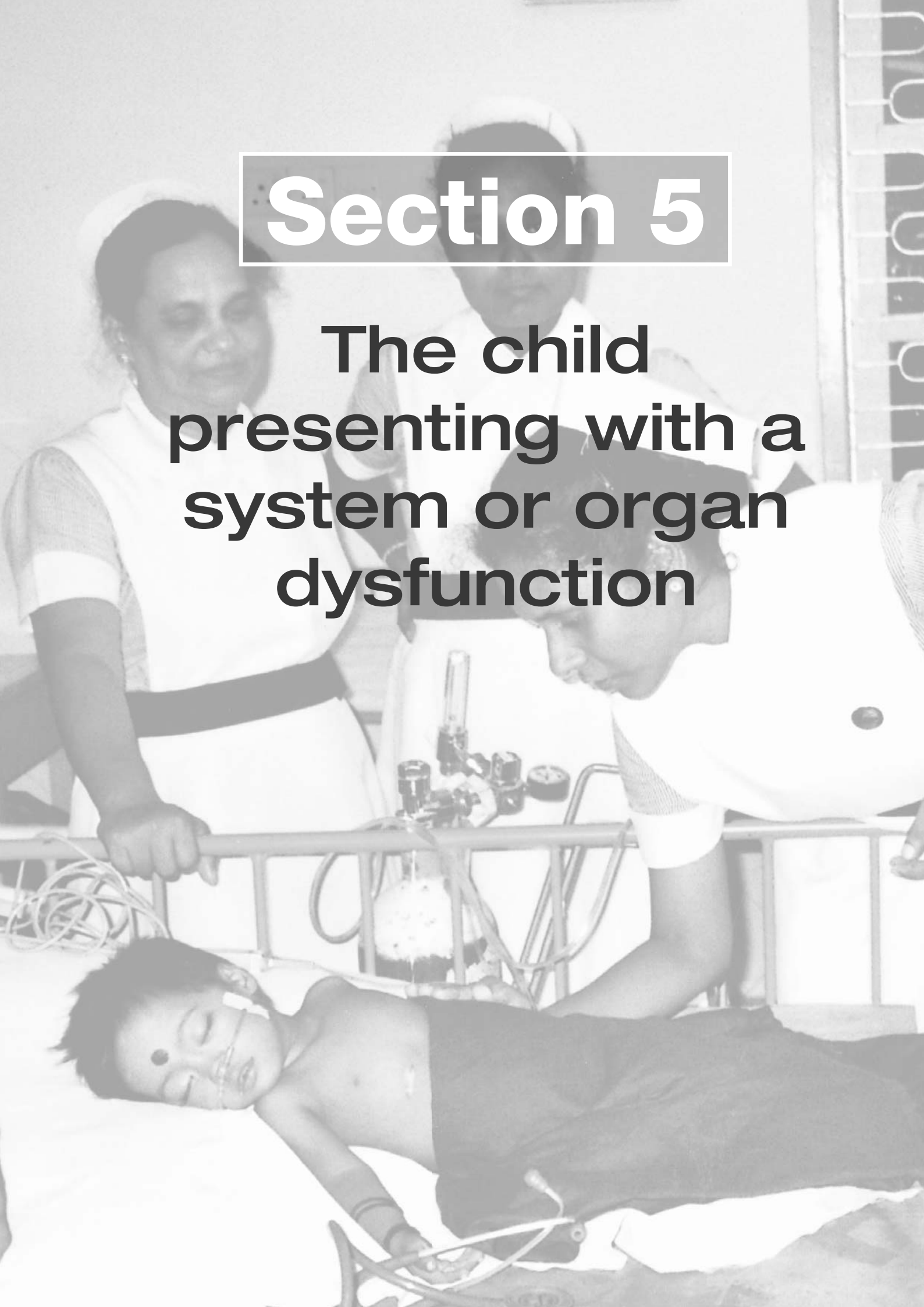

Section 5

The child presenting with a system or organ dysfunction

5.1 Upper airway disorders

5.1.A Acute upper airway infections: croup and epiglottitis

BOX 5.1A.1 Minimum standards
- Dexamethasone/prednisolone.
- Nebulised 1 in 1000 adrenaline.
- Choking management skills.
- Intubation.
- Cricothyrotomy or tracheostomy.
- Antibiotics: cefuroxime, chloramphenicol, ceftriaxone, ceftazidime.
- *Haemophilus influenzae* immunisation.
- Measles immunisation.

Introduction

Obstruction of the upper airway (larynx and trachea) is potentially life-threatening. The cardinal feature is stridor (a harsh noise during inspiration), which is due to narrowing of the air passage in the oropharynx, subglottis or trachea. If the obstruction is below the larynx, stridor may also occur during expiration. **Like the wheeze in asthma, the loudness of the stridor does not indicate the severity of the obstruction.** There may also be hoarseness and a barking or seal-like cough. The severity of the obstruction is best assessed by the degree of sternal and subcostal recession, and the respiratory and heart rate. Increasing agitation or drowsiness, or central cyanosis, indicates severe hypoxaemia and hypercapnia and the need for urgent intervention.

The major causes of severe stridor are viral croup (caused by measles or other viruses), foreign body, retropharyngeal abscess, diphtheria, and trauma to the larynx.

Differential diagnosis of upper airway obstruction

1 Collapse of airway due to muscle tone loss or build-up of secretions due to poor cough reflex:
   - Depressed conscious level from any cause.
   - Drug or alcohol intoxication or overdose.
   - Bulbar palsy.
   - Myopathy.

2 Airway inflammation and oedema:
   - Infective:
     - Upper respiratory tract infection in an infant.
     - Viral croup.
     - Bacterial tracheitis.
     - Epiglottitis.
     - Severe tonsillitis.
   - Non-infective:
   - Recurrent croup.
   - Anaphylaxis.

3 Space-occupying lesion or structural abnormality:
   - Intranasal, pharyngeal or in upper trachea:
     - Adenoidal hypertrophy.
     - Foreign body.
     - Retropharyngeal abscess.
     - Tumour.
     - Extrinsic haematoma (e.g. post thyroidectomy).
   - Congenital pharyngeal, laryngeal or upper tracheal abnormalities:
     - Choanal atresia.
     - Laryngomalacia.
     - Subglottic stenosis.
     - Laryngeal web or haemangioma.

For diagnosis of a space-occupying lesion or structural abnormality, a specialist ENT examination under anaesthetic may be needed (if available).

Croup

Croup is a condition characterised by inspiratory stridor, hoarse voice, barking cough and a variable degree of respiratory distress.

This definition embraces several distinct disorders.

- **Acute viral laryngotracheobronchitis (viral croup).** This is the commonest type of laryngotracheal infection (representing over 95% of cases). Peak incidence is in the second year of life, and most hospital admissions are between 6 months and 5 years of age. The stridor is usually preceded by fever (< 38.5°C) with coryza, and symptoms tend to be worse at night. If narrowing is minor, the stridor will be present only when the child hyperventilates or is upset. As the narrowing progresses, the stridor becomes both inspiratory and expiratory, and is present even when the child is at rest. Children under 3 years in particular may develop features of increasing obstruction and hypoxaemia with marked sternal and subcostal recession, tachycardia and agitation. If the infection extends distally to the bronchi, wheeze may also be audible.
- **Recurrent or spasmodic croup.** Some children have repeated episodes of croup without preceding fever and coryza. The symptoms are of sudden onset at night, and often persist for only a few hours. The condition is associated with atopic disease (e.g. asthma, eczema, hay fever). The episodes can be severe, but are more commonly self-limiting.
- **Bacterial tracheitis or pseudomembranous croup.** This dangerous condition is one of the important complications of measles but may occur without that antecedent. Infection of the tracheal mucosa with *Streptococcus pneumoniae*, *Staphylococcus aureus* or *Haemophilus influenzae* B results in copious purulent secretions and mucosal necrosis. The child appears

toxic with a high fever, with marked signs of respiratory obstruction. In the UK, over 80% of these children need intubation and ventilatory support to maintain an adequate airway. The croupy cough and the absence of drooling help to distinguish this condition from epiglottitis. Clinical and radiological signs of segmental collapse and consolidation related to bronchial occlusion are usual. The cough is often persistent and ineffective in clearing the secretions, the illness has a prolonged course, and the restoration of normal mucosa usually takes several weeks. The condition is much less common than the two preceding ones.

TABLE 5.1.A.1 Severity of croup

Sign	Mild	Moderate	Severe
Upper airway noise	Hoarse voice, barking cough, mild stridor intermittently on inspiration only	As before, with stridor constant and also some on expiration	Stridor usually decreases as exhaustion occurs
Effort of breathing	Mild increase, some intercostal recession	Further increase in effort, nasal flare, tracheal tug, accessory muscle usage	Major increase in effort gives way to exhaustion and poor but gasping effort
Efficacy of breathing	Not distressed by effort. No cyanosis, SaO_2 may be normal	Distressed by effort. Cyanosis not usually visible but SaO_2 is low	Cyanosis visible if haemoglobin is in normal range, SaO_2 is very low
Conscious level	Alert, usually still playing	Anxious and distressed. Not playing, little interaction, drowsy	Conscious level severely reduced, causing respirations to slow, reflex gasps and apnoeas
Cardiovascular	Mild increase in heart rate	Rapid heart rate	Severe tachycardia progresses to bradycardia and hypoxic cardiac arrest

Emergency treatment of croup

- These children (and their parents) may be very frightened. **Do not alarm them further by putting instruments in the child's throat, by giving painful injections or by trying to place an IV cannula.** Crying increases their oxygen demand and may increase laryngeal obstruction **and even cause total airway obstruction**. Keep the child on their parent's lap and explain the condition and the treatment. Tell the mother to alert the nurses or doctors if the child breathes more quickly or has marked sternal recession. **These are danger signs for hypoxaemia.**
- Ensure adequate oral fluid intake.

Many children who are admitted to hospital have hypoxaemia. Humidified oxygen should be given through nasal cannulae or a face mask held just in front of the child's face by the parent. **Do not use nasopharyngeal catheters to give oxygen, as these can precipitate dangerous paroxysms of coughing and total airway obstruction.**

Milder cases of croup should not routinely be given oxygen, as this can frighten the child.

- Croup can be a very painful condition. Even if the child does not have a high temperature, prescribe regular paracetamol, but do not force the child to take this.
- There is very good evidence that steroids help. Children with mild, moderate or severe croup all benefit from steroids. Give 0.6 mg/kg dexamethasone once or twice a day. This should be given orally, **as it works just as well as if given parenterally. If the child vomits, repeat it or give the same dose intramuscularly**. An expensive but effective treatment is nebulised budesonide 2 mg in 2 mL; it may be repeated 30–60 minutes later.
- Nebulised adrenaline (5 mL of 1 in 1000 adrenaline nebulised, preferably with oxygen) will bring rapid and effective relief for severe croup. The relief lasts only for about 1 hour, but it can be repeated (although the effect diminishes), and this treatment gives the steroids time to start working. **Arrange for the child to be seen quickly by an anaesthetist.** Monitor the oxygen saturation with a pulse oximeter.
- A few children need intubation. This should be done under general anaesthetic. **If there is doubt about the diagnosis, or difficulty in intubation is anticipated, an ENT surgeon capable of performing a tracheostomy should be present.** In intubated children, 1 mg/kg prednisolone every 12 hours reduces the duration of intubation.
- Severely ill or toxic children and those with measles croup should receive an antibiotic effective against *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Staphylococcus aureus*. If available, cefuroxime 150 mg/kg/day in four doses IV or ceftriaxone 80 mg/kg IV or IM once daily. An alternative is chloramphenicol 25 mg/kg IV 6-hourly.

Inhaled foreign body (*see* Section 5.2.C)

Suspect the diagnosis if there has been a sudden onset of cough and stridor in a well child. Ask the parents and child whether there has been any access to peanuts or other food, toys or other small objects that could have been put in the mouth.

Management

If the foreign body is causing symptoms of stridor, coughing and respiratory distress, emergency management of choking is required (*see* Section 1.12 on Basic Life Support, which describes acute choking management).

In addition, call an ENT surgeon for laryngoscopy (if available). A laryngeal foreign body may present very acutely with cyanosis or loss of consciousness. Therefore urgent direct laryngoscopy may be necessary.

In the absence of an ENT surgeon, tracheostomy or cricothyrotomy may be necessary (*see* Section 8.2 for cricothyrotomy procedure).

Acute epiglottitis

This is a severe infection caused by *Haemophilus influenzae.* Peak incidence is at 2–3 years of age. It is less common than croup, but important, as **the diagnosis needs to be made fast because rapid progression of stridor in the ill toxic child may be fatal within hours if not promptly treated.** Cough is not a prominent feature, and the stridor has a soft quality, often with an expiratory component. The child tends to drool and assume an upright posture.

Unlike croup, epiglottitis is always severe and progression is rapid. It is always a medical emergency. Fortunately, since the introduction of *Haemophilus influenzae* type B (HiB) vaccine the disease has become much less common in those countries where the vaccine is used.

Do not:	Do:
Examine the throat	Reassure the child and their parents, and calm the child
Lie the child down	Attach a pulse oximeter
X-ray the neck	Give oxygen if SpO_2 is < 94% using a face mask held close to **but not on** the child's face by the parent with the child sitting on their lap
Perform invasive procedures	Call an anaesthetist and an ENT surgeon
Use a nasopharyngeal tube to give oxygen	Arrange examination under anaesthesia
	Arrange for high-dependency care to be available

Management

- Elective intubation under general anaesthetic is the treatment of choice. Often a much smaller diameter than the usual endotracheal tube for the child's age will be needed because the airway is so swollen internally. The endotracheal tube still needs to be the right length for the child's age. This is why children's endotracheal tubes should not be pre-cut to size. The diagnosis is confirmed by laryngoscopy under general anaesthetic just prior to intubation ('cherry-red epiglottis'). **An ENT surgeon must be present if possible.**
- While the child is anaesthetised, the following procedures should be performed: blood cultures, throat swab and IV line.
- Recommended antibiotic therapy is chloramphenicol 50 mg/kg IV immediately, then 25 mg/kg IV 6-hourly. If available, cefuroxime or cefotaxime 50 mg/kg IV 6-hourly or ceftriaxone 80 mg/kg once daily IV or IM should be effective.
- Following intubation the child will be able to breathe humidified air spontaneously, ideally with nasal continuous positive airway pressure (CPAP) (*see* Section 1.25 and 8.3). Sedation (discuss with anaesthetist) may be required in order to prevent self-extubation, but the child will then usually require assisted ventilation. Most children will be ready for extubation after 48 hours.

TABLE 5.1.A.1 Contrasting features of croup and epiglottitis

Feature	Croup	Epiglottitis
Onset	Over days	Over hours
Preceding coryza	Yes	No
Cough	Severe, barking	Absent or slight
Able to drink	Yes	No
Drooling saliva	No	Yes
Appearance	Unwell	Toxic, very ill
Fever	38.5ºC	38.5
Stridor	Harsh, rasping	Soft
Voice muffled	Hoarse	Reluctant to speak
Need for intubation	1%	80%

An alternative is to fix the child's arms to their thorax using a bandage to stop them pulling out the endotracheal tube but the stress to the child caused by this may have a deleterious effect on recovery. If possible, have a relative sit with the child to reassure them.

Angioneurotic oedema

See Section 5.1.B on anaphylaxis.

There are usually areas of painless swelling obvious in other areas of skin and mucous membranes. The eyes, lips and tongue are particularly likely to be affected. Stridor is caused by laryngeal oedema.

Management

- Give adrenaline, 10 micrograms/kg IM.
- Give adrenaline, 5 mL of 1 in 1000 nebulised with 100% oxygen.
- Give 100% oxygen.
- Give hydrocortisone, 4 mg/kg IV over 15 minutes or IM and repeat 8 hourly as required.
- Give chlorphenamine, 250 micrograms/kg IV or orally (maximum dose 2.5 mg) or
  - 6 months to 6 years 2.5 mg and repeat up to 4 times in 24 hours
  - 6–12 years 5 mg and repeat up to 4 times in 24 hours
  - 12–18 years 10 mg and repeat up to 4 times in 24 hours.
- Give Ringer-lactate or Hartmann's solution or 4.5% albumin (if available), 10–20 mL/kg, if the child is shocked.
- Intubation or even tracheostomy may be required (contact the ENT team).

Airway/inhalational burns (*see* Section 7.3.I.b)

Such burns are caused by inhalation of hot gases or toxic vapours. They may be associated with extensive skin burns. **Be aware that airway obstruction may develop even if it is not obvious on first assessment.**

Management

- **Admit the child to a high-dependency unit** (if available).
- Give hydrocortisone, 4 mg/kg IV 6-hourly.
- Give Ringer-lactate or Hartmann's solution or 4.5% albumin boluses (10–20 mL/kg) for shock as required.
- Intubation or tracheostomy may be necessary if indicated by assessment.

Diphtheria (*see* Section 6.1.C for further details on management)

Diphtheria is characterised by gradual onset of stridor in a child (usually 2 to 3 years old) with neck oedema and ulcerating lesions of the tonsillar bed forming a grey membrane. Bleeding may occur at the site and down the nose. The diagnosis may be confirmed by throat swab and **urgent Gram stain**. There will usually be no evidence of DTP vaccination.

5.1.B The child with anaphylaxis

BOX 5.1.B.1 Minimum standards

- ABC of resuscitation.
- Adrenaline.
- Oxygen.
- Salbutamol by nebuliser or spacer.
- Hydrocortisone.
- Antihistamine.

Introduction

Anaphylaxis is an immunologically mediated reaction to ingested, inhaled or topical substances, which may progress to life-threatening shock and/or respiratory distress.

Common causes include allergies to penicillin, anaesthetic agents, blood transfusion, **radiographic contrast media**, and certain foods, especially nuts.

Consider the diagnosis of anaphylaxis if any of the following symptoms are present when there is a history of previous severe reaction, rapidly progressive or increasingly severe symptoms, a history of asthma, eczema or rhinitis (atopy).

This situation is potentially life-threatening and may result in a change in conscious level, collapse, or respiratory or cardiac arrest.

Management

See **Figure 5.1.B.1.**

Remove the source of allergen if possible (e.g. take down the blood giving set if blood transfusion is the cause).

The key to anaphylaxis treatment is intramuscular adrenaline.

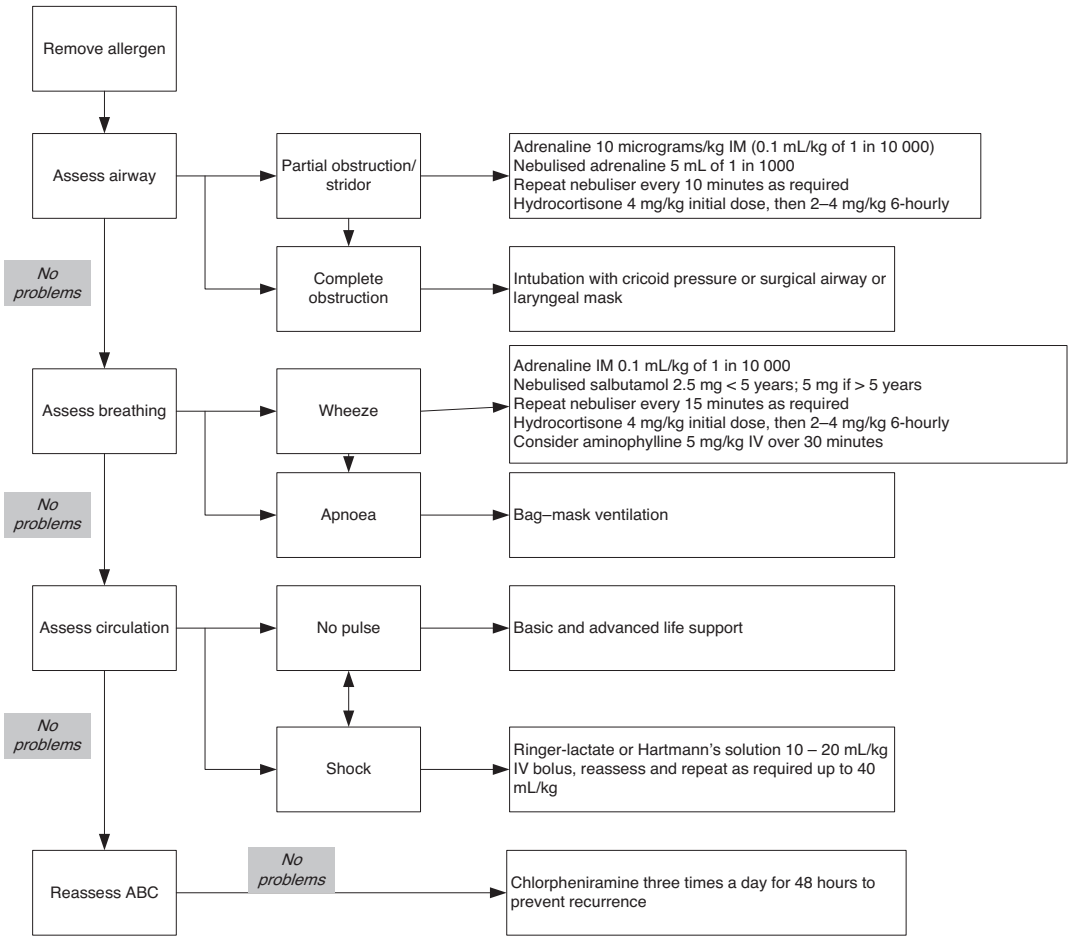

FIGURE 5.1.B.1 Pathway of care for anaphylaxis in a child. Note: Adrenaline should be repeated every 5 minutes. If repeated doses are ineffectual, use an IV infusion of adrenaline (see below)

Airway: assessment and resuscitation

- If there is no problem with the airway, assess **B**reathing.
- If stridor is present there is obstruction (usually at the larynx):
  - Give 10 micrograms/kg adrenaline IM, then 5 mL adrenaline 1 in 1000 nebulised.
  - Give 100% oxygen.
  - Consider intubation, and call for anaesthetic and ENT assistance.
- If there is stridor with complete obstruction, intubate or create a surgical airway (*see* Section 8.2).

Breathing: assessment and resuscitation

- If there is no problem with breathing, assess the **C**irculation.
- If there is no breathing, give five rescue breaths using a bag-valve-mask with 100% oxygen and assess the circulation.
- If the child is wheezing, give 10 micrograms/kg adrenaline IM and salbutamol (either by nebuliser 2.5 mg if under 5 years of age or 5 mg if over 5 years, (nebulised with 100% oxygen) or 1000 micrograms (5 puffs) of a metered dose inhaler via a spacer and repeated as required).

Circulation: assessment and resuscitation

- If there is no problem with the circulation, observe the child.
- If there is no pulse, start basic life support, assess the rhythm and treat.
- If the child is shocked, give 10 micrograms/kg adrenaline IM and 20 mL/kg IV bolus of Ringer-lactate or Hartmann's solution. It may be necessary to give adrenaline IV if shock is present (see below for dosage).

Reassess ABC and continue to give 100% oxygen

- If there is airway deterioration, repeat IM adrenaline 10 micrograms/kg with or without intubation.
- If the child is still wheezy, repeat IM adrenaline 10 micrograms/kg and hydrocortisone 4 mg/kg IV by slow Injection. Consider giving aminophylline 5 mg/kg by slow IV injection over 20–30 minutes followed by a 1 mg/kg/hour IV infusion or salbutamol 4–6 micrograms/kg IV slow injection followed by an IV infusion of 0.5–2.0 micrograms/kg/minute.
- If the child is still shocked, repeat IM adrenaline 10 micrograms/kg and give a further bolus of 10 mL/kg Ringer-lactate or Hartmann's solution. If there is a poor response then give a further 10 mL/kg and consider giving an adrenaline infusion (see below). Intubation and ventilation may be needed if there is a poor response as now a total of 40 mL/kg of crystalloids have been given by bolus.
- If there is no problem, observe the child.
- If there are no symptoms other than rash or itching:
  - Give oral antihistamine (chlorphenamine, 250 micrograms/kg).
  - Give oral steroids (0.5–1 mg/kg oral prednisolone).

TABLE 5.1.B.1 Features of anaphylaxis

Severity	Symptoms	Signs
Mild	Burning sensation in mouth Itching lips, mouth and throat Feeling of warmth Nausea and abdominal pain	Urticarial rash Angio-oedema Conjunctivitis Red throat
Moderate	Coughing and wheezing Loose stools Sweating Irritability	Bronchospasm Tachycardia Pallor
Severe	Difficulty with breathing Faintness or collapse Stridor Vomiting Uncontrolled defecation	Severe bronchospasm Laryngeal oedema Shock Respiratory arrest Cardiac arrest

Adrenaline

Adrenaline is given intramuscularly unless there is intractable shock or cardiac arrest, in which case it should be given IV or by the intra-osseous route.

If repeated IM injections of adrenaline are not effective or last only a short time, start giving adrenaline IV. For treatment of children in severe shock:

- Place 1 mg (1 mL of 1 in 1000 adrenaline) in 50 mL of Ringer-lactate solution.
- Then give 2–5 mL (40–100 micrograms) in a child (depending on size) and 1 mL (20 micrograms) in an infant under 1 year of age. Give IV **slowly** using a peripheral vein or ideally a central vein, if possible with ECG monitoring.
- Repeat as required.
- An infusion of adrenaline at 0.05–2.0 micrograms/kg/minute may be needed (preferably via a central vein and using a syringe pump).

5.1.C The child with tonsillitis, otitis media, mastoiditis or retropharyngeal abscess

BOX 5.1.C.1 Minimum standards

- Antibiotics: penicillin/amoxicillin/erythromycin.
- Quinolone antibiotic ear drops.
- Adrenaline nose drops.
- Wicking.

Tonsillitis

Tonsillitis is a common childhood disorder. The bacteria most commonly involved are beta-haemolytic streptococci, *Streptococcus pneumoniae* and *Haemophilus influenzae*, and around 50% of attacks are viral.

Classic symptoms include pyrexia and sore throat.

Swallowing solid food is difficult, and fluid intake must be encouraged. Painful cervical lymphadenopathy is the rule, and referred earache from the IXth cranial nerve is common. Febrile convulsions may occur in younger children, who may also present with acute abdominal pain without any throat symptoms, due to mesenteric lymphadenitis.

Examination

- Tender lymphadenopathy beneath and/or behind the mandible.
- Red enlarged tonsils with or without purulent exudate.

Differential diagnosis

Diphtheria and infectious mononucleosis (*see* Section 6.1.C for diphtheria and later in this section for infectious mononucleosis).

Treatment

- Give paracetamol (20 mg/kg 4- to 6-hourly) for pain relief. Bear in mind that attacks are often viral, and often antibiotics are not needed.
- Penicillin is still an effective antibiotic, and in **serious cases** in hospital give penicillin 12.5 mg/kg four times daily orally. If the child is allergic to penicillin, erythromycin may be used.
- Rarely there is acute partial airway obstruction due to massive tonsillar enlargement. In this case use IV benzylpenicillin 25 mg/kg 6-hourly and IV hydrocortisone 4–8 mg/kg initially, and then a further dose 4 hours later if needed at 4 mg/kg.

Recurrent tonsillitis

- If the number of attacks increases with age rather than decreasing, tonsillectomy is appropriate if it is safe to perform in the healthcare facilities available.
- As a rule of thumb, six attacks per year for 2 years over the age of 5 years could indicate a case for tonsillectomy.
- It is often said that peritonsillar abscess (quinsy) is an indication, but one attack of quinsy is not enough to warrant the operation.

Indications for tonsillectomy

In the past, tonsillectomy was performed all too often. Sleep-related upper airway obstruction (*see* Section 5.1.D) is a good reason for undertaking tonsillectomy, and about 10% of tonsil operations are currently done for this reason.

Peritonsillar abscess (quinsy)

This is a complication of tonsillitis, and it presents with a unilateral swelling of the soft palate, deflecting the uvula to the opposite side, with associated trismus. Surgical drainage is often necessary as well as IV penicillin as described above.

Acute suppurative otitis media (ASOM)

Acute suppurative otitis media is a mucosal infection of the middle ear and mastoid air cells, arising via the Eustachian tube. *Streptococcus pneumoniae* and *Haemophilus influenzae* are the bacteria most commonly involved, and about 50% of cases are caused by viruses.

The symptoms are hearing loss, earache and fever. Pain is due to the bulging tympanic membrane from accumulated pus. Rupture leads to otorrhoea with rapid symptom improvement. Localising signs may be absent in infants, who may present with fever and systemic illness. On examination the tympanic membrane is red and bulging.

Treatment

- **Many cases of otitis media are incorrectly diagnosed:** any child who is crying or has a fever will tend to have pink eardrums. Earache often presents at night. This is usually due to Eustachian tube obstruction occurring when the child is sleeping, from accumulated mucus in the postnasal space resulting in a negative pressure in the ear, which wakes the child up with discomfort. Paracetamol, plus sitting up and drinking, will open the Eustachian tube and thus relieve the symptoms. Antibiotics are unnecessary.
- In true otitis media with bulging eardrums, treat the child as an outpatient and **always give an antibiotic as described below. It is not safe to withhold antibiotic treatment**. Give oral amoxicillin 40 mg/kg twice a day for 7–10 days. If amoxicillin is not available give co-trimoxazole (trimethoprim 4 mg/kg/sulfamethoxazole 20 mg/kg twice a day) for 7–10 days.
- Paracetamol relieves pain and reduces fever.
- Ephedrine nose drops (0.5%) given 8-hourly for a maximum of 5 days may help to open the Eustachian tube and speed resolution.
- If the eardrum is perforated, the ear must be kept dry until the resulting perforation has healed. This is achieved by teaching the parent to undertake wicking as follows. Roll a clean soft absorbent cotton cloth or strong tissue paper into a wick. **Never use a cotton-tipped applicator, or flimsy paper that will fall apart in the ear, or a stick of any kind.** Place the wick in the ear and remove it after a few seconds, when it is wet. Repeat until the ear is dry. Wicking should be undertaken at least three times daily, usually for 1 to 2 weeks, until pus is no longer present. **The parent must not leave anything in the ear after wicking, must not put oil or any other fluid in the ear, and should prevent the child from going swimming or putting their head under water until the ear has been dry for at least 2 weeks.**
- Check that the child has recovered at follow-up 1 week later. If ear pain or discharge persists, treat the child for 5 more days with the same antibiotic and continue wicking the ear. Follow up in 5 days.

Chronic otitis media

If pus has been draining from the ear for 2 weeks or longer and there is perforation of the ear drum, the child has a chronic otitis media infection.

Treatment

- Treat as an outpatient.
- Keep the ear dry by wicking (*see* above).
- Instil topical antibiotic ear drops (always without steroids, which must not be used in children) three times daily for 2 weeks. Drops containing quinolones (norfloxacin, ofloxacin, ciprofloxacin) are more effective than other antibiotic drops; 0.3% ciprofloxacin drops (5 drops twice daily) have been most researched.
- Oral antibiotics are not indicated unless there is an acute otitis media.
- Topical antiseptics and steroids should not be used.

Follow-up after 1 week

If the ear discharge persists despite ear wicking and ciprofloxacin drops, consider IV antibiotic treatment with antibiotics that are effective against *Pseudomonas* (such as gentamicin, azlocillin and ceftazidime), in addition to wicking. Do not give oral antibiotics for a chronically draining ear.

If chronic suppurative otitis media (CSOM) continues despite the above treatment, do not forget the possibility of TB.

Secretory otitis media

This may lead to recurrent attacks of acute suppurative otitis media (ASOM) because the exudate acts as a culture medium for repeated infections. **Occasionally, myringotomy with grommet insertion is necessary.** The alternative treatment is long-term low-dose oral antibiotics (trimethoprim 2 mg/kg once daily (maximum dose 100 mg) at night for 3 months). Eustachian tube function may also be improved by adenoidectomy.

Acute mastoiditis

This is a complication of ASOM. The mucosa of the mastoid system is always inflamed in ASOM. Mastoiditis occurs when the mucosal inflammation spreads to the adjacent bone, causing osteitis, and eventually the outer cortex of the mastoid is breached, leading to a subperiosteal abscess behind the ear. The symptoms are similar to those of ASOM, but the signs include a forward displaced pinna with a tender fluctuant swelling in the post-auricular sulcus.

Complications

Not only is the outer cortex of the mastoid involved, but also the bone adjacent to both the middle and the posterior cranial fossa can be affected, occasionally leading to **extradural abscess, meningitis and brain abscess. Facial nerve paralysis** may occur from the pressure of pus on an exposed facial nerve.

Treatment

- Give IV benzylpenicillin 50 mg/kg IV 6-hourly **plus** chloramphenicol 50 mg/kg 8-hourly IV OR plus flucloxacillin 50 mg IV 6 hourly both for 5 days and then orally (penicillin 25 mg/kg four times daily and chloramphenicol 50 mg/kg 8-hourly) for another 5 days. Alternatively, give ceftriaxone 100 mg/kg IV/IM for 10 days. If there is no improvement within 24–48 hours or the child's condition deteriorates, surgical drainage is necessary.
- The key is to provide drainage for the mastoid system. **If it is not possible to do a full-scale mastoidectomy (due to lack of equipment or expertise)**, a dramatic improvement, in conjunction with intravenous antibiotics, may be obtained by incising the abscess (avoiding the mastoid tip in the small child where the facial nerve may be exposed) and opening into mastoid air cells.
- If signs of meningitis or a brain abscess (indicated by a reduced level of consciousness, a fit or localised neurological signs) are seen or suspected, give high-dose IV antibiotics as for meningitis (*see* Section 5.16.B) and refer the child immediately to an appropriate specialist.

Glandular fever/infectious mononucleosis

This is caused by the Epstein–Barr virus and may be similar in presentation to diphtheria.

Diagnosis

There are atypical lymphocytes on blood, monospot and Paul-Bunnell tests (usually but not always positive).

Management

- **Do not give ampicillin, amoxicillin or Augmentin** for throat infections until glandular fever has been excluded (there is a risk of severe skin reaction). Antibiotics are unhelpful in glandular fever. Treatment is symptomatic.
- Give IV maintenance fluids if swallowing problems are causing dehydration.
- Give IV hydrocortisone 4 mg/kg 6-hourly if signs of airway obstruction occur.
- Intubation/tracheostomy is rarely indicated.

Retropharyngeal abscess

Most common in infants and young children, retropharyngeal abscess (RPA) is an abscess located behind the posterior pharyngeal wall (the retropharyngeal space).

RPA is usually caused by a bacterial infection originating in the nasopharynx, tonsils, sinuses, adenoids or middle ear, and can also result from a penetrating injury or a foreign body. It may result from suppuration of retropharyngeal lymph nodes from infected tonsil, adenoid, tooth or penetrating foreign body. The most common causative organisms are beta-haemolytic streptococci, *Staphylococcus aureus, Haemophilus parainfluenzae* and anaerobic organisms.

RPA is a relatively uncommon illness, and therefore may not receive prompt diagnosis in children presenting with stiff neck (limited neck mobility or torticollis), some form of palpable neck pain (which may be in 'front of the neck' or around the larynx), malaise, difficulty swallowing, high fever, stridor, trismus, dribbling of saliva, croupy cough or enlarged cervical lymph nodes. Early diagnosis is essential. Infection in the retropharyngeal space can pass down behind the oesophagus into the mediastinum, producing an extremely dangerous mediastinitis.

Peroral surgical drainage of the abscess by incision under anaesthetic (or without anaesthetic in an emergency) is often required. An ENT specialist (if available) must be called urgently.

Surgery may be required urgently to relieve obstruction, but not all patients with retropharyngeal abscesses require surgery. One study found that of 162 paediatric patients with retropharyngeal abscess, 126 required surgery initially, and of the 36 patients who were initially treated conservatively with high-dose antibiotics, 17 required surgery. Surgery is best undertaken using general anaesthesia undertaken by an experienced anaesthetist, as there is risk of rupture of the abscess during intubation. In patients who present with severe airway obstruction, tracheostomy may be required before surgical drainage.

High-dose IV antibiotics, such as ampicillin plus flucloxacillin plus metronidazole, cefuroxime or ceftriaxone plus metronidazole, or clindamycin plus metronidazole, are required in order to control the infection, and can be used to reduce the size of the abscess prior to surgery.

Chronic retropharyngeal abscess is usually secondary to tuberculosis of the cervical spine or spread from an infected lymph node, and the patient needs to be started on anti-TB treatment as soon as possible.

A CT scan (if available) is the definitive diagnostic test.

A lateral X-ray of the neck will usually show swelling of the retropharyngeal space, with the following:

- increased prevertebral soft tissue shadow
- air and fluid level in the pre-vertebral area
- concavity or straightening of the cervical vertebral column
- the air column is pushed forward.

If the retropharyngeal space is more than half of the size of the C2 vertebra, it may indicate retropharyngeal abscess.

A chest X-ray will also be valuable to exclude pneumonia and to show the size of the mediastinum.

Mediastinal tumours (*see* Section 5.14)

These often present with the slow onset of stridor in a child with other symptoms and signs (e.g. pallor, lethargy) may be precipitated or aggravated by mediastinal radiotherapy used for treatment of malignant causes.

Management

- X-ray the chest and mediastinal inlet.
- Intubation may be required as a temporary measure.
- Treat the primary cause.

5.1.D The child with sleep-related upper airway obstruction

BOX 5.1.D.1 Minimum standards

- Appropriate surgery (especially tonsillectomy and adenoidectomy).
- Steroids: topical nasal and, for acute use, oral.

Introduction

The incidence of sleep-related upper airway obstruction depends on the method of diagnosis (it affects 1–3% of preschool children). It is associated with both enlargement of the tonsils/adenoids and reduced tone or diameter in the upper airway.

Groups at risk are children with any of the following:

- Pierre-Robin sequence
- craniofacial syndromes
- Down's syndrome
- cerebral palsy
- neuromuscular disease
- sickle-cell disease
- Prader–Willi syndrome.

Presenting features

- Snoring: this occurs in more than 10% of healthy 4- to 5-year-olds, and in most cases is benign.
- Sleep disturbance and restlessness.
- Apnoeic episodes followed by inspiratory gasps.
- Sleeping with the head extended.
- Subcostal and sternal recession during sleep.
- Mouth breathing and halitosis.
- Daytime hyperactivity, poor concentration and irritability (young children).
- Daytime sleepiness (older children).
- Pulmonary hypertension.
- Heart failure.

These features may be associated with developmental delay, impaired cognitive function and behavioural disorders. The disorder is insidious – the child may appear completely normal when awake, and the problem is most or only apparent during rapid eye movement (REM) sleep.

Investigations

A sleep observation or study is most useful. This can be done either by direct observation of the child during sleep with the chest and face exposed, or by video recording at home during sleep by the parents, looking for the following:

- chest wall recession
- snoring
- sleep position
- nocturnal restlessness.

It is also useful to monitor oxygen saturation (SpO_2) during sleep. An abnormal result would be a lowest level of less than 87% or more than three dips below 90% during the night.

Also consider the following investigations:

- barium swallow: to assess bulbar function and exclude tracheal compression
- upper airway endoscopy: to assess the structure and dynamics of the upper airway
- lateral X-ray of the post-nasal space: to assess the size of the adenoids.

Measurement of oxygen saturation (SpO_2)

Methodological issues that affect this measurement include the following:

- the instruments used (e.g. functional vs. fractional haemoglobin)
- exclusion of motion artefact
- averaging
- altitude
- inclusion of apnoeic pauses.

Normal data

In children outside infancy, a normal oximetry recording should have the following:

1. a median SpO_2 level of ≥ 95%
2. no more than four desaturations of ≥ 4% per hour
3. no abnormal clusters of desaturation defined as ≥ 5 in a 30-minute period.

Widely used criteria for abnormality in nocturnal oximetry recordings are falls of more than 4% below baseline and

desaturations below 90%. The measure that correlates best with poor academic performance is the lowest level of SpO_2 (nadir) during the night (normal value is > 87.5%).

Adverse effects of hypoxaemia

These include the following:

- poor weight gain
- developmental delay
- poor cognitive function
- pulmonary hypertension
- cyanotic apnoeic episodes.

Treatment

- Time: the airway enlarges with growth.
- Obstruction is worse with infections and may need a rescue course of steroids (e.g. prednisolone 0.5 mg/kg once daily for up to 7–10 days).
- Topical steroids/decongestants.
- Tonsillo-adenoidectomy.
- Nasal CPAP.
- Nasopharyngeal tube (in infants).
- Tracheostomy.

Nasal CPAP (see Section 1.25)

This is an effective non-invasive treatment, but it is associated with the following potential problems:

- compliance
- side effects:
  - skin sores
  - nose bleeds
  - conjunctivitis
  - aerophagy.

Reference

British Lung Foundation. *OSA in Children*. A leaflet for the parents of children with obstructive sleep apnoea. www.blf.org.uk/Conditions/Detail/OSA-in-children#overview.

5.2 Lower airway disorders

5.2.A Bronchiolitis

BOX 5.2.A.1 Minimum standards

- Oxygen.
- Oxygen saturation monitor.
- Bag-valve-mask system.
- Cannulae for thoracostomy.
- Antibiotics.
- Nasal CPAP.

Introduction

Wheezing is a whistling noise heard during expiration. The child who has cough or difficulty breathing **and** wheezing will fit into one of the following categories:

- bronchiolitis (mainly less than 1 year old)
- asthma (over 1 year old)
- pneumonia with wheezing (any age).

In pneumonia with wheezing in children over 1 year of age and in asthma, a bronchodilator provides important symptomatic relief. An aerosol and large-volume spacer (which may be improvised) is the best way of administering a bronchodilator (see below). Bronchodilators are not routinely effective in bronchiolitis, but may be tried in some cases.

A lower respiratory viral infection, typically most severe in young infants, occurs in annual epidemics, and is characterised by airways obstruction and wheezing. Respiratory syncytial virus is the most important cause. Secondary bacterial infection may occur and is common in some settings. Episodes of wheeze may occur for months after an attack of bronchiolitis, but will eventually stop. Some babies who have had bronchiolitis go on to have asthma, but both bronchiolitis and asthma are common conditions, and a causal relationship has not been established.

Clinical features of bronchiolitis

- Infants are coryzal, have a troublesome cough and may feed poorly or even be unable to suck and feed. There may be vomiting.
- The nose is often obstructed by secretions.
- On examining the chest, there may be hyperinflation, chest wall indrawing, nasal flaring, grunting, wheeze and fine crackles at the lung bases.
- Young infants may present with apnoeic/hypoxaemic episodes which may be recurrent and life-threatening.
- There may be hypoxaemia, with SaO_2 less than 94%, with or without cyanosis.
- Some infants will have such severe respiratory distress that there is gasping; this is pre-terminal.

Treatment

Only supportive treatment (e.g. oxygen, gentle suction of the nose, and fluids) is of benefit. Antibiotics and bronchodilators have no role. However, in the most severe cases and unless you are **certain** that pneumonia is not present,

it is safer to give antibiotics and a trial of a bronchodilator (stop the bronchodilator if it is not helping).

Non-invasive respiratory support to help to overcome small airway obstruction (nasal CPAP and continuous negative extrathoracic pressure (CNEP)) may be valuable (*see* Section 1.25 and Section 8.3). CNEP may be more effective because of the nasal blockage that accompanies bronchiolitis.

- Give oxygen by nasal cannulae to keep SaO_2 in the range 94–98%. Check that the nasal cannulae are in the correct place, and check frequently that they are not blocked by secretions.
- Nasal clearance. Gentle nasal suction should be used to clear secretions in patients in whom nasal blockage is thought to be causing respiratory distress. This may be aided by saline nasal drops or spray.
- Ensure that daily maintenance fluids are achieved. If this is not possible by mouth, use nasogastric feeding. This should be considered in any patient who is unable to maintain oral intake or hydration (use the mother's expressed breast milk if possible and if tolerated).
- If the patient is vomiting despite nasogastric feeding, or severe respiratory distress is present, give fluids IV.
- If there are signs of pneumonia, give antibiotics (*see* Section 5.3.A).
- If fever (≥ 39°C or ≥ 102.2°F) is causing distress, give paracetamol. High fever is the exception rather than the rule in bronchiolitis, and should make you suspect bacterial infection.

Failure to improve

If the condition worsens suddenly, consider pneumothorax, although this is uncommon. Tension pneumothorax associated with major respiratory distress and shift of the heart requires immediate relief by needle thoracocentesis (i.e. placing a needle to allow the air that is under pressure to escape) (*see* Section 8.3). If needle thoracocentesis is helpful, insert a chest tube with an underwater seal until the air leak closes spontaneously and the lung expands (*see* Section 8.3). **The signs of pneumothorax in severe bronchiolitis may be difficult to detect clinically. However, needle thoracocentesis in the absence of a pneumothorax may cause one, so if you are unsure, take a chest X-ray.** Even on a chest X-ray, the diagnosis may be very difficult due to the areas of hyperlucency in bronchiolitis caused by air trapping.

If respiratory failure develops, nasal continuous positive airways pressure (CPAP) or continuous negative extrathoracic pressure (CNEP) may be of benefit (*see* Section 8.3).

If apnoeic episodes develop (this is most likely in premature infants), give bag-valve-mask resuscitation, then nasal CPAP or CNEP. Sometimes intubation and ventilation may be needed in a high-dependency ward (if available); if so, contact an anaesthetist urgently.

Infection control

Bronchiolitis is infectious and easily transmitted to other infants and young children in hospital. Babies in the neonatal unit are particularly at risk. The following strategies may reduce the risk of cross-infection (*see* Section 1.2):

- hand washing between patients
- the wearing of gloves and aprons
- ideally isolate the affected patient, but close observations are needed
- restrict visiting by anyone with symptoms of upper respiratory tract infection.

5.2.B Asthma

BOX 5.2.B.1 Minimum standards

- Inhaled bronchodilators (with spacers).
- Inhaled steroids.
- Prednisolone/hydrocortisone.
- Nebulised bronchodilators.
- Oxygen.
- Salbutamol, magnesium sulphate, adrenaline and aminophylline.
- Pulse oximetry.

Introduction

Asthma is a condition characterised by episodic or recurrent symptoms of cough, prolonged expiration with wheeze, chest tightness and shortness of breath without fever (although some episodes are precipitated by an upper respiratory tract infection which may have an accompanying fever). It is due to variable and reversible airway obstruction associated with chronic airway inflammation. Asthma has become more prevalent over the last 20 years, along with the other atopic conditions such as allergic rhinitis and eczema. This is particularly so in well-resourced countries, where it is reported to occur in up to 10–15% of children.

Young children (under 5 years of age) often have 'asthma-like' symptoms (cough, wheeze and shortness of breath) in response to respiratory infections, but with no demonstrable problem between infections. This tendency often stops in the early school years. In these children, treatment of episodic symptoms with acute asthma therapies ('relievers') may still provide relief of symptoms, but 'preventers' (i.e. inhaled steroids) will not usually be of benefit unless the child has continuous symptoms or is likely to be atopic (e.g. due to a personal or family history of asthma, eczema or allergic rhinitis). In the youngest children (less than 2 years old) with severe episodes or symptoms continuing between infections (interval symptoms), it is necessary to consider other diagnoses, such as bronchiectasis, tuberculosis, foreign body and cystic fibrosis.

Diagnosis of asthma between episodes

The diagnosis is clinical, and is based on a **history** of the following:

- recurrent cough (mostly dry, becoming productive with exacerbations), wheeze, shortness of breath or chest tightness
- symptoms worse at night, and on exertion

- symptoms worsened by respiratory infections, inhaled irritants (e.g. cigarette smoke), cold air, animal fur, excitement or upset
- a personal or close family history of eczema, rhinitis or asthma.

Examination may identify any of the following:
- no abnormalities
- slow growth
- overinflation of the chest, Harrison's sulci
- wheeze, particularly on forced expiration
- rhinitis or eczema.

Investigations

Investigations are not usually needed, but may help to support the diagnosis or exclude other conditions:

1 Chest X-ray. This is normal or shows overinflation (flat diaphragms and hyperlucency, particularly when severe or acute), or increased perihilar linear markings.
2 Peak flow (in children aged 7–8 years or over). This may show the following:
   - more than 15% variability from morning to night (keep a peak flow diary)
   - a fall after 5–10 minutes of hard exercise
   - a rise after a dose of inhaled bronchodilators (e.g. salbutamol)
   - **spirometry will show FEV1:FVC of less than 85% and concavity in the flow-volume loop, which is at least partially reversed by a dose of inhaled bronchodilators.**

Skin prick tests, or IgE RASTs, do not aid the diagnosis, and only infrequently help in the management.

Symptoms that resolve with bronchodilators with or without steroids support the diagnosis, but bear in mind that conditions other than asthma may also show reversibility.

Ongoing management

- Avoid allergic/irritant factors (e.g. smoke, chemical fumes, house dust mites, animal fur). Discourage cigarette smoking and acquiring new pets at home.
- Do not prevent the child from exercising, but pre-dose them 5–10 minutes beforehand with a dose of inhaled beta-2 agonist bronchodilators (e.g. salbutamol).

Use of 'reliever' medication

- Occasional symptoms (e.g. on 2 to 4 days per week) may be managed with only the use of a bronchodilator (a 'reliever'), and do not usually need a 'preventer' (see below).
- Use inhaled drugs where possible, except in acute severe or life-threatening attacks, when the IV route may be used.

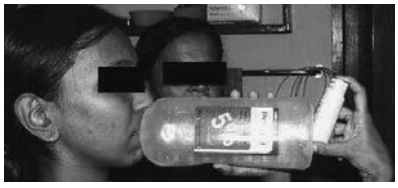

FIGURE 5.2.B.1 'Spacer' made from a large plastic bottle in use with an inhaler.

- Use an aerosol spray (metered-dose inhaler) with a spacer (first choice):
  - A commercial medium- to large-volume spacer (e.g. Volumatic, AeroChamber), or a large (2-litre) plastic bottle with the aerosol sealed into one end, and the open end held closely over the nose and mouth (*see* Figure 5.2.B.1).
  - Use 200–1000 micrograms of salbutamol (2–10 sprays); more may be needed in younger children, or if the patient is acutely breathless (and repeated).
  - Each spray or puff should be inhaled individually in turn with 4 to 5 breaths, rather than filling the spacer device with multiple sprays.
  - For children under 5 years of age, attach a face mask (e.g. inverted adult mask) to the mouthpiece of a spacer.

Clean the spacer with soapy water and leave it to dry naturally to reduce static electrical charges on the inside. Alternatively, use a nebuliser to deliver salbutamol (this is less portable).

Children with asthma should always have immediate access to their usual reliever inhaler device. Children over 7–8 years of age may keep their device with them.

Use of 'preventer' medication

More frequent symptoms, regular nocturnal symptoms or daily use of a bronchodilator should be treated with regular medication aimed at controlling airway inflammation (a 'preventer'), such as inhaled steroids. Use inhaled (preferably through a spacer) beclomethasone propionate or budesonide, 200–400 micrograms twice daily.

- Rinse the mouth (if feasible) after each dose of inhaled steroid.
- Aim for rapid control of symptoms, and then tail down the dose over a period of months.
- Gaining control may be helped by a short course (7–10 days) of systemic steroid (e.g. prednisolone 500 micrograms/kg once daily after food or milk, maximum daily dose 40 mg).
- Continue with bronchodilator use for symptom relief (but avoid regular use).

For frequent or severe symptoms, consider:

- whether the diagnosis is correct
- aggravating factors (e.g. rhinitis, stress, gastro-oesophageal reflux)
- whether the medication is being taken, and whether it is being taken correctly
- increasing the inhaled steroid dose (beclomethasone to 400–800 micrograms twice daily) **or**
- **adding leukotriene antagonists (e.g. montelukast), which are useful in preschool children, or a long-acting inhaled drug (e.g. salmeterol) or**
- oral methylxanthines (e.g. theophylline 5 mg/kg three to four times a day)
- **as a last resort**, use of alternate-day oral prednisolone (start at 500 micrograms/kg on alternate days and reduce rapidly to 100 micrograms/kg on alternate days, to the nearest 1 mg or 5 mg tablets). Stop as soon as possible.

Children on inhaled or oral steroids should have regular

checks of their growth and be watched for steroid side effects (e.g. oral thrush)

The control of asthma should be regularly reviewed (e.g. 3-monthly) and medication stepped up or down depending on the symptoms and on peak flow measurements **or spirometry *in*** those over 7 years of age. Families should be given written instructions and helped to change the treatment themselves, with support.

Management of an episode of acute asthma

Initial treatment of a mild to moderate acute attack of asthma is as follows:

- Reassure the child and their parents, and avoid upset as this may exacerbate respiratory distress.
- Give a regular inhaled beta-2 agonist bronchodilator, such as salbutamol aerosol 200–1000 micrograms (2 to 10 sprays each of 100 micrograms, with each spray given after every four to five breaths) via a spacer every 30 minutes to 2-hourly until the child is better.
- If the child does not respond to the spacer, give 2.5 mg salbutamol for children under 5 years and 5 mg salbutamol for those over 5 years via a nebuliser 2- to 4-hourly (use oxygen to drive the nebuliser if possible).
- Give systemic steroids: oral prednisolone 1 mg/kg (maximum dose of 40 mg) for 3–5 days, depending on the duration of symptoms; administer with food or milk to avoid gastric irritation.
- Treat or remove any exacerbating factors (see the 'Diagnosis' section above).
- Give antibiotics only if there are signs of pneumonia, especially a persistent fever.

Very severe or life-threatening asthma

Features of severe or life-threatening asthma include the following:

- being too breathless to feed, drink or talk
- marked recession/use of accessory muscles
- respiratory rate of more than 50 breaths/minute
- pulse rate of more than 140 beats/minute
- poor chest movement or silent chest
- exhaustion, agitation or reduced conscious level (due to hypoxia or hypercapnia)
- hypoxaemia (SaO_2 less than 90% in air or cyanosis) (this is a very late sign).

Treat immediately (use the 'ABC' approach):

- Give **100% oxygen** via a face mask with reservoir bag held by the parent or nurse close to the child's face at 10–15 litres/minute to keep SaO_2 in the range 94–98%.
- Give salbutamol inhaled from a nebuliser, 2.5 mg nebules for children under 5 years and 5 mg for those over 5 years, and repeated as required (drive the nebuliser with oxygen at 6–8 litres/minute rather than compressed air). Sometimes nebulisers may be needed continuously (described as 'back to back', i.e. as each nebule finishes, repeat with another).
- If a nebuliser is not available, use inhaled salbutamol via a spacer (but now without a valve that needs opening with each breath; *see* Figure 5.2.B.1, in which the home-made 'spacer' has no valve) as described above in acute asthma. That is, give salbutamol aerosol 1000 micrograms (10 sprays each of 100 micrograms, with each spray given after every four to five breaths) via the spacer every 5–10 minutes initially and then, once there is some improvement, 10 sprays over four to five breaths each, every 10–30 minutes until the child is better. Children under 4 years of age are likely to require a face mask connected to the mouthpiece of a spacer for successful drug delivery. Inhalers should be sprayed into the spacer in individual sprays and inhaled immediately by tidal breathing.
- If nebulised or inhaled beta-agonist bronchodilators are not available or are not effective and the child is deteriorating, give an intramuscular injection of adrenaline: 10 micrograms/kg (0.01 mL/kg of 1 in 1000 solution, up to a maximum of 300 micrograms), measured accurately with a 1-mL syringe (**ensure that the needle is not in a vein before injecting**). If there is no improvement after 15 minutes, repeat the dose once.
- **In addition to the bronchodilator treatment, give systemic steroids either as** IV/IM hydrocortisone 4 mg/kg 4- to 6-hourly (preferable) or as **oral** prednisolone (see above) until recovery. Start the steroids as soon as possible. A soluble preparation dissolved in a spoonful of water is preferable in those unable to swallow tablets. Use a dose of 20 mg for children aged 2–5 years. Repeat the dose of prednisolone in children who vomit, and give IV (or IM if a venous cannula cannot be inserted) hydrocortisone (4 mg/kg repeated 4-hourly) in those who are unable to retain orally ingested medication. Treatment for 3–5 days is usually sufficient, but the length of the course should be tailored to the number of days necessary to bring about recovery. Weaning is unnecessary unless the course of steroids exceeds 14 days.

If two to three doses of inhaled bronchodilator and systemic steroids do not result in improvement, or if life-threatening features are present, use:

- IV beta-2-agonist salbutamol (loading dose 5 micrograms/kg over 10–15 minutes in children under 2 years of age and 15 micrograms/kg over 2 years of age). If resources allow (i.e. only where high-dependency or intensive care is available), this can be followed by 1–2 micrograms/kg/minute (maximum of 5 micrograms/kg/minute) adjusted according to response and heart rate, and with monitoring of serum potassium levels as this electrolyte falls when salbutamol is given IV (see below)
- **or** IV magnesium sulphate 40 milligrams/kg (maximum of 2 grams) over 20 minutes
- **or** both of the above
- an alternative to the above treatments is to give aminophylline (loading dose 5 mg/kg over 20 minutes, followed by 1 mg/kg/hour by IV infusion in children aged 1–12 years and 500 micrograms/kg/hour in patients aged over 12 years or under 1 year). Do not give the loading dose if the child has already received any form of aminophylline or caffeine in the previous 24 hours. Side effects include nausea, vomiting, tachycardia or tachyarrhythmia and seizures, and consequently this treatment is less preferred.

Severe and life-threatening hypokalaemia may occur with IV salbutamol, potentiated by steroids. If possible, monitor the ECG continuously and check potassium levels 12-hourly. ECG signs of hypokalaemia are ST depression, T-wave

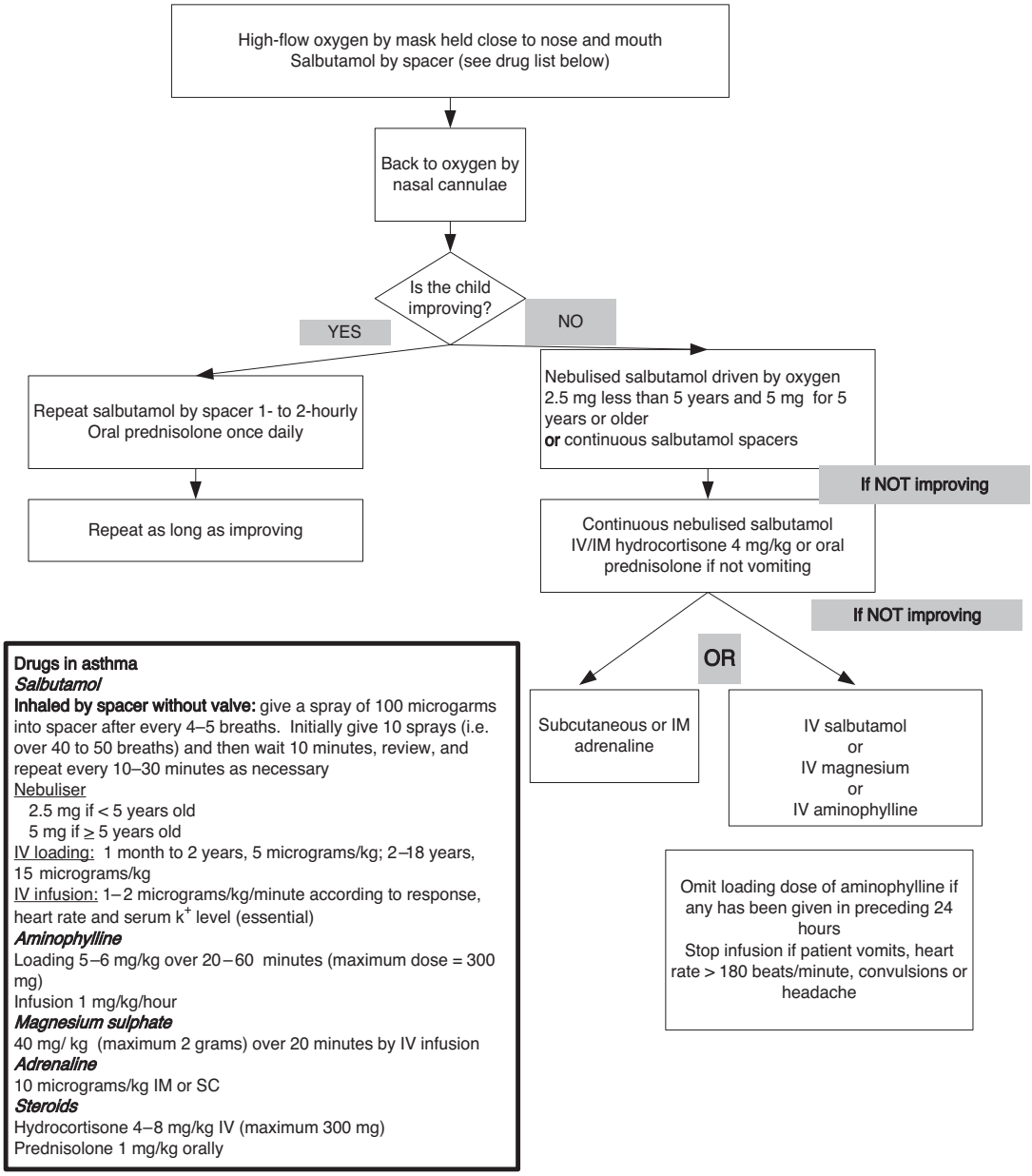

FIGURE 5.2.B.2 Pathway of care for very severe or life-threatening asthma.

reduction and prominent U waves. Ensure that maintenance potassium intake is given in the infusion fluid.

If there is a poor response to the above treatment, or the child's condition worsens suddenly, obtain a chest X-ray to look for evidence of pneumothorax. In the presence of hyperinflation from asthma, detection of a pneumothorax on the chest X-ray may be difficult.

Monitor the above clinical features regularly, and also monitor oxygen saturation, by pulse oximeter if available. Keep SaO_2 in the range 94–98% by administering oxygen, either by face mask or by nasal cannulae. Use oxygen to drive nebulisers.

If the above measures do not result in improvement, or the child is tiring and gasping, this may progress to a respiratory arrest. Positive airway pressure would be the usual next step. Some respiratory support can be given by the use of a bag-valve-mask system to increase tidal breaths, but beware of aspiration (insert a nasogastric tube).

Transcutaneous pCO_2 monitoring is valuable in severe asthma.

In cases that do not respond to the above measures, obtain a chest X-ray and consider mechanical ventilation (slow rate, long expiration). A blood gas measurement showing respiratory acidosis can be valuable at this time, but remember that invasive procedures can worsen respiratory distress.

If intubation and ventilation become essential, ketamine induction followed by inhalational anaesthetic gases (e.g. halothane) may assist bronchodilatation.

Indications for intubation and ventilation (if available) in severe asthma include the following:

- increasing exhaustion
- progressive deterioration in clinical condition
- oxygenation decreasing and/or oxygen requirement increasing

- pCO_2 increasing (if measurable from arterial/capillary gas)
- sudden deterioration – and always consider the possibility of a pneumothorax.

Follow-up care

Once the child has improved sufficiently to be discharged home, prescribe inhaled salbutamol through a metered-dose inhaler with a suitable commercially available or home-made spacer (*see* Figure 5.2.B.1), and instruct the parents in how to use this.

Following any acute episode, review asthma control and management, including correct use of medications and the need for a step up in 'preventive' treatment.

5.2.C The child with an inhaled foreign body

BOX 5.2.C.1 Minimum standards

- Chest X-ray.
- Antibiotics.
- Physiotherapy.
- Bronchoscopy.

Introduction

Any small object that can get through the trachea or large bronchi, such as a seed, a peanut or an eraser from the top of a pencil, can lodge in the lower airway. If the object is too small to cause life-threatening choking it will enter the lower respiratory tract and cause subacute respiratory symptoms after an initial coughing bout.

Diagnosis

There may be a clear history from the parent or child of an episode of coughing or choking, followed by difficulty in breathing.

- On examination of the child's chest, look to see whether there is less chest expansion on one side when breathing in.
- Feel the trachea. It may be pushed away from the midline by air trapping on the side affected by the foreign body.
- This may also be seen on a chest X-ray (if available) (*see* Figure 5.2.C.1), ideally an expiratory and inspiratory film.

An inhaled foreign body in a young child can go down the right or left side. In older children and adults, a foreign body on the right side is more common. There may be a harsh wheezing noise heard on the side of the chest where the foreign body has lodged.

Treatment

Air may be trapped in the lungs beyond the point where the foreign body has lodged, or this part of the lung may become infected. Give the child antibiotics. Chloramphenicol, 25 mg/kg every eight hours, is a good first choice, but add flucloxacillin or cloxacillin 25 mg/kg six hourly if there is a suspicion of or proven infection with *Staphylococcus aureus*. If there is evidence of severe pneumonia use the antibiotic combination in Section 5.3.A for severe pneumonia. Removal of a foreign body is a specialised procedure that must be carried out using a bronchoscope. Treat the infection until the child can be transferred to a hospital where this procedure can be performed. Some gentle physiotherapy may help, but take care not to dislodge the foreign body, as this will cause infection and obstruction in another part of the lung.

If the foreign body is not removed there will be subsequent bronchiectasis and recurrent chest infections (*see* Section 5.3.B).

For the management of choking, *see* Section 1.12.

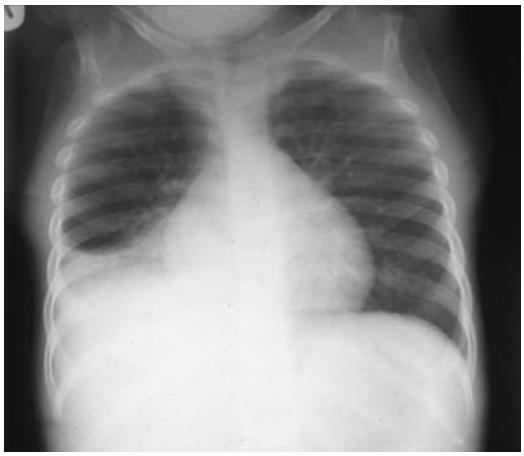

FIGURE 5.2.C.1 Chest X-ray of a child with a foreign body occluding the right middle and right lower lobe bronchi. The right upper lobe of the lung shows air trapping due to a 'ball-valve' effect. The foreign body is not visible because it is not radio opaque.

5.3 Lung disorders

5.3.A Pneumonia

BOX 5.3.A.1 Minimum standards
- Oxygen.
- Pulse oximeter.
- Antibiotics.
- Immunisations: pneumococcal.
- Chest X-ray.
- TB and HIV testing.

Acute respiratory infection

There are two categories of acute respiratory infection (ARI).

- **Acute upper respiratory infection (AURI):** above the vocal cords and epiglottis. These infections include colds, tonsillitis and otitis media. They are not life-threatening, but may lead to disability (e.g. otitis media is a leading cause of deafness in resource-limited countries) and complications (e.g. rheumatic fever following streptococcal pharyngitis).
- **Acute lower respiratory infection (ALRI):** below and including the vocal cords and epiglottis. These infections include croup (and other infectious causes of upper airway obstruction), pneumonia and bronchiolitis. Acute upper airway obstruction is described in Section 5.1.

Importance of acute respiratory infection

Pneumonia is responsible for around two million deaths annually in children under 5 years of age. In resource-limited countries, most of these infections are bacterial, and the most common causative bacteria are *Streptococcus pneumoniae* and *Haemophilus influenzae*. **In severely malnourished children, *Klebsiella pneumoniae* and *Staphylococcus aureus* are the most common causative organisms.**

Immunisation

Pneumococcal conjugate vaccine has been introduced to the primary immunisation schedule in many well-resourced countries, and reduces the incidence of X-ray-proven pneumonia in infants by around one-third. The HiB vaccine (against encapsulated *Haemophilus influenzae* type B) will not protect against unencapsulated *H. influenzae*, which causes some cases of pneumonia in resource-limited countries. Nevertheless, the HIb vaccine is very effective against other very serious infections caused by *H. influenzae* (e.g. meningitis, epiglottitis), and should be given to all infants in every country. Unfortunately, around 34 million children do not receive routine immunisations, and most of these are **living** in resource-**limited** countries.

Management of the child with acute upper respiratory infection

Coryza or pharyngitis

These are common self-limiting viral infections that require only supportive care. Antibiotics should not be given. Wheeze or stridor may occur in some children, especially infants. Most episodes end within 14 days. Cough lasting 30 days or more may be caused by tuberculosis, asthma or pertussis.

Presentation

These infections present with cough, running nose, fever and sore throat, but **not** with fast breathing, chest indrawing, stridor or danger signs for pneumonia (see below). Wheezing may occur in young children (*see* Section 5.2.A).

Treatment

- Treat the child as an outpatient.
- Soothe the throat and relieve the cough with a safe remedy, such as a warm sweet drink.
- Relieve high fever (≥ 39°C or ≥ 102.2°F) with paracetamol if it is causing distress.
- Give normal fluid requirements plus extra breast milk or fluids if there is a fever. Small frequent drinks are more likely to be taken and less likely to be vomited.
- Clear secretions from the nose before feeds using a cloth which has been soaked in water and twisted to form a pointed wick.
- Do not give any of the following:
  - antibiotics (they are not effective for viral illnesses and do not prevent pneumonia)
  - remedies containing atropine, codeine or codeine derivatives, or alcohol (which may be harmful)
  - medicated nose drops.

Advise the mother to feed the child normally, to watch for fast or difficult breathing, and to return if either develops or if the child is unable to drink or breastfeed.

Inform the mother that the child has mucus in the upper airways that 'drops' in the lungs, so the child coughs in order to remove it, and this means that the cough in itself is not dangerous.

Management of the child with acute lower respiratory infection (ALRI)

Children at greatest risk of dying from an ALRI have the following risk factors:

- age under 1 year
- malnutrition

- pneumonia as a complication of infection with measles, pertussis, malaria or HIV.

Diagnosis of ALRI

In many hospitals in resource-limited countries, special tests (e.g. blood culture, microbiology of respiratory secretions, X-rays) may be limited or unavailable. However, because the prevalence of bacterial pneumonia is high, the diagnosis must usually be made clinically. This will not be 100% accurate, so a few children may receive antibiotics unnecessarily (i.e. clinical diagnosis has less than 100% **specificity**). However, it is more important not to miss children who do need antibiotics (i.e. clinical diagnosis should have a good **sensitivity**). Clinical diagnosis may be as accurate as an X-ray and more helpful in deciding whether treatments such as oxygen are indicated. The clinical features will also help to decide how severe the child's infection is and what treatment is appropriate.

The following clinical features should be recorded:

- The presence of **cyanosis**, which is best seen in the lips or tongue. It may be missed if the lighting is poor or if the child is anaemic (e.g. due to co-infection with malaria), and it can be difficult to detect in black children. Cyanosis is a late sign of respiratory problems, and if possible oxygenation should be assessed with a pulse oximeter. Normal saturation at sea level (SaO_2) is greater than 94%.
- Inability of the child to drink.
- The presence of chest wall indrawing (an inward motion of the lower chest wall when the child breathes in).
- The presence of grunting (expiratory braking).
- The presence of hyperinflation (asthma or bronchiolitis).
- Elevated respiratory rate. Respiratory rate is measured over 1 minute, using a suitable timing device. The respiratory rate in children varies with age. Table 5.3.A.1 lists the abnormal values for respiratory rate for various age groups.

TABLE 5.3.A.1 WHO definition of abnormally fast breathing

Age	Abnormally fast breathing
< 2 months	≥ 60 breaths/minute
2–12 months	≥ 50 breaths/minute
12 months to 5 years	≥ 40 breaths/minute

Remember that conditions such as severe anaemia, dehydration and high fever are accompanied by a raised respiratory rate.

A high fever in a child with breathing difficulties may be due to pneumonia, bacterial tracheitis or even epiglottitis. If the airway is clear, the most likely diagnosis is pneumonia. Although high fever and respiratory signs are the usual way for pneumonia to present, pneumonia should always be considered in the list of causes of abdominal pain and neck stiffness.

Clinical examination (or chest X-ray) cannot reliably differentiate between a viral pneumonia and a bacterial one, so all cases are treated with antibiotics.

Features of pneumonia include the following:

- fever, cough, breathlessness and lethargy
- pleuritic chest pain, abdominal pain and neck stiffness (these indicate pleural involvement)

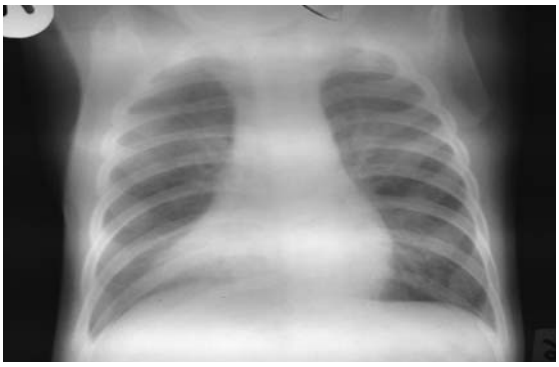

FIGURE 5.3.A.1 Right middle lobe pneumonia. Note the loss of the right heart border.

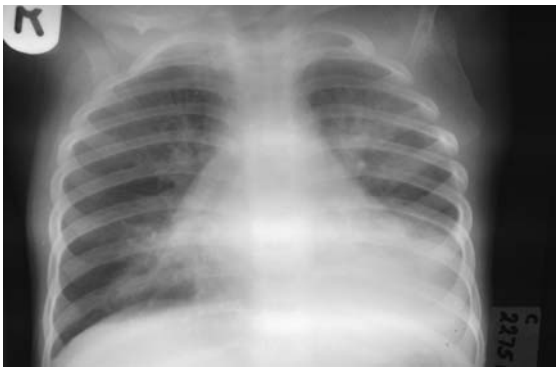

FIGURE 5.3.A.2 Left lower lobe pneumonia. Note that the silhouette of the diaphragm cannot be seen on the left. The right middle lobe is also affected.

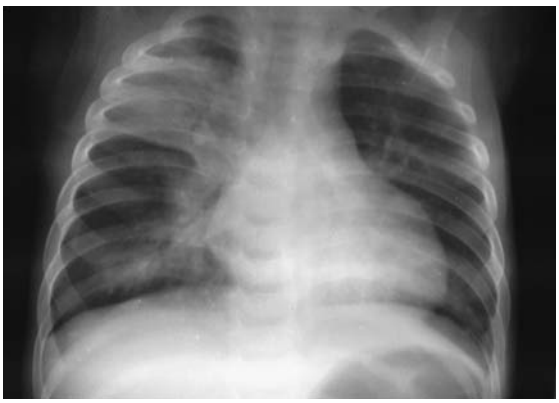

FIGURE 5.3.A.3 Right upper lobe pneumonia. Note that the horizontal fissure is pulled up.

- signs of consolidation:
  - dull percussion
  - reduced breath sounds
  - bronchial breathing may be absent in an infant
- chest X-ray may show pleural effusion or empyema as well as consolidation.

Auscultation should always be undertaken, **but only after first checking for cyanosis, observing the breathing pattern and the other signs as described above**. Important clinical signs include evidence of the following:

- consolidation or effusion/empyema
- wheeze

- bronchiolitis (hyperinflation with crackles at the lung bases)
- alveolitis (e.g. in HIV-induced *Pneumocystis* pneumonia) with end-inspiratory crackles.
- pericardial involvement (rare)
- pneumothorax (rare).

A chest X-ray may be helpful if there is any doubt about the diagnosis or if the child is seriously ill.

Figures 5.3.A.1, 5.3.A.2 and 5.3.A.3 show the appearance of lobar pneumonia affecting different lobes.

Additional features of ARLI usually include a fever and a cough. Pleuritic chest pain (which may radiate to the abdomen) may also be present in older children if the diagnosis is pneumonia.

Table 5.3.A.2 gives guidelines for the assessment and treatment of acute respiratory infection. Children with the following features should be managed differently, as described elsewhere in this book:

- stridor (*see* Section 5.1.A)
- wheeze (*see* Sections 5.2.A and 5.2.B)
- severe malnutrition (*see* Section 5.10.B)
- signs suggesting meningitis (*see* Section 5.16.B).

Diagnosis of severe pneumonia

This is diagnosed by the presence of cough or difficult breathing plus at least one of the following:

- central cyanosis
- inability to breastfeed or drink, or vomiting after every drink
- convulsions, lethargy or unconsciousness
- severe respiratory distress.

In addition, some or all of the other signs of pneumonia may be present, such as the following:

- fast breathing:
  - age < 2 months: ≥ 60 breaths/minute
  - age 2–11 months: ≥ 50 breaths/minute
  - age 1–5 years: ≥ 40 breaths/minute
- nasal flaring
- grunting (in young infants)
- lower chest wall indrawing
- chest auscultation signs of pneumonia:
  - decreased breath sounds
  - bronchial breath sounds
  - crackles
  - abnormal vocal resonance (decreased over a pleural effusion, and increased over lobar consolidation)
  - pleural rub.

Obtain a chest X-ray and SaO_2 (if available).

For children with no evidence of pneumonia but with signs suggesting a chest infection, look for ear and throat infections or infections in another system and treat accordingly.

TABLE 5.3.A.2 The management of children with different severities of acute lower respiratory tract infection (ALRI) (modified from the WHO *Pocket Book of Hospital Care for Children*, second edition 2014)

Sign or symptom	Classification	Treatment
Central cyanosis and/or SaO_2 < 90% Severe respiratory distress (e.g. head nodding, gasping, chest wall indrawing, grunting) Fast breathing as below under 'pneumonia that is not severe' Decreased breath sounds and/or bronchial breathing Crackles in the lung fields Vocal resonance and percussion suggesting consolidation and/or effusion Pleural rub Inability to drink, vomiting, reduced consciousness **Plus** signs of pneumonia in the row below	Severe pneumonia	Admit to hospital Give IV/IM appropriate antibiotics* Give oxygen Manage the airway Treat high fever if present If the child has HIV infection, refer to specific guidelines (and *see* Section 6.2.D)
Fast breathing but no chest wall indrawing: ≥ 60 breaths/minute in a child aged < 2 months ≥ 50 breaths/minute in a child aged 2–11 months ≥ 40 breaths/minute in a child aged 1–5 years Definite crackles on auscultation	Pneumonia that is not severe	Home care (but depends on home circumstances and overall clinical state of the child) Give an appropriate antibiotic* Advise the mother when to return if treatment fails on amoxicillin and more appropriate second-line treatment is needed Follow up in 2 days
No signs of pneumonia or severe pneumonia	No pneumonia Cough or coryza	Home care Advise the mother to return for follow-up in 5 days if not improving If coughing for more than 14 days, consider investigations for TB, asthma, inhaled foreign body, pertussis, HIV, bronchiectasis and lung abscess (*see* Figure 5.3.C.1).

* See details of antibiotics, routes of administration and durations for different categories of pneumonia in section 'Antibiotics' below

Oxygen

Children with severe or very severe pneumonia are likely to be hypoxaemic. However, cyanosis is a late sign of hypoxaemia.

Oxygen must always be available in sufficient quantity to provide 24-hour treatment without depending on the availability of a reliable electricity supply.

Give oxygen if the child shows any of the following:

- restlessness (if oxygen makes the child more comfortable)
- severe chest wall indrawing
- a breathing rate of more than 70 breaths/minute (in a child aged 2 months to 5 years)
- grunting (in an infant under 2 months of age)
- gasping
- if a pulse oximeter is available, SaO_2 of less than 94% (at sea level; lower values will be normal at high altitude, and normal values of SaO_2 should be known for healthy local children in your area if it is at high altitude). Aim to maintain SaO_2 in the range 94–98%.

Give oxygen until the signs of hypoxia (e.g. severe lower chest wall indrawing, high breathing rates and/or SaO_2 < 94% in air) are no longer present.

Oxygen delivery

A good source of oxygen is an oxygen concentrator. This is a durable piece of equipment, but it requires a continuous supply of mains electricity to provide oxygen. It works on the 'molecular-sieve' principle, removing nitrogen from room air. The alternative is cylinder oxygen, but cylinders must be replenished regularly and need to be available at all times, which is expensive and may give rise to transport difficulties. **A combination of the two supplies of oxygen is essential.** An oxygen generator which can provide oxygen and fill cylinders when the electrical power is available (e.g. Diamedica equipment). The concentrator or cylinder should be connected to a low-flow meter. The use of a flow splitter will allow up to four children to receive oxygen from one source. The oxygen should be delivered to the child using nasal cannulae. **These should be only 2–3 mm long, to avoid nasal irritation.**

Figure 5.3.A.4 shows the delivery of oxygen through nasal cannulae.

A mask should be used to give high-flow oxygen during resuscitation.

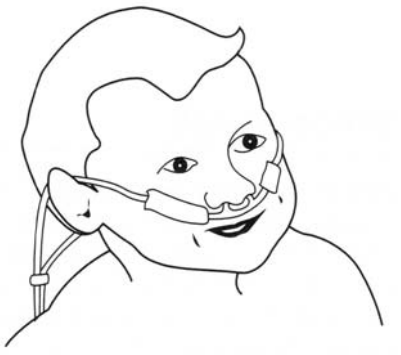

FIGURE 5.3.A.4 Nasal cannulae for delivering oxygen. The cannula has been taped to the child's cheeks, close to the nostrils. The tubing is run under the child's shirt to stop them pulling it, and leads to the low-flow meter and oxygen concentrator or cylinder. A flow splitter may be used.

Nurses should check frequently that the nasal cannulae are not blocked with mucus and are in the correct position, and that all connections are secure.

Antibiotics

Children who are vomiting or who require IV fluids should have their antibiotics given intravenously (preferably), or intramuscularly **if vascular access is difficult to achieve or maintain**, for the first 48 hours. Some antibiotics, such as gentamicin, are always given IV or IM. Certain antibiotics are reserved for specific circumstances, such as high-dose co-trimoxazole for suspected *Pneumocystis jirovecii* pneumonia, and flucloxacillin or cloxacillin for pulmonary abscess or bacterial tracheitis where *Staphylococcus aureus* is likely to be responsible. These are described at the end of the section on antibiotics.

For severe pneumonia:

- Give ampicillin 50 mg/kg IM/IV or benzyl penicillin 50 000 units/kg that is 30 mg/kg IM or IV every 6 hours plus gentamicin 7.5 mg/kg IM or IV once a day for 5 days. Then, if the child responds well, complete treatment with oral amoxicillin (25 mg/kg three times a day, maximum 500 mg, or 1 gram in severe cases) plus IM or IV gentamicin 7.5 mg/kg once daily for a further 5 days.
- Alternatively, if the above are not available, give chloramphenicol (25 mg/kg IM or IV every 8 hours) until the child has improved. Then continue orally four times a day for a total course of 10 days.
- **Or** use ceftriaxone (80 mg/kg IM or IV once daily) or cefotaxime (50 mg/kg IV 6-hourly) for 10 days.
- If the child does not improve within 48 hours, switch to gentamicin (7.5 mg/kg IM or IV once a day) and cloxacillin (50 mg/kg IM or IV every 6 hours), as described below for possible staphylococcal pneumonia.

For pneumonia that is not severe:

- Treat the child as an outpatient.
- Give amoxicillin 40 mg/kg twice a day for 5 days.
- Give the first dose at the clinic, and teach the mother how to give the other doses at home.
- In infants aged 2–12 months who have some of the signs suggestive of non-severe pneumonia without a high fever but **with** wheeze, the most likely diagnosis is bronchiolitis. This is caused by a virus, and in the absence of signs suggesting the development of secondary bacterial infection (severe pneumonia), antibiotics are not necessary (*see* Section 5.2.A). The WHO recently published the following conclusion: **Antibiotics are not routinely recommended for children aged 2 months to 5 years with non-severe pneumonia (that is, fast breathing with no chest indrawing or danger signs) with a wheeze but no fever (temperature below 38°C), as the cause is most likely to be viral.**

Symptomatic and supportive treatment for children with all degrees of pneumonia

Nurse the child in a thermoneutral environment (lightly clothed in a warm room at around 25°C).

Fever:

- Remember that fever may not be simply due to the child's pneumonia. Consider other diagnoses, such as malaria.
- If the child has fever (≥ 39°C or ≥ 102.2°F) that appears

to be causing distress, give paracetamol oral or rectally, 10–15 mg/kg 4- to 6-hourly.
- Remove by gentle suction under direct observation any thick secretions in the throat which the child cannot clear.
- Ensure daily maintenance fluids appropriate for the child's age, but avoid over-hydration.
- Encourage breastfeeding and oral fluid intake.
- If the child cannot drink, insert a nasogastric tube and give maintenance fluids in frequent small amounts. If the child is taking fluids adequately by mouth, do not use a nasogastric tube, as it increases the risk of aspiration pneumonia. Encourage eating as soon as food can be taken. When the child is recovering, nutritional rehabilitation may be necessary.

Failure to start to improve within a few days

If the child has not improved after 2 days, or if their condition has worsened, re-examine them thoroughly, looking for signs of pleural effusion/empyema and other causes of fever. If possible, obtain a chest X-ray. This may show a pleural effusion or empyema (*see* Section 5.3.B) into which antibiotics cannot penetrate, or it may show the characteristic pneumatocoeles (lung abscesses) of staphylococcal pneumonia.

Also consider *Mycoplasma pneumoniae* or *Bordetella pertussis* infections. **Pertussis should be recognisable because of the characteristic nocturnal emetic cough and the whoop in the child over 2 years of age.**

Prescribe **erythromycin** if either of these infections is suspected. It should be given orally as follows:
- 125 mg 6-hourly (children aged 1 month to 2 years)
- 250 mg 6-hourly (children aged 2–8 years)
- 500 mg 6-hourly (children over 8 years of age).

Pneumonia that does not respond to standard antibiotics within 2 weeks

Tuberculosis

A child with persistent fever for more than 2 weeks and signs of pneumonia should be evaluated for tuberculosis. If another cause of the fever cannot be found, tuberculosis should be considered and treatment for tuberculosis, following national guidelines, may be initiated and response to anti-tuberculous treatment evaluated (*see* Section 6.1.N).

Children who are HIV-positive or in whom HIV is suspected

Some aspects of antibiotic treatment are different in children who are HIV-positive or in whom HIV is suspected. Although the pneumonia in many of these children has the same aetiology as in children without HIV, pneumocystis pneumonia (PCP), often at the age of 4–6 months, is an important additional cause which must be treated when present (*see* Section 6.2.D). While confirming the diagnosis, give ampicillin plus gentamicin as described above for severe pneumonia.

Staphylococcal pneumonia

Staphylococcal pneumonia is suspected if there is rapid clinical deterioration despite treatment, a pneumatocoele or necrotising pneumonia with effusion on chest X-ray, numerous Gram-positive cocci in a smear of sputum, or heavy growth of *Staphylococcus aureus* in cultured sputum or empyema fluid.
- Treat with cloxacillin (50 mg/kg IM or IV every 6 hours) and gentamicin (7.5 mg/kg IM or IV once a day) for at least 7 days.
- When the child improves, continue cloxacillin/flucloxacillin orally four times a day for a total course of 3 weeks. Note that cloxacillin can be substituted by another anti-staphylococcal antibiotic, such as oxacillin, flucloxacillin or dicloxacillin.

Severe dehydration

This may be a problem in pneumonia, arising from high fever and poor fluid intake (*see also* Section 5.12.A for the treatment of diarrhoea and Section 5.5.A for the management of shock).

Look for signs of dehydration or shock (tachycardia, weak pulse, poor peripheral circulation, and capillary refill time prolonged by more than 3 seconds).
- **If the child is shocked:** Site an intravenous line and give a bolus of crystalloid – for example, Hartmann's solution, Ringer-lactate or colloid 10–20 mL/kg (10 mL/kg in a neonate).
- **If the child is not shocked but is clinically dehydrated** (*see* Section 5.12.A): Give oral rehydration solution (ORS), 15–20 mL/kg/hour for 2 hours orally or via nasogastric tube. Encourage breastfeeding.

Management of ALRI in special circumstances

Management of the child under 6 months of age

Young infants with severe ALRI/pneumonia may not cough, but rather they may present with apnoea, poor feeding or hypothermia. Remember that in infants under 2 months of age, the abnormal respiratory rate cut-off is higher (> 60 breaths/minute). For infants aged 2–12 months the cut-off is > 50 breaths/minute.
- Some chest wall indrawing is normal during REM (dream) sleep.
- **All infants with severe ALRI/pneumonia should be admitted to hospital for treatment.**
- Bronchiolitis is a frequent cause, and usually involves hypoxaemia due to ventilation to perfusion mismatch. Oxygen is usually required. Additional respiratory support (*see* Section 5.2.A) may also be necessary, especially if there is apnoea or severe respiratory distress leading to exhaustion.
- Grunting (a short expiratory noise at the start of expiration) is **common and usually an indication for oxygen**.
- **Avoid using chloramphenicol in infants under 2 months of age** (there is a risk of development of 'grey baby syndrome'). Use benzylpenicillin or ampicillin plus gentamicin instead.
- Respiratory infection in neonates may rapidly develop into septicaemia, shock and death, so it is essential to act quickly (*see* Section 3.4).

Further reading

World Health Organization and UNICEF (2013) *Ending Preventable Child Deaths from Pneumonia and Diarrhoea by 2025: the integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD)*. http://apps.who.int/iris/bitstream/10665/79200/1/9789241505239_eng.pdf

5.3.B Pleural effusion, empyema and bronchiectasis

BOX 5.3.B Minimum standards
- Oxygen.
- Pulse oximeter.
- Chest drain.
- Antibiotics.
- Physiotherapy.
- Chest X-ray/ultrasound.

Pleural effusion

A pleural effusion is a collection of fluid between the chest wall and the lung. A small effusion of clear fluid is common in children with pneumonia. Effusion should be suspected when one side of the chest sounds very dull to percussion and the breath sounds are very quiet. It can also be seen as usually unilateral shadowing on the X-ray. Usually this fluid will quickly disappear once the infection has been treated. However, if treatment is started late, or the child is unlucky, this clear fluid can become infected, too. This leads to pus accumulating in the chest cavity (an empyema).

On examination, the chest is dull to percussion and breath sounds are reduced or absent over the affected area. A pleural rub may be heard at an early stage before the effusion is fully developed. A chest X-ray shows fluid on one or both sides of the chest.

An ultrasound examination may be helpful for identifying the size of the effusion and guiding drainage.

When empyema is present, fever persists despite antibiotic therapy, and the pleural fluid is cloudy or frankly purulent.

Treatment

If a pleural effusion is suspected, X-ray the chest if possible. If this confirms your suspicions, perform a diagnostic tap as follows:

1 In the case of young children, the child should sit on the mother's lap, facing her. The mother then holds the child tightly in a bear hug. Older children can sit or lie on a bed, but it is important to explain carefully to them what is being done and have an assistant to hold the child steady.
2 Percuss out the area of dullness, put on sterile gloves and clean the skin with alcohol.
3 Gently inject some local anaesthetic (1% lidocaine) under the skin, down to the rib, using an orange (25-gauge) or blue (23-gauge) needle.
4 Then take a fresh 20-gauge needle or butterfly needle connected to a syringe and press the needle though the chest wall just below the level where the percussion note becomes dull. **Remember to go just above the rib (to avoid the intercostal blood vessels)** and aspirate all the time. Ultrasound support is ideal if available.
5 When fluid appears, aspirate a diagnostic specimen and send this for microscopy, protein, glucose, cell count, Gram and Ziehl–Neelsen stain (low yield for acid-fast bacilli), and culture for bacteria and tuberculosis. Remember that a clear fluid aspirate can suggest another diagnosis, such as tuberculosis or lymphoma (especially if bloodstained).
6 Aspirate as much fluid as possible during the procedure to allow the child to breathe more comfortably. A three-way tap connected to the catheter can be helpful. **Ensure that air cannot enter the pleural space.** If clear fluid (straw coloured or brown) is aspirated, remove sufficient fluid to relieve distress and then remove the needle.

If more than a few millilitres of fluid containing pus (opaque) are aspirated, and this does not easily pass down the needle, a chest drain will be required. This must be a sterile procedure, and is performed as follows:

1 Select a drain, the largest that will comfortably pass through the intercostal space into the cavity by holding the tip of the tube in the forceps. Do not use the stylet, as this can damage the lung.
2 Position the child and locate the effusion in the same way as for the diagnostic tap.
3 Use sufficient local anaesthetic (1% lidocaine).
4 Make an incision in the skin and part the underlying muscle with artery forceps.

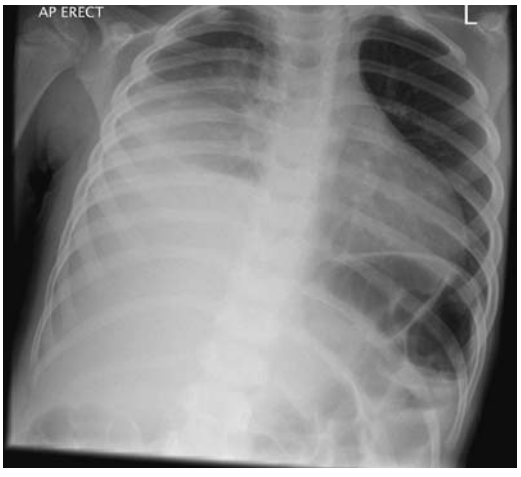

FIGURE 5.3.B.1 Chest X-ray of right-sided empyema. Note that this 5-year-old boy had a 1-week history of fever and shortness of breath. There was dullness to percussion and reduced air entry at the right lung base.

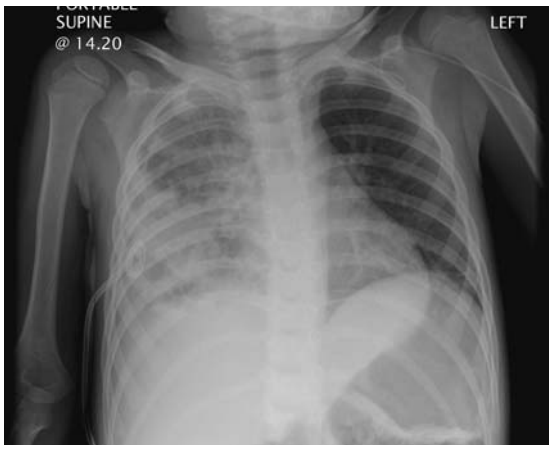

FIGURE 5.3.B.2 Chest X-ray in the same child after placement of a right-sided chest drain.

5 Avoid the neurovascular bundle on the inferior part of the rib by keeping the incision and passage of the drain on top of the rib.
6 When the pleura is reached, puncture it with the forceps and thread the chest drain through the pleural hole.
7 Ensure that all of the drainage holes of the catheter are inside the chest.
8 Fix the drain with a gauze dressing, tape and a suture.
9 Connect to an underwater seal. If the drain has been placed correctly, fluid will flow out and the fluid level will 'swing' with respiration.

Give ampicillin or cloxacillin/flucloxacillin 50 mg/kg IV or IM every 6 hours plus gentamicin 7.5 mg/kg IM/IV once daily. After at least 7 days IV/IM antibiotics, and providing the child is improving, continue flucloxacillin/cloxacillin orally 50 mg/kg 6 hourly for a total of 3 weeks from the onset of the antibiotics.

If the patient does not improve despite adequate chest drainage and antibiotics consider HIV and/or TB.

Figures 5.3.B.1 and 5.3.B.2 show the chest X-ray in a child with empyema, and the effect of placing a chest drain.

Lung abscess

Diagnosis

A lung abscess is a collection of pus in the lung. This can result from an untreated foreign body, aspiration of other material (e.g. vomit), infection with *Staphylococcus aureus*, or as a complication of bronchiectasis. When examining the child, the findings may be similar to those in the child with pneumonia, though they will often have been ill for longer. A chest X-ray (if available) will be helpful. Ultrasound scanning can show whether the abscess lies close to the posterior chest wall.

Treatment

Antibiotics are the most important form of treatment, and a long course (4–6 weeks) must be given. Give ampicillin or flucloxacillin/cloxacillin 50 mg/kg IV/IM every 6 hours plus gentamicin 7.5 mg/kg IM/IV once daily. Continue, as in empyema, for up to 3 weeks. If you are certain that the abscess lies close to the posterior chest wall, it can be aspirated in the same way as an empyema (see above).

A chest drain must never be placed in a pulmonary abscess, as this can create a fistula.

Surgical management may be required for a large abscess, especially if haemoptysis or a deterioration despite appropriate antibiotic therapy occur.

If the child has been ill for weeks, ensure good nutrition.

Bronchiectasis

Diagnosis

Bronchiectasis occurs when the bronchi become baggy and full of mucus and pus. Bronchiectasis may follow infection such as tuberculosis, pertussis and measles. It may be due to congenital problems such as cystic fibrosis (*see* Section 5.3.C) and rarer lung diseases in which there are abnormal cilia or abnormal cilial activity, or an inhaled foreign body that has not been removed (*see* Section 5.2.C).

Sometimes a child who has had lobar pneumonia does not recover fully, and develops bronchiectasis in the affected lobe. There are other rare causes, such as some viral infections.

Children with bronchiectasis usually cough and produce sputum every day. Their symptoms may become much worse at times due to secondary infection. The child may have finger clubbing, a hyperinflated chest and coarse crackles in many parts of the lung. Look for thickened bronchi and areas of consolidation on the chest X-ray.

Treatment

Bronchiectasis cannot be cured, although **occasionally symptoms can be improved by removing the lung lobe that is most severely affected**. The child and their parents must understand that daily treatment with chest physiotherapy and frequent courses of antibiotics will be needed. The use of physiotherapy is described in Section 8.3.

5.3.C Cystic fibrosis

BOX 5.3.C.1 Minimum standards
- **Diagnostic testing.**
- Pancreatic enzyme supplements.
- Fat-soluble vitamins (A, D and E).
- Daily chest physiotherapy.
- Early use of antibiotics, including flucloxacillin, amoxicillin, chloramphenicol, ciprofloxacin, gentamicin and ceftazidime.

Introduction

Pathophysiology

In the cells lining the airways of patients with cystic fibrosis (CF), chloride ions cannot leave the cell to enter the bronchial lumen. The cell cytoplasm has a high salt content, and water moves from the airway lumen into the cell by osmosis. The mucus within the lumen then becomes dehydrated. Sticky mucus interferes with the action of the respiratory cilia, and this leads to bacterial colonisation of the airway, with chronic inflammation and neutrophil damage. There are also viscid secretions in the biliary tract, pancreas and reproductive system, causing poor fat digestion and very low fertility in male patients.

Cystic fibrosis is an autosomal-recessive genetic disorder that affects the lung, digestive system, sweat glands, liver, pancreas and reproductive system. Most deaths from cystic fibrosis are caused by respiratory failure. In well-resourced countries, many patients now survive well into adulthood.

Incidence

The incidence of cystic fibrosis in countries such as the UK and the USA is around 1 in 2500 live births, and around 1 in 25 of the population are carriers. Very little is known about

the frequency of the disorder in resource-limited countries. Diagnosis relies on the sweat test, which is difficult to perform where laboratory facilities are limited. The incidence of cystic fibrosis among black South Africans is thought to be between 1 in 700 and 1 in 14000, with between 1 in 14 and 1 in 60 of the general population being carriers. In some well-resourced countries there is routine screening of newborn infants from heelprick blood samples.

The CF gene

The CF gene is on chromosome 7. The commonest mutation causing disease is DF508, and it occurs all over the world. (It is as common in cystic fibrosis patients in North Africa as it is in those in Northern Ireland.) Over 1000 other mutations have been found, many of which are rare. The gene product is a protein which sits on the apical membrane of epithelial cells and regulates the movement of chloride ions. As cystic fibrosis is a recessively inherited condition, two abnormal genes, one from each parent, are required for the disease to occur, and then this protein is defective and chloride transport is disrupted.

Presentation

Meconium ileus

In the newborn period, babies may present with a triad of:

- failure to pass meconium in the first 24 hours
- abdominal distension
- vomiting.

This picture may also occur in surgical conditions (e.g. Hirschsprung's disease, imperforate anus), and any sick newborn infant may develop non-specific abdominal distension. Around 15% of babies with cystic fibrosis present with meconium ileus (i.e. difficulty passing thick, sticky meconium, leading to small bowel obstruction).

Presentation in older children

This includes the following:

- malabsorption (pale, greasy stools)
- failure to thrive
- rectal prolapse
- chronic and recurrent chest infections
- partially digested material with a high fat content may block the ascending colon (distal intestinal obstruction syndrome).

Differential diagnosis

The differential diagnosis of chronic cough and failure to thrive includes the following:

- pulmonary tuberculosis
- bronchiectasis (especially following measles, which may also cause chronic diarrhoea)
- HIV infection.

Figure 5.3.C.1 shows a flow diagram for investigation of the child with chronic cough and failure to thrive, in areas where pulmonary tuberculosis and HIV infection are prevalent.

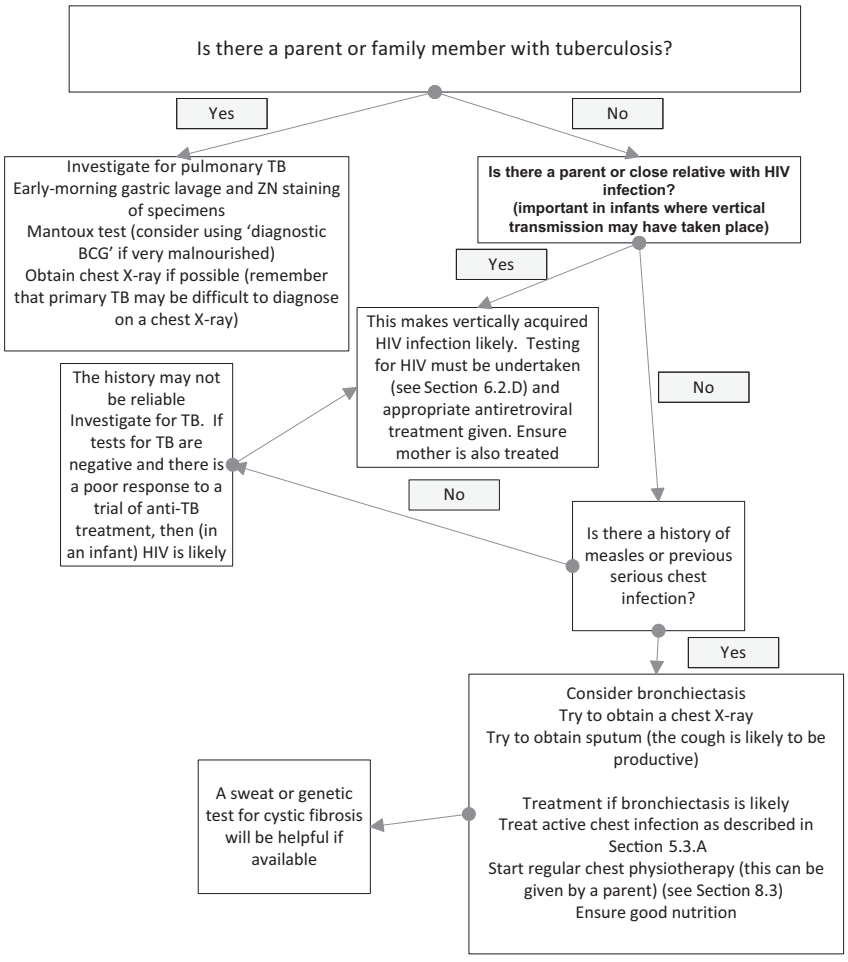

FIGURE 5.3.C.1 Differential diagnosis of the child with chronic cough and failure to thrive.

Diagnosing cystic fibrosis

The sweat test

This detects the high levels of chloride and sodium in sweat that occur in cystic fibrosis patients. The principle of the test is to allow pilocarpine to diffuse into the skin of the forearm using an electric current (pilocarpine iontophoresis), which stimulates sweating via cholinergic receptors in sweat glands. The sweat is collected on filter paper and the weight, chloride and sodium concentrations are calculated. At least 100 mg of sweat are needed. Values highly suggestive of cystic fibrosis are concentrations of chloride and sodium of greater than 60 mmol/litre, with a higher concentration of chloride than sodium. False-negative and false-positive results are usually a consequence of faulty test technique, which is why there is a need for a specialised laboratory and experienced technician, which should be available in at least one hospital in every country.

Genetic tests

These can be performed on very small amounts of blood, collected as a dried blood spot on filter paper. It is possible to send dried blood spots to a genetics laboratory for analysis. A negative genetic test does not rule out cystic fibrosis (only common genes are tested).

Management

Treatment of children with cystic fibrosis in resource-limited countries has been identified as a priority area by the WHO. For practical reasons, children with cystic fibrosis can be seen regularly in a clinic alongside children with bronchiectasis. It is important that the child's parents understand that cystic fibrosis cannot be cured. However, these children can lead active lives with minimal symptoms initially, provided that daily treatment is given and deteriorations are treated promptly.

Pancreatic enzyme supplements

Most children with cystic fibrosis will require pancreatic enzyme supplements (e.g. Creon, Solvay Healthcare, or Pancrease, Janssen-Cilag). Young infants are given half a capsule per milk feed. Older children may need over 10 capsules per meal. The capsules contain protease, lipase and amylase. The lipase is the most important component for preventing malabsorption. Most brands contain 5000–10 000 units of lipase per capsule. The correct dose of pancreatic enzyme supplements is not necessarily related to age, but rather it is the amount required to control symptoms of steatorrhoea and achieve normal growth. The maximum dose (expressed as units of lipase) is 10 000 units/kg/day.

Fat-soluble vitamins

The child should be given extra fat-soluble vitamins. Appropriate doses are vitamin E, 50 mg once daily in infants and young children (aged 0–5 years), 100 mg/day in older children (aged 5–12 years), and 200 mg/day in patients over 12 years of age. Vitamin E may be given as vitamin E suspension 100 mg/mL or as 50 mg tablets. Multivitamin drops, such as Abidec, which contains vitamin A 4000 units/6 mL and vitamin D_2 400 units/6 mL, are also required.

Abidec should be given as follows:

- 0.3 mL/day for newborn infants
- 0.6 mL/day for infants aged 1–12 months
- 1.2 mL/day for children over 1 year of age.

Remember that an adequate calorie intake is vital. **Do not restrict fat in the diet.**

Chest physiotherapy

Routine daily chest physiotherapy should be started as soon as the diagnosis is suspected. The most common method is percussion and postural drainage. In young infants this can be performed with the child across their parent's lap, whereas in preschool children a foam 'wedge' helps the child to achieve the correct position for postural drainage. The percussion element of the treatment involves firm 'clapping' movements with the flat of the hand against the child's chest. Older children and teenagers should be encouraged to take a more active part in their physiotherapy. A technique incorporating periods of diaphragmatic breathing followed by a forced expiration or 'huff', causing coughing, is suitable at this age.

(For physiotherapy techniques, *see* Section 8.3)

Antibiotics

Children with cystic fibrosis have intermittent or chronic infection with *Staphylococcus aureus* in the first 2 to 3 years of life. *Haemophilus influenzae* is also seen in the early years and should be treated as a pathogen. In most children, chronic infection with *Pseudomonas aeruginosa* becomes established sooner or later. Later still, a variety of opportunistic organisms colonise the lungs. If the results of sputum or 'cough swab' cultures are available, these will allow you to choose an appropriate antibiotic. If not, the likely organisms in the age groups described above will be a rough guide. Ideally, the child's respiratory microorganisms should be monitored on a frequent and regular basis so that the appropriate antibiotic can be given promptly.

Antibiotic prophylaxis

In well-resourced countries, a continuous prophylactic oral antibiotic is often given to children with cystic fibrosis, up until 2 years of age. An antibiotic active against *S. aureus*, **usually flucloxacillin**, is chosen. In resource-limited countries this may not be an option, either because the diagnosis is made late or because continuous antibiotics are too expensive. However, flucloxacillin (125 mg twice daily) should be prescribed if possible for children under 2 years of age. Once mucoid *Pseudomonas aeruginosa* has become established, respiratory deterioration occurs, so in well-resourced countries various antibiotic regimes are used to reduce the bacterial burden in the lungs and slow down lung damage. Oral ciprofloxacin, inhaled nebulised colistin or intravenous ceftazidime and tobramycin are variously used. Up-to-date details on antibiotic treatment for cystic fibrosis can be found on the website of the charity the Cystic Fibrosis Trust (www.cysticfibrosis.org.uk).

Treatment of exacerbations

If the cough worsens or the child produces more sputum, a full course of antibiotics should be started and continued for at least 2 weeks. Longer courses of antibiotics are given than in most other conditions. The following antibiotics are suitable.

Flucloxacillin

TABLE 5.3.C.1 Oral flucloxacillin doses

Age (years)	Dose	Number of doses/day
< 1 year	125 mg	4
1–6 years	250 mg	4
7–12 years	500 mg	4
> 12 years	500–1000 mg	4

Amoxicillin or ampicillin

TABLE 5.3.C.2 Oral amoxicillin or ampicillin doses

Age (years)	Dose	Number of doses/day
< 1 year	125 mg	4
1–7 years	250 mg	4
> 7 years	500 mg	4

Flucloxacillin, combined with amoxicillin, has good activity against *S. aureus* and *H. influenzae*.

An alternative is chloramphenicol, which is active against *S. aureus* and *H. influenzae*. Its activity against *P. aeruginosa* is poor. Children with cystic fibrosis may receive many courses of antibiotics in their lifetime, and it is important to limit the number of courses of chloramphenicol that they receive, because of the risk of aplastic anaemia. However, because chloramphenicol is cheap and readily absorbed when given orally, it is justified to use it sparingly in cystic fibrosis. The oral dose of chloramphenicol is 12.5 mg/kg 6-hourly.

If *P. aeruginosa* has been identified in sputum, or infection is suspected, use one of the following antibiotics.

Gentamicin

Dose: 7.5 mg/kg, once daily for 2 weeks.

Monitor gentamicin levels if possible. Peak is 5–10 micrograms/mL and trough is < 1 microgram/mL.

Patients with cystic fibrosis often have more rapid renal clearance and have lower levels for a given dose than other patients. If possible, combine gentamicin with another antipseudomonal antibiotic, such as ceftazidime.

Ciprofloxacin

Dose:
Age < 1 year: 7.5 mg/kg/dose.
Age 1–3 years: 62.5 mg.
Age 3–7 years: 125 mg.
Age 7–12 years: 250 mg.

All age groups should have two doses of ciprofloxacin daily, and a course will last 2 weeks.

Ceftazidime

Dose: 50 mg/kg, three times daily, given over 30 minutes for 2 weeks.

Other manifestations and complications of cystic fibrosis

In addition to those features mentioned above under clinical presentation, the following may occur:

- haemoptysis (not usually a major problem)
- pneumothorax (usually small because of chronic pleural thickening)
- bronchiectasis
- biliary cirrhosis, portal hypertension and oesophageal varices
- diabetes mellitus (requiring insulin)
- infertility (in men)
- women may become pregnant but will need careful management of their chest problems
- 'meconium ileus equivalent' (obstructed bowel occurring in older children)
- arthropathy.

With the best care or in those rare patients with mild disease, survival is possible into the fourth decade. Careful management will improve the quality of life greatly for children in resource-limited countries. Sadly, most patients with cystic fibrosis, in any part of the world, ultimately die of respiratory failure.

5.4 Cardiac disorders

5.4.A Congenital and rheumatic heart disease

BOX 5.4.A.1 Minimum standards
- Electrocardiograph.
- Chest X-ray.
- Prostaglandin E.
- Oxygen.
- Beta-blockers.

Introduction

Congenital heart disease occurs in 5–8 in 1000 live births.

Every country should have immediate access to a hospital that can surgically correct the easily curable acquired or congenital heart defects. The reality is very different with more than 90% of countries without access to such facilities.

Investigations or treatments, which are likely to be unavailable or irrelevant in the absence of a specialist cardiac centre are highlighted.

TABLE 5.4.A.1 Percentage frequency of common congenital heart defects in the UK

Ventricular septal defect (VSD)	32%
Persistent ductus arteriosus (PDA)	12%
Pulmonary stenosis	8%
Atrial septal defect (ASD)	6%
Coarctation of the aorta	6%
Tetralogy of Fallot	6%
Aortic stenosis	5%
Transposition of the great arteries	5%
Hypoplastic left heart syndrome	3%
Atrioventricular septal defect (AVSD)	2%

Cardiac defects may present as any of the following:
- cyanosis in the newborn period
- cyanosis in the older infant
- cardiovascular collapse in the newborn period
- cardiac failure in infancy
- an asymptomatic murmur.

This section explains how to recognise the presence of congenital heart disease in each of these clinical scenarios, and provides enough information to make a working diagnosis. Management decisions can then be made when modern imaging techniques are not immediately available.

The cyanotic newborn

Is there a cardiac problem?

When a child is referred as a 'blue baby', first check to see whether there is genuine central cyanosis. Examine the lips and tongue for blue discoloration, and confirm the clinical impression by measuring the oxygen saturation (less than 94% is abnormal). If there is central cyanosis this may have a cardiac or respiratory cause.

TABLE 5.4.A.2 Features that distinguish cardiac from respiratory cyanosis in the neonate

Cardiac cyanosis	Respiratory cyanosis*
Mild tachypnoea but no respiratory distress May have cardiac signs on examination Arterial blood gas: $pO_2\downarrow$, $pCO_2\downarrow$ or normal Fails hyperoxia test	Respiratory distress Chest X-ray: abnormal lung fields Arterial blood gas: $pO_2\downarrow$, $pCO_2\uparrow$ or normal Passes hyperoxia test

*A respiratory cause for cyanosis is more likely in infants born preterm.

The hyperoxia test is performed as follows:
1 Ensure that there is good IV access.
2 Monitor oxygen saturations continuously.
3 Give 100% oxygen for 10 minutes.
4 Take an arterial blood gas sample in the right arm (preductal).
   - If pO_2 is lower than 20 kPa (150 mmHg), a cardiac cause of cyanosis is likely (the test is 'failed').
   - If pO_2 is higher than 20 kPa, a respiratory cause of cyanosis is likely (the test is 'passed').
   - Although pulse oximetry cannot reliably be used in place of an arterial blood gas, a resting saturation of less than 80% and a saturation of less than 90% after 10 minutes in 100% oxygen suggests cyanotic heart disease requiring early intervention.
   - **Note: Oxygen administration could cause closure of the arterial duct, precipitating profound hypoxaemia in some types of cyanotic congenital heart disease.**
   - Prostaglandin E (which opens the duct) should therefore be available at the time of the test and should be given if oxygenation deteriorates.

Persistent pulmonary hypertension of the newborn (PPHN) may often mimic cyanotic heart disease using these clinical criteria. However, PPHN is usually distinguished by a history of fetal distress, resuscitation is often needed at birth, and there may be neurological signs. Improvements

in oxygenation may be possible after intubation and ventilation, and saturations in the right arm may be significantly higher than those in the feet, suggesting right-to-left shunting across the arterial duct.

What type of cardiac defect is present?

Cyanotic cardiac defects can be divided into three broad categories, as described below.

Once cyanotic congenital heart disease is suspected, attempt to place the defect in one of the three categories. This may be done using Table 5.4.A.3, which describes the typical findings in each physiological category. These guidelines assist the clinician but are not infallible, and the nature of the defect is sometimes only clear after echocardiography.

Cyanotic heart diseases

Low pulmonary blood flow

In defects where there is low pulmonary blood flow the physiology is the same regardless of the precise anatomy of the defect. Deoxygenated blood returning from the systemic veins cannot flow through the right side of the heart to the lungs. The pulmonary blood supply is therefore via the arterial duct. The deoxygenated blood from the right side of the heart shunts to the left side of the heart (via either an atrial or a ventricular septal defect), and the left ventricle receives both deoxygenated blood from the right heart and oxygenated blood from the pulmonary venous return. Blood entering the aorta is therefore not fully oxygenated, and the child appears cyanosed. If the duct closes, the infant becomes profoundly cyanosed and is unlikely to survive unless pulmonary blood flow is rapidly restored. This is **duct-dependent pulmonary circulation**, an example of which is shown in Figure 5.4.A.1.

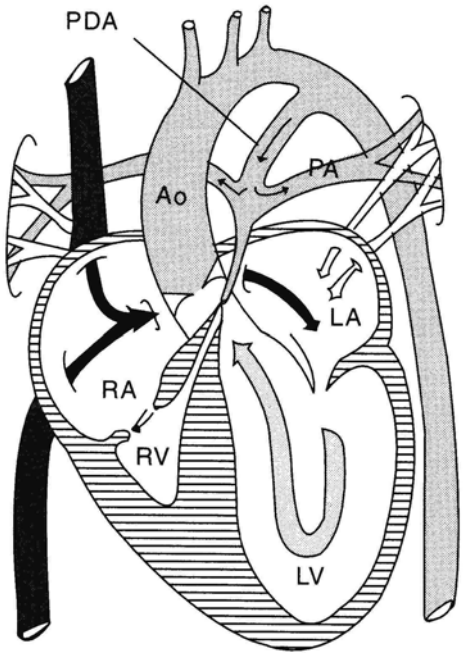

FIGURE 5.4.A.1 The circulation in pulmonary atresia with intact ventricular septum. PDA, patent ductus arteriosus; Ao, aorta; PA, pulmonary artery; LA, left atrium; LV, left ventricle; RV, right ventricle; RA, right atrium.

Complete transposition of the great arteries (TGA)

Here the aorta arises from the right ventricle and the pulmonary artery arises from the left ventricle (*see* Figure 5.4.A.2). Systemic venous return enters the right side of the heart and is recirculated to the systemic arteries. Pulmonary venous return enters the left side of the heart and is recirculated to the lungs. Oxygenated blood and deoxygenated blood are therefore separated in two parallel circuits. Oxygenated blood enters the systemic circulation only when there is mixing between the two circuits. Mixing occurs at atrial level (across the foramen ovale) and at ductal level (while

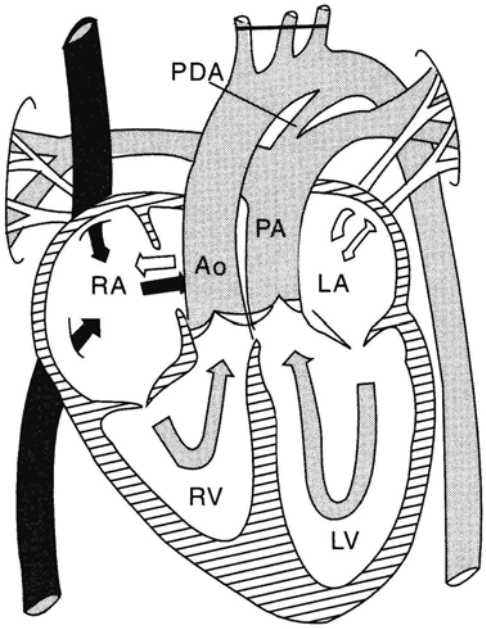

FIGURE 5.4.A.2. Transposition of the great arteries. For explanation of abbreviations, see legend to Figure 5.4.A.1.

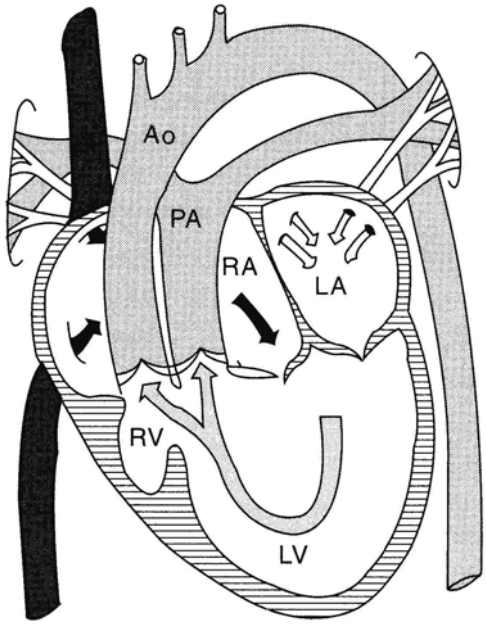

FIGURE 5.4.A.3 The circulation in double-outlet left ventricle. For explanation of abbreviations, see legend to Figure 5.4.A.1.

the duct remains open). Systemic oxygen saturation reflects the amount of mixing (which in turn depends on the size of these communications). If the atrial communication is small, oxygenation may therefore be duct dependent.

Common mixing lesions

In common mixing lesions, oxygenated pulmonary venous blood and deoxygenated systemic venous blood mix in one of the cardiac chambers. An example is shown in Figure 5.4.A.3. The systemic output is therefore only partly oxygenated. The relative amounts of pulmonary and systemic blood in the mixture determine the oxygen saturation and the mode of presentation. If pulmonary blood flow is high, cyanosis is minimal, and the child usually presents at about 2 months of age in heart failure. If pulmonary blood flow is low (the complex lesion may coexist with pulmonary stenosis), cyanosis is severe and is often detected early.

Once the defect has been placed in one of these categories, immediate management decisions can be made. Although it is not imperative to reach a more specific diagnosis, an anatomical diagnosis can sometimes be made using clinical information and simple investigations.

TABLE 5.4.A.3 Features that help to distinguish the three types of cyanotic congenital heart defect

	Low pulmonary blood flow	Complete TGA	Common mixing lesion
pO_2 at rest SaO_2 at rest	Often ≤ 35 mmHg < 80%	Often ≤ 35 mmHg < 80%	Often ≥ 45 mmHg 80–90%
pO_2 hyperoxia test SaO_2 hyperoxia	Often ≤ 50 mmHg < 90%	Often ≤ 50 mmHg < 90%	75–200 mmHg 90–100%
Chest X-ray	Reduced pulmonary vascular markings	Normal or increased pulmonary vascular markings with or without narrow mediastinum	Normal or increased pulmonary vascular markings

TABLE 5.4.A.4 Conditions with low pulmonary blood flow

Critical pulmonary stenosis
Pulmonary atresia with intact ventricular septum
Tetralogy of Fallot (with severe right ventricular outflow tract obstruction)
Pulmonary atresia with ventricular septal defect
Absent right atrioventricular connection

Pulmonary atresia with intact ventricular septum and critical pulmonary stenosis

These two conditions are similar pathologies with either complete or almost complete closure of the pulmonary valve. Both are often associated with hypoplasia of the right ventricle. There is either no murmur or a soft murmur at the lower left sternal border (tricuspid regurgitation). The chest X-ray usually shows a normal heart size. The precordial leads on the ECG usually show decreased right ventricular voltages (small R waves in leads V1 and V2) and dominant left ventricular voltages (prominent S waves in leads V1 and V2 and prominent R waves in leads V5 and V6).

Tetralogy of Fallot and pulmonary atresia with ventricular septal defect

These two pathologies are also similar, but in Fallot's tetralogy the right ventricular outflow tract is patent, albeit narrow, generating a high-pitched ejection systolic murmur at the upper left sternal border. In both defects, the cardiac silhouette on the chest X-ray has a concavity on the left heart border where there is usually a convexity produced by the right ventricular outflow tract and pulmonary artery. The ECG shows dominant right ventricular voltages (normal neonatal RS progression).

Absent right atrioventricular connection (also known as tricuspid atresia)

There is often a long harsh systolic murmur (this may arise from a restrictive ventricular septal defect or pulmonary stenosis). The precordial leads on the ECG show decreased right ventricular voltages and dominant left ventricular voltages. The QRS axis is characteristically directed to the left and superiorly between 0 and –90 degrees.

Complete transposition of the great arteries

There is usually no murmur. The ECG shows dominant right ventricular voltages (normal neonatal RS progression). Therefore, if a newborn is severely cyanosed and otherwise appears clinically normal, actively look for a narrow mediastinum on the chest X-ray to help to make the diagnosis.

Management of defects with low pulmonary blood flow or complete TGA

- Do not give oxygen after the hyperoxia test, as it may precipitate ductal closure.
- Start IV prostaglandin E (PGE) to maintain ductal patency. There are two formulations, namely prostaglandin E1 (PGE1) and prostaglandin E2 (PGE2). Commence PGE1 at 25 nanograms/kg/minute or PGE2 at 5 nanograms/kg/minute.
- PGE infusion is made up by adding 30 micrograms/kg of prostaglandin to 50 mL of 5% dextrose (if the pump runs at 1 mL/hour this is equivalent to 10 nanograms/kg/minute).
- If saturations are initially very low and fail to improve 10 minutes after starting PGE, intubate and ventilate the baby in air and increase the PGE dose to 50 nanograms/kg/minute. The dose can be increased further to a maximum of 100 nanograms/kg/minute if there is still no response. Prostaglandin sometimes causes vasodilation, so fluid boluses may be required at high doses of PGE in order to maintain blood pressure.
- PGE often causes hypoventilation and apnoea (particularly at doses of PGE2 above 10 nanograms/kg/minute). If oxygen saturations initially improve with PGE and then start to fall, assess respiratory effort. If respiration is shallow or slow, intubate and ventilate in air.
- If oxygen saturations start to fall after PGE is started, and respiratory effort appears adequate, increase the

PGE dose stepwise until a response is seen. At doses over 10 nanograms/kg/minute watch very carefully for hypoventilation.
- Arrange for an urgent paediatric cardiology review and transfer the child to a cardiac centre.
- Defects with poor pulmonary blood flow usually require a systemic to pulmonary artery shunt (modified Blalock–Taussig shunt) to provide a stable pulmonary blood supply. Where special interventional expertise is available it may be possible to implant a coronary stent in the duct to maintain patency and avoid surgery.
- TGA often requires enlargement of the interatrial communication by balloon atrial septostomy, followed by an arterial switch operation if surgical expertise is available.
- For critical pulmonary valve stenosis or pulmonary atresia, early intervention to open the pulmonary valve is required. This can be done by the transcatheter route if interventional expertise is available.

Management of common mixing lesions

- Monitor the child on the neonatal unit.
- Arrange for an echocardiogram as soon as possible to define the anatomy.
- If oxygen saturations fall progressively to less than 70%, commence PGE and arrange for an urgent paediatric cardiology review.
- Once the anatomy is defined it may be possible to discharge the baby without further treatment (after paediatric cardiology advice has been obtained).

The older infant with cyanosis

Is there a cardiac problem?

When an older infant presents with cyanosis, cardiac pathology is likely if:
- Respiratory distress is not severe.
- There is no carbon dioxide retention.
- Respiratory pathology is not evident on the chest X-ray.
- The cardiovascular examination is abnormal (see below).

What type of cardiac defect is present?

The cyanotic defects that commonly present after the neonatal period are tetralogy of Fallot and cyanotic defects with high pulmonary blood flow. They may escape detection at birth because cyanosis is initially only mild. In tetralogy of Fallot, there is right ventricular outflow tract obstruction and a large ventricular septal defect (VSD) (right ventricular hypertrophy and aortic override are the other components of the tetralogy). The right ventricular outflow tract obstruction limits blood flow to the pulmonary arteries, causing deoxygenated blood to shunt right to left across the VSD, resulting in cyanosis. With time, the right ventricular outflow tract obstruction usually becomes more severe, causing further reductions in pulmonary blood flow, more right to left shunting, and increasing cyanosis.

Cyanotic defects with high pulmonary blood flow

In cyanotic defects with high pulmonary blood flow (mostly common mixing defects), pulmonary flow increases as pulmonary vascular resistance decreases over the first few weeks of life, resulting in progressively worsening cardiac failure.

TABLE 5.4.A.5 Cyanotic defects with high pulmonary blood flow

Truncus arteriosus
Total anomalous pulmonary venous connection
Double-outlet left ventricle
Absent right atrioventricular connection with large ventricular septal defect (tricuspid atresia)
Pulmonary atresia with large or multiple aorto-pulmonary collateral arteries
TGA with large ventricular septal defect

Findings in defects with high pulmonary blood flow

- May present with cardiac failure at 2–6 weeks of age.
- Active praecordium.
- Murmur usually present (may be systolic, diastolic or continuous).
- Increased pulmonary vascular markings on chest X-ray.

Management of cyanotic defects with high pulmonary blood flow

Define the anatomy by echocardiography. Manage cardiac failure medically (*see* Section 5.4.B). Surgical correction or pulmonary artery banding will be necessary in most cases.

Findings in tetralogy of Fallot

- May present with increasing cyanosis.
- May present with an ejection systolic murmur at the upper left sternal border.
- Reduced pulmonary vascular markings on chest X-ray, and concavity on the left heart border where there is usually a convexity produced by the right ventricular outflow tract and pulmonary artery.
- Children are often asymptomatic, but there may be sudden periods of increased cyanosis known as hypercyanotic spells.

Characteristics of hypercyanotic spells

- Spells often occur on waking from sleep or after feeding.
- The infant becomes restless and agitated.
- There is increased cyanosis and pallor.
- Respiration is often rapid and shallow.
- In severe spells, crying is followed by limpness or loss of consciousness.
- Spells usually last 1–5 minutes, but may last longer when severe.
- The ejection systolic murmur shortens or becomes inaudible.

Management of tetralogy of Fallot

The anatomy should be confirmed by echocardiography, preferably within a few weeks of presentation, and surgical correction should be carried out between 6 and 12 months of age (although it can be carried out later).

Hypercyanotic spells may be life-threatening. If a child starts to have such spells, discuss this with a paediatric cardiologist immediately, as it is an indication for urgent surgery.

If hypercyanotic spells are more than a few minutes in duration, treat them urgently as follows:
- Knee–chest position.
- Give oxygen by face mask.
- Give an IV bolus of Ringer-lactate or Hartmann's solution

10–20 mL/kg, as during spells children are often relatively hypovolaemic.
- Give IV or IM morphine, 100 microgram/kg (or IV ketamine 1 mg/kg).
- Give IV propranolol at an initial dose of 20 micrograms/kg with a maximum of 100 micrograms/kg (have isoprenaline ready in case of excessive β–blockade).
- Adrenaline may make spells worse.
- General anaesthesia and artificial ventilation are needed in intractable cases.
- If cyanosis persists, consider an emergency aorto-pulmonary shunt.

Neonatal cardiovascular collapse

Is there a cardiac problem?

When a child presents in shock in the first month of life, the working diagnosis is often dehydration or sepsis. The following features help to distinguish cardiac causes of poor systemic output from non-cardiac causes:
- collapse in the first 2 weeks of life
- poor feeding, lethargy and tachypnoea prior to collapse
- hepatomegaly
- pulmonary oedema and cardiomegaly on chest X-ray
- lack of response to intravascular volume expansion.

What type of cardiac defect is present?

Left heart obstruction is the most likely cardiac cause of cardiovascular collapse with low systemic output in the first 2 weeks of life:

TABLE 5.4.A.6 Left heart obstruction

Critical aortic stenosis
Hypoplastic left heart syndrome (HLHS)
Coarctation of the aorta
Interrupted aortic arch

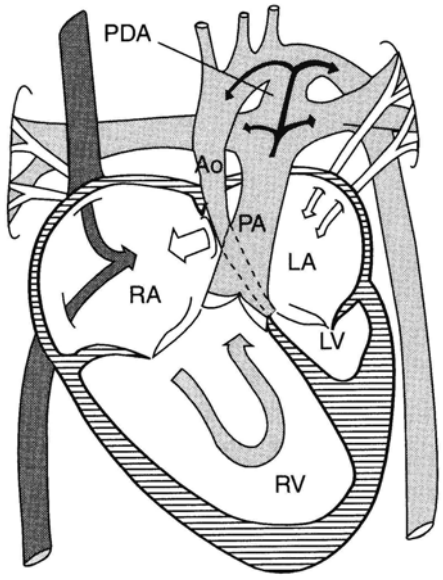

FIGURE 5.4.A.4 Hypoplastic left heart. For explanation of abbreviations, see legend to Figure 5.4.A.1.

Hypoplastic left heart syndrome

In hypoplastic left heart syndrome all of the left heart structures are small (*see* Figure 5.4.A.4). There is insufficient forward flow through the left ventricle and the aortic valve to support the systemic circulation. Pulmonary venous return cannot pass through the left heart, so it crosses the atrial septum and enters the right atrium, mixing with systemic venous return. Mixed pulmonary and systemic venous blood enters the right ventricle and is pumped to the pulmonary arteries and also across the arterial duct to supply the systemic circulation. Ductal flow passes to the descending aorta and retrogradely around the aortic arch to supply the head and neck vessels and the coronary arteries. Ductal flow is not fully oxygenated, so there is a degree of central cyanosis. When the duct closes, the cardiac output falls precipitously, the infant becomes shocked, and cardiac failure develops. This is duct-dependent systemic circulation. The haemodynamics are the same in **critical aortic stenosis**.

Coarctation of the aorta

Coarctation of the aorta consists of a narrowing in the descending aorta close to the aortic end of the arterial duct. Contractile tissue may extend from the duct into the aorta so that when the duct closes it draws in the adjacent section of aorta, causing obstruction. Flow to the head and neck vessels is maintained, but flow to the lower body distal to the coarctation site is dramatically reduced. The infant becomes shocked and acidotic. Cardiac failure develops secondary to high systemic afterload. This is also an example of the systemic circulation depending on ductal patency (although systemic blood flow may not directly depend on a right-to-left shunt through the duct). In **interrupted aortic arch**, perfusion to the lower part of the body depends on right-to-left ductal flow and presentation is similar to that with coarctation.

The following features help to distinguish between the lesions:
- If all of the pulses are weak or absent, consider HLHS or critical aortic stenosis.
- If the right arm pulses are palpable and the femoral pulses are weak or absent, consider coarctation or interrupted aortic arch (note, however, that all pulses may initially be impalpable if the cardiac output is poor).
- If four limb blood pressures demonstrate significantly lower blood pressures in the legs than in the right arm (a gradient of more than 20 mmHg), consider coarctation or interrupted aortic arch.
- Coarctation often presents towards the beginning of the second week of life.
- HLHS often presents in the first 2 days of life.
- In HLHS, the ECG shows reduced left ventricular voltages (small R waves in leads V5 and V6).

Other cardiac causes of cardiovascular collapse in the first few weeks of life are supraventricular tachycardia (SVT) (*see* Section 5.4.C) and cyanotic congenital heart disease with duct-dependent pulmonary blood flow (when the duct closes, the ensuing profound hypoxaemia causes acidosis and cardiovascular collapse). SVT should be evident on the ECG and cyanotic heart disease should be suspected when the oxygen saturation remains low after instituting the management described below for left heart obstruction.

Emergency management of low systemic output secondary to left heart obstruction

1 Check the ECG (to exclude SVT as a cause of collapse).
2 Obtain peripheral IV access if not already established (if IV access is difficult, intra-osseous access should be obtained).
3 Give a fluid bolus of 10 mL/kg Ringer-lactate or Hartmann's solution if not already given.
4 Intubate and ventilate if there is significant respiratory distress (high PEEP, 8–10 cmH_2O).
5 Once ventilated, commence prostaglandin E_1 or E_2 at 100 nanograms/kg/minute (give for 30 minutes, then reduce to 25 nanograms/kg/minute, reducing again to 10 nanograms/kg/minute when stabilised). If the initial clinical condition is not poor, commence PGE_2 at a lower dose of 10 nanograms/kg/minute, which should avoid PGE-related apnoea and the need for ventilation.
6 Admit the child to the paediatric ICU.
7 Check blood sugar levels, full blood count, urea and electrolytes, coagulation, calcium levels and magnesium levels, and correct abnormalities.
8 Take blood cultures and treat with IV antibiotics, as sepsis cannot be excluded.
9 Check arterial blood gas (using the right arm if possible).
10 Give IV furosemide 1 mg/kg if the chest X-ray shows pulmonary oedema.
11 Insert central venous access and an arterial line.
12 Reassess whether further intravascular volume is needed (give if the central venous pressure is low).
13 Give dopamine 5–10 micrograms/kg/minute if perfusion remains poor or the blood pressure remains low.
14 Give adrenaline 0.1–0.2 micrograms/kg/minute if perfusion remains poor or the blood pressure remains low (by central venous access only).
15 If acidosis is profound and not improving with other measures, give IV sodium bicarbonate 4.2%.
16 Ask for an urgent paediatric cardiology review and advice.

Asymptomatic murmurs

When a child presents with an asymptomatic murmur, first examine them for cyanosis and measure the oxygen saturation. If there is desaturation, refer the child for an echocardiogram, as cyanotic congenital heart disease requires a detailed anatomical assessment. Tetralogy of Fallot is the most likely diagnosis. If cyanosis is excluded, the child may have an innocent cardiac murmur or one of the following defects.

TABLE 5.4.A.7 Initially asymptomatic heart lesions

Left-to-right shunts	Left or right heart obstruction
Small to moderate-sized VSD	Pulmonary stenosis
Small to moderate-sized PDA	Aortic stenosis
Atrial septal defect (ASD)	Coarctation of the aorta
Partial AVSD	

Innocent murmurs are characterised as follows:

- The Still's murmur is a vibratory short systolic murmur heard at the lower left sternal border or apex.
- The venous hum is a soft continuous murmur heard best below the clavicles, and is abolished by pressure over the jugular vein or lying down with the neck flexed.
- The pulmonary flow murmur is a soft ejection systolic murmur at the upper left sternal border, and may be confused with an ASD or mild pulmonary stenosis.
- The neck bruit is an ejection systolic murmur that is maximal above the clavicle and may be confused with aortic stenosis.

The cardiac defects are characterised as follows:

- In **coarctation**, the right arm blood pressure is often elevated, the femoral pulses are weak or impalpable, and there is brachiofemoral delay.
- The **patent ductus arteriosus (PDA)** has a continuous murmur that is loudest in the left infraclavicular region.
- The **ventricular septal defect (VSD)** has a harsh pansystolic murmur that is loudest at the lower left sternal border radiating to the lower right sternal border.
- **Aortic stenosis, pulmonary stenosis, atrial septal defect (ASD)** and **partial atrioventricular septal defect (AVSD)** all have an ejection systolic murmur at the upper left sternal border.
  - In **aortic stenosis** the ejection systolic murmur is harsh and may be heard at the upper right and left sternal border. The murmur radiates to the carotid arteries and there is often a carotid thrill. There may be an ejection click at the apex if the stenosis is at valvar level.
  - In **pulmonary stenosis**, the ejection systolic murmur is harsh and radiates to the back. There may be an ejection click along the left sternal border if the stenosis is at valvar level.
  - In an **atrial septal defect (ASD)** there is a soft ejection systolic murmur at the upper left sternal border from increased flow across the pulmonary valve. There is sometimes a fixed widely split second heart sound, and there may be a mid-diastolic murmur at the lower left sternal border (from increased flow across the tricuspid valve) when the left-to-right shunt is large.
  - In **partial atrioventricular septal defect (AVSD)** there is an abnormal atrioventricular valve and a defect in the atrial septum. There may be a blowing pansystolic murmur at the lower left sternal border or apex from atrioventricular valve regurgitation. The ejection systolic murmur may mimic an ASD, but the defect is distinguished by a superior QRS axis on the ECG.

Unless the murmur is clearly innocent, perform an ECG and chest X-ray.

Right ventricular hypertrophy (RVH) is indicated by an R wave in lead V1 > 98th centile for age (³ 20 mm is always abnormal), a neonatal RS progression beyond the neonatal period (dominant R waves in lead V1 and dominant S waves in lead V6) or an upright T wave in lead V1 before the teenage years.

Left ventricular hypertrophy (LVH) is indicated by T inversion in leads V5 and V6, loss of the Q wave in lead V6 or the amplitude of the R wave in lead V6 plus S wave in lead V1 > 98th centile for age (³ 50 mm is always abnormal). RVH may indicate significant right heart obstruction or high pulmonary artery pressure (secondary to a large left-to-right shunt or pulmonary vascular disease). LVH may indicate significant left heart obstruction. Cardiomegaly and

increased pulmonary vascular markings on the chest X-ray may indicate a large left-to-right shunt.

Any child who is thought to have an anatomical defect on the basis of the clinical examination, or any child with an abnormal ECG or chest X-ray, should if possible be referred to a paediatric cardiologist for an echocardiogram and opinion. If there is evidence of a significant left-to-right shunt (*see* Section 5.4.B) in a VSD or PDA, the referral should be as soon as possible, as there is still a risk of pulmonary vascular disease even when the child does not present in heart failure.

Rheumatic fever

For the diagnosis and treatment of rheumatic fever, *see* Section 5.13.

Long-term consequences of rheumatic fever

After an attack of acute rheumatic fever there may be permanent valve damage. Rheumatic heart disease occurs when acute valve inflammation is followed by scarring and fibrosis, resulting in various degrees of shortening, thickening, rigidity, deformity, retraction and fusion of the valve cusps. The commonest valve lesions are mitral regurgitation, mitral stenosis and aortic regurgitation.

Rheumatic heart disease is most severe and progressive in (1) children who initially have severe carditis in (2) children who have recurrent attacks of acute rheumatic fever. The prognosis is more favourable if recurrences are prevented (residual cardiac disease may disappear or improve and valve damage only worsens in a few cases). It is therefore crucial to maintain continuous antibiotic prophylaxis to prevent further valve damage, particularly as children are prone to develop a recurrence after the initial attack (below).

Mitral regurgitation

Mitral regurgitation is the commonest valve lesion in children with rheumatic heart disease. Patients are often asymptomatic during childhood as symptoms are caused by left ventricular failure which may take as long as two decades to develop. However, cases may present before adolescence and mitral regurgitation may be rapidly progressive in regions where the incidence of rheumatic fever is high and recurrent rheumatic fever is common. Mitral regurgitation may be diagnosed by the presence of a blowing apical pansystolic murmur radiating to the left axilla. There may also be a third heart sound and a short low frequency mid-diastolic murmur from increased transmitral flow.

Features of severe mitral regurgitation:

- Easy fatigue (caused by low cardiac output)
- Shortness of breath on exertion (caused by pulmonary oedema)
- Hyperdynamic apical impulse and pansystolic murmur
- Apical impulse displaced laterally and inferiorly
- The chest X ray demonstrates cardiomegaly and left atrial enlargement (a double density on the right heart border and elevation of the left main bronchus)
- The ECG demonstrates left atrial enlargement (broad bifid P waves in lead II and a prominent negative component to the P in V1) and left ventricular hypertrophy
- Signs of pulmonary hypertension (see below).

If there are features of severe mitral regurgitation, the child should be urgently referred for a paediatric cardiology opinion as surgery is likely to be necessary. Ideally all children with mitral regurgitation should be evaluated by echocardiography annually, as progressive left heart dilation may result in irreversible left ventricular dysfunction if referral is delayed until symptoms develop. Medical treatment should be given for heart failure (captopril is particularly useful) but children who are unwell enough to require this often need either a mitral valve repair or a mitral valve replacement with a mechanical valve or bioprosthesis.

Mitral stenosis

If there is effective antibiotic prophylaxis, mitral stenosis usually develops slowly over 5–10 years and is often not sufficiently severe to cause symptoms in childhood. The reality in countries where there is inadequate prophylaxis and recurrent attacks of rheumatic fever are common is that mitral stenosis may progress much more rapidly and symptoms may be evident 6 months to 3 years after the first attack. Mild stenosis does not cause symptoms, moderate stenosis causes shortness of breath on exertion and severe stenosis causes easy fatigue, shortness of breath at rest, orthopnoea, paroxysmal nocturnal dyspnoea and haemop-tysis. Mitral stenosis may be diagnosed by the presence of a low frequency mid-diastolic murmur maximal at the apex. The murmur may be accentuated by exercise and is often accompanied by a loud first heart sound and a diastolic opening snap. The murmur becomes longer as the severity of the stenosis increases. In severe cases there are also signs of pulmonary hypertension.

Signs of pulmonary hypertension:

- Left parasternal heave
- Loud second heart sound
- Early diastolic murmur of pulmonary regurgitation at the upper left sternal border
- Elevated JVP and hepatomegaly if there is right heart failure.

The chest X ray and ECG often show left atrial enlargement when there is moderate mitral stenosis. Radiographic signs of pulmonary oedema may be evident when stenosis is severe. ECG changes of right ventricular hypertrophy and right axis deviation are present when there is pulmonary hypertension. Symptoms should be treated with diuretics and a low-sodium diet. Digoxin is only indicated in rare cases where there is atrial fibrillation secondary to left atrial enlargement. Symptomatic children and children with signs of pulmonary hypertension should be referred for paediatric cardiology review as surgery is often necessary. The options for treatment are open or closed mitral commissurotomy, mitral valve replacement and percutaneous catheter balloon mitral commissurotomy.

Aortic regurgitation

Aortic regurgitation is less common than mitral regurgitation and frequently occurs in combination with mitral valve disease. Affected children usually remain asymptomatic for many years as symptoms only become evident when left ventricular dysfunction develops secondary to chronic left ventricular volume overload. Severe symptomatic aortic regurgitation may however become established within 1–2 years of the initial attack of rheumatic fever if recurrence is not prevented. Once symptoms appear deterioration is often rapid. Symptoms include exercise intolerance, shortness of breath on exertion and chest pain in a few severely affected cases. Examination reveals a blowing decrescendo

early diastolic murmur maximal at the mid to lower left sternal border. The murmur is loudest sitting forward with the breath held in expiration.

Signs of moderate to severe aortic regurgitation:

- The murmur lengthens and may be throughout diastole
- Hyperdynamic apex
- Apical impulse displaced laterally and inferiorly
- Wide pulse pressure
- Collapsing pulses
- Visible pulsations in the suprasternal notch and neck vessels
- Systolic murmur at the upper right sternal border (from increased aortic valve flow).

If patients are symptomatic or have signs of severe aortic regurgitation they should be referred for paediatric cardiology assessment as surgery may be necessary. Marked cardiomegaly on the chest X ray or multiple ventricular ectopics on the ECG should also prompt referral. Ideally all children with aortic regurgitation should have an echocardiogram at least annually as it is important to assess left ventricular dilation and function to ensure that surgery is carried out before irreversible left ventricular dysfunction develops. Exercise tolerance may be improved by captopril treatment and medical treatment for heart failure may be necessary in severe cases. Surgical options include aortic valve reconstruction, aortic valve replacement with an aortic homograft or mechanical valve and transferring the patient's own pulmonary valve to the aortic position (Ross procedure).

5.4.B The child with heart failure and cardiomyopathy

BOX 5.4.B.1 Minimum standards

- Electrocardiograph.
- Chest X-ray.
- Furosemide.
- Spironolactone.
- Anticoagulant.

Introduction

Heart failure occurs when the heart is unable to pump enough blood to meet the metabolic needs of the body. The term is often used to indicate the clinical changes that occur when the cardiac pump cannot meet the workload it is presented with. This may occur either because the pump is weak (due to a primary abnormality of the cardiac muscle) or because the workload imposed on the heart is higher than normal. The latter is the case in congenital heart disease, where heart failure occurs because the heart is pumping against a high resistance (in the case of obstructive lesions) or because it is volume loaded (commonly in left-to-right shunting cardiac lesions).

Left-to-right shunting cardiac defects are the commonest cause of heart failure in infancy identified in well-resourced countries.

In resource-poor countries most heart failure is related either to severe anaemia or to fluid overload when treating infections or severe malnutrition, particularly with IV fluids or during blood transfusion (see below).

The physiology of left-to-right shunts

A large defect between the ventricles or great arteries allows free communication between the left and right sides of the heart. Left and right heart pressures therefore equalise, and pulmonary artery pressure is maintained at systemic level. The pulmonary vascular resistance then determines the pulmonary blood flow. In the newborn period the pulmonary vascular resistance is high, which limits the pulmonary blood flow and therefore the left-to-right shunt across the defect. Over the first 6 weeks of life, the pulmonary vascular resistance gradually falls, allowing pulmonary blood flow and the left-to-right shunt to increase. This gives rise to heart failure, which usually appears after 4 weeks of age. If the pulmonary arteries are exposed to high pressure and flow for a prolonged period, pulmonary vascular disease develops. This normally becomes significant between 12 and 18 months of age. High pulmonary vascular resistance secondary to pulmonary vascular disease reduces the left-to-right shunt, and symptoms of heart failure gradually resolve. Eventually, pulmonary resistance becomes so high that flow across the defect becomes right to left, and cyanosis develops (Eisenmenger's syndrome). The pulmonary artery pressure remains high throughout, and it is only the amount of flow through the lungs that changes.

Is heart failure present?

TABLE 5.4.B.1 Diagnosis of heart failure secondary to congenital heart disease in infancy

Symptoms	Signs
Easily tired	Failure to thrive
Poor feeding	Tachypnoea
Breathlessness (particularly during feeds)	Increased respiratory effort
Sweaty (particularly during feeds)	Tachycardia > 160 bpm
	Sweating
	Pallor
	Hepatomegaly
	Gallop rhythm

What type of cardiac defect is present?

Heart failure in the first few weeks of life is a medical emergency.

The following causes should be considered:

- supraventricular tachycardia
- complete atrioventricular block
- high-output cardiac failure
- left heart obstruction.

Perform an ECG to detect supraventricular tachycardia and heart block. Check the haemoglobin level, as severe anaemia may cause high-output cardiac failure. Also examine the baby for cranial and hepatic bruits, as cranial and hepatic arteriovenous malformations are a potential (although very rare) cause of high-output cardiac failure.

If these tests are negative, refer the child to a paediatric cardiologist, as a left heart obstructive lesion is likely and there may be duct-dependent systemic circulation. Consider the use of prostaglandin to keep the ductus arteriosus open until the referral can be achieved (*see* Section 5.4.A).

Heart failure in infancy presenting after the first few weeks of life may be caused by any of the following:

- the left-to-right shunting lesions listed in Table 5.4.B.2
- cyanotic congenital heart defects with high pulmonary blood flow
- the same causes that present in the first few weeks of life
- myocarditis or cardiomyopathy.

TABLE 5.4.B.2 Common left-to-right shunting lesions that cause heart failure

Large ventricular septal defect (VSD)
Atrioventricular septal defect with large ventricular component (AVSD)
Large persistent ductus arteriosus (PDA)

Examine the child for cyanosis and measure the oxygen saturation. It should be possible to detect those children with cyanotic defects immediately (note, however, that children with AVSD are sometimes mildly desaturated). Next, attempt to detect the children with left-to-right shunts, looking for the following features which are present in significant shunts:

- hyperdynamic precordial impulse
- apical impulse displaced laterally and inferiorly
- apical mid-diastolic murmur (from increased flow across the mitral valve)
- loud second heart sound (from increased pulmonary artery diastolic pressure)
- cardiomegaly and increased pulmonary vascular markings on the chest X-ray
- signs of heart failure and pulmonary oedema on the chest X-ray in severe cases.

If these examination findings are not present and there is no evidence of SVT or a hyperdynamic circulation (see above), a left heart obstructive lesion should be considered. **Some of these are eminently treatable conditions** and if they are suspected the child should be referred for paediatric cardiology review without delay.

If there is evidence of a large left-to-right shunt, refer the child to a paediatric cardiologist within a few weeks. These signs must not be missed, as a remediable cardiac defect is rendered inoperable by delay.

Although it is not imperative to make a more specific diagnosis, the following clinical features discriminate between the three most common left-to-right shunts:

- The persistent arterial duct has a continuous murmur that is maximal in the left infraclavicular area.
- A large ventricular septal defect has a quiet pansystolic murmur that is maximal at the lower left sternal border radiating to the lower right sternal border. There may also be a soft ejection systolic murmur at the upper left sternal border from increased flow across the pulmonary valve.
- An atrioventricular septal defect with a large ventricular component may have a blowing pansystolic murmur at the lower left sternal border or apex from atrioventricular valve regurgitation. The ECG shows a characteristic superior QRS axis (between –30 and –180 degrees).

Heart failure in later infancy and childhood

In addition to the symptoms seen in early infancy (easily tired, poor feeding, breathlessness particularly during feeds, excess sweating particularly during feeds), older children may have decreased exercise tolerance, shortness of breath on exertion and when lying flat.

The signs of heart failure are cyanosis or $SaO_2 < 94\%$, basal lung crepitations, failure to thrive, tachypnoea > 50 breaths/minute for children aged 2–12 months, tachypnoea > 40 breaths/minute for children aged 12 months to 5 years and the cut-offs for tachycardia are > 120 bpm aged 1–5 years and > 100 bpm after age 5 years.

There is usually increased respiratory effort, sweating, pallor and hepatomegaly.

In older children the hepatomegaly may be tender, a gallop rhythm may be heard and a raised jugular venous pressure may be observed.

In addition to the congenital heart defects described in Section 5.4.A the following causes of heart failure should be considered:

- Severe anaemia
- Severe malnutrition
- Excessive intravenous fluids
- Rheumatic fever
- Myocarditis
- Cardiomyopathy
- Infective endocarditis
- Constrictive pericarditis (rare and most often caused by tuberculosis) (*see* Section 6.1.N).

Anaemia is a common and often severe problem in poorly resourced settings (*see* Section 5.11.A). When the haemoglobin falls below 7 g/dl cardiac output must increase to maintain oxygen delivery and heart failure frequently develops with a haemoglobin < 5 g/dl). The treatment is careful blood transfusion, but the increase in intravascular volume may precipitate worsening heart failure. Blood must therefore be infused slowly in small boluses and an exchange transfusion may be needed if there is clinical deterioration. Furosemide 1 mg/kg IV may be given during transfusion (*see* Section 5.11.A).

Protein-calorie malnutrition is also an important cause of cardiac failure in disadvantaged countries (*see* Section 5.10.B) with specific contributions from certain vitamin deficiencies (*see* Section 5.10.A). Although cardiac failure is unusual at presentation, it may occur after several days of refeeding. Rapid refeeding can cause a hypermetabolic state, demanding an increase in cardiac output which cannot be met by the malnourished heart which has a decreased cardiac reserve. The problem is exacerbated by coexisting anaemia, blood transfusion, inappropriate intravenous fluid administration and high sodium diets.

The other common causes of cardiac failure are dealt with individually in the sections below.

Management of heart failure

Monitor heart and respiratory rates, respiratory distress and oxygenation regularly during treatment of acute heart failure. It is necessary to both control the symptoms of failure and to determine and treat the underlying cause.

- Treat severe anaemia if present, be careful with IV fluids and ensure adequate nutrition.
- Nasogastric feeding if there is inadequate oral intake.
- For older children nurse sitting up with legs dependent
- Treat hypoxaemia with oxygen to keep SaO_2 > 94%.
- In an emergency where there is pulmonary oedema, give furosemide 1 mg/kg IV which should produce a diuresis within 2 hours. If the initial dose is ineffective, give 2 mg/kg IV and repeat after 12 hours if necessary.
- For chronic heart failure give oral furosemide 1 mg/kg once a day, twice a day or three times a day.
- Spironolactone 1 mg/kg once a day or twice a day in combination with furosemide, matching the dose frequency, to enhance diuresis and prevent furosemide-related hypokalaemia.
- If furosemide is used without spironolactone, oral potassium 3–5 mmol/kg/day, should be given (supplemental potassium is not required if furosemide is given for less than 4 days).

If more than twice daily diuretics are required, consider using captopril. Captopril should be commenced in hospital with a 100 microgram/kg test dose. The dose should then be increased gradually over a number of days 100–300 microgram/kg 2–3 times a day to a maximum total dose of 4 mg/kg daily. After the test dose and each increment monitor the blood pressure carefully, as hypotension is common. Reduce the dose if significant hypotension occurs. Monitor urea and electrolytes daily while building up the dose, as renal failure is a well-recognised side effect. Stop spironolactone when the captopril dose is greater than 500 micrograms/kg per day as both drugs cause potassium retention. Do not give captopril if there is left heart obstruction.

Cardiomyopathy and myocarditis

Myocarditis and dilated cardiomyopathy both cause impairment of myocardial contractility. This results in a dilated poorly functioning heart. Children present with heart failure, sometimes in association with shock. They may also more rarely present with ventricular arrhythmias.

The unexpected onset of heart failure in a previously well child should suggest the diagnosis. However, in the first 3 months of life, heart failure associated with cardiomegaly is more likely to be caused by congenital heart disease than by heart muscle disease. Echocardiography is therefore particularly important in this age group, to discriminate between the two potential causes of heart failure.

In addition to the features of heart failure listed earlier in Table 5.4.B.1, signs may include lateral displacement of the apex beat and an apical pansystolic murmur from mitral regurgitation. The chest X-ray often demonstrates cardiomegaly. It is not essential to identify whether the child has cardiomyopathy or myocarditis, as the management of both conditions is the same. However, the latter may be suggested by a preceding viral illness or evidence of acute myocardial damage with elevated blood levels of creatinine kinase or troponin. Myocarditis may be confirmed by identifying enterovirus by polymerase chain reaction (PCR) or serology.

In most cases, the cause of the cardiomyopathy remains unknown. However, it is important to perform a 12-lead ECG in all cases of cardiomyopathy, as it may reveal two particular conditions that are reversible causes of poor heart function:

- Incessant tachyarrhythmias may cause cardiomyopathy. In cardiomyopathy there is often sinus tachycardia, which appears on the ECG as a heart rate faster than that expected for the child's age, with each QRS complex being preceded by a P wave that is positive in both lead I and lead aVF. If the QRS complexes are not preceded by P waves, or P-wave morphology is unusual, the rhythm is not sinus rhythm and a tachyarrhythmia must be suspected. Sometimes the tachyarrhythmia heart rate is only marginally higher than that expected for the child's age, but many months of mild tachycardia have resulted in poor function. If the arrhythmia is successfully controlled with anti-arrhythmic drugs or radiofrequency ablation, the heart function should normalise.
- Anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) presents with severely impaired cardiac function at around 3 months of age. The ECG will show transmural anterolateral myocardial infarction in most cases. If the coronary artery is reimplanted in the aortic root the function will usually recover.

Post-intervention management is aimed at supporting the heart while function spontaneously recovers. It includes the following:

- Furosemide and spironolactone (see above, under heart failure)
- Captopril (see above, under heart failure)
- Digoxin:
  - 5 micrograms/kg orally twice a day (in children under 5 years old).
  - 3 micrograms/kg orally twice a day (in children over 5 years old).
  - Plasma levels should be in the range 0.8–2.0 micrograms/litre (check the level after 5 days, and at least 6 hours after giving a dose).
- Aspirin 3–5 micrograms/kg once a day if function is poor, to prevent thromboembolism.
- Anticoagulation if cardiac function is very poor:
  - Heparin IV, initially 20 U/kg/hour, titrated to APTT 2–3 times normal.
  - Warfarin if anticoagulation is needed long term.
- Intubation and ventilation if pulmonary oedema is severe.
- Inotropic support (dobutamine 5–10 micrograms/kg/minute, dopamine 5–10 micrograms/kg/minute, milrinone maximum dose of 0.7 micrograms/kg/minute). Ventilation and inotropic drugs should be a last resort if the child is deteriorating despite other measures, as it can be difficult to wean them off intensive care support once these steps are taken.
- Once the child is stabilised, introduce carvedilol at a dose of 50 micrograms/kg (maximum dose 3.125 mg) twice a day, doubling the dose at intervals of at least 2 weeks up to an upper limit of 350 micrograms/kg (maximum 25 mg) twice a day. Use echocardiography to check that cardiac function has not deteriorated before each dose increment, and monitor blood pressure for 4 hours after every dose increment. Carvedilol promotes myocardial remodelling.

Bacterial endocarditis

Endocarditis should always be suspected in a child with

a cardiac defect when there is a fever without a focus. Infection develops on injured areas of endothelium or on abnormal or damaged heart valves. In some cases the onset may be sudden with obvious signs of sepsis and cardiac fail-ure (secondary to valve damage). However, in most cases the onset is insidious and the diagnosis is unclear. There may be fever, malaise, fatigue, arthralgia, anorexia and weight loss. It may occur in a child previously thought to have a normal heart but with an undiagnosed congenital heart defect or undiagnosed episode of rheumatic fever.

Signs of endocarditis:

- Pyrexia
- Microscopic haematuria
- Splenomegaly
- Changing heart murmur
- Petechiae
- Neurological abnormalities (caused by cerebral abscess or infarction)
- Splinter haemorrhages, Janeway lesions, Osler's nodes and Roth's spots (characteristic but rare).

The diagnosis is made by isolating bacteria from the blood. At least three sets of blood cultures must be obtained from different puncture sites. If possible, antibiotics should be witheld until multiple blood cultures have been obtained and should only be started when the diagnosis is clear or there is a pressing clinical urgency. Blood cultures will be negative in 10–15% of cases. Echocardiography helps to make the diagnosis if vegetations are seen, but a negative echocardiogram does not exclude the diagnosis.

Organisms most commonly isolated in endocarditis:

- *Streptococcus viridans* (commonest overall)
- *Staphylococcus aureus* (most cases of fulminant endocarditis)
- Coagulase-negative staphylococci (if the patient has a central venous line or is immunocompromised e.g. with HIV).

If the organism is *Streptococcus viridans*, IV benzylpenicillin 25 mg/kg 6 hourly and gentamicin 7.5 mg/kg once daily are given for two weeks, followed by a further two weeks of oral amoxycillin. If the organism is *Staphylococcus aureus*, IV flucloxacillin 25 mg/kg 6 hourly is given for 4 weeks, coupled with IV gentamicin 7.5 mg/kg once daily (or sodium fucidate) 6–7 mg/kg 8 hourly for the first two weeks. Vancomycin 10 mg/kg 6 hourly is used in place of flucloxacillin if the organism is a coagulase negative Staphylococcus or the patient is allergic to penicillin.

The effectiveness of treatment is monitored by symptoms and inflammatory markers (WBC, ESR and CRP).

Surgery is necessary when the organism cannot be eradicated, when there is evidence of embolisation, where there is a large mobile vegetation at risk of embolisation or when there is severe cardiac failure from valve damage.

5.4.C The child with a cardiac arrhythmia

BOX 5.4.C.1 Minimum standards

- Electrocardiograph.
- Defibrillator.
- Adenosine.
- Beta-blockers.
- Flecainide.
- Amiodarone.
- Atropine.

Supraventricular tachycardia

Supraventricular tachycardia (SVT) is the commonest tachyarrhythmia in childhood.

It may present with poor systemic output and heart failure in infancy, or palpitations and dizziness in later childhood. SVT can be distinguished from sinus tachycardia because the rate is usually more rapid (200–300 beats/minute) than can be explained by the child's level of activity, fever, agitation or pain. The ECG in most cases shows narrow QRS complexes without a preceding P wave. The commonest cause of SVT in childhood is an accessory pathway, which is an abnormal bundle of muscle fibres bridging from the atrium to the ventricle. In accessory pathway-mediated tachycardia, depolarisation passes down from the atrium to the ventricle through the atrioventricular node, and then returns back up to the atrium using the accessory pathway. If the electrical wavefront then passes down the atrioventricular node again and once again returns up to the atrium via the accessory pathway, SVT has initiated. Some, but not all, accessory pathways are evident on the resting ECG because forward conduction across the accessory pathway in sinus rhythm causes a slurred stroke just before the QRS complex, known as a delta wave. The condition is often known as the Wolff–Parkinson–White (WPW) syndrome. The best method of treating this condition is by radiofrequency ablation of the abnormal pathway by means of a catheter passed into the atria, but this is a skilled technique that is only available in specialist centres.

Some patients have a different type of SVT, where the electrical wavefront loops back on itself to form a 'short circuit' entirely within the atrioventricular node. This is less often seen in early childhood, but becomes more common towards adolescence. A totally different mechanism of tachycardia occurs when there is an abnormally rapid atrial discharge (atrial flutter or atrial ectopic tachycardia). This is relatively rare in childhood.

Management of SVT

1. Record a 12-lead ECG in tachycardia,
2. While attempts are made to terminate the tachycardia, record a rhythm strip (this can often be easily run off a standard defibrillator).
3. In the infant, try to terminate the SVT by facial immersion in ice-cold water.
4. To terminate symptomatic or prolonged attacks of SVT in the older child, try vagal manoeuvres such as ice-cold packs on the face, the Valsalva manoeuvre or carotid sinus massage.
5. If tachycardia persists, obtain IV access (via a large antecubital vein if possible) and give a rapid bolus of

adenosine 100 micrograms/kg followed by a rapid crystalloid flush.

6 If the SVT is not terminated, give larger doses of adenosine, doubling the dose until a maximum dose of 400 micrograms/kg is reached.
7 If adenosine terminates the tachycardia transiently, and then SVT re-initiates, anti-arrhythmic drug treatment needs to be initiated straight away to prevent constant recurrence of the arrhythmia.
8 If adenosine successfully terminates the tachycardia, it is not compulsory to initiate anti-arrhythmic treatment. As SVT is not dangerous beyond infancy, anti-arrhythmic drugs are only given if the child wants to avoid further attacks (this decision is usually influenced by the frequency and duration of attacks). In infancy, SVT may cause serious haemodynamic compromise. In view of this, all infants who present with SVT should be started on anti-arrhythmic medication, which should be continued until the child's first birthday.
9 If adenosine does not terminate the tachycardia at all, carry out synchronised DC cardioversion, after anaesthesia, intubation and ventilation with 0.5 joules/kg, rising to 2 joules/kg in steps if the first shocks are unsuccessful.
10 In rarer cases, adenosine causes only transient block of the atrioventricular node, revealing rapid atrial activity in the form of P waves or sawtooth flutter waves. When atrioventricular nodal conduction returns after a few seconds, the tachycardia is re-initiated. These tachycardias require either anti-arrhythmic drug treatment to be initiated straight away or DC cardioversion.

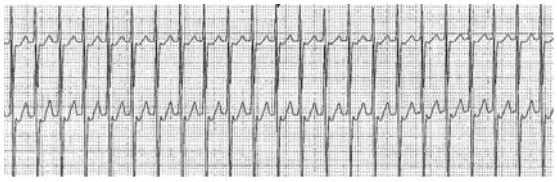

FIGURE 5.4.C.1 Supraventricular tachycardia (SVT).

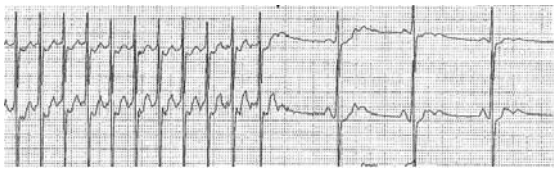

FIGURE 5.4.C.2 Termination of supraventricular tachycardia (SVT).

FIGURE 5.4.C.3 Administration of adenosine during atrial tachycardia shows underlying rapid P waves.

Ventricular tachycardia

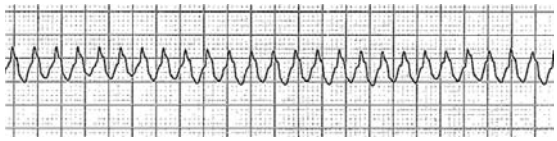

FIGURE 5.4.C.4 Ventricular tachycardia.

Ventricular tachycardia (VT) is normally diagnosed when there is a broad complex tachycardia. However, the latter is more often seen in childhood when there is SVT with bundle branch block. In view of this, adenosine should be given if a child presents with regular broad complex tachycardia. If the adenosine terminates the tachycardia, this proves that SVT was the correct diagnosis. If there is irregular broad complex tachycardia, do not give adenosine (this pattern indicates a dangerous arrhythmia). If the tachycardia persists even after high-dose adenosine, ventricular tachycardia is likely. Not all childhood ventricular tachycardia is dangerous. If the child is haemodynamically stable, attempts can be made to terminate the tachycardia with anti-arrhythmic drugs (see below). If there is haemodynamic compromise, immediate DC cardioversion is required.

Direct current (DC) cardioversion

Sedate or anaesthetise the child unless they are in extremis. Use paediatric paddles if the child weighs less than 10 kg. Place one paddle over the apex of the heart in the mid-axillary line and the other immediately below the clavicle just to the right of the sternum. If there are only adult paddles and the child weighs less than 10 kg, place one on the back and one over the lower chest anteriorly. The first shock should be 0.5 joules/kg, and subsequent shocks should be increased stepwise to a maximum of 2 joules/kg.

Anti-arrhythmic drugs

This is only a guide, and other types of drug within a class can be given.

First choice

Beta-blockers (oral doses given)

Infants: propranololol 1 mg/kg/dose three times a day.

Children (when cannot swallow tablets): atenolol 1–2 mg/kg once a day.

Older children (when can swallow tablets): bisoprolol 0.2–0.4 mg/kg once a day (tablets come as 2.5 mg, so use multiples of this amount).

Second choice

Flecainide (oral doses given)

Under 12 years of age: initially 2 mg/kg/dose twice a day. It is possible to increase to 3 mg/kg/dose if tachycardias persist (maximum of 8 mg/kg/day).

Over 12 years of age: 50–100 mg twice a day (maximum of 300 mg a day).

It is preferable to measure the flecainide level after 5 days just before the next dose is due to be administered, to check that the plasma level has not exceeded 800 micrograms/litre.

Avoid feeds for 30 minutes before or after giving oral flecainide, as the absorption of the drug is significantly affected by milk and dairy products.

Third choice

Beta-blocker and flecainide together

If the tachycardia does not respond to the above drugs in the acute setting, or the child's haemodynamic status is borderline, IV amiodarone is the safest option.

IV amiodarone

Give a loading dose of 5 mg/kg over 2 hours (dilute with 5% dextrose only). Then continue infusion at a rate of

5–20 micrograms/kg/minute (maximum of 1.2 grams in 24 hours).

Consider stopping the infusion 4–8 hours after the SVT has resolved.

If tachycardia recurs after stopping amiodarone, give a further loading dose and recommence infusion, continuing for at least 1 day after tachycardia resolution.

As amiodarone has a large number of side effects, consider switching to either a beta-blocker or flecainide once the tachycardia has been controlled and the child is haemodynamically stable.

Make up the amiodarone infusion as follows:
15 mg/kg in 50 mL of 5% dextrose (1 mL/hour = 5 micrograms/kg/hour: such a slow infusion will need an electrically driven syringe pump).

Amiodarone is incompatible with sodium chloride. Therefore do not make up with and do not flush lines with this solution.

Amiodarone can be given through a peripheral line, but serious tissue damage may be caused by the drug if extravasation occurs, so central access is preferred. If peripheral access is used, dilute the infusion to a concentration between 600 micrograms/mL and 2 mg/mL. This dilution will be more appropriate in situations where electrically driven syringe pumps are not available, but the infusion needs close monitoring.

Congenital complete heart block

- Consider this in any newborn who has a consistent bradycardia without apparent cause, such as terminal respiratory failure or very severe shock.
- P waves are dissociated from QRS complexes on the 12-lead ECG.
- Perform an echocardiogram to exclude structural heart disease.
- Check for anti-Ro and anti-La antibodies in the child's mother (the underlying cause in the majority of cases).
- Monitor the heart rate for 24–48 hours.
- Assess perfusion and blood pressure, and examine for signs of heart failure.
- Arrange for a permanent pacemaker if there is inadequate cardiac output, heart failure, structural heart disease or the heart rate is < 50 beats/minute.
- Atropine 20 micrograms/kg or isoprenaline infusion 0.02–0.2 micrograms/kg/minute can be used for emergency treatment of severe bradycardia with inadequate cardiac output.

5.5 Shock

5.5.A Shock

Introduction

'Shock' occurs when the circulatory system fails to deliver adequate amounts of primarily oxygen, but also nutrients, to the tissues, and fails to remove unwanted metabolites from the tissues for excretion.

Pathology at cell level

At a cellular level, the end result of shock is anaerobic metabolism (oxygen-depleted metabolism). This is an inefficient mechanism and requires much more energy than aerobic metabolism (the normal oxygen-dependent system). In addition, anaerobic metabolism builds up excess toxic acid products in the cells which cannot be removed by the failed circulation. Cellular function deteriorates and there is a downward spiral of increasing loss of homeostasis, the onset of disseminated intravascular coagulation, and after a short while so much cell death occurs in vital organs that recovery is impossible and the patient dies.

In the early stages of shock the body has mechanisms to try to combat this process. The circulatory system is under the control of the sympathetic nervous system. This system regulates the flow of blood in health and in disease to all organs so as to respond to demands on different organs. In health, more blood is sent to muscles if a person is exercising, more to the digestive system if they are eating, and more to the skin if their body is too warm.

In shock, the sympathetic nervous system attempts to protect the vital organs by diverting blood away from muscle, skin and the digestive system and directing it to the heart, brain and kidneys. This gives rise to some of the earlier signs of shock, such as cold peripheries, increased capillary refill time, cerebral anxiety or agitation, tachycardia to increase cardiac output, and reduced urine output as the kidneys conserve fluid.

Later signs such as depressed consciousness, weak pulses, falling blood pressure and acidotic breathing show that the body's compensation mechanisms are failing. It can be seen that it is vital to recognise and treat shock in the patient as soon as possible, as this will give the best chance of patient recovery.

Clinical diagnosis of shock

The signs of shock are listed below, although not all of them are present in all types of shock.

- **Tachycardia** (best measured with a stethoscope).

- **Weak pulse** (ideally central – brachial, femoral or carotid, but difficult to gauge).
- Low blood pressure (this is a **late sign** and very difficult to measure in young children).
- Extreme central pallor (severe anaemia).
- Raised respiratory rate (due to acidosis).
- **Cold skin with poor circulation.**
- **Prolonged capillary refill time (CRT) > 3 seconds.**
- Increased skin sweating in some cases.
- Agitation and anxiety (this is an early sign).
- **Reduced conscious level.**
- Reduced urine output (this is an early sign).

The WHO diagnosis of shock includes all of the above signs that are highlighted in bold type.

The problem is that shock is quite difficult to diagnose in the early stages, as some signs also occur as a result of medical causes other than shock. The diagnosis in the early stages depends on the following:

- tachycardia, which is a very useful sign of shock, but also occurs with fever and with anxiety or fear
- anxiety and/or agitation
- prolonged capillary refill time, which also occurs in dehydration and is influenced by environmental temperatures and by how hard the nail bed or sternum is pressed
- cold skin, which is also dependent on environmental temperature
- reduced urine output, which is also dependent on fluid intake.

It is vital that if any of these early signs are noted in a patient that they are not dismissed as some unrelated cause, but are seriously considered as likely to be indicating the development of shock.

This is why it is so useful to have regular vital signs (pulse, respiration, conscious level, temperature and blood pressure) observations on patients, so that abnormal trends can be detected early.

It is also important to note that shock is not diagnosed on the basis of one physical sign alone, but on the basis of several signs occurring together. For example, a tachycardia alone does not diagnose shock, but if you note a tachycardia, you should look for cold limbs, prolonged capillary refill time, or a history suggestive of a cause of shock, such as a fever, severe diarrhoea or bleeding.

Pathological mechanisms that can cause shock

The circulatory system is complex, so there are many causes of shock. The organs, systems and pathologies that can be the primary cause of the shock include the heart itself, the blood vessels, restriction to the flow of blood, failure of the oxygen-carrying capacity of the blood, and loss of blood or fluid from the body. The main mechanisms of shock can be summarised as follows:

- loss of fluid or blood: **hypovolaemic shock** (e.g. diarrhoea, blood loss)
- failure of the heart pump: **cardiogenic shock** (e.g. dysrhythmias, cardiomyopathy, myocarditis, malnutrition)
- abnormal function of vessels supplying nutrients and oxygen to tissues: **distributive shock** (e.g. sepsis, anaphylaxis)
- inadequate capacity of the blood to release oxygen: **dissociative shock** (e.g. severe anaemia, carbon monoxide poisoning)
- restriction of circulation to the tissues: **obstructive shock** (e.g. some congenital heart diseases, tension pneumothorax, cardiac tamponade, pulmonary embolus).

In an individual with shock, often several of these mechanisms may coexist. Therefore the clinician must consider which emergency treatments will be effective **and which will be harmful** for any particular patient. One of the most difficult situations is in the anaemic malnourished child with sepsis, where fluid is required to expand the circulating volume, but the heart is already failing and cannot cope with a rapid fluid infusion (*see* Section 5.10.B).

Basic management of shock

Shock is managed according to the following principles:

- High concentrations of oxygen are safe and must be given regardless of the cause of shock.
- Airway and breathing stability or support must be established promptly first (the only exception is to control exsanguinating external bleeding in trauma or major obstetric haemorrhage concurrently with airway and breathing; *see* Sections 7.3.A, 2.5.D.i and 2.5.D.iv).
- Frequent reassessment, at least after every therapeutic manoeuvre, is vital to avoid both under-infusing and over-infusing fluids.
- The underlying pathology must be treated to arrest the pathological process.

The clinical diagnosis of the cause of shock is not easy or definitive. Shock is a spectrum of conditions and mechanisms, and it is a clinical challenge.

Immediate resuscitation is needed to maintain oxygenation and perfusion of vital organs. Once this is under way, the cause of shock needs to be found and treated.

Diagnosis depends on history, clinical examination, and response to treatment given. It is often possible to identify the cause of shock with a good history and a careful examination.

Investigations

- Haemoglobin measurement is essential.
- Blood glucose measurement is essential, as some signs of shock are the same as signs of hypoglycaemia.
- Plasma electrolyte measurements are helpful, especially sodium and bicarbonate.
- Lactate measurement is helpful (if available).
- Central venous pressure (CVP) measurement is useful, if skilled staff are available to undertake the procedure and measurement (not an emergency procedure, but helpful if in high-dependency care).

Choice of intravenous fluid

Fluid infused into the circulation should approximate to plasma in its electrolyte content, osmolality and pH.

Dextrose-only fluids

It is clear that although glucose or dextrose is necessary to prevent or manage hypoglycaemia, fluids containing only dextrose should **never** be used for IV fluid replacement

TABLE 5.5.A.1 Diagnostic pointers to the clinical causes of shock (each is discussed in the sections indicated)

Diarrhoea and/or vomiting with signs of severe dehydration	Gastroenteritis (*see* Section 5.5.B and Section 5.12.A), volvulus, intussusception (*see* Section 5.19)
Fever, non-blanching (purpuric) rash	Meningococcal septicaemia (*see* Section 5.5.C and Section 6.1.G), dengue haemorrhagic fever (*see* Section 6.2.B)
Urticaria, wheeze, oedema, exposure to allergen	Anaphylaxis (*see* Section 5.1.B)
Trauma	Blood loss, tension pneumothorax, internal bleeding, spinal cord transection (*see* Section 7.3.A)
Major obstetric haemorrhage in children who are pregnant	Blood loss: ruptured ectopic pregnancy, antepartum haemorrhage, postpartum haemorrhage (*see* Section 2)
Burns	Fluid loss from burns (*see* Section 7.3.I.b)
Pallor, tachycardia, severe malaria, severe acute malnutrition	Severe anaemia, often with malnutrition (*see* Section 5.10.B) and malaria (*see* Section 6.3.A.d)
Fever, signs of shock and a very sick child	Septicaemia (*see* Section 5.5.C) and malaria (*see* Section 6.3.A.d)
Baby < 4 weeks old: cyanosis, with no response to oxygen, very weak pulses	Congenital heart disease (*see* Section 5.4.A)
Very fast pulse, heart failure	Arrhythmia (*see* Section 5.4.C) and cardiomyopathy (*see* Section 5.4.B)
Dehydration, polyuria, polydipsia, high glucose levels	Diabetic ketoacidosis (*see* Section 5.8.A)
History of sickle-cell disease or diarrhoeal illness and low haemoglobin levels	Haemolysis with severe anaemia (*see* Section 5.11.C)

or maintenance, or for the emergency management of shock.

The reason for this is that the dextrose is rapidly metabolised, so the effect of a dextrose-only IV fluid on the child's body is as if pure water had been given. The outcome of this treatment would be severe hyponatraemia, which could quickly lead to brain damage or death.

In addition, this pure water is rapidly moved out of the circulation and into the cells, and the state of shock is then worse than before the infusion.

Sodium-containing fluids

The fluid traditionally infused into the circulation for the management of shock has been 'normal saline' (0.9% sodium chloride, NaCl). This fluid has increasingly been shown to be potentially dangerous, especially in the sick patient. An infusion of normal saline causes a hyperchloraemic acidosis (a high chloride concentration leading to an acidosis), which in the shocked patient, who is already acidotic, causes a deterioration in the health of cells in vital organs, even though perfusion of the cells has been improved by the increased circulating volume.

There are sodium-containing alternatives to normal saline which are safer as they approximate more closely to human serum in content (*see* Table 5.5.A.2), although they are a little more expensive. We recommend the use of either of these alternatives (**Ringer-lactate and Hartmann's solution** are widely available) for all fluid replacement. Recognising that not all hospitals will have access to these solutions immediately, there may sometimes be no alternative but to start fluid replacement with normal saline. However, if more than 20 mL/kg needs to be given, one of the safer alternatives should be used in these very sick children if at all possible.

Note that hospitals and clinics will need to have access to some 0.9% NaCl (normal saline), usually in 5 mL or 10 mL ampoules. This will be used for dissolving or diluting drugs for IV injection. If a specific fluid is indicated as the diluent for a particular drug (e.g.0.9% NaCl, 5% dextrose, water for injection), **this fluid must be used**. If drugs are infused using the wrong fluid, their effect on the patient may be altered.

Clinicians should try to ensure that their hospital facility does have access to these safer infusion fluids, such as Ringer-lactate or Hartmann's solution.

TABLE 5.5.A.2 Comparison of electrolytes, osmolality and pH levels in IV fluids with those in human serum

Fluid	Na^+ (mmol/litre)	K^+ (mmol/litre)	Cl^- (mmol/litre)	Ca^{2+} (mmol/litre)	Lactate or bicarbonate (mmol/litre)	Osmolarity (mOsm/litre)	pH
Human serum/plasma	135–145	3.5–5.5	98–108	2.2–2.6	22–30	276 to 295	7.35–7.45
Ringer-lactate or Hartmann's solution	131	5.0	111	2.0	29	279	6.0
0.9% 'normal' saline	154	0	154	0	0	310	5.4

Initial management of shock

Even though it may be clear on initial inspection that the child is in shock, the first priority must still be to call for help, manage the airway, manage breathing and then manage the circulation.

Call for help.

Airway

At this stage also stop any obvious exsanguinating bleeding.

Assess the airway by the simple technique of asking the child 'Are you all right?'

Any vocalisation such as a reply or crying indicates an open airway and some ventilation. In the absence of a response, formally open the airway with a head tilt/chin lift or a jaw thrust manoeuvre (*see* Section 1.12), and assess breathing by looking, listening and feeling for its presence.

Stop any obvious exsanguinating bleeding by applying external pressure (or in the case of postpartum haemorrhage, *see* Section 2.5.D.iv).

Breathing

All children with suspected shock must receive high-flow oxygen.

In the absence of spontaneous breathing, give assisted ventilation with a bag-mask (*see* Section 1.13).

Circulation

Intravenous access with a short wide-bore venous cannula, or placement of **an intra-osseous line** (*see* Section 8.4.B), is vital. More than one line is preferable, as rapid fluid resuscitation may be needed, although always start treatment as soon as the first access has been achieved and insert the second line when possible. Take blood samples for the

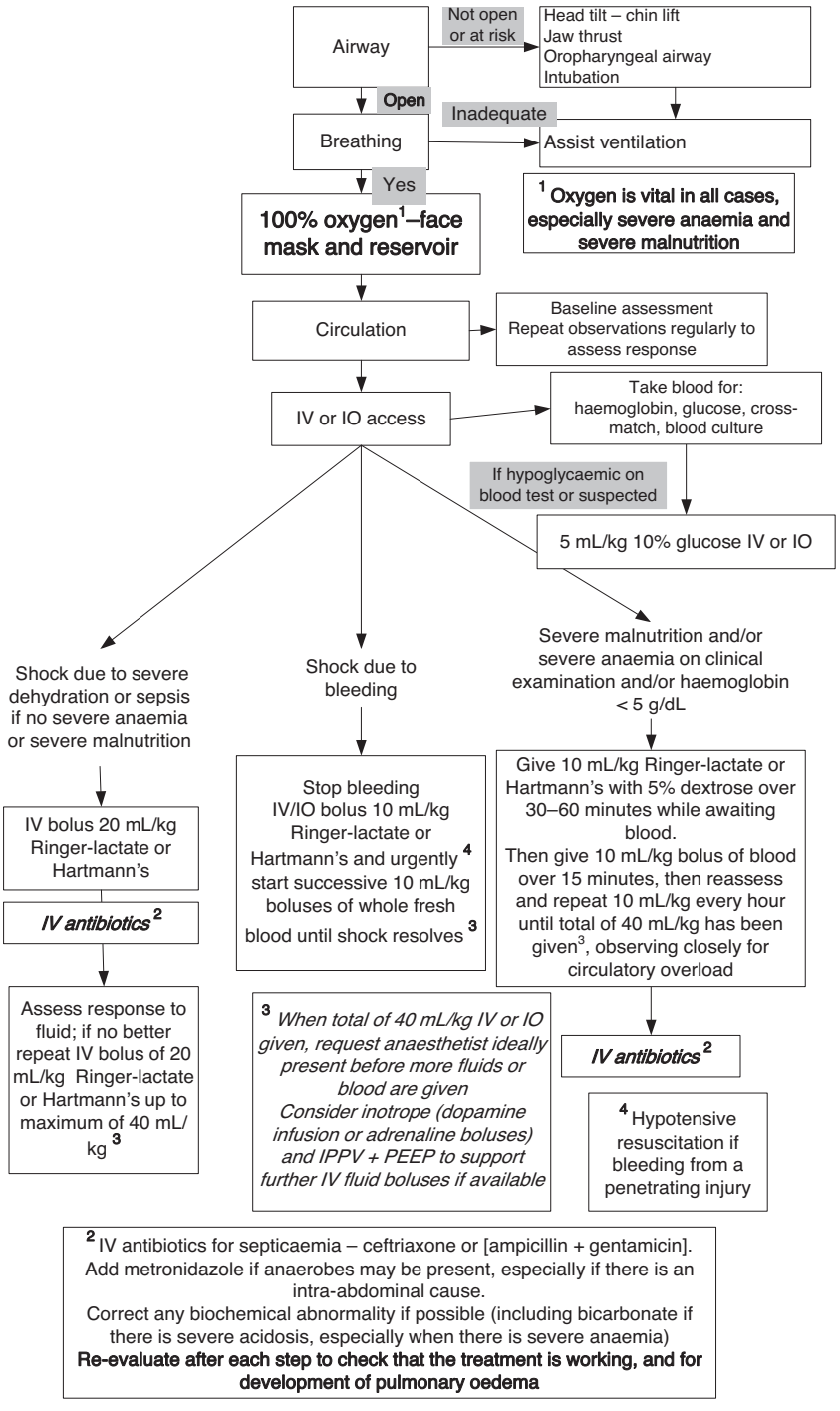

FIGURE 5.5.A.1 Pathway of care for the child with shock that is not cardiac in origin.

following investigations: full blood count, glucose levels, electrolytes, blood culture (and, if relevant, cross-matching and malarial parasite test).

Nutritional status

While starting to give fluid, assess the child's nutritional status (*see* Section 5.10.B). Look for visible severe wasting or **marasmus**. The WHO recommended criteria are as follows: 'Look at the arms, legs and chest. The marasmic child does not look just thin, but appears to be all skin and bone. The skin looks too large for the body, there is no fat on the child and you will see the outlines of the ribs. There is also severe muscle wasting of the arms, legs and buttocks. The head may appear relatively large because of wasting of the body.' Use the mid upper arm circumference (MUAC) (*see* Section 9) to assess marasmus, as the urgency of the child's need for treatment precludes a weight and height measurement.

Look also for kwashiorkor. Check for oedema of both feet. Look at the bare feet. Press the top of the foot gently with your thumb for a few seconds. Oedema is present if a definite dent is left in the tissues. Look and feel to determine whether the child has oedema of both feet.

Some assessment of weight will be necessary to calculate the amounts of fluid and antibiotics to be given. If the child is not malnourished, use the following formula:

weight in kg = 2 (age in years + 4).

If the child is malnourished, this formula can still be used, but perhaps a percentage such as 25–50% subtracted from the result.

Severe anaemia

In very anaemic children (with either obviously pale palms or haemoglobin levels of less than 3–4 grams/dL), crystalloid alone will worsen oxygen delivery to the tissues. These children need blood, either packed cells or a partial exchange transfusion, in addition to initial **slow** fluid resuscitation (*see* Section 5.10.B, Section 5.11.A and Section 8.4.B).

The next step is to **give fluid intravenously**. In most cases this should be a crystalloid such as Hartmann's or Ringer-lactate solution, but give normal saline (0.9%) if this is all that is available. In children, the volume of fluid to be given is usually 20 mL/kg, which is 25% of the child's circulating volume (10 mL/kg in severe anaemia or severe malnutrition while awaiting blood for transfusion). Shock is not usually clinically evident until 25% of the circulation has been lost, so any child with signs of shock must have lost at least this amount of fluid from the circulation.

The concept of **targeted crystalloid fluid resuscitation** is important if the cause of hypovolaemic shock in a child is haemorrhage from a penetrating injury. Here the initial boluses of IV crystalloids required to treat shock should only be given to keep the vital organs (especially the brain, heart and kidneys) perfused before life-saving surgery and blood transfusion can be undertaken. Fresh blood is particularly useful to combat the coagulopathy that occurs in major blood loss if specific coagulation components such as platelets are unavailable.

Giving too large a volume of IV fluids can increase the blood pressure and thus increase bleeding by disrupting early clot formation. IV crystalloid also dilutes the red cells in the circulation, but whether or not this could reduce oxygen-carrying capacity requires further research.

We suggest that when giving boluses of crystalloid or blood to patients in shock due to bleeding, only the amount needed to keep the blood pressure at a level sufficient to perfuse the vital organs should be given. There is no clear evidence to indicate the precise blood pressure that should be achieved in a child in shock due to haemorrhage from penetrating injury. **Adequate perfusion of vital organs may best be indicated by the following: in the child over 2–3 years of age, a radial pulse that can be palpated and a conscious level of A or V on the AVPU scale (i.e. the child is either awake or will respond by opening their eyes when spoken to). In children under 2–3 years of age the radial pulse may be difficult to feel, and in children with shock due to haemorrhage the presence of a palpable brachial pulse may be the best available indicator at present.**

In this situation, therefore, and to maintain a palpable radial or brachial pulse, start with IV boluses of 10 mL/kg of crystalloid, or ideally blood, and reassess after each bolus.

The next very important step is to reassess the patient's vital signs to see whether the fluid has helped, and to ensure that circulatory overload has not given rise to a situation where more IV fluids may produce very dangerous heart failure (see below for clinical signs of this).

During this reassessment, give IV antibiotics, as shock without obvious fluid loss is probably sepsis (*see* Section 5.5.C).

At this point, some children will need more crystalloid fluid, while others will not, or they will need other fluids (e.g. plasma expanders such as albumin or blood). Many will need additional treatments. The next two sections (Sections 5.5.B and 5.5.C) deal with two of the commonest causes of shock in children, and the reader is referred to the sections indicated in Table 5.5.A.1 for details of the various other causes of shock.

5.5.B The child with shock from dehydration

BOX 5.5.B.1 Minimum standards
- Oral rehydration solution (ORS), including ReSoMal.
- Crystalloid infusion fluids (preferably Hartmann's solution or Ringer-lactate solution, but normal saline may be used if it is the only available alternative).
- Blood transfusion.
- Antibiotics.
- Furosemide.
- MUAC tapes.

Dehydration

- Dehydration is loss of water, sodium and other essential electrolytes.
- The most common cause in resource-limited countries is gastroenteritis (from a number of different organisms; *see* Section 5.12.A).
- Most cases can be treated with low-osmolarity oral rehydration solution (ORS) administered by mouth or nasogastric tube.
- In children with severe malnutrition, use a solution with lower sodium content, such as ReSoMal.
- It is important to also consider diabetic ketoacidosis (*see* Section 5.8.A) and surgical causes of dehydration, such as intussusception and volvulus (*see* Section 5.19).

Dehydration classification

Dehydration is classified by estimating the percentage of body water lost according to clinical criteria (except in malnutrition, where clinical signs are more difficult to interpret; see below).

'No dehydration'

If there is less than 3% weight loss there are **no clinical signs**.

'Some dehydration'

If there is 3–9% weight loss, the following signs are seen:
- increased thirst
- drinks eagerly
- dry mucous membranes
- loss of skin turgor, tenting when pinched
- sunken eyes
- sunken fontanelle in infants
- restless or irritable behaviour
- decreased capillary refill time (> 3 seconds)
- decreased urine output.

'Severe dehydration'

If there is ≥ 10% weight loss, the following signs are seen:
- more pronounced signs than those seen in moderate dehydration
- lack of urine output
- lack of tears when crying
- inability to drink or drinking poorly (because of reduced conscious level)
- lethargy

plus
- **hypovolaemic shock**, including:
  - rapid and weak low-volume pulse (radial pulse may be undetectable) (use a stethoscope for measuring heart rate)
  - altered consciousness or coma
  - low or undetectable blood pressure
  - cool and poorly perfused extremities
  - severe nail bed or sternum decreased capillary refill time
  - peripheral cyanosis
  - rapid deep breathing (from acidosis).

It is important to realise that the above classification is made only to guide the start of treatment. **Levels of dehydration are a continuous spectrum, not three separate and distinct categories.** The only way to be absolutely certain about the percentage dehydration of a child is to compare an accurate weight measured just before the onset of the diarrhoeal illness with an accurate current weight. It is very unlikely in most cases that the former weight will be available. In the case of the shocked patient, immediate treatment takes precedence over weighing the child (estimate the child's weight from the formula:

weight (kg) = 2 (age in years +4)

for previously well children before puberty, or read it from a weight/age chart (*see* Section 9)).

However, if the clinical situation is not so critical, the weight of the child on presentation is very helpful for subsequent management, and should be measured and recorded as a daily routine.

Emergency treatment of severe dehydration: principles of treatment

- Recognise and treat shock.
  - Give a fluid bolus, 20 mL/kg IV of Hartmann's or Ringer-lactate solution (0.9% saline, or 'normal' saline, can be used if there is no alternative; *see* Section 5.5.A).
  - A second bolus may be needed if the child does not respond (*see* the 'shock' pathway in Figure 5.5.A.1).
  - It is unusual to need more than two boluses in cases of dehydration due to gastroenteritis alone, unless they are due to cholera (*see* Section 5.12.A). Consider other causes, such as septicaemia, diabetic ketoacidosis (check blood sugar levels), volvulus or intussusception (check whether vomit is bile-stained, and whether there is fresh blood in stools; *see* Section 5.19).
  - If septicaemia is suspected, treat with IV antibiotics.
- Think of the most likely cause of the dehydration.
- Estimate the level of dehydration (see above) to calculate the fluid deficit, maintenance needs and ongoing losses (see below).

Shock recognition and treatment

Children with shock associated with dehydration will have a high and increasing heart rate, weak pulse, poor

skin circulation time with prolonged capillary refill time (> 3 seconds), depressed conscious level, and low or even unmeasurable blood pressure.

These children require immediate resuscitation (ABC) and emergency treatment.

Call for help (summon an anaesthetist if possible).

Airway (in cases of reduced conscious level)

Use an opening manoeuvre if the airway is not open or if it is partially obstructed. Keep the airway open. If there is immediate improvement but the airway closes without active opening support, consider airway adjuncts to support the airway.

Suction if necessary under direct vision, but not routinely.

If the child is deeply unconscious (P or less on the AVPU scale), the airway may need to be secured by intubation using experienced senior help (if available).

Breathing

Give 100% oxygen (using a mask with reservoir and a flow rate of at least 6 litres/minute) regardless of SpO_2 (this increases oxygen delivery as well as improving tissue oxygenation). For inadequate ventilation or depressed conscious level (check with the AVPU scale) with hypoventilation, respiration should be supported with oxygen via a **bag and mask**, and experienced senior help should be summoned (if available).

Circulation

- Obtain vascular access to give IV boluses quickly. Insert an IV cannula and send blood for a full blood count, urea and electrolytes, cross-matching (if the patient is anaemic) and clotting. If peripheral veins are difficult to access, the **external jugular vein** or **long saphenous vein cut-down** are good alternatives, as is an **intra-osseous infusion** (*see* Section 8.4.B). If a skilled operator is available, an internal jugular or femoral vein central line is ideal, as it can also allow central venous pressure (CVP) measurements (if available).

Some assessment of weight will be necessary to calculate the amounts of fluid and antibiotics to be given. If the child is not malnourished, use the formula:

weight (kg) = 2 (age in years +4).

If the child is malnourished, this formula can still be used but perhaps a percentage such as 25–50% subtracted from the result.

Children with normal nutrition

- **If the child is not malnourished**, give an initial **rapid** bolus of 10–20 mL/kg of Ringer-lactate or Hartmann's solution, but give normal saline (0.9%) if this is all that is available. It is essential that the bolus is given as rapidly as possible. **Do not use 5% glucose or 0.18% saline/4% glucose solutions for resuscitation, which can be dangerous (risk of hyponatraemia and cerebral oedema).** Boluses should be manually pushed in using a 20- to 50-mL syringe (with a three-way tap and linked to an IV giving set).
- When this bolus of fluid has been given, review the child's condition, looking to see whether there has been any improvement in pulse rate, conscious level, respiratory rate, capillary return and limb warmth, and blood pressure.
- A further 10–20 mL/kg bolus will be required if signs of shock remain. Once a **total** of 40 mL/kg of boluses has been given IV, complications such as pulmonary oedema are more likely to occur. In a child with shock from severe dehydration caused by diarrhoea, it would be unusual to need more than 40 mL/kg to improve the child's circulation, unless cholera was the cause. In severe cases, where more than a total of 40 mL/kg is considered essential, intubation, ventilation, CVP monitoring and inotrope support might be indicated (if available), but **the diagnosis should be reviewed as this need is unusual in straightforward gastroenteritis.** Reconsider the diagnosis. For example:
  - surgical abdominal pathology, such as intussusception, peritonitis or volvulus (bile-stained vomiting, abdominal distension or tenderness) (*see* Section 5.19)
  - additional pathology, severe anaemia, septicaemia or a cardiac problem.

Children with severe malnutrition or severe anaemia

- **If the child is malnourished and/or has severe anaemia, fluid must be given much more carefully.** Give 15 mL/kg IV over 1 hour. The recommended solution is Ringer-lactate or Hartmann's solution, each with 5% glucose (insert 50 mL of 50% dextrose into a 500-mL bag of the bolus fluid, ideally after first removing 50 mL from the bag: not essential), but give normal saline (0.9%) if this is all that is available, also with 5% dextrose. At the same time, insert a nasogastric tube and give ReSoMal, 10 mL/kg/hour. Monitor carefully for signs of over-hydration: reassess the respiratory and heart rates every 15 minutes. It is also wise to give IV antibiotics in this situation, as it can be very difficult to distinguish septic shock from dehydration shock in children with malnutrition.

Nutritional status

- **While starting to give fluid, assess the child's nutritional status** (*see* Section 5.10.B). Look for visible severe wasting or **marasmus**. Follow the WHO criteria: 'Look at the arms, legs and chest. The marasmic child does not look just thin, but appears to be all skin and bone. The skin looks too large for the body, there is no fat on the child and you will see the outlines of the ribs. There is also severe muscle wasting of the arms, legs and buttocks. The head may appear relatively large because of wasting of the body.'
- Use the mid upper arm circumference (MUAC) (*see* Sections 5.10.B and 9) to **assess marasmus**, as the urgency of the child's need for treatment precludes a weight and height measurement.
- **Look also for kwashiorkor.** Check for oedema of both feet. Look at the bare feet. Press the top of the foot gently with your thumb for a few seconds. Oedema is present if a definite dent is left in the tissues. Look and feel to determine whether the child has oedema of both feet.

Severe anaemia

In very anaemic children (with either obviously pale palms or haemoglobin levels less than 3–4 grams/dL), crystalloid

alone may worsen oxygen delivery to the tissues. These children need blood, either packed cells or a partial exchange transfusion, in addition to initial **slow** fluid resuscitation (*see* Section 5.10.B and Section 8.4.B).

- **If after 1 hour** the child is improving but still severely dehydrated, stop the IV fluids, but continue nasogastric ReSoMal 10 mL/kg/hour for up to 5 hours (*see* Section 5.10.B for further details).
- A child with a haemoglobin level of less than 5 grams/dL will also need a transfusion of 10 mL/kg of packed cells over 4 hours, watching continuously for evidence of pulmonary oedema. If pulmonary oedema develops, furosemide 1 mg/kg IV may be required, but if possible pulmonary oedema of severity requiring diuretics should be avoided by a slow and vigilant approach to therapy in these very sick children.
- Keep the patient warm, but do not overheat them, as this will cause peripheral vasodilatation and reduce the blood supply to vital centres. Hypothermia will exacerbate poor peripheral perfusion, acidosis and coagulation abnormalities.
- Elevate the patient's legs (raise the foot of the bed).
- A central venous pressure (CVP) line is potentially helpful for avoiding under-transfusion or fluid overload. Insertion should not delay initial resuscitation, but if peripheral access is inadequate this route may be used for volume replacement. If disseminated intravascular coagulation (DIC, a clotting disorder) has become established, CVP insertion is hazardous, must be undertaken by an expert, especially via the subclavian vein.
- If the child has a reduced level of consciousness or has a convulsion, particularly if they are an infant or a young child, hypoglycaemia may be present. Always measure the blood glucose concentration in this situation. However, if blood glucose measurement is not possible, always treat as for presumed hypoglycaemia and, in addition to the IV fluids given above, give 5 mL/kg of 10% glucose IV or, if there is no IV access, by intra-osseous needle.

While treating shock, reassess the child, ideally continuously, until signs of shock have resolved.

When signs of shock have resolved

When shock has resolved and the patient's level of consciousness has returned to normal, the remaining estimated fluid deficit MUST be taken by mouth or by gastric tube, especially if there is malnutrition and/or anaemia (due to the danger of a large IV fluid volume). Use WHO Plan B (*see* Appendix to Section 5.12.A).

- Check the serum sodium concentration, and if it is higher than 155 mmol/litre, reduce it **slowly** with oral rehydration solution over 48 hours. Too rapid a reduction in sodium levels leads to cerebral oedema.
- Further tests might include abdominal X-ray or ultrasound scanning, if there is concern about a distended abdomen.
- A surgical opinion is needed if there is bile-stained vomiting or abdominal signs.

Fluid requirements

WHO Plans A, B and C for gastroenteritis in children (*see* Appendix to Section 5.12.A) include estimates of total fluid requirements, and assume that most children will be drinking by 4 hours into treatment and thus able to 'self-regulate'. For patients for whom this is not the case, the following guidelines can be used.

Estimating fluid requirements

The amount of fluid needed in a 24-hour period must be calculated. It is the sum of:

estimated fluid deficit + maintenance requirements + ongoing losses.

Deficit

If an accurate recent pre-illness weight is available, subtract the current weight to estimate lost fluid (1 kg = 1 litre of fluid).

For example, a child who weighed 9.2 kg is seen with diarrhoea and a weight of 8.3 kg. The estimated fluid loss in this case is (9.2 – 8.3) kg = 0.9 kg = 900 mL deficit, i.e. 10% dehydrated.

If no recent reliable weight is available:

1 Estimate the degree of dehydration.
2 Weigh the child or estimate their weight from their age as follows:

$$\text{weight (kg)} = 2\,[\text{age (years)} + 4].$$

3 Use the formula: percentage dehydration × weight (kg) × 10 = deficit (in mL).

For example, a child whose weight is estimated to be 10 kg is 10% dehydrated. The estimated fluid loss in this case is 10 × 10 × 10 = 1000 mL (i.e. 40 mL/hour if replaced over 24 hours).

Maintenance

The estimated maintenance fluid requirements based on body weight for a child are shown in Table 5.5.B.1.

TABLE 5.5.B.1 Fluid requirements per day

Body weight	Volume of fluid needed per day	Volume of fluid needed per hour
First 10 kg of body weight	100 mL/kg	4 mL/kg
Second 10 kg	50 mL/kg	2 mL/kg
Subsequent kg	20 mL/kg	1 mL/kg

Ongoing losses

Estimated ongoing fluid losses are shown in Table 5.5.B.2.

TABLE 5.5.B.2 Estimates of ongoing fluid losses in gastroenteritis

For each diarrhoea stool	Age < 2 years: give 50–100 mL Age ≥ 2 years: give 100–200 mL
For each vomit	2 mL/kg oral rehydration solution: give small frequent volumes (e.g. 5 mL every minute for a child) via a spoon, syringe or cup
For nasogastric tube aspirates	Replace volume for volume with either oral rehydration solution or Hartmann's or Ringer-lactate solution with 5% or 10% glucose or normal saline with 5% or 10% glucose and 5 mmol/litre of potassium chloride

Over-hydration

Signs of over-hydration, especially if there is cardiac failure (e.g. in severe malnutrition) are as follows:

- tachycardia, increased respiratory rate, oedematous (puffy) eyelids, crepitations at lung bases, enlarged liver and raised jugular venous pressure (JVP)
- pulmonary oedema on chest X-ray.

Management

- Stop giving IV fluids or oral rehydration solution, but give breast milk or plain water and food.
- Do not give a diuretic unless there is pulmonary oedema (crepitations in lungs), in which case give furosemide 1 mg/kg IV.

Reassess:

- ABC.
- The state of intravascular rehydration.
- Plasma electrolytes (if possible).
- Urine output and urine electrolytes.
- Glucose levels.

Reduce fluid intake and continue to monitor, responding to changes in the child's condition as described above.

5.5.C The child with septic shock

BOX 5.5.C.1 Minimum standards

- High-dependency care.
- Ringer-lactate or Hartmann's solution (or 0.9% saline if no other crystalloid is available).
- Urgent blood transfusion.
- Antibiotics: cefotaxime, flucloxacillin, gentamicin, metronidazole and penicillin.
- Dopamine and adrenaline.
- MUAC tapes.

Introduction

Septic shock develops when a number of different mechanisms of shock operate in the context of an invasive bacterial infection (an exception is dengue, which is caused by a viral agent; *see* Section 6.2.B). These mechanisms are as follows:

- **hypovolaemic:** there is abnormal capillary permeability, fever and accompanying vomiting and diarrhoea
- **distributive:** there is loss of the normal sympathetic nervous system control of vascular tone, so that blood is lost from vital organs into non-vital areas
- **cardiogenic:** there is impaired cardiac function secondary to hypovolaemia and the toxic effects of the pathogen.

These multiple factors make septic shock difficult and complex to treat, and they contribute to a high mortality rate in these conditions.

The bacteria that cause septic shock include *Meningococcus*, *Staphylococcus*, *Streptococcus pneumoniae* and *Streptococcus pyogenes*, together with Gram-negative organisms such as *E. coli* which particularly affect **patients who are at risk due to lower immunity**, such as the newborn, those with HIV/AIDS, and the malnourished.

Diagnosis of septic shock

The early recognition and treatment of septic shock is key to a good outcome, so a high degree of vigilance for this condition is necessary.

In a child who has an infection, with a fever (although the **at-risk** group mentioned above may have a normal or subnormal temperature), the development of a change in mental status, such as irritability, drowsiness, lack of interaction or reduced or absent eating or breastfeeding is often the first feature to alarm parents, and is the result of the effect of poor cerebral perfusion and possible accompanying hypoglycaemia on the child's brain.

The signs which should then be sought include the following:

- tachycardia (best measured with a stethoscope)
- weak pulse (ideally central – brachial, femoral or carotid, but difficult to gauge)
- reduced urine output (this is an early sign)
- cold skin with poor circulation, or sometimes peripheral skin vasodilatation
- prolonged capillary refill time (CRT) > 3 seconds
- agitation and anxiety
- increased skin sweating in some cases
- extreme central pallor (in cases with severe anaemia)
- raised respiratory rate (due to acidosis)
- reduced conscious level (**this is a serious and dangerous sign**)
- low blood pressure (this is a **late sign** and difficult to measure in young children; the correct-sized cuff is needed).

Difficulties in managing septic shock

In well-resourced countries or well-resourced areas of countries with specialist paediatric intensive care units (PICUs) or high-dependency units, some cases of septic shock are still difficult to manage and some children die.

In resource-limited countries the following additional difficulties need to be taken into account:

- **Severe malnutrition:** this makes the diagnosis of septic shock more difficult, as the child's malnourished body does not respond with the same physical signs as that of a well-nourished child. In addition, malnourished children may have poor myocardial function and almost always have severe anaemia. This will result in cardiac failure and probable death if rapid infusions of large and repeated boluses of fluid (an important part of septic shock management) are given (*see* Section 5.10.B).
- **Severe anaemia:** as shock is a failure of oxygen delivery to the tissues, clearly anaemia will make this worse. Rapid crystalloid fluid infusion will dilute the blood further and worsen the heart failure which may be present in severe anaemia. These children need early **fresh**

whole blood transfusion, where the red blood cells will improve oxygen-carrying capacity, and the plasma will support the circulation and supply coagulation factors. If only stored blood is available, it should be packed to provide predominantly red blood cells. In the absence of a suitable centrifuge, hanging the bag vertically allows the red cells to fall to the bottom of the pack and these can be transfused first.

- **HIV/AIDS:** again diagnosis may be difficult, as physical signs and laboratory tests may be unreliable. A low threshold for treatment of suspected sepsis with broad-spectrum antibiotics is recommended (*see* Section 6.2.D).
- **Lack of PICU or high-dependency care facilities:** even in children with good nutrition, no severe anaemia and no other long-term debilitating condition, the amount of fluid infusion required to successfully treat some cases of septic shock is sufficient to induce heart failure and pulmonary oedema. If facilities are available, intubation and ventilation, IV infusion of inotropic drugs such as dopamine and adrenaline, invasive cardiovascular monitoring, renal dialysis and other aspects of paediatric intensive care are required. The absence of these facilities limits the treatment that can be offered to children with septic shock.

Initial management of septic shock

Even though it may be clear on initial inspection that the child is in shock, the first priority must still be to call for help, manage the airway, manage breathing, and then manage the circulation.

Call for help.

Airway

Assess the airway by the simple technique of asking the child 'Are you all right?'

Any vocalisation such as a reply or crying indicates an open airway and some ventilation. In the absence of a response, formally open the airway with a head tilt/chin lift or a jaw thrust maneouvre (*see* Section 1.12), and assess breathing by looking, listening and feeling for its presence.

Breathing

All children with suspected shock must receive high-flow oxygen.

If possible, this should be given through a mask with a reservoir to achieve the higher concentrations. In the absence of spontaneous breathing give assisted ventilation with a bag-mask (*see* Section 1.13).

Circulation

Some assessment of weight will be necessary to calculate the amounts of fluid and antibiotics to be given. If the child is not malnourished, use the following formula:

weight in kg = 2 (age in years + 4).

If the child is malnourished, this formula can still be used, but perhaps a percentage such as 25–50% subtracted from the result.

Intravenous access with a short wide-bore venous cannula, or placement of **an intra-osseous line** (*see* Section 8.4.B), is vital. More than one line is preferable, as rapid fluid resuscitation may be required, and other drugs may need to be given simultaneously, but start IV treatment as soon as the first line is in place before seeking additional IV access (unless sufficient staff are available). Take blood for the following investigations: full blood count, glucose levels, electrolytes (including calcium and lactate levels if possible), blood grouping and blood cross-matching in all cases. Treat hypoglycaemia if it is identified (*see* Section 5.8.B).

Nutritional status: severe malnutrition

While starting to give fluid, assess the child's nutritional status (*see* Section 5.10.B). Look for visible severe wasting or **marasmus**. Follow the WHO criteria: 'Look at the arms, legs and chest. The marasmic child does not look just thin, but appears to be all skin and bone. The skin looks too large for the body, there is no fat on the child and you will see the outlines of the ribs. There is also severe muscle wasting of the arms, legs and buttocks. The head may appear relatively large because of wasting of the body.' Use the mid upper arm circumference (MUAC) (*see* Section 9) to **assess marasmus**, as the urgency of the child's need for treatment precludes a weight and height measurement.

Look also for kwashiorkor. Check for oedema of both feet. Look at the bare feet. Press the top of the foot gently with your thumb for a few seconds. Oedema is present if a definite dent is left in the tissues. Look and feel to determine whether the child has oedema of both feet.

Severe anaemia

In very anaemic children (with either obviously pale palms or haemoglobin levels of less than 3–4 grams/dL), crystalloid alone will worsen oxygen delivery to the tissues. These children need blood, either packed cells or a partial exchange transfusion, in addition to initial **slow** fluid resuscitation (*see* Section 5.10.B, Section 5.11.C and Section 8.4.B).

First fluid

The next step is to give fluid and antibiotics intravenously.

Malnourished and/or severely anaemic children

- **If the child is malnourished and/or anaemic (haemoglobin concentration < 5 grams/dL), fluid must be given much more carefully**. Give 10 mL/kg IV over 30–60 minutes. The recommended solution is Ringer-lactate solution or Hartmann's solution, each with 5% glucose (insert 50 mL of 50% dextrose into a 500-mL bag of the bolus fluid), but give normal saline (0.9%) if this is all that is available, also with 5% dextrose. For antibiotic treatment, see below.
- Give a bolus of 10 mL/kg of fresh blood (if available) or stored blood over 15 minutes as soon as possible.
- Assess the child and **if they are not in clinical heart failure**, give another 10 mL/kg bolus of fresh or stored blood over 15 minutes.
  - **If the child is in heart failure**, give 10 mL/kg of blood as packed red cells over 2–3 hours, or use a partial exchange transfusion as follows: using a cannula in a large vein, withdraw 5–10 mL of the patient's anaemic blood (depending on the child's size) and infuse 10–20 mL, respectively, of new blood over 5 minutes and repeat 10 times.
- If the child is not improving after having been given the above treatment and antibiotics (see below), further

clinical interventions must be determined by the individual situation.

Normal nutrition

- **If the child is not malnourished**, infuse a crystalloid such as Hartmann's or Ringer-lactate solution as quickly as possible, but give normal saline (0.9%) if this is all that is available. In well-nourished children, the initial bolus volume of fluid to be given is usually 20 mL/kg, which is 25% of the child's circulating volume. Shock is not usually clinically evident until 25% of the circulation has been lost, so any child with signs of shock must have lost at least this amount of fluid from the circulation. For example, a child weighing 12 kg would need 240 mL of crystalloid. This fluid should be given as quickly as possible, usually over 5–10 minutes. It is easily given by pushing the fluid in using a 50-mL syringe.

Antibiotics

- While giving the first bolus of IV fluid, also give IV antibiotics if sufficient staff are available to avoid introducing delays with the first fluid bolus. The choice of antibiotics will depend on the clinical clues as to the infecting organism. In the presence of a purpuric rash (and in a non-endemic dengue area), meningococcus is the likely organism. Otherwise *Streptococcus* or *Staphylococcus* or Gram-negative organisms are candidates. A third-generation cephalosporin such as ceftriaxone or a combination of gentamicin and a penicillin would be advisable. Flucloxacillin should be added if *Staphylococcus* is suspected (e.g. if there are boils or a known abscess). In newborn infants or children with suspected intra-abdominal sepsis, Gram-negative organisms are likely. Metronidazole should be given to cover anaerobic organisms if clinically appropriate.

Reassessment

- The next very important step before a second IV bolus is given is to **reassess the patient's vital signs** to see if the fluid has helped. Check the pulse rate, capillary return, limb temperature and blood pressure, and pay particular attention to the child's mental status. Observe the parent–child interaction. Is the child more or less responsive to the parent? Look for signs of heart failure (i.e. raised jugular venous pressure, enlarged liver, and crackles in the lung bases).
- If the child still shows the signs of shock, give further fluid. If there are signs of fluid overload with or without heart failure, stop the IV fluid.

Further fluid

- If there has been a little improvement or no improvement, give **a further bolus of 10–20 mL** of fluid. Reassess the child after each 10 mL/kg of fluid, checking the pulse rate, capillary return, limb temperature, blood pressure and alertness, and looking for signs of heart failure, raised jugular venous pressure, enlarged liver, and crackles in the lung bases.
- Once a total of 40 mL of fluid have been given, there is an increasing risk that you will cause fluid overload with pulmonary oedema, which will make the child worse, not better. The problem is that there may still be leakage of fluid out of the circulation (into which you have been infusing the crystalloid or other fluid), which makes the tissues oedematous but leaves the circulation still hypovolaemic and the tissues under-perfused.

Inotropes

- One response to this situation is to give an infusion of a drug that stimulates the heart to pump harder and supports the circulation (an inotrope). **Dopamine is a very potent drug and must be given carefully.** It should be given into a peripheral vein or intra-osseously at a starting dose of 5 micrograms/kg/minute. The dose can be increased in steps up to 20 micrograms/kg/minute if lower doses do not help.

Dopamine infusion

- Make up 0.3 mg/kg of dopamine in 500 mL of Ringer-lactate or Hartmann's solution or normal saline. This will give 0.1 microgram/kg/minute if run at a rate of 1 mL/hour. Use an 100-mL paediatric burette in the infusion line for this fluid. The burette can then be filled with a further 100 mL and a further dose of dopamine added when necessary. To give 5.0 micrograms/kg/minute, give 50 mL/hour of this dilution for a child. Do not forget that the fluid that you are using for the infusion must be included in your calculations of total fluid given. If higher doses of dopamine are needed, a more concentrated solution of dopamine should be used or too much fluid will be given.
- If dopamine is not available or is not having any significant effect in the larger doses, then adrenaline, which is more potent than dopamine, may be tried.

Intermittent adrenaline infusions

- Dissolve 0.1 mL of 1 in 1000 adrenaline or 1 mL of 1 in 10 000 adrenaline in 10 mL of 0.9% saline and give 1 mL IV in a child (100 microgram) or 0.2 mL in an infant (20 micrograms). Check the response (in particular of blood pressure), and repeat after 15–30 minutes if it helps to improve perfusion. Then intermittently give further doses as required (1 mL of this solution contains 100 micrograms).
- It must be emphasised that in the absence of paediatric intensive care, the above infusions of inotropic (circulation-supporting) drugs are an attempt to save a child in extremis, and may not be effective.
- Once the infusion of inotropes has been started and the child's vital signs reassessed, fluid may cautiously be continued, reassessing frequently and stopping the infusion if signs of heart failure appear.
  - If there is a skilled operator (an anaesthetist or surgeon) available, the placing of a central venous line would be very helpful for monitoring the venous pressure (around + 8 mmHg is a good target) and for infusing the dobutamine or adrenaline centrally.
  - Once 60 mL/kg have been given in total along with inotropes, further fluid is unlikely to be beneficial unless skilled ventilation is available.
  - In this situation, provided that adequate facilities and expertise are available, positive pressure ventilation through an endotracheal tube (usually with positive end-expiratory pressure) can assist the circulation and help to manage the effects of any pulmonary oedema.

Reviewing the full blood count and biochemistry

- Blood tests were taken at the beginning of treatment, but it is useful to check the blood tests again (taking the blood from a vein with no IV in place).
  - Check the haemoglobin level to see whether there is now a need for a blood transfusion (fresh blood would be best). Studies have shown that the haemoglobin concentration should ideally be above 10 grams/dL when treating shock in children.
  - Check the blood glucose level and treat with 2 mL/kg of 10% dextrose in a neonate and 2–5 mL/kg of 10% dextrose in an older infant or child if the level is less than 2.5 mmol/litre. Also add glucose to any infusion fluid.
  - Check the calcium level, and if the concentration of ionised calcium is less than 1 mmol/litre, give 0.3 mg/kg of 10% calcium gluconate IV slowly (over 30 minutes, as calcium can cause cardiac arrest if given too quickly).
- Consider giving 0.5–1 mmol/kg of sodium bicarbonate (0.5–1 mL/kg of 8.4% sodium bicarbonate) over 15 minutes IV for refractory acidosis that is not responding to fluid resuscitation and effective ventilation.

Steroids

- There is some evidence that IV steroids can be helpful in some cases of septic shock. If the suspected organism is meningococcus or the child has previously been on a prolonged course of steroid treatment (e.g. for nephrotic syndrome), IV hydrocortisone can be given at a dose of 1–2 mg/kg/day in divided doses or as a continuous infusion. Occasionally higher doses up to 50 mg/kg/day have been used.

Further treatment

- Many children with septic shock may respond to the above treatments. For those who have not done so, paediatric intensive or high-dependency care is needed. If this is available, contact should be made with the PICU team as soon as it becomes clear that the child has septic shock. Advice on their care can then be given by experts and arrangements made, if possible, for the child to be 'retrieved' by the intensive care team coming to stabilise and transfer them.

5.6 Renal disorders

5.6.A Medical renal disorders

BOX 5.6.A.1 Minimum standards

- Accurate weight-measuring scales.
- Fluid input and output charts.
- Urine microscopy, culture and sensitivity.
- Antibiotics: trimethoprim, cephalosporins, amoxicillin, nitrofurantoin, gentamicin, penicillin.
- Blood biochemistry: urea, creatinine, sodium, potassium, chloride, bicarbonate.
- Urinary electrolytes.
- Full blood count.
- Ultrasound scan.
- Blood pressure measurement.
- Furosemide and chlorothiazide.
- Nifedipine or amlodipine, hydralazine, propranololol or atenolol, captopril or enalapril.
- Prednisolone, levamisole and cyclophosphamide.
- IV albumin.
- Analgesia: morphine.
- IV Ringer-lactate solution, Hartmann's solution, phosphamide and 5% albumin.
- IV glucose 10% and insulin.
- Sodium bicarbonate, calcium gluconate, calcium resonium and calcium carbonate.
- Antihypertensive drugs.

Introduction

Common renal investigations: plasma or serum biochemistry

Electrolytes

Sodium (Na^+) and potassium (K^+) assays are essential for the logical management of children with kidney dysfunction. Bicarbonate (HCO_3^-) is also extremely helpful, but more difficult to measure.

Problems with fluid and electrolyte balance are common in ill children. They can occur in a wide variety of clinical situations and with a wide range of underlying diagnoses. A methodical approach to history taking and clinical examination is therefore essential, and interpretation of biochemical results must always be done in the context of the clinical situation.

TABLE 5.6.A.1 Maintenance water, sodium and potassium requirements

	Age Preterm	Term	1 year	5 years	12 years
Sodium (mmol/kg/24 hours)	5	3	2	2	1
Potassium (mmol/kg/24 hours)	5	3	2	2	1
Water (mL/kg/24 hours)	200	150	100	75	50
Fluid (mL/kg/hour)	8	6	4	3	2

Dehydration and hypovolaemia

Fluid within the body is distributed between the intracellular fluid (ICF) and extracellular fluid (ECF) compartments, the ECF being composed of the intravascular and interstitial components. Differential solute composition of the ICF and ECF compartments is maintained by cell membrane pump activity and solute size and electrical charge. Fluid movement is regulated by a balance between osmotically active solutes and hydrostatic pressure.

It is useful when clinically assessing the fluid volume status of a patient to try to consider which compartment has insufficient or excess volume.

The effects of ECF volume depletion are usually shared between the intravascular and interstitial compartments, and are seen as hypovolaemia and dehydration, respectively. However, assessment can be complex. For example, in a condition like nephrotic syndrome, on examination there may be weight gain and oedema. However, since there is hypoalbuminaemia, and albumin is the primary intravascular osmotic component, the intravascular fluid volume may be low but the total ECF volume is high. Conversely, in acute renal failure there can be weight gain and oedema in a situation where both the total ECF and the intravascular volume are high. In heart failure, oedema can be present with high, normal or low intravascular volume, depending on other additional pathologies. In summary, oedema can occur with high, normal or low intravascular fluid volume, which makes the clinical history and a full examination vitally important for understanding the individual patient.

Often, in dehydration, sodium and water have been lost in an approximately normal ratio and therefore the deficit should be replaced as Ringer-lactate or Hartmann's solution. Normal saline can be used if these two solutions are unavailable, but it is less satisfactory because large volumes cause the patient to develop a hyperchloraemic acidosis, due to the larger chloride load in normal saline than there is in plasma.

Practical point

When prescribing rehydration fluids:

A Make an assessment of volume deficit and replace this as Ringer-lactate or Hartmann's solution.
B Calculate maintenance fluids and insensible losses.
C Initially estimate, and then measure, ongoing losses and replace them appropriately in volume and content.

Fluid prescription should consist of A + B + C.

Aim to treat cardiovascular collapse or 'shock' quickly over the first 1–2 hours. Infuse Ringer-lactate or Hartmann's solution to restore the circulating blood volume, reviewing to assess the response (*see* Section 5.5.A), and thereafter use a slow replacement rate so that the total deficit is replaced over at least 24 hours.

In hypernatraemic dehydration, after an acceptable cardiovascular state has been restored, aim to reduce plasma sodium levels slowly over 24–48 hours by altering the sodium concentration of the infusion fluid appropriately, and repeatedly monitoring the rate of fall of the plasma sodium and urinary sodium concentration.

Fluid and electrolyte disorders

Good management depends on measurement of input and output, plus **repeated:**

- clinical examination
- biochemical data on urine and blood
- weight measurements.

Hyponatraemia

Hyponatraemia is defined as a plasma sodium concentration of less than 130 mmol/litre, and it occurs when there is:

- sodium loss in excess of water loss
- **or** water gain in excess of sodium gain.

The total body sodium level may be high, low or normal, and therefore initial and ongoing clinical assessment of the extracellular fluid volume is essential.

Hypernatraemia

Hypernatraemia is defined as a plasma sodium concentration greater than 150 mmol/litre, and occurs when there is:

- water loss in excess of sodium loss
- **or** sodium gain in excess of water gain.

Again, the total body sodium level may be high, low or normal.

TABLE 5.6.A.2 Clinical estimation of ECF volume deficit in dehydration

Mild 3–5% weight loss	Thirsty Mucous membranes dry Decreased skin turgor
Moderate 5–10% weight loss	Increased severity of the above Depressed fontanelle Sunken eyes Tachycardia
Severe 10–15% weight loss	Increased severity of the above Drowsiness, confusion or coma 'Shock' Cool peripheries Prolonged capillary refill time Hypotension

Hypernatraemic dehydration: water loss in excess of sodium loss

Because sodium is the principle ECF osmole, the ECF volume is relatively well maintained, and signs of dehydration and hypovolaemia are less apparent.

Creatinine

Plasma creatinine concentration is the best available, most clinically useful and relatively inexpensive guide to glomerular renal function. It is easily, quickly and cheaply measured on a small blood sample. Individual measurements are of use in determining whether renal function is within the normal range. Sequential measurements are useful for following deterioration or improvements in renal function over a short time scale of hours or days, or over a long time scale of months or years. Although formulae can be used, the following guidelines allow the glomerular filtration rate (GFR) to be estimated in most clinical situations.

The plasma creatinine concentration depends on the bulk of the patient's muscle (where it is produced) and the patient's height, so on average men have higher values than women, and older children have higher values than babies, except in the first few days of life (*see* Table 5.6.A.3).

For example, a creatinine concentration of 150 mmol/litre in a well-nourished 5-year-old girl would be three times the upper limit of normal, indicating a GFR of one-third normal. The same creatinine concentration in a very undernourished girl with little muscle bulk would imply a GFR considerably lower than one-third.

TABLE 5.6.A.3 Upper limit of normal plasma creatinine concentrations

Subject	Plasma creatinine concentration (micromol/litre)	Plasma creatinine concentration (mg/dL)
Well-nourished average man	100	1.15
Well-nourished average woman	75	0.85
Well-nourished average 10-year-old child	60	0.70
Well-nourished average 5-year-old child	50	0.65
Well-nourished average baby or toddler	40	0.45
Baby aged 3 days to 3 weeks	Variable	
Baby in first 2 days of life	Maternal	

Urea

Although useful for managing children with renal failure, urea concentration is an inaccurate way of measuring renal function because it is also highly dependent on hydration, and on carbohydrate and protein intake.

Urine biochemistry

Concept of fractional excretion

Clearance of any substance which is filtered by the glomeruli and then reabsorbed by the tubules can be compared to the clearance of creatinine which is filtered and then excreted largely unmodified by the tubule. The fractional excretion is that fraction of substance *x* that has been filtered at the glomerulus that actually reaches the urine.

$$\text{Fractional excretion (FE) } x\ \% = \frac{\text{urine } x}{\text{filtered } x} \times 100$$

Fractional excretion of sodium

Normally, most of the filtered sodium (Na^+) is reabsorbed; the majority of this reabsorption occurs in the proximal tubule. When plasma sodium is normal and the patient is not shocked, physiologically fractional excretion of sodium can vary. However, calculating FE Na can give useful clues in pathological states.

The normal renal response to intravascular fluid volume reduction is to excrete urine with a low sodium content. It does this by a number of mechanisms, including reduction of glomerular filtration rate (GFR) and aldosterone-stimulated sodium reabsorption, which requires intact tubules.

Fractional excretion of sodium (FE Na) is calculated from the urine (U) and plasma (P) concentrations (check that P and U creatinine values are expressed in the same units), using the following formula:

$$\text{FE Na (\%)} = \text{U/P sodium} \times \text{P/U creatinine} \times 100.$$

TABLE 5.6.A.4 Interpretation of excretion of sodium in pathological processes

	FE Na	Interpretation
Shock	< 1%	Tubules functioning = pre-renal failure
	> 1%	Acute tubular necrosis (ATN)
Hyponatraemia	< 1%	Salt loss or water overload (appropriate renal response)
	> 1%	Renal salt wasting (tubular disease)
Hypernatraemia	< 1%	Renal concentration defect
	> 1%	Salt overload (may be abuse)

Urine collection and examination

Collecting urine from babies can be time consuming, but is important in establishing a diagnosis.

Methods of urine collection

- Clean catch into a sterile pot.
- Sterile collecting pads are cheaper and easier to use than an adhesive bag.
- For toddlers it is fine to use a potty or equivalent which has been thoroughly washed in hot water and detergent (using antiseptics or bleach, or scalding with boiling water, are unreliable).
- Suprapubic or catheter urine sampling is useful in ill children when antibiotics need to be started without delay.

Stick testing of urine and protein measurement

- Dipstick testing for blood, protein and glucose is useful and reliable.
- Stick testing for nitrite to identify urinary tract infections (UTIs) is useful when positive to rule in UTIs, but unreliable when negative because it remains negative in 50% of cases.
- Stick testing for white cells to diagnose UTIs is unreliable because they may occur without white cells, and because white cell numbers also increase in the urine of febrile children without UTIs.

Laboratory measurement of protein in urine

Urine protein should be < 20 mg protein/mmol creatinine in an early-morning sample of urine.

In nephrotic syndrome there is typically > 500 mg protein/mmol creatinine.

Microscopy of urine

Microscopy of unspun fresh urine can provide a cheap and reliable way of rapidly diagnosing UTIs (by identifying bacteria directly, rather than by counting white cells), and of diagnosing schistosomiasis.

Red blood cells can be identified as being due to glomerulonephritis (when they are small, fragmented and of varied and distorted shapes), or due to other causes, such as trauma, stones or bladder inflammation (when they are all similar, and typically biconcave).

A standard light microscope with a magnification of × 400 is sufficient. Using a counting chamber (or a microscope slide with a scratched surface) and cover slip ensures that the microscope is focused at the correct plane, otherwise it is not possible to tell when microscoping a normal urine. A counting chamber with a mirrored surface is not essential, but makes identification of bacteria easier. Phase contrast makes identification even easier. A highly reliable, almost pocket-sized microscope (McArthur) is available with phase contrast.

Urinary tract imaging techniques

All renal imaging techniques are relatively expensive, and many will have limited availability.

Ultrasound scanning

Useful information can only be obtained from ultrasound scanning by a skilled operator using an adequate machine. It demonstrates anatomy, but not function. It is ionising radiation free, and, when available, is now the first choice for initial imaging of most renal conditions in children. It is excellent at demonstrating cysts, stones and dilatation, and has a similar sensitivity to the intravenous urogram (IVU) for demonstrating long-standing or extensive scarring. Nephritis causes echo brightness of the kidneys. Tumours and cysts are easily seen, usually before they are visible by other modalities. Stones can be easily identified, but may be misinterpreted by the inexperienced because the whole stone is not seen; a bright line identifies where the ultrasound hits the front edge of the stone, and an acoustic shadow is thrown behind it. Nephrocalcinosis can be detected easily as white renal pyramids long before it can be seen on X-rays.

Ultrasound scanning during the acute phase of the UTI will often show dilation of the ureters. It is therefore suggested that this investigation should be undertaken 2–3 weeks after the infection. Any dilation of the ureters should then be regarded as significant.

Micturating cystogram (MCUG)

This is still the most reliable way to assess vesico-ureteric reflux (VUR), but unfortunately depends on invasive urethral catheterisation, and depending on the equipment used it may require a relatively high dose of radiation. It should be reserved for use when the result will affect management. (Reflux is less commonly found in Afro-Caribbean children.)

This investigation is very important to confirm posterior urethral valves, one of the commonest obstructive uropathies seen in Afro-Caribbean children. The age of presentation is variable. When it presents in the neonatal period there is usually severe renal involvement.

Plain abdominal X-ray

This demonstrates radio-opaque stones, but these and nephrocalcinosis are usually easier to see on an ultrasound scan.

Urinary tract infections (UTIs)

Background

UTIs are very common. The risk of UTI is increased in babies with anatomical nephro-urological abnormalities, those with obstruction, those with VUR, and in girls. Management of VUR is controversial (*see* Section 5.6.B). Recent studies have shown that about 10% of girls and 3% of boys will have had a UTI diagnosed by the age of 16 years in the UK. Most children with UTIs have no underlying renal tract problem and suffer no serious consequences. However, UTI may be the first indicator of underlying renal tract abnormality, and may be associated with acquired renal scarring. Distinguishing the small group of children with important findings in this common condition remains a challenge, and the question of how intensively to investigate children after UTI remains controversial.

Large scars may cause renal failure, but even small ones can cause hypertension, often in later childhood or in adulthood. **To prevent serious sequelae of hypertension, children with scars should have lifelong blood pressure monitoring, as symptoms do not occur until serious irreparable disease is present.**

Infants are the most vulnerable to scarring, and most children who will acquire scarring will have started to do so by the age of 4 or 5 years. Animal studies and case series suggest that a UTI in a vulnerable individual may cause permanent scarring rapidly, in a matter of a very few days.

Diagnosis

Symptoms

Older children may present with typical 'cystitis' symptoms, typically due to bladder and urethral irritation, such as frequency and dysuria. Loin pain suggests likely upper renal tract involvement, but some children have few or no symptoms. Younger children (under 2 years of age) often only have non-specific symptoms such as anorexia, failure to thrive, unexplained fever or prolonged jaundice. Therefore all young children with an unexplained illness, particularly with a fever, should have a UTI excluded.

Urine testing

A diagnosis is usually made by culture of a pure growth of one species of bacteria (most commonly *E. coli*) at a concentration of more than 10^5/mL. Any concentration of bacteria in a suprapubic urine sample suggests infection. White blood cells (> 50/microlitre) are usually considered helpful in making the diagnosis, but UTIs can occur without any white cells (sometimes because they lyse in minutes), and urinary white blood cells can be found in children with fever who have some other cause and do not have a UTI.

As stated above, the organism most commonly involved is *E. coli.* If unusual organisms such as *Pseudomonas* are cultured at the first episode of UTI, it is mandatory to rule out an underlying urinary tract abnormality.

Microscopy

Microscopy of freshly voided unspun urine is a quick, reliable and cheap way to diagnose UTIs if a × 400 microscope is available, and it enables an immediate diagnosis to be made. This allows the best-guess antibiotic to be started at once. Infected urines need to be cultured to obtain antibiotic sensitivities. Infected urine will contain many bacteria, up to thousands per high-power field, depending slightly on the depth of urine under the cover slip. The bacteria will all look the same, and are typically rods of identical length. Occasionally, UTIs are caused by streptococci, which are seen as long chains of dots. Separate small dots that appear to be swimming are not streptococci, but are phosphate crystals (the shimmering movement is due to Brownian motion). Most but not all children with UTIs will also have > 50 white blood cells/microlitre, or at least 1 per 10 high-power fields.

If no bacteria are seen in about 5 high-power fields, the urine is not infected; the samples therefore need no further testing and can be discarded. Urine samples containing less than 1 bacterium per high-power field, or mixtures of rods and cocci, are likely to have been contaminated. Because this can be identified quickly, further samples can and should be collected until a clearly uninfected or infected one is obtained.

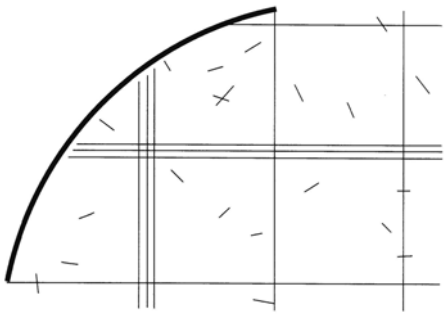

FIGURE 5.6.A.1 Rods seen in 10 high-powered fields.

Imaging

Imaging after the first UTI is controversial. Young children and infants warrant more intensive investigation, as do those with a family history of renal disease.

Ultrasound scanning

This should be undertaken for all children after their first recognised UTI in order to identify structural abnormalities, and to try to identify scars. The likelihood of detecting a scar is much greater if it is large, involving multiple renal segments, or several years old, so that it will have had time to shrink and distort. Negative scans in young children (under 4 years) therefore need to be interpreted with caution.

Ultrasound scanning during the acute phase of the UTI will often show dilation of the ureters. It is therefore suggested that this investigation be undertaken 2–3 weeks after the infection. Any dilation of the ureters should then be regarded as significant.

Micturating cystogram (MCUG)

It is probably ideal to perform an MCUG on very young children who have had a definite UTI. It is recommended that an MCUG be performed on all those under 1 year of age, because about a third will have an anatomical abnormality detected, usually vesico-ureteric reflux (VUR). However, there is not universal agreement about this, as there is a high percentage of normal results.

Posterior urethral valves may present with a UTI, especially in parts of the world where there is little or inadequate antenatal scanning. Thus in baby boys who have had a UTI, a good view of the urethra is essential.

Children with VUR are at risk of developing scars with UTI. Therefore finding VUR should make you suspect that the child may have a scar that was not identified by ultrasound.

Management of VUR is controversial (*see* Section 5.6.B). Prophylactic antibiotics may reduce the recurrence of infection; awareness and rapid treatment of infection is important. Most VUR is self-resolving and the aim of medical treatment is to keep free of UTI while allowing natural resolution (over a period of years). The possibility of VUR should be considered and, if possible, tested for if scarring is identified on ultrasound scanning.

Most VUR resolves with time; the lower the grade, the more likely it is that resolution will occur (80–90% resolution of grade 1–2 over 5 years).

Treatment of UTIs

Encourage a high fluid intake to produce dilute urine and reduce the symptoms of dysuria.

Treat the child for 7 days initially with:

- oral trimethoprim (4 mg/kg twice daily)
- **or** cephalexin (10 mg/kg three times daily)
- **or** amoxicillin (1 month to 1 year 62.5 mg: 1–5 years 125 mg: 5–18 years 250 mg, all three times daily)
- **or** nitrofurantoin (3 months to 5 years: 750 micrograms/kg 4 times daily, 12–18 years: 50 mg 4 times daily).

Intravenous antibiotics may be necessary for very unwell children (particularly under 2 years of age) for as long as they are unable to tolerate oral medication. This may include **gentamicin** 7.5 mg/kg as a loading dose and then 7.5 mg/kg once daily only after confirmation that the plasma creatinine concentration is normal. If there is renal failure, no more should be given after the single dose, unless blood levels are available to guide the dosage. If necessary, change the antibiotic according to the laboratory sensitivity testing, when and if it is available.

Use of prophylactic antibiotics is controversial. Use may reduce recurrence of UTI and should be considered when there is VUR. A night-time dose of trimethoprim (2 mg/kg) or cephalexin (12.5 mg/kg maximum 125 mg) or nitrofurantoin

(1 mg/kg) may be used. Do not use amoxicillin for prophylaxis, because resistant organisms are likely to emerge.

In many resource-limited countries where there may be inadequate procedures for ensuring that antibiotics are used appropriately and where disposal of body fluids containing antibiotics may contaminate drinking water supplies, UTIs are resistant to trimethoprim but remain sensitive to cephalosporins and amoxicillin. Ideally, where available, cultures for antibiotic sensitivity should be undertaken.

Hypertension

Background

There is a steady increase in blood pressure with age, and definitions of hypertension are arbitrary. However, in most children with hypertension the blood pressure becomes very much higher than normal (unlike the majority of adult hypertension patients, whose blood pressure is only moderately elevated, causing a skewed frequency distribution curve). Primary hypertension is rare in children, and in more than 80% of them hypertension is secondary, and in at least 75% it is renal in origin. Diagnosis of the underlying cause is therefore very important in management. Children are relatively intolerant of hypertension, so they are at major risk of sequelae, especially encephalopathy, blindness and death.

Measurement

Blood pressure is best measured with a simple sphygmomanometer, as automatic blood pressure machines may be unreliable. It is more reliable to use the largest cuff that will fit on to the upper arm, rather than using 'formulae' that relate the cuff size to the child's size. A cuff that is too large will not significantly underestimate the blood pressure, but one that is too small will overestimate it. In children, it is best to use systolic blood pressure; it is just as important as diastolic pressure for diagnosis and treatment, and is easier and more reliable to measure. In most children, palpating the reappearance of the pulse at the wrist is as accurate as using a stethoscope at the antecubital fossa, or a Doppler (if available) may be used at the wrist to detect the reappearance of the pulse. High values should be confirmed with the child relaxed to reduce the effects of anxiety. Measurements should be repeated several times if they are abnormal. Table 5.6.A.5 shows the upper limit of normal blood pressure ranges according to age.

TABLE 5.6.A.5 Mean, upper limit of normal and dangerous levels of systolic blood pressure in children of different ages

Value	1 month	1 year	5 years	10 years	15 years
Mean (mmHg)	75	85	95	105	115
Upper limit of normal (mmHg)	80	90	100	110	125
Needing urgent treatment (mmHg)	100*	120	130	140	150

*In infants, the likeliest cause of hypertension is coarctation of the aorta.

TABLE 5.6.A.6 Oral hypotensive drugs* for children, with maximum doses

Class of drug	Example	Maximum dose (mg/kg/day)
Calcium-channel blocker	Nifedipine	1
Vasodilator	Hydralazine	10
Beta-blocker	Atenolol	1
Angiotensin-converting-enzyme (ACE) inhibitor†	Captopril	5

* These are often given in combination to achieve a powerful effect with fewer side effects.

† ACE inhibitors must be started by giving a very low test dose first and building up slowly. They must be used with great care if renal artery stenosis is suspected.

Causes and diagnosis

It is important to find the underlying cause of the hypertension to guide management. Sometimes the cause is clear from the history, examination or urine testing, and sometimes it requires diagnostic imaging. Ultrasound is the most useful screening technique, but is quite operator dependent. Hypertension can be caused by renal scarring that is difficult to detect with ultrasound.

Treatment

If the hypertension is known to be of recent onset, as in acute glomerulonephritis, it is safe to reduce the blood pressure quickly. Usually salt and water overload is a major factor; if so, restrict sodium and give furosemide 1–2 mg/kg (the oral route is as effective as the intravenous one).

In other cases, treat the blood pressure slowly because cerebral arterial vasoconstriction may have occurred to protect the brain parenchyma from the impact of the hypertension, and made the cerebral blood flow dependent on a high blood pressure being sustained.

A rapid fall in blood pressure may cause cerebral infarction and blindness. Reduction over 2 days or more allows the vascular tone to return to normal. **Slow control may be achieved by introducing oral hypotensive drugs slowly at well below the maximum dose.**

Glomerular disease

Glomerular disease is characterised by proteinuria with or without haematuria. It may be caused by a primary glomerular disease or be secondary to a systemic illness, and it can cause a wide spectrum of clinical pictures, including the following:

- nephrotic syndrome
- acute glomerulonephritis
- chronic glomerulonephritis
- asymptomatic proteinuria or haematuria.

TABLE 5.6.A.7 Renal and arterial causes of hypertension in childhood

Diagnosis	Notes	Renal ultrasound
Reflux nephropathy	Also called pyelonephritis (*see* UTI)	Focal scars or shrunken kidney
Glomerulonephritis Post-infective Other causes	Typically have proteinuria and glomerular haematuria. Typically after a streptococcal infection, sore throat/skin infection. Give a 10-day course of penicillin May have evidence of Henoch–Schönlein purpura or lupus; if not, renal biopsy is needed	Echo bright
Inherited polycystic disease Infantile type (recessive) Adult type (dominant)	Kidneys large at birth, typically severe hypertension, renal failure in early life Seldom causes renal failure in childhood, but may cause hypertension. Screen blood pressure of children of affected parents	Huge, homogeneous, echo bright Discrete cysts develop through childhood
Narrowed arterial supply Coarctation of the aorta Renal artery stenosis	Check femoral pulses; may need surgical treatment or balloon angioplasty Requires long-term medical treatment. May occur with neurofibromatosis; screen for this	May be small, and difficult to diagnose without expensive imaging

Nephrotic syndrome

Background and clinical features

The clinical picture is of proteinuria, hypoalbuminaemia and oedema.

It must be differentiated from other causes of hypoalbuminaemia, such as protein malnutrition (*see* Section 5.10.B) and protein-losing enteropathy (*see* Section 5.12.D).

It is traditionally classified as early-onset (congenital, diagnosed at under 6 months of age) and later-onset types.

Early onset

Children with congenital nephrotic syndrome frequently do not survive, many of them dying early of protein malnutrition, infection or thrombosis unless they are aggressively treated.

Those with severe proteinuria, including the recessively inherited Finnish type, tend to fare worst. Diffuse mesangial sclerosis is a similar condition, but is usually less acute. Congenital syphilis can cause neonatal nephrotic syndrome which may respond to penicillin treatment. Some early nephrotic syndromes are self-resolving, but this is uncommon.

Treatment is often difficult. Early-onset nephrotic syndrome is generally not responsive to steroids. Treatment may be supportive, including frequent albumin infusions, and in the most severe cases may require early unilateral or even bilateral nephrectomy, leading to dialysis and transplantation. Reduction of proteinuria by the use of ACE inhibitors or indomethacin may be attempted, but very careful monitoring is required.

Later onset

Most children with nephrotic syndrome presenting in childhood (after the age of 1 year and before the teenage years) are steroid responsive, losing their proteinuria within 1 to 2 months of treatment. They share clinical characteristics (*see* Table 5.6.A.8). Children with steroid-resistant nephrotic syndrome may have a range of diagnoses, including focal segmental glomerulosclerosis, Henoch–Schönlein purpura, lupus and mesangiocapillary glomerulonephritis. There is a strong association with infections, especially malaria and hepatitis B, as well as hepatitis C and HIV.

Acute management

It is reasonable to attempt to induce a remission with steroids, unless the clinical picture virtually excludes the possibility of steroid sensitivity.

- Use prednisolone 60 mg/m^2 daily (*see* Section 9 to convert from body weight to surface area) for up to 6 weeks (about 95% of children who are going to respond do so within 1 month). Monitor carefully for the development of hypertension on steroids.
- Limit fluid retention by imposing a tight dietary sodium restriction.
- Prevent secondary pneumococcal infection with prophylactic penicillin V (125 mg twice daily up to 5 years of age, and 250 mg twice daily thereafter).
- Avoid the sequelae of hypovolaemia (thrombosis).
- Intravascular hypovolaemia is a high risk and should be monitored clinically by the appearance of cold peripheries and sometimes abdominal pain. There may be initial paradoxical hypertension, and hypotension may not occur until late. The best laboratory test is a urinary sodium concentration of less than 15 mmol/litre, especially if combined with a urine osmolality of over 800 osmol/kg. Blood tests are seldom helpful.
- Treatment of hypovolaemia should be with 1 gram/kg

TABLE 5.6.A.8 Clinical characteristics of steroid-sensitive and steroid-resistant nephrotic syndrome

Feature	Steroid-sensitive nephrotic syndrome	Steroid-resistant nephrotic syndrome
Gender	Male > female	Varies with condition
Age	1–3 years	Usually older
Blood pressure	Normal	Often elevated
Speed of onset	Rapid (days or weeks)	Usually weeks or months
Haematuria	Microscopic	Often macroscopic
Plasma creatinine concentration	Normal or low unless hypovolaemic	May be elevated

of IV 20% albumin over 4 hours, preferably with 2 mg/kg of IV furosemide given halfway through. If shocked, give 10 mL/kg of 4.5% albumin.
- Avoid the use of furosemide in the acute situation without adequate volume replacement.

Subsequent management if steroid-sensitive

This is ideally based on daily home monitoring of the morning urine protein level by stick testing. A common definition of a relapse is ++ proteinuria for 7 consecutive days, or +++ for 3 days, and it should be responded to by reintroducing salt restriction, penicillin V and prednisolone.

Protocols for doses and duration of use of prednisolone and steroid-sparing agents vary. The following is a proposed example:

First presentation: give prednisolone 60 mg/m^2 daily (*see* Section 9), and if the patient responds (by loss of proteinuria), complete 6 weeks of 60 mg/m^2 daily, followed by 40 mg/m^2 on alternate days for a further 6 weeks.

Subsequent relapse: restart 60 mg/m^2 daily until there is no proteinuria for 3 days, then give 40 mg/m^2 on alternate days for a further 4 weeks.

Frequent relapses: give prophylactic low-dose (e.g. 200 micrograms/kg) alternate-day prednisolone. Titrate the dose up until either relapses are prevented, or steroid side effects develop.

If steroid prophylaxis causes unacceptable side effects, add prophylactic levamisole 2.5 mg/kg on alternate days (approximately 50% of cases will benefit), which can be used relatively long term.

If levamisole is ineffective, consider giving cyclophosphamide 2.5–3 mg/kg daily for 12 weeks, monitoring weekly with white blood cell count, and reducing the dose if the absolute neutrophil count falls below 1 × 10^9/litre, or stopping if it falls below 0.5 × 10^9/litre. Or give 6 × monthly cyclophosphamide infusion (600 mg/m^2). Note that this is potentially dangerous in resource-limited circumstances where infections are frequent.

Subsequent management if steroid resistant

Persistent haematuria and hypertension at the first presentation may be early warning signs of steroid resistance. Steroids should be used with caution, as the hypertension may be aggravated.

There is a wide range of conditions that may induce steroid-resistant nephrotic syndrome. These include infective agents, autoimmune diseases, some drugs and poisons, and unknown causes. The cause may be apparent from the history and examination and other tests, but **in most cases the diagnosis relies on the accurate interpretation of a kidney biopsy**.

The infective causes include hepatitis B, HIV, *Schistosoma mansoni*, leprosy, tuberculosis and malaria. These conditions should be sought in those parts of the world where they are likely to be found, and treated appropriately. Hepatitis B typically causes a membranous nephropathy which tends to improve spontaneously. Post-streptococcal glomerulonephritis may cause nephrotic syndrome, but it is seldom the presenting feature. Although it is not the only cause of this clinical picture, **it is sensible to treat any child who develops nephrotic syndrome after an acute nephrotic illness with 10 days of oral penicillin V, 1–6 years 125 mg, 6–12 years 250 mg, 12–18 years 500 mg per dose 6-hourly.**

The autoimmune causes of nephrotic syndrome include Henoch–Schönlein purpura and IgA nephritis, lupus, mesangiocapillary glomerulonephritis, and some cases of membranous nephropathy. The commonest cause of steroid-resistant nephrotic syndrome in many parts of the world is focal segmental glomerulosclerosis (FSGS), the pathophysiological mechanism of which is unknown. In some of these conditions (including lupus, mesangiocapillary glomerulonephritis and FSGS), some children do respond to steroids. However, many children with steroid-resistant nephrotic syndrome do not respond to any treatment at all. Most of those who do only respond to more powerful immunosuppressants, such as cyclophosphamide or cyclosporine. Some conditions have been treated with plasmapheresis, but in most conditions the evidence for this is purely anecdotal. These treatments are difficult to use because they are expensive, and they require close monitoring for side effects. Even under ideal medical conditions with considerable resources, many cases still progress to end-stage renal failure.

Protein in the diet

Children with nephrotic syndrome may lose huge quantities of protein in their urine. If they are on a low-protein diet they will quickly lose muscle mass as the body proteins are utilised to synthesise plasma albumin. A relatively high-protein diet will be muscle sparing, but will make no significant difference to the plasma albumin concentration.

Glomerulonephritis

Glomerulonephritis (GN) strictly refers to inflammation of the glomeruli with cellular proliferation, although it is often used to include other glomerulopathies such as FSGS and membranous nephropathy, both of which typically cause steroid-resistant nephrotic syndrome.

The commonest cause of childhood glomerulonephritis varies widely across the world. In resource-limited countries, acute post-streptococcal glomerulonephritis is the commonest type. In wealthier countries this is now becoming more unusual, and IgA nephropathy predominates.

Post-streptococcal glomerulonephritis

This is caused by antibodies produced in response to specific strains of streptococci. These bacteria typically cause throat and skin infections. The antibodies then form complexes and are deposited within the glomeruli along with C3. Because it takes time for antibody production to occur, the signs and symptoms of nephritis do not usually begin to appear until 10–20 days after the start of the infection.

The inflamed glomeruli leak blood and protein, so the first symptom is usually the child passing smoky or frankly bloody urine. The glomerular filtration rate usually falls slightly, so the plasma creatinine concentration is typically slightly elevated. Also the tubules reabsorb sodium and water excessively, which causes water retention out of proportion to the fall in glomerular filtration rate. This leads to swelling, which is most easily noticed around the eyes and face, and in the legs, but which does not pit as easily as oedema does in the nephrotic syndrome. The water retention also leads to hypertension. Most children with acute post-streptococcal glomerulonephritis do not lose enough protein into the urine to cause nephrotic syndrome as well, although some do, producing a mixed nephrotic–nephritic picture.

A presumptive diagnosis is made by examination of the urine for the presence of protein (using stick tests) and glomerular red cells and casts (by microscopy; *see* Section 8.S), in a child with a history of a recent sore throat or skin infection. Culture of a specific strain of *Streptococcus* from a throat or skin swab may confirm the diagnosis.

It is not reliable to make a diagnosis from a single titre of an anti-streptococcal antibody such as the ASOT or the anti-DNase B, because many children have an elevated level from previous exposure to other strains of streptococci. Confirmation requires a significant rise between two titres taken at least 10 days apart.

If plasma complement levels (C3 and C4) can be measured, they may give a clue to the underlying diagnosis but are not confirmatory. In post-streptococcal glomerulonephritis the plasma C3 concentration is reduced, and often stays subnormal for up to 6 weeks before rising back to normal. The plasma C3 level is usually low in mesangiocapillary glomerulonephritis, and the C3 and C4 levels are often both low in lupus, and these conditions may present clinically identically to post-streptococcal glomerulonephritis.

Treatment

If post-streptococcal glomerulonephritis is suspected, immediately start penicillin V, 1–6 years 125 mg, 6–12 years 250 mg, 12–18 years 500 mg per dose four times daily for 10 days, to eradicate the organism. There is always a delay in obtaining bacteriological confirmation, either from culture or from paired titres, so it is best to start the penicillin at once, and use these tests as retrospective confirmatory evidence.

It is essential to measure the child's fluid intake and losses accurately as well as daily weighing, and restrict the amounts of sodium and water allowed. This should be to balance the losses, or to cause net fluid reduction if the child is significantly fluid-overloaded. The insensible loss is about 300 mL/m^2 daily, but will be higher in a hot dry climate. (Estimate the surface area from Table 9.16 in Section 9.) **Salt restriction is far more important than water restriction**, and is sometimes all that is required for a child to maintain fluid balance. This is because the tubules retain sodium avidly, so any salt that is eaten will be retained in the body and cause hypernatraemia. This drives an intense thirst, and it then becomes almost impossible to stop the child drinking. By contrast, a tight salt restriction will minimise the thirst, which aids management.

If the plasma albumin concentration is normal or only slightly reduced, it is safe to give an oral dose of furosemide, 1–2 mg/kg. This will increase the urinary excretion of sodium and water, and thus improve fluid overload and hypertension. It will also increase potassium loss, which is helpful if the fall in glomerular filtration has led to hyperkalaemia. It may be repeated as needed. However, if the child has a very low plasma albumin concentration from a mixed nephrotic–nephritic picture, giving furosemide may precipitate hypovolaemia. Because of this, either give intravenous albumin combined with furosemide (*see* section on acute management of nephrotic syndrome), or give furosemide under close observation and be prepared to give albumin if hypovolaemia occurs. Cold peripheries and abdominal pain (from splanchnic vasoconstriction) are important signs of this.

The raised blood pressure is frequently fully controlled by salt and water restriction and furosemide, but in some cases hypotensive agents are also needed (*see* Table 5.6.A.5). Under such acute conditions it is safe to reduce the blood pressure rapidly.

In children with post-streptococcal glomerulonephritis, the kidneys usually make a full recovery, and progression to renal failure is rare. Therefore most of these children will have no sequelae, provided that their fluid and electrolyte balance and blood pressure are carefully managed.

IgA nephropathy (Berger's disease)

The typical presentation is of a child aged 5–15 years who develops an acute upper respiratory tract illness, and simultaneously has heavy haematuria that lasts for several days. Urine microscopy reveals distorted 'glomerular' red cells (see above). Usually the urine then clears completely, but the haematuria may return with subsequent illnesses. Some children with IgA disease have a more insidious illness with little or no macroscopic haematuria.

The diagnosis is suggested in children who present with recurrent heavy glomerular haematuria. There may be a family history. The plasma IgA concentration may be elevated in affected children, but this test is a poor discriminator. In children with a less obvious clinical picture the diagnosis can only be made on a kidney biopsy. Antibody staining will show granular deposits of IgA in glomeruli that have mesangial proliferation. Histologically, IgA disease is identical to Henoch–Schönlein nephritis.

The best prognostic indicator in IgA nephropathy is the amount of proteinuria that persists between the acute episodes of haematuria. Most children have heavy haematuria but little or no proteinuria between attacks, and virtually all of these grow out of the condition, usually without any sequelae. Often the ones with the most dramatic haematuria recover particularly well. The children with a more insidious onset are more likely to have persistent proteinuria, and to continue with the condition into adulthood, eventually developing end-stage renal failure by middle age. There is no good evidence for treatments to prevent this happening. However, adequate blood pressure control is important in slowing the progression of renal disease.

Rarely, IgA disease first presents as a severe rapidly progressing glomerulonephritis. The picture is one of an acute nephritis in which the creatinine level rises rapidly and inexorably. It is therefore clinically indistinguishable from any other rapidly progressive glomerulonephritis, other than by renal biopsy. Treatment options include various immunosuppressive drugs and plasmapheresis. These have not been subjected to controlled trials, are expensive and may lead to serious complications.

Haematuria

- Urine test sticks are highly sensitive and detect the smallest traces of blood.
- **For most conditions that can cause haematuria, the clinical significance is best predicted by the quantity of protein present, so always test for that, too.**
- **The most important test for determining the cause of haematuria is to check the shape of the red cells, ideally under phase-contrast microscopy** (see above).

Macroscopic glomerular haematuria

The presence of distorted red cells may be due to any

form of glomerulonephritis, as listed above. The history of a simultaneous infection may suggest IgA nephropathy, while a recent infection points to post-streptococcal glomerulonephritis. The presence of a rash, or joint involvement, or abdominal pain might suggest Henoch–Schönlein or lupus nephritis as causes, but most other types can only be diagnosed on renal biopsy.

Macroscopic non-glomerular haematuria

The presence of red cells with a normal biconcave appearance indicates bleeding into the urine, and excludes glomerulonephritis as a cause. This may be due to trauma, but this would have to be major, because the renal tract is physically well protected. Minor trauma will only cause bleeding if the kidney is enlarged with cysts, as in adult-type (dominantly inherited) polycystic kidney disease, or if it is vulnerable due to being ectopically positioned. Urinary tract stones can also cause bleeding.

The cystitis caused by a urinary tract infection or by *Schistosoma mansoni* may cause frank haematuria. These can be distinguished on phase-contrast microscopy of a fresh sample, when either bacteria or ova are easily visible.

Although bleeding into the urine can be due to a malignancy, this is rare in childhood, and is then usually from a Wilms' tumour. Frank haematuria in a newborn suggests a renal vein thrombosis, which may be unilateral or bilateral, and the affected kidney is usually easily palpated.

Trauma, stones, an ectopic kidney, adult polycystic disease, a Wilms' tumour and renal vein thrombosis can each be identified by their characteristic appearance on ultrasound scanning. In cases for which no cause has been found, cystoscopy should be considered.

Microscopic glomerular haematuria

Blood may be detected in urine that looks completely clear. Rarely, the red cells appear normal on microscopy; these children should be investigated as for frank non-glomerular haematuria. Most children with microscopic haematuria have distorted 'glomerular' red cells. In this group, management depends on how much proteinuria they have. Those with massive nephrotic-level proteinuria should be assessed and managed in the same way as for other children with nephrotic syndrome. Those with moderate proteinuria are likely to have a form of glomerulonephritis. The vast majority of children will not have any proteinuria with their microscopic haematuria. Investigation of this group is unlikely to identify a cause. If the renal ultrasound scan is normal, these children should be monitored annually with just a urine stick test and blood pressure measurement. If the blood disappears, follow-up may be discontinued. If it persists without proteinuria or hypertension developing, continue the annual reviews. If proteinuria or hypertension appears, the child needs to be investigated accordingly.

Haemolytic uraemic syndrome (HUS)

HUS is a common cause of established (parenchymal) acute renal failure (see above). Children with HUS fall broadly into two groups, according to their pathophysiological mechanisms. It is important to divide them clinically into diarrhoea-associated HUS (D + HUS) and diarrhoea-negative HUS (D – HUS).

D + HUS

This is the common type, and it occurs in otherwise normal children, often in outbreaks or clusters of cases. It is triggered by a toxin that is produced by some colonic bacteria, including *Shigella* and some strains of enteropathic *E. coli*. Infection is from ingestion of contaminated food or fluids. Public health measures to identify a source of the organism are important in preventing and limiting outbreaks. Typically the child has several days of bloody diarrhoea, and then becomes pale and mildly jaundiced (from haemolytic anaemia), may bruise and have petechiae (from thrombocytopenia), and develops oligo-anuria. A blood film shows fragmented red blood cells and a low platelet count.

Antibiotics are not of benefit, and may worsen the condition by causing the acute release of more bacterial toxin. Blood transfusion may be needed (usually when the haemoglobin level falls below 6 grams/dL). Platelet transfusion may exacerbate the condition, and should only be used in the face of uncontrolled bleeding. There is no evidence that any specific medication is of benefit. Management is as for other children with acute renal failure (see above). Mortality from this condition has decreased with active management of fluid and electrolyte imbalance and dialysis.

In a minority of cases, D + HUS can affect other organs, sometimes severely. Effects can include bowel perforations, pancreatitis with diabetes mellitus, and cerebral involvement, with fits, coma and death.

The long-term outcome for children who survive the acute episode of D + HUS is relatively good. Most appear to fully recover renal function, although up to 25% have persistent hypertension or proteinuria. Few develop end-stage renal failure.

D – HUS

This variant is very rare, and is often associated with a functional or actual deficiency of factor H, so a minor trigger (such as a minor viral illness) can precipitate the typical clinical and haematological HUS picture, but without a diarrhoeal prodrome. Typically, D – HUS patients fare much worse long term than D + HUS patients.

Confusing findings

Blood may be present on stick testing without any red cells visible on microscopy. This indicates acute haemolysis such as may occur in glucose-6-phosphate dehydrogenase (G6PD) deficiency or malaria.

Large quantities of urate make the urine brick red. Although families may think the colour resembles blood, it is easily distinguished visually. Porphyria is a very rare cause of confusion. Ingestion of red vegetables, especially beetroot, causes red urine. Rarely, but this possibility must not be forgotten, a parent may place their own blood in a child's urine, leading to unnecessary investigations. This condition is called fabricated or induced illness (FII).

Urinary tract stones

Background

There is wide geographical variation in the frequency of stone disease, and there have been major changes in prevalence with time within populations. The incidence appears to be influenced by a wide range of factors, such as climate, race, diet, dehydration, infections and socio-economic status.

Causes

There are three broad causes of urinary tract stones (which may coexist in individual children).

Proteus urinary tract infections

The mechanism is twofold. The infection results in turbid urine containing cells and debris, and secondly *Proteus* splits urea to form ammonia, which raises the urinary pH. Because calcium ammonium phosphate is relatively insoluble in alkaline urine, it will co-precipitate readily on to the urinary debris under these conditions to form thick sludge initially, and subsequently a stone. This explains why these stones take up the shape of the tract they form in ('staghorns' in the pelvi-calyceal system, 'date stones' in the lower ureter, and round stones in the bladder). Preschool boys are affected much more than any other groups.

Relative dehydration and possibly dietary factors

The mechanisms of stone formation are probably similar to those for infection stones, with chemicals normally found in the urine reaching relatively high concentrations due to low urine volumes, and high dietary intake and consequent excretion rates of relatively insoluble chemicals.

Rare inherited metabolic conditions

These result in excessive urinary excretion of poorly soluble chemicals. Calcium stones are most commonly caused by isolated hypercalciuria (without hypercalcaemia), and more rarely by hypercalciuria combined with hypercalcaemia in hyperparathyroidism. Cystine stones are seen due to an inherited (dominantly or recessively) failure of the proximal tubules to reabsorb this amino acid. Oxalate stones may be due to excessive gut absorption of oxalate when the calcium is unavailable to precipitate it, such as with steatorrhoea. Rarely it is also produced and excreted in excess due to a recessive liver enzyme deficiency.

Presentation and diagnosis

Children may pass a stone or present with severe colicky abdominal pain (typically in one loin), often with frank haematuria. Ultrasound scanning is a sensitive imaging tool, showing the front edge as a bright line, with an acoustic shadow thrown behind it, rather than showing the whole stone. Nephrocalcinosis associated with hypercalciuria is seen as white (echo-bright) renal pyramids.

A plain abdominal X-ray will show radio-opaque stones, and is thus useful for distinguishing the type. Similarly, the appearance of a passed stone or fragment may aid identification. Infection and dehydration stones are usually grey, and only moderately X-ray dense, and take up the shape of the collecting system. Calcium (white) and cystine (yellow) stones are very X-ray dense, may grow up to 2 cm or more in diameter, and are typically smooth, and round or oval wherever they form. Oxalate stones are yellowish-buff coloured and typically grow to 5 mm, with irregular spiky edges. A high oxalate load will result in many small stones rather than large individual ones.

If the type of stone is not clear from the history, chemical measurements can be made and compared with urinary creatinine measurements on an untimed 'spot' urine sample collected during the morning (but not the overnight sample).

The **upper normal limits** of the ratio of the chemical x to creatinine concentrations, both in mmol/litre, are as follows:

- calcium:creatinine ratio of < 0.8
- cystine:creatinine ratio of < 25
- oxalate:creatinine ratio of < 0.18.

These ratios will be normal in children with infection stones, or those secondary to dehydration.

Treatment

Removal of stones

Small stones may be passed spontaneously. Ureteric colic may be excruciatingly painful and should be treated with powerful opiate analgesia (*see* Section 1.15). Spasmolytics such as hyoscine butylbromide (age 6–12 years: 5–10 mg IV or orally; age > 12 years: 20 mg IV or orally) are sometimes used, but are often not effective. Larger stones may need surgical removal by open surgery or cystoscopy. Percutaneous nephrostomy or lithotripsy may be used where specialist facilities exist.

Preventing recurrences

Infection stones should not recur in the absence of infection. Stones due to metabolic causes and those related to dehydration are all helped by a consistently high fluid intake, but it is probably even more important to avoid episodes of acute dehydration (e.g. with vomiting or diarrhoea) than increasing daily fluid intake.

Chlorothiazide up to 10 mg/kg twice daily reduces urinary calcium excretion; its dose can be titrated in hypercalciuria to keep the urinary calcium:creatinine ratio in the normal range. Furosemide should be avoided because it increases urinary calcium excretion.

Children with hyperparathyroidism may require parathyroidectomy.

In cystinuria, it is essential to maintain a lifelong high fluid intake. Alkalinising the urine increases the solubility of cystine. Give oral sodium bicarbonate supplements (start with 1 mmol/kg daily) until the urine pH is usually ≥ 7 on home testing with strip test paper.

With oxalate stones due to malabsorption, treat the underlying bowel problem. Inherited hyperoxaluria typically leads to renal failure and widespread calcification of soft tissue.

5.6.B The child with vesico-ureteric reflux

BOX 5.6.B.1 Minimum standards
- Ultrasound scanning.
- Micturating cystogram.
- Antibiotics: trimethoprim, nitrofurantoin, nalidixic acid.
- Paediatric surgery.

Introduction

Vesico-ureteric reflux (VUR), which is the abnormal flow of urine from the bladder into the upper urinary tract, occurs in about 1 in 100 members of the general population and is more common in girls. Reflux nephropathy is a cause of hypertension and chronic renal failure in children and young adults.

Renal scarring is an acquired phenomenon that usually occurs during the first few years of life, and rarely after the age of 5 years.

Grades of VUR (International Reflux Study Group classification)

These are as follows:
- Grade I: partial filling of an undilated ureter.
- Grade II: total filling of an undilated upper urinary tract.
- Grade III: dilated calyces but sharp fornices.
- Grade IV: blunted fornices and degree of dilatation greater than in lower stages.
- Grade V: massive hydronephrosis and tortuosity of the ureters.

Figure 5.6.B.1 illustrates the different grades of VUR.

Clinical presentation

- VUR almost always occurs in conjunction with an associated UTI.
- It is rarely a cause of flank pain.
- Fever is the single most important symptom for differentiating children with upper tract infections (pyelonephritis) from those with lower tract infections (cystitis).

Investigations

The minimal acceptable standards of investigation would include the following:
- ultrasonography (useful for detection of dilatation, but not for demonstrating scars or reflux)
- micturating cystourethrogram

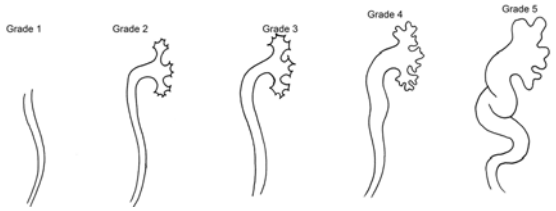

FIGURE 5.6.B.1 The different grades of vesico-ureteric reflux (VUR) according to the International Reflux Study Group classification.

- investigations in siblings: VUR occurs in up to 30% of siblings, and families should be made aware of this.

Medical management

- Spontaneous resolution occurs most often in the first 2–3 years after diagnosis and then at the rate of 10–15% per year.
- The main goal is the prevention of ascending UTI and renal scarring.

The following measures should be used to prevent UTI:
- Proper wiping techniques (girls should be taught to wipe their bottoms backwards, and to avoid using soap on the vulva if possible; they should be discouraged from wearing nylon knickers).
- Frequent voiding.
- Avoidance of constipation.
- Low-pressure voiding.
- Continuous antibiotic prophylaxis, usually maintained for 2 years. Trimethoprim, 2 mg/kg/day, is the usual prophylactic agent. If breakthrough infections that are resistant to this occur, a suitable alternative prophylactic such as nitrofurantoin (1 mg/kg/day) or nalidixic acid (7.5 mg/kg twice daily) may be used.

In children of all ages the preferred initial treatment is medical, but they need regular follow-up. The need for surgery is becoming increasingly uncommon, but re-implantation of the ureters is occasionally necessary if the VUR is not resolving, is bilateral, in late presentations and in children, or with higher grades of VUR and with antenatally detected hydronephrosis.

5.6.C Acute renal failure

BOX 5.6.C.1 Minimum standards
- **Peritoneal dialysis.**
- ECG monitoring.
- Nebulised salbutamol.
- Vitamin D with serum calcium monitoring.
- Blood transfusion.
- Low protein and sodium diet.
- Furosemide.
- Antibiotics.

Types of acute renal failure

Acute renal failure (ARF) may be caused by a wide variety of insults to the renal tubule cells. Each type of ARF has a different management. It is therefore important to distinguish them clearly.

Pre-renal failure

This is caused by poor perfusion and hypovolaemia secondary to gastroenteritis, septic shock, haemorrhage, burns, nephrotic syndrome or cardiac failure.

Established (intra-) renal failure

Established renal failure most commonly results from more extreme or more prolonged versions of the same insults that cause pre-renal failure, leading to acute damage to the kidney cells. Other causes include haemolytic–uraemic syndrome and drug toxicity and acute rapidly progressive glomerulonephritis. The prognosis for recovery depends on the underlying cause, whether only the tubule cells are damaged, and whether the glomeruli are also involved.

Post-renal failure

Acute complete obstructions of the renal tract causing failure of urine production are rare, but include posterior urethral valves, obstruction of a single kidney, bilateral stones and trauma.

Diagnosis and initial management of ARF

Pre-renal ARF

Pre-renal failure is essentially a reversible renal dysfunction due to the kidneys being under-perfused, but where the perfusion is still sufficient to prevent necrosis of the renal tissue.

The clinical diagnosis is made by recognising the signs of shock, the commonest of which are a delayed capillary refill time, cool peripheries, a weak pulse, and usually a low blood pressure. However, the blood pressure may also be unexpectedly high because of the powerful renin drive in response to hypovolaemia. An important feature is that the child may complain of abdominal pain (induced by splanchnic ischaemia as blood flow is diverted from the gut to more vital organs).

Laboratory support of the clinical diagnosis is made by measuring the fractional excretion of sodium (FE Na; *see* Section 5.6.A). This requires measurement of the sodium and creatinine concentrations in a sample of blood and urine. If the FE Na is less than 1% this indicates that the renal tubule cells are still alive, and able to respond to shock by reabsorbing sodium avidly. This therefore confirms a diagnosis of pre-renal failure. No other tests, including measurements of osmolality, urinary sodium concentration alone, or urine microscopy, can reliably differentiate pre-renal from established renal failure. Ultrasound scanning is useful to exclude obstruction, but cannot differentiate pre-renal from established renal failure.

Treatment

This consists of urgent volume expansion followed by furosemide. Percentage dehydration should be estimated, and rehydration should be with Hartmann's or Ringer-lactate solution, plasma, 4.5% albumin or other similar isotonic fluid or plasma substitute. Give 10–20 mL/kg as rapidly as possible initially, and repeat if necessary. If urine output does not commence after adequate volume replacement and furosemide, consider whether this is actually established renal failure, and **do not continue repeating fluid boluses**. Thereafter give Hartmann's or Ringer-lactate solution to fully correct the fluid deficit within 2–4 hours. The deficit can be estimated by multiplying the child's weight by the estimated percentage dehydration. For example, a 6 kg infant estimated to be 10% dehydrated is deficient of approximately 600 mL. According to the above guidelines he would receive 60–240 mL of plasma or plasma substitute very rapidly, and the rest of the 600 mL as Hartmann's or Ringer-lactate solution over a few hours.

Once rehydration has started, give furosemide 2 mg/kg orally or IV. **If there is a urine output response to furosemide this will usually indicate that the renal failure can recover.** If the blood pressure remains markedly depressed after rehydration, it may be due to cardiogenic shock, so consider administering inotropes (*see* Section 5.5.C).

Established ARF

Established failure is due to acute parenchymal damage to the kidneys. In most cases the causes are exactly the same as for pre-renal failure, but an increased severity or duration of the insult has led to death of some of the renal cells. Therefore the pertinent history and clinical signs are usually the same as for pre-renal failure. Other cases are due to directly toxic effects of drugs such as gentamicin, or poisons to the tubular cells. Some forms of glomerulonephritis may lead to ARF (*see* Section 5.6.A), as may the arteriolar disease, haemolytic–uraemic syndrome.

The laboratory diagnosis of established renal failure due to under-perfusion or an ischaemic insult can be made reliably by calculating the FE Na from a measurement of the sodium and creatinine concentrations in a plasma sample and a spot urine sample. The FE Na is typically greater than 2% because the damaged tubules are usually unable to reabsorb sodium avidly. Again, attempts to use other laboratory criteria are unreliable. The history, clinical examination and laboratory confirmation of glomerulonephritis and haemolytic–uraemic syndrome are described in Section 5.6.A.

The most vulnerable region of the kidney is the highly metabolically active mass of proximal tubule cells. If these cells alone die from the insult, this causes acute tubular necrosis (ATN), which will fully recover in 2–4 weeks if the child is maintained in good health during that period of renal failure (likely to require dialysis). More severe insults

may result in damage to some or all of the glomeruli as well, which are in the renal cortex. Glomerular damage is irreversible, and acute cortical necrosis may therefore result in chronic or end-stage renal failure.

Fluid repletion and furosemide administration will not result in recovery of renal function. If an FE Na is not available to distinguish between pre-renal and established ARF, it is sensible to give a trial of fluid bolus and furosemide. Management consists of correcting the dehydration, as for pre-renal failure, and thereafter careful maintenance of fluids (usually restriction) and electrolyte balance and nutrition (restricting potassium intake) while it is hoped that some recovery of tubule cells will lead to recovery of kidney function. **This is likely to require dialysis.** If recovery is going to happen it is likely to have begun by 4 weeks, but can occur up to 2 or even 3 months later. There are no reliable imaging techniques for determining whether the child has recoverable ATN or irrecoverable cortical necrosis, but renal biopsy if available may distinguish between these.

Post-renal ARF

Post-renal causes are due to obstruction to all of the urinary flow, and are uncommon. This will not occur if the flow from just one kidney is blocked (unless a single kidney is present). Causes in a child with two kidneys include congenital urethral valves, or a bladder stone obstructing the urethra. Causes in a child with a single kidney include a ureteric stone, or a pelvi-ureteric junction narrowing (which is congenital, but often blocks intermittently and presents late).

All of these pathologies cause severe acute colicky abdominal pain. This is well localised in older children to either unilateral pain with ureteric obstruction, or lower abdominal pain with bladder neck obstruction. An ultrasound scan will reveal stones and dilatation of the urinary tract proximal to the site of the obstruction.

Treatment

The treatment of post-renal ARF is to remove or bypass the obstruction. For a bladder neck stone obstruction, catheterise the child. Giving pain relief with an opiate analgesic may allow time for an obstructing urethral stone to pass, or for the intermittent blockage from a pelvi-ureteric junction narrowing to clear. If not, the stone may need to be removed cystoscopically or by ureterolithotomy, or the upper renal tract can be drained by insertion of a percutaneous nephrostomy under ultrasound guidance. Once removal of the obstruction has allowed the renal function to recover, procedures such as surgical repair of the pelvi-ureteric junction may be performed.

Ongoing management of persistent ARF

General management

The management of ARF consists of the provision of good general care for an acutely ill child, plus the specific management of fluid and electrolyte balance, blood pressure, and the adjustment of some drug dosages. In many instances the limitations that need to be imposed to keep in metabolic balance compromise the care that can be given in other areas.

The safe management of these children requires the maintenance of meticulous fluid balance. To achieve this it is necessary to accurately measure all intake and losses. For babies, stool and urine losses are best estimated by weighing their clean and dirty nappies. Insensible water losses need to be estimated. This is done most reliably by assuming it to be 300 mL/m^2 in temperate conditions, and higher in hotter climates and at low humidity (for estimation of body surface area, *see* Table 9.16, Section 9). The best guide to the overall changes in fluid balance is to weigh the child twice daily.

Nutrition, fluid and electrolyte balance

Adequate nutrition is important for recovery, but may be difficult to provide. If a child is old enough and well enough to eat solid food they are relatively easy to manage because they can obtain their requirements with little water. Aim to provide their normal calorie intake from carbohydrates and fats, and limit their protein intake to about 1 gram/kg/day to minimise uraemia. It is necessary to limit the salt intake to prevent sodium retention and hypernatraemia, which leads to insatiable thirst and hence fluid overload. It may be necessary to provide some of the sodium as bicarbonate to prevent acidosis, typically at a starting dose of 1 mmol/kg/day (note that 1 mL of an 8.4% sodium bicarbonate solution contains 1 mmol, and 1 gram of powder contains 12 mmol).

Dietary potassium must be restricted (avoid in particular bananas, tomatoes, coconut, citrus fruits or juices, and chocolate) to decrease the risk of hyperkalaemia. Dietary phosphate must be restricted (restrict milk and dairy products but not breastfeeding) to reduce the risk of hyperphosphataemia.

Giving calcium carbonate with the food (e.g. 0.5–2 grams with each meal) will bind the intestinal phosphate and reduce hyperphosphataemia as well as reducing the tendency to hypocalcaemia.

Young infants who normally take milk, and children who are too ill to eat solid food, or who have gastrointestinal involvement, will need either nasogastric tube feeding **or intravenous nutrition**. **The enteral route should always be used if possible.** However, adequate nutrition has to be delivered in a relatively large fluid volume. If the child has polyuric renal failure, or has high non-renal water losses (e.g. from diarrhoea or drain fluids), this can be achieved. However, if the child is oligo-anuric it is very difficult (and often impossible) to give sufficient nutrition without causing fluid overload, which can lead to hypertension and pulmonary oedema. Concentrated fat-based oral feeds can be made up from ingredients such as double cream. **Specialist parenteral nutrition solutions will be required if they are to be used for a child in renal failure.**

The need for dialysis

Although severe fluid and electrolyte restriction is possible for short periods of time while awaiting spontaneous recovery of renal function, it is not possible to both provide adequate nutrition and maintain stable water and chemical balance over a prolonged period in a child with oligo-anuria. If such a child does not start to regain renal function, they will die unless they are dialysed.

The main indications for starting dialysis (where available) are as follows:

- Hyperkalaemia: this is discussed below.
- Fluid overload causing pulmonary oedema and/or hypertension.
- Severe metabolic acidosis: this is another important reason for dialysis (if available). Treatment with sodium bicarbonate is limited because this may lead to massive

sodium overload, and thus to dangerous levels of hypernatraemia, and to greater fluid retention. Fluid overload is worsened if hypoglycaemia occurs (this needs to be treated with IV glucose solutions) and if other fluids are required (e.g. platelets).

- Uraemia: clinical symptoms are apparent at concentrations above 40 mmol/litre, but uraemia is not as acutely life-threatening as hyperkalaemia or pulmonary oedema. It needs to be reduced by providing more non-protein calories.

Hyperkalaemia

Hyperkalaemia causes life-threatening arrhythmias, especially in acute renal failure, where other metabolic changes may exacerbate the risk (e.g. hypocalcaemia). Aim to keep the plasma potassium concentration below 6.5 mmol/litre in older children and below 7.0 mmol/litre in neonates (who appear to tolerate hyperkalaemia better).

There are three pharmacological approaches to managing children with hyperkalaemia.

1. **Reduce the risk of it causing arrhythmias.** Reduce the effect of hyperkalaemia by increasing the plasma calcium concentration. Give 0.5 mL/kg (0.1 mmol/kg) of calcium gluconate 10% IV.
2. **Remove potassium from the body.** Give calcium resonium 1 gram/kg orally or rectally, and repeat with 0.5 grams/kg 12-hourly. This ion-exchange resin exchanges potassium for calcium. It is not well tolerated. If volume status and urine flow permit, furosemide will increase urinary potassium excretion.
3. **Push potassium into the cells.** This last option only results in a temporary improvement, because as soon as the treatment stops the potassium moves back out of the cells. Essentially this approach is only a holding treatment while a more effective therapy such as dialysis is prepared:
   - Give a beta-2-adrenergic agonist, such as salbutamol. Nebulise 2.5 mg for children under 25 kg, and 5 mg for larger children, or give 4 micrograms/kg IV. This works rapidly, but the potassium will move back out of the cells within a few hours.
   - Alternatively, infuse a high concentration of glucose. Monitor the plasma glucose concentration and be prepared to infuse insulin beginning at a dose of 0.05 units/kg/hour if it exceeds 12 mmol/litre. It is unsafe to mix the glucose and insulin and infuse them together in children, as this may cause hypoglycaemia. This necessitates close monitoring, an inevitable fluid load, and only lasts while it is continued.
   - Bicarbonate infusions push potassium into the cells. A dose of 2.5 mmol/kg may be infused over 15 minutes. If a solution of 8.4% is used, containing 1 mmol/mL, it will increase the plasma sodium concentration by approximately 5 mmol/litre very quickly, which may be hazardous. It is better to use a solution of 1.26% which is isonatraemic, but this requires that a volume of 17 mL/kg be infused, adding to fluid overload.

Acute peritoneal dialysis

Indications

Children with acute renal failure can be considered for peritoneal dialysis if their biochemical control is not safe despite careful treatment (see section on management of acute renal failure above). Although the specific indications for initiating peritoneal dialysis vary from case to case, the commonest reason is a high and rising plasma potassium concentration (e.g. above 6.5 mmol/litre in an older child, or above 7 mmol/litre in a neonate). Others indications include a urea concentration above 40 mmol/litre, a phosphate concentration above 3.5 mmol/litre, or acidosis with a bicarbonate concentration below 12 mmol/litre, as well as hypertension or pulmonary oedema due to fluid overload.

The primary underlying reason for needing to proceed to dialysis is usually anuria or severe oliguria. This is because even a moderate urine flow will prevent fluid overload if the intake is restricted, and because it 'makes space' for biochemically appropriate replacement fluid. Even poor-quality urine contains potassium, so replacement with potassium-free fluid allows a net loss. Also, urinary sodium losses can be replaced with IV sodium bicarbonate to counter acidosis, and a high infused glucose concentration will reduce catabolism and so minimise urea, potassium and phosphate production. Take advantage of all fluid losses; diarrhoeal losses will 'make space' just as effectively as urine losses.

Practical techniques

PD Catheter

Ideally, a catheter with side holes should be inserted so that its tip lies in or near one of the iliac fossae. The ideal catheter is a cuffed silastic Tenckhoff which has a series of side holes and an end which is cut off straight, but these are expensive and need to be inserted through a peel-away sheath (usually in the midline below the umbilicus). It is possible to dialyse adequately using other more readily available catheters that have side holes, such as chest drains. These are usually inserted over a metal trocar, and have a tapered tip with an end hole that is considerably smaller than the diameter of the tube lumen, which can lead to difficulties with blockage with omentum (see below).

Insertion of catheter

- This must be a strictly aseptic technique performed either under general anaesthetic, or under sedation/systemic analgesia (*see* Section 1.15) and local anaesthetic. The catheter may be placed directly percutaneously or with a subcutaneous tunnel or with full surgical procedure.
- If the catheter is not tunnelled, to prevent fluid leakage it is essential that it is inserted through the skin with a very tight fit; using a larger skin hole and stitching it closed will inevitably result in leakage in time. Cut a skin slit that is obviously smaller than the tube, and stretch it with a surgical clip or stitch holder.
- Before introducing the catheter, insert an IV cannula through the skin cut and fill the abdomen with about 40 mL/kg of Ringer-lactate solution or 0.9% saline until the abdominal wall is fairly tense.
- To insert the catheter through a tight hole requires some force, and this is best done by pushing the catheter and trocar tip into the dilated skin slit as far as possible, and then suddenly advancing it with a sharp force through the tense abdominal wall. Grip the catheter and trocar tightly about 3 cm from its tip to act as a stop as it pops into the abdomen (the risk of causing damage is greatly reduced by the presence of sufficient instilled fluid).
- To further minimise the risk of trauma, it is better to

enter the upper quadrant lateral to the rectus sheath, and aim towards the opposite iliac fossa, than to use an infra-umbilical approach. Be aware of the possibility of an enlarged spleen or liver.
- Once sited, test to check that fluid flows rapidly in and out, before securing with a skin stitch and sterile dressing.

Problems with omentum

It is common for omentum to wrap around the end of the catheter, and for some to enter the end hole. This slows or stops drainage because the omentum is sucked further into the lumen, but has little effect on filling because the omentum is washed back towards the catheter tip, and the fluid exits through the side holes. Deal with it as follows:
- The omentum can often be forced out by rapidly injecting up to 50 mL of dialysis fluid, Ringer-lactate solution or 0.9% saline into the catheter under pressure.
- If this fails, withdraw the catheter from the abdomen using full aseptic technique. If the omentum has become detached, simply reinsert the catheter, and resume dialysis.
- If (as usually happens) the catheter comes out with the omentum attached, detach it, and gently pull more omentum out, tie round it with an absorbable suture near to the skin surface, cut off the excess, and return the omentum into the abdomen, using the stitch to obtain easy purchase, and replace the catheter.

Fluid and cycles
- Run the dialysis fluid in through a giving set with a burette, and with the bag held about 1 metre above the patient, and leave it to dwell for 30 minutes. Allow it to drain by gravity through a Y-connector into a sealed bag for about 10–15 minutes; by then, it should have drained about as much as was instilled, and the flow should have stopped.
- The osmolality of the dialysis fluid determines the amount of water that is drawn off (ultra-filtered) during each peritoneal dialysis cycle, and this is adjusted by varying the glucose content. Typical glucose concentrations available are 1.36% (standard) and 3.86% (high-osmolality) bags. Start with 1.36% glucose.
- Add heparin, 1000 units/litre, to the fluid initially to prevent any blood from the insertion clotting the catheter. Discontinue it once the effluent fluid looks clear.
- Start with 10 mL/kg cycles of dialysis fluid for the first 2 days. Using this small volume minimises the risk of a peritoneopleural leak of dialysate.
- The first cycle balances are unreliable because there is always a sump of fluid left, but after that the ultra-filtrate required is the volume of fluid that needs to be removed to correct any overload, plus an amount equivalent to the urine that would normally be passed (so just a little less than the normal fluid intake).
- If there is too little ultra-filtrate, increase the glucose concentration of the dialysate by giving some cycles of 1.36% glucose and some of 3.86% glucose. Continue to review the fluid balance, and vary the proportion of cycles of each strength as necessary.
- Increase the cycle volume by 10 mL/kg every 2 days until tolerance occurs, or a maximum of 40 mL/kg. As the cycle volume increases, it is not necessary to dialyse so intensively. Either continue with 30-minute dwells, but just for part of the day (e.g. 8 hours overnight), or lengthen the dwells, eventually moving to chronic ambulatory peritoneal dialysis (CAPD), in which the fluid is left in the peritoneum all the time, and exchanged four to six times per day.

Biochemical control

The sodium, calcium and magnesium content of the dialysis fluid is similar to that of plasma, and the fluid contains lactate, which is converted to base, so is equivalent to bicarbonate. Cycling therefore tends to keep the plasma concentrations stable. Peritoneal dialysis fluid contains no potassium, urea or creatinine, so these are removed.
- Urea equilibrates rapidly, so is cleared well, allowing the child to have a normal protein intake.
- Creatinine is removed slowly, so peritoneal dialysis never restores the plasma levels to normal. This is useful because creatinine is not toxic, and its plasma concentration continues to provide a measure of intrinsic renal function and renal recovery.
- Sometimes the dialysis required to control fluid or urea excretion is sufficient to cause hypokalaemia. If so, reduce the potassium dialysis clearance by adding up to 3 mmol/litre potassium chloride to the dialysate bags (do not use more than this; if the potassium concentration is still too low, give extra orally or intravenously).

Peritonitis

Infection is the major hazard of peritoneal dialysis, and produces a cloudy dialysis effluent in the drainage bag due to white blood cells. Prevention is crucial, by scrupulous hand washing and avoiding touching the open tubing ends while changing peritoneal dialysis bags, and by changing connections as infrequently as possible.
- Monitor constantly by inspecting the clarity of the effluent fluid.
- Undertake daily microscopy for white blood cells (there should be < 50 white blood cells/mL; *see* Section 8.5).
- If the effluent fluid is cloudy, and microscopy confirms the presence of large numbers of white blood cells (over 100, but typically several hundred), culture a sample of fluid, and start treatment at once by adding heparin (to stop blockage of the tube holes with fibrin) and antibiotics to peritoneal dialysis bags and revert to continuous cycling if not still doing that. Start with vancomycin and ceftazidime, and adjust according to the culture and sensitivity results. Concentrations of antibiotics that may be added to peritoneal dialysis fluid are as follows:
  - vancomycin, 25 mg/litre
  - ceftazidime, 125 mg/litre
  - ampicillin, 125 mg/litre
  - flucloxacillin, 250 mg/litre
  - gentamicin, 8 mg/litre.
- Continue continuous cycling until a count of < 50 white blood cells/mL is obtained for two samples taken 12 hours apart. Then return to previous dialysis cycles, adding peritoneal dialysis antibiotics for 14 days.
- If accidental contamination occurs, such as touching the open dialysis catheter during a bag exchange, or a fluid leak from a connection or punctured bag, add vancomycin and either ceftazidime or gentamicin to the dialysis fluid for the next 12 hours.
- Fungal peritonitis is difficult to clear. It is best to remove

the catheter and treat systemically until the peritonitis resolves.

The urine output must be measured throughout the procedure.

Analgesia for the procedure and throughout the dialysis is likely to be required.

Chronic renal failure

Background

Chronic renal failure (CRF) is more frequent in boys than in girls. Its commonest cause is congenital renal abnormalities such as dysplasia associated with severe antenatal vesicoureteric reflux, and often also with posterior urethral valves. It can also follow almost any form of acute renal failure.

It is relatively easy to improve the quality of life of children with milder forms of CRF by simple treatments, especially in the case of older children. In its more severe forms, CRF is very difficult to treat effectively, requiring expensive drugs and intensive laboratory monitoring.

Very young children with CRF are particularly difficult to manage, as they usually have marked anorexia and failure to thrive. Successful treatment requires a massive family and medical input, highly expensive drugs, and a complex medical infrastructure of a kind that has only limited availability worldwide at present. **Each country should have a specialised centre that can provide care for such children.**

Progression of CRF

CRF tends to worsen progressively through childhood. This is mainly because dysplastic or damaged kidneys may not grow in parallel with body growth, and renal function becomes outstripped by demand. Deterioration is likely to be quicker if the child has hypertension, or has recurrent urinary infections with continuing reflux, both of which require active treatment.

Management

Water, sodium and potassium

Children with dysplastic kidneys usually have **polyuric renal failure** in which they lose water and salt, and often potassium, in an uncontrolled way. Consequently, they have a persistent thirst, and can become dehydrated extremely rapidly if they vomit persistently. They need IV fluids early, particularly if there is an episode of gastroenteritis.

Hyperkalaemia due to severe CRF occurs relatively late in children with polyuria.

Supplementing with sodium bicarbonate or salt, as needed, can improve well-being and growth. For each of these, start by adding about 1 mmol/kg per day. For bicarbonate, increase daily until the plasma concentration is in the normal range. The total extra sodium needed is best judged by measuring lying and standing blood pressures to detect postural hypotension; a fall in plasma sodium concentration is a very late event. Note that:

- For bicarbonate, 1 mmol is equivalent to 84 mg, so 1 gram contains about 12 mmol bicarbonate. For intravenous use, 8.4% bicarbonate solution contains 1 mmol/mL.
- For sodium chloride (salt), 1 mmol is equivalent to 57 mg, so 1 gram contains about 18 mmol sodium. For intravenous use, each litre of 0.9% saline contains 150 mmol (*see* Table 5.5.A.2 in Section 5.5.A on 'shock' for details of electrolyte concentrations in other more physiological infusion crystalloids, such as Ringer-lactate and Hartmann's solution), and strong sterile sodium chloride solutions can be used to increase the sodium concentrations of standard IV fluids (e.g. a 30% solution contains 5 mmol sodium/mL).

Children with **oliguric renal failure** are more difficult to manage because they require salt and water restriction to prevent hypertension, and potassium restriction to prevent hyperkalaemia.

When dialysis is available, indications to begin this treatment are often multiple, and include an intolerable diet or fluid restriction, and symptoms such as poor growth and lethargy as important factors, rather than just specific biochemical parameters.

Calcium and phosphate

CRF can lead to abnormalities of the plasma calcium and phosphate concentrations, and these can cause rickets and hyperparathyroidism (renal osteodystrophy), which can result in bone pain, limb deformities, and fractures (especially slipped femoral capital epiphyses). The primary problem is phosphate retention due to a reduced glomerular filtration rate. This causes a high plasma phosphate concentration, which in turn leads to a low plasma calcium level by mass action, and by suppressing the enzyme 1-alpha-hydroxylase, thus lowering the concentration of circulating activated 1-alpha-hydroxyvitamin D. A primary lack of 1-alpha-hydroxylase enzyme from destruction of kidney tissue is rare except in very severe CRF.

Treatment is therefore aimed at reducing the phosphate intake, either directly by dietary restriction (reducing the intake of meat and dairy products), or by **giving calcium carbonate** with meals. This binds with the phosphate in the gut, and prevents its absorption. The dose needed is very variable. Start at about 50–100 mg/kg, divided among the day's meals, and titrate the dose (if biochemical monitoring is available) to keep plasma phosphate levels at the lower end of the normal range. This commonly also results in a rise in plasma calcium levels into the normal range. Because of this, it is seldom necessary to treat mild CRF with 1-alpha-hydroxyvitamin D_3. If it is needed, in more severe CRF, start with about 20 nanograms/kg once daily, and titrate the dose up until the plasma calcium concentration is normalised. It is extremely potent, and using it without regular monitoring can easily lead to severe hypercalcaemia, which can result in permanent calcification of tissues, including the renal medullae.

Anaemia

Severe CRF leads to anaemia because the kidneys fail to produce enough erythropoietin. Treatment by repeated transfusions is unsatisfactory because blood is often scarce, carries infective risks, is always expensive, and eventually leads to iron overload. Recombinant erythropoietin (if available) should be used, after adequate iron levels have been achieved (folate and vitamin B_{12} supplementation is seldom required, but levels should be checked if possible).

Growth

Many factors lead to growth failure in children with CRF.

In older children, attention to fluid and electrolyte intake,

prevention of acidosis with bicarbonate supplements, and control of the bone biochemistry help considerably. Control of uraemia by encouraging a diet containing about 1 gram of protein/kg daily and a high carbohydrate intake will also contribute to good growth.

In young children, the problems are much greater. They are often extremely anorexic; most babies with severe CRF virtually do not feed, and only survive if tube fed for months or even years. Many also vomit excessively. Even when supplemented with tube feeds, very young children with CRF often remain small.

Transplantation

Renal transplantation (if it is available) from a living or deceased donor gives the best quality of life for children with end-stage renal failure.

5.7 Liver disorders

5.7.A Acute liver failure

BOX 5.7.A.1 Minimum standards

- Vitamin K.
- IV glucose 10%.
- Oxygen.
- Lactulose.
- Blood transfusions and clotting factors.
- Ranitidine/antacids.
- Antibiotics and antifungal treatment.
- High-carbohydrate diet.
- N-acetylcysteine.
- Measurements of prolonged blood clotting times.

Introduction

In contradistinction to fulminant liver failure in adults, acute liver failure (ALF) in children may not be accompanied by encephalopathy, which tends to be a late feature, or if it occurs early in the course suggests a metabolic cause.

Prolonged prothrombin time (PT) or international normalised ratio (INR) indicates coagulopathy due to the absence of liver-synthesised coagulation factors, and is the basis of the definition of ALF. However, coagulopathy in the presence of liver dysfunction can also result from vitamin K deficiency (usually due to prolonged cholestasis) and consumption of coagulation factors due to disseminated intravascular coagulation (DIC).

Definition

Based on the above, ALF is present in children when coagulopathy accompanies liver disease but is not due to DIC or a lack of vitamin K (*see* Table 5.7.A.1). Administration of IV or IM vitamin K (300 micrograms/kg for children aged 1 month to 12 years: 10 mg for those over 12 years of age) ensures that remaining coagulopathy is due to failed production (liver failure) or excess consumption (DIC). Markers that suggest DIC, rather than ALF, include a low platelet count, compatible blood film (fragmented cells, schistocytes) and a serum bilirubin that is predominantly unconjugated.

TABLE 5.7.A.1 Clinical features of ALF

1.	Nausea and vomiting is a frequent early feature.
2.	Bruising, petechiae and bleeding secondary to deranged clotting (INR > 4 is associated with 90% mortality).
3.	Jaundice with tender hepatomegaly or a liver that is enlarged but reducing in size in days.
4.	Encephalopathy latterly complicated by features of raised intracranial pressure.
5.	Metabolic alkalosis from failure of the urea cycle associated with a low serum potassium concentration.
6.	Failure to maintain normoglycaemia.

Diagnosis of ALF

- The history may establish a recent episode of shock including severe dehydration, sepsis or heatstroke, evidence of ingestion of toxic mushrooms or drugs (including those bought over the counter or obtained from any non-conventional source), or exposure to infection such as *Salmonella typhimurium* (*see* Table 5.7.A.2).
- The possibility of bloodborne or other parenteral infection with hepatitis B up to 6 months previously should be explored.
- Examination may show features of acute portal hypertension with liver tenderness suggesting Budd–Chiari syndrome or a veno-occlusive disease, or lymphadenopathy suggesting malignancy.
- Urine should be tested for bilirubin, urobilinogen and reducing substances.
- Stools should be examined for colour.
- **Tests to establish many of the causes of ALF require sophisticated laboratory facilities which may not be available.**
- The cause may be diagnosed from local epidemiology.
- A blood film and an INR or prothrombin ratio should be measured.
- A full septic screen, **excluding lumbar puncture because of coagulopathy**, should be performed (including fungal cultures and chest X-ray).

TABLE 5.7.A.2 Causes of acute liver failure

Type	Cause
Infective Viral	Hepatitis A, B, C or D, HIV, parvovirus, herpes virus, enterovirus, adenovirus, echovirus varicella, yellow fever, Lassa fever, Ebola virus, Marburg virus, dengue
Bacterial, protozoal	Leptospirosis, typhoid, malaria
Metabolic	Wilson's disease, tyrosinaemia, urea cycle disorders, galactosaemia, mitochondrial disorders, haemochromatosis, Niemann–Pick disease type C
Drugs	Paracetamol, anti-TB drugs, halothane, carbamazepine, sodium valproate
Toxins	*Amanita phalloides*, heatstroke, shock (all causes)
Autoimmune	Anti-smooth-muscle antibodies and anti-liver-kidney microsome (LKD) antibodies, antibody-positive giant cell hepatitis with haemolytic anaemia
Vascular	B Budd–Chiari syndrome, veno-occlusive disease (may follow bush tea ingestion)
Cryptogenic	Non-A, non-B hepatitis

TABLE 5.7.A.3 Four grades of hepatic encephalopathy

Grade I
Irritable, inappropriate behaviour
Lethargy
Mildly depressed awareness
Tremor or flap (slow wave in outstretched extended hand)
Grade II
Aggressive outbursts, bad language
Unable to stay still
Pulling at IV cannulae, plaster, etc.
Grade III
Mood swings
Irritable, odd behaviour
Not recognising parents
Photophobia
Grade IVa
Mostly sleeping, but rousable
Incoherent, sluggish pupils
Hypertonia with or without clonus and extensor spasm
Grade IVb
Absent reflexes
Irregular gasps with imminent respiratory failure
Bradycardia
Unresponsive to painful stimuli

Complications of ALF

These include the following:

- Encephalopathy and raised intracranial pressure, convulsions.
- Hepatorenal syndrome.
- High-output cardiac failure.
- Hepatopulmonary syndrome.
- Acid–base disturbance; initially alkalosis with hypokalaemia, followed by metabolic acidosis from multi-organ failure.
- Gastrointestinal bleeding, including early development of oesophageal varices.
- Pancreatitis.
- Bone-marrow aplasia.
- Sepsis, particularly Gram-negative and fungal, pulmonary (including aspiration) and septicaemia.

Fluids in ALF

- Fluids in ALF should be restricted to two-thirds of normal maintenance (*see* **Section 9 Appendix**).
- When albumin needs to be infused, the dose is 5 mL/kg of 20% albumin, and for fresh-frozen plasma the dose is 10–20 mL/kg.
- Do not give any potassium if the patient is anuric.
- Treat hypoglycaemia in the usual way (*see* **Section 5.8.B**).

Management of children with ALF

- **In the absence of liver transplantation, conservative management relies on liver recovery, which will occur in many cases of ALF, taking place before irrecoverable damage occurs in another organ, particularly the brain. The best possible high-dependency care may improve the likelihood of this occurring.**
- Refer the child to a specialised centre if one exists in that country. Undertake frequent reviews and clinical observations and high-dependency nursing.
- Blood tests for coagulation, electrolytes, blood glucose levels and blood count should be performed frequently (ideally 8-hourly).
- Hypoglycaemia and hypokalaemia must be detected and corrected.
  - Maintain blood glucose levels in the range 4–9 mmol/litre using a restricted fluid volume (two-thirds of maintenance) consisting of a minimum concentration of 10% glucose (given IV or orally); 20% glucose is the preferred solution, but is irritant to peripheral veins and is best given into a central vein or, better still, if tolerated, orally or via a nasogastric tube.
  - A metabolic alkalosis resulting from a failure of the urea cycle may cause hypokalaemia as a result of a shift of potassium into the cells. This hypokalaemia can worsen encephalopathy, and should be corrected enterally or IV.
- Children with encephalopathy should be nursed with their head elevated at 30 degrees above the horizontal and without neck flexion (to decrease intracranial pressure and minimise cerebral irritability). Children with agitated encephalopathy of grade II or III represent a major management problem, as they may pull out monitoring equipment and IV lines. **Sedation will worsen their encephalopathy.**
- Strict fluid balance is essential.
  - Allowance should be made for a hot climatic environment by giving 10–20% extra fluid, and 10% extra fluid should be given for each degree of fever.
  - Strict monitoring of urinary output and fluid balance is required. Aim for a urine output of not less than

0.5 mL/kg/hour (determined by weighing nappies or measuring output).
  - Daily weights are useful if the child can be moved, and will allow greater precision in fluid balance.
- If possible and appropriate, insert a central venous line and aim to provide a central venous pressure (CVP) of 6–10 cmH_2O if necessary to give a normal blood pressure. Increased CVP may be required to compensate for an increased cardiac output, or to treat the reduced cardiac performance that is seen as liver failure progresses.
  - Patients who require inotropes despite adequate central venous filling are developing multi-organ failure and have a very poor prognosis.
- Stop oral protein initially, and during recovery gradually reintroduce 0.5–1 gram/kg/day in oral or nasogastric feeding.
- A high-energy intake, predominantly of dietary carbohydrate, should be promoted to prevent protein catabolism with an increased serum ammonia level. In the absence of products such as Maxijul, uncooked cornstarch may be used as a source of carbohydrate. It may be given up to 2-hourly to provide predicted energy requirements, and may also help to maintain normoglycaemia.
- Lactulose, 5–10 mL two to three times a day, is given to produce two to four soft and acid stools per day (it should be omitted if diarrhoea occurs).
- Maintain normothermia by environmental measures (**but NOT with paracetamol, aspirin or ibuprofen**).
- Give one dose of IV or IM vitamin K (300 micrograms/kg for children aged 1 month to 12 years: 10 mg for those over 12 years of age) to attempt correction of prolonged clotting time.
- If there is frank bleeding (gastrointestinal or other), consider giving fresh blood, fresh-frozen plasma or **cryoprecipitate** at 10 mL/kg IV.
- A prophylactic H_2-blocking agent (e.g. ranitidine 2 mg/kg twice daily orally or IV) is given with oral antacid (e.g. sucralfate 250 mg four times a day for children aged 1 month to 2 years, 500 mg four times a day for those aged 2–12 years, 1 gram four to six times a day for those aged 12–18 years) to prevent gastric and/or duodenal ulceration.
- Treat any confirmed sepsis aggressively.
  - Broad-spectrum antibiotics, such as a cephalosporin plus amoxicillin, or penicillin plus gentamicin, should be used prophylactically.
  - Systemic fungal infection may require IV amphotericin (250 micrograms to 1 mg/kg/day) or oral fluconazole (10 mg/kg once daily).
  - Give prophylactic oral nystatin mouthwashes (100 000 IU (1 mL) four times a day).
- Manage hypotension with IV colloids and **possibly dopamine and nor-adrenaline infusions if central venous access has been obtained** (*see* Section 5.5.C).

Paracetamol overdose

If paracetamol overdose is suspected or confirmed, N-acetylcysteine must be started immediately, whatever the time between the alleged overdose and the visit to the hospital. Histories after overdose are often misleading, with multiple administrations and other drugs not immediately admitted. N-acetylcysteine is given IV at 150 mg/kg over 15 minutes as a loading dose, then 100 mg/kg over 12 hours, then 100 mg/kg/day as a continuous infusion until the INR is normal.

Prognosis for ALF

The most important prognostic parameter for ALF is metabolic acidosis. Even in the presence of a very prolonged INR, a patient who is not acidotic will have an 80% chance of survival. A plasma pH of < 7.25 (if blood gas measurement is available) indicates a 95% risk of mortality.

Other factors that predict a poor outcome are grade III or IV hepatic encephalopathy and oliguric renal failure (usually occurring 3–4 days after onset).

Risk factors

- Age < 2 years.
- INR ≥ 4 (associated with a mortality of > 90%).
- Serum bilirubin concentration > 350 micromol/litre.
- Grade III or IV encephalopathy.
- Non-A non-B hepatitis.
- Drug-induced ALF.

Poisoning or toxic reactions associated with the development of ALF

These include the following:

- paracetamol
- mushrooms, particularly *Amanita phalloides* and similar species
- carbon tetrachloride
- copper
- iron
- halothane and other volatile anaesthetic agents
- sodium valproate
- carbamazepine
- phenytoin
- phenobarbitone
- isoniazid
- cytotoxic drugs
- irradiation.

Galactosaemia

- A defect of galactose-1-phosphate uridyl transferase is revealed in the perinatal period when affected infants are first exposed to milk feeding.
- Infants present with vomiting, hepatitis, liver failure and DIC, often with septicaemia.
- Symptoms settle within 2–3 days when feeding with milk is discontinued.
- Hypoglycaemia is seen in the majority of cases.
- Cataracts may be detected.
- Fanconi's nephropathy explains the presence of galactose in the urine giving the characteristic 'Clinistix negative, Clinitest positive' side-room test pattern when the infant is receiving feeds.
- Management consists of the **removal of galactose from the diet** and standard management of liver failure and sepsis.

5.7.B Chronic liver disease

BOX 5.7.B.1 Minimum standards
- Hepatitis B vaccine.
- Vitamin K.
- Fat-soluble vitamins (A, D, E and K).
- Cholestyramine.
- Specific nutritional support.

Introduction

The liver is anatomically strategically positioned between the gastrointestinal tract and the systemic circulation to perform its nutritional homeostatic role. Through the portal system, it filters organic and inorganic substances, microorganisms and their breakdown products, including endotoxins. It also stores and processes nutritional substrates and coordinates nutritional status through endocrine carrier proteins. The liver is therefore the major organ of nutritional homeostasis.

It can be helpful in diagnostic and prognostic terms to think of clinically evident liver dysfunction as having degrees of severity in three simultaneous dimensions: cholestasis, portal hypertension (with hypersplenism) and synthetic function (although homeostasis of ammonia and blood glucose levels may fit better into this synthetic group). The clinical features are summarised in Table 5.7.B.1.

Clinical symptoms and signs of chronic liver disease (CLD)

TABLE 5.7.B.1 Clinical features of CLD

Clinical feature	Cholestasis	Portal hypertension	Cell dysfunction
Jaundice	Conjugated	–	Mixed if severe
Pruritis	+	–	–
Leuchonychia	+	–	–
Fat-soluble vitamin deficiency	+	–	–
Xanthomas	+*	–	–
Splenomegaly	–	+	–
Cutaneous shunts	–	+	+
Other cutaneous stigmata	–	+	+
Hypersplenism	–	+	–
Hepatopulmonary syndrome	–	+	+
Oesophageal varices	–	+	–
Ascites	–	+	+
Encephalopathy	–	+	+
Dependent oedema	–	–	+
Malnutrition	+	+	+

*Not in familial intrahepatic cholestasis.

Jaundice

Accompanied by dark urine and pale stools, jaundice is characteristic of cholestatic liver disease. The urine of infants should not contain significant colour or stain the nappy, and yellow urine strongly suggests bile obstruction. Yellow sclerae suggest cholestatic jaundice but are difficult to detect in small infants, and children with deep skin pigmentation may have some scleral pigmentation. There is no substitute for personal examination of stool and urine, as the history can be misleading. White stool, or stools the colour of cream cheese or uncooked pastry, are clearly abnormal, whilst pale yellow, pale green or pale brown stools may also raise concern about liver function. Comparison with a stool colour chart (www.yellowalert.org/file_download.aspx?id=7358) can be extremely helpful if there is doubt.

Hepatomegaly

Healthy infants may have up to 2 centimetres of liver edge palpable below the costal margin, but the texture is soft. An abnormally hard texture or irregular inferior margin strongly suggests established liver disease with fibrosis/cirrhosis. Changed liver conformation with prominence in the mid-line but an impalpable right lobe suggests collapse, regeneration and the development of cirrhosis. Tenderness of a smoothly enlarged liver suggests a rapid recent increase in liver size (e.g. in acute hepatitis and also congestive cardiac failure).

Splenomegaly

Newborns may normally have a palpable spleen tip. Later palpable spleen suggests splenomegaly, possibly from portal hypertension, but as children get older a larger spleen can be accommodated beneath the ribs, so the sign becomes less sensitive.

Coagulopathy

With cholestasis, coagulopathy results from a failure of absorption of sufficient vitamin K. In infants this may present as haemorrhagic disease of the newborn, who should not

normally suffer spontaneous bleeding. Routine vitamin K is given to newborns in some countries. Fresh blood from sites such as the umbilicus or nares should always prompt a search for evidence of vitamin K malabsorption or liver disease even when jaundice seems trivial.

In liver disease and coagulopathy unresponsive to vitamin K, but without consumptive coagulopathy, liver synthetic failure must be present. **The degree of coagulopathy is the most sensitive index of liver impairment in children.**

Hypoglycaemia

Hypoglycaemia may suggest a metabolic disease as a cause of liver dysfunction or profound failure of liver function.

Encephalopathy

More common in acute liver failure (*see* Section 5.7.A), chronic hepatic encephalopathy may be insidious, with educational failure, poor impulse control, bizarre behaviour and absences noted intermittently over months or years. Improvement may be associated with a low-protein diet reduced to 1 gram/kg/day, with lactulose to give acid stools and change the gut flora in favour of organisms that are less likely to produce the amines associated with encephalopathy.

Ascites

This is seen in advanced CLD, being a function of the balance between plasma oncotic pressure, which is mostly contributed by serum albumin, and hydrostatic pressure from portal hypertension.

Cutaneous manifestations

Pruritus, liver palms, cutaneous shunts, clubbing, white nails and xanthomas are well-recognised signs.

Hepatopulmonary syndrome

Progressive cyanosis occurs without lung disease, associated with low pulmonary artery pressure. Exertional dyspnoea is a frequent early feature. Type 1 implies pulmonary capillary vasodilatation and improves at least in part with inspired oxygen, whereas type 2 implies fixed intrapulmonary shunts without a response to oxygen.

Other presentations

Chronic liver disease may be present without detectable symptoms or signs. For example, chronic viral hepatitis B can be present for decades, proceeding to cirrhosis without any external evidence.

TABLE 5.7.B.2 Laboratory features of CLD

Laboratory feature	Cholestasis	Portal hypertension	Cell dysfunction
Serum bilirubin	Conjugated	Normal	Normal or mixed
Serum albumin	Normal	Normal	Low
Serum cholesterol	High†	Normal	Low
Prothrombin time/ratio	Normal‡	Normal*	Prolonged if severe

* Implies minor prolongation seen in portal vein thrombosis.

† Except in familial intrahepatic cholestasis types 1 and 2.

‡ If there is adequate vitamin K.

Investigations into CLD

Consider liver dysfunction according to the following three categories (*see* Table 5.7.B.2):

- **cholestasis:** impairment of bile flow with a consequent reduction in intraluminal bile salt concentration and associated conjugated hyperbilirubinaemia and malabsorption
- **portal hypertension (PHT)** with associated hypersplenism and the effects of portosystemic shunting
- **hepatocellular impairment** (cell dysfunction) with failure of synthetic and homeostatic function, such as hyperammonaemia and hypoglycaemia.

Clinical findings (*see* Table 5.7.B.1) can be interpreted according to this classification, although some (e.g. ascites) are represented in more than one category. Serum albumin concentration reflects liver synthetic function but also depends on nutritional status and losses (e.g. via the gastrointestinal tract or kidneys). Thus it is necessary to consider all clinical features supported by basic laboratory parameters when possible to evaluate the severity of liver disease.

A precise diagnosis of the various causes of CLD is often not possible without specialised and expensive investigations, yet use of the above clinical assessment may allow a general if unconfirmed diagnosis.

Outcome of CLD

Although CLD can often only be cured in specialised centres in countries where transplantation is available (costs are over $120 000 per case), much can be done to relieve suffering in children with CLD, and most notably Wilson's disease can be treated successfully for US$1–2 per day depending on the patient's size and age.

Cholestatic CLD: diagnosis and management

Cholestasis is most frequently seen as a complication of the neonatal hepatitis syndrome. The commonest defined diagnosis is **biliary atresia**, an obliterative inflammatory condition of the intra- and extrahepatic biliary system exclusive to the perinatal period. Infants typically present with jaundice, pale stools and dark urine. If left untreated, biliary atresia progresses to biliary cirrhosis and death from complications of decompensated liver function within 2 years in 95% of cases. It is the commonest individual cause of severe liver disease in childhood in all populations, occurring in 1 in 9000 to 1 in 16 000 live births.

Causes of cholestatic CLD that are rare and difficult to treat include the following:

- **Alagille syndrome:** a condition characterised by

TABLE 5.7.B.3 Basic investigations in liver disease

Investigation	Role
Serum bilirubin, total and conjugated	Conjugated bilirubin is elevated in cholestasis Unconjugated bilirubin is elevated in hepatocellular injury
Urine bilirubin	Present in cholestasis
Serum aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transpeptidase	Elevated in hepatocellular injury plus cholestasis
Serum sodium, potassium, urea, creatinine, albumin and glucose	Hepatocellular injury
Full blood count, prothrombin time or INR	Coagulopathy in liver failure and in cholestasis from vitamin K malabsorption
Hepatitis A antigen, toxoplasma, rubella, herpes, CMV, syphilis antibodies	Congenitally acquired infection
Serum total protein and immunoglobulins	Abnormal in autoimmune disease
Alpha fetoprotein	Elevated in liver tumour
X-ray of spine, cardiac	Alagille syndrome, dextrocardia rarely in biliary atresia
Ultrasound scanning	Biliary, portal and parenchymal abnormalities
Eye review for Kayser–Fleischer rings and embryotoxon	Wilson's disease, Alagille syndrome

cholestasis of variable severity associated with syndromic features.

- **Progressive familial intrahepatic cholestasis (PFIC):** a series of clinical syndromes of cholestasis representing impairment of bile salt transport or handling that may present as neonatal giant-cell hepatitis or drug- or viral-induced cholestasis.
- **Neonatal sclerosing cholangitis:** a rare condition which may mimic biliary atresia, although stools may show variable pigmentation.

The consequences of cholestasis include **pruritus**. This is a particularly troublesome symptom, resulting in disruption for the whole household, especially at night. Persistent scratching can be complicated by secondary infection of broken skin and bloodstaining of clothes and bedclothes. Early onset, before 7 months of age, implies profound cholestasis and a poor prognosis. Treatment is often difficult. First-line management is with **cholestyramine**, at a starting dose of 1 gram/day for under 1 year olds, 2 grams (sachets)/day for children under 6 years, or 4 grams (sachets)/day for those over 6 years, up to 6 sachets/day according to response, but not given within 4 hours of vitamins or other medicine, Second-line treatment is **rifampicin**, 2–4 mg/kg (maximum 300 mg) twice daily, and third-line treatment is **ursodeoxycholic acid**, 5–10 mg/kg two to three times a day up to 15 mg/kg two to three times a day.

Fat-soluble vitamin deficiencies (A, D, E and K) are frequently encountered in cholestasis unless patients receive prophylactic treatment. Clinical features of **rickets**, such as splayed epiphyses, especially swollen wrists, rickety rosary and craniotabes should be sought regularly. Metabolic bone disease should, if possible, be screened for by measurements of serum phosphate, calcium and parathormone levels and regular wrist X-rays. Prothrombin time or INR should be measured to ensure adequate vitamin K repletion.

Vitamin A replacement is 5000–10 000 units per day or 100 000 units by deep IM injection every 2 to 4 months. Vitamin D deficiency may be refractory to oral calciferol (vitamin D_2) tablets or cholecalciferol (vitamin D_3), but 10 000–25 000 units (250 micrograms) for 1–12 years and 10 000–40 000 for 12–18 years per day of either may help. More water-soluble preparations such as 1-alpha-calcidol, 15–30 nanograms/kg for 1 month to 12 years and 250–500 nanograms for 12–18 years once daily, are more effective. **They may also cause hypercalcaemia.** Vitamin E deficiency is associated with hypotonia, peripheral neuropathy, developmental delay and haemolysis, and is the most frequently encountered vitamin deficiency in liver disease. The dose of vitamin E for all age groups is initially 100–200 mg/day adjusted according to response up to 200 mg/kg once daily, to increase until normal plasma levels are maintained. Vitamin K replacement for infants orally is 1 mg/day, and for children it is 5–10 mg/day.

Nutritional management applies to all three categories of CLD, and is discussed below.

Portal hypertension (PHT): diagnosis and management

The complications of portal hypertension can be divided into:

- those related to the increased pressure (e.g. enteropathy, hypersplenism)
- those related to the anatomy of any collateral circulation (e.g. bleeding varices, haemorrhoids)
- those related to the effects of substances bypassing the liver by porto-systemic shunting (e.g. hepatic encephalopathy, hepatopulmonary syndrome, porto-pulmonary syndrome, hepatorenal syndrome). In this group complications may increase as shunting increases and portal pressure then falls.

The aetiology of PHT has conventionally been divided into the following:

- **pre-hepatic causes**, including portal vein thrombosis and other congenital and acquired portal vein anomalies, including arterioportal fistulae
- **hepatic causes**, including all causes of cirrhosis, especially cystic fibrosis and other biliary diseases, congenital hepatic fibrosis, and causes of non-cirrhotic portal hypertension, including portal vein sclerosis

- **post-hepatic causes**, including hepatic venous outflow obstruction such as Budd–Chiari syndrome, various causes of veno-occlusive disease and problems of inferior vena caval flow or right heart function; particularly difficult to detect are constrictive pericarditis and IVC webs.

Treatment of bleeding varices

BOX 5.7.B.2 Minimum standards: oesophageal varices

- Vitamin K.
- Blood transfusion (ideally fresh blood) and blood-clotting factors (if available).
- Propranololol.
- Antacids (aluminium hydroxide or magnesium carbonate).
- Ranitidine.

Acute management

1 Advise the parents not to panic, but to stay with the child.
2 Unless the CLD is very advanced, or the child is vitamin K deficient, the bleed will probably stop spontaneously, although the child may be shocked by that time.
3 Give oxygen by face mask.
4 Gain IV access and obtain cross-matched blood if possible. Resuscitation with 10–20 mL/kg boluses of Ringer-lactate or Hartmann's solution is appropriate in the acute situation while waiting for blood for transfusion.
5 Give IV vitamin K slowly over 5 minutes 250–300 microgram/kg up to a maximum of 10 mg (or 1 mg for children under 1 year; 3 mg for those aged 1–4 years; 5 mg for those aged 5–12 years; 10 mg for those over 12 years). Repeat according to the results of clotting studies.
6 Start antacids (see below).
7 Arrange skilled endoscopy with sclerotherapy or banding (if available).

Prevention

- Propranololol is beneficial as primary and secondary prophylaxis for variceal bleeding, particularly when given early in the course of PHT. Give 500 micrograms/kg orally twice daily (adjust according to the heart rate; aim to reduce the rate by up to 25%). Around 30% of patients who receive propranololol have side effects, including wheeze and systemic vasoconstriction.
- Antacids. If there is a tendency to diarrhoea, use aluminium hydroxide (children aged 6–12 years: 5 mL three to four times a day between meals; children over 12 years: 10 mL three to four times a day). If there is a tendency toward constipation, use magnesium carbonate in the same dosage. The two may be used in combination.
- Avoid aspirin, ibuprofen and other gastric irritants.
- H_2-receptor antagonists are of no proven value but are often used (ranitidine 1 mg/kg for 1–6 months, 2–4 mg/kg 6 months to 12 years, 150 mg 12–18 years ALL twice daily).

Hepatocellular liver disease: diagnosis and management

Chronic viral hepatitis B, C and D

Hepatitis B

Millions of children worldwide are infected with hepatitis B virus (HBV), and many ultimately die in adulthood from its complications, particularly decompensated cirrhosis and hepatocellular carcinoma. The population prevalence may exceed 10%, making HBV a major international public health problem. Spread may occur vertically at the time of birth or shortly afterwards, but also horizontally, especially in poor communities. Unlike HIV infection, surface contact with very small amounts of infected blood (e.g. as a result of sharing toothbrushes) can result in infection. A neonate exposed to HBV for the first time has more than a 90% risk of becoming chronically infected, a child has a 25% risk, and an adult has a 10% risk.

Risk factors associated with the development of cirrhosis and hepatocellular carcinoma include eAg+, a high level of HBV DNA, and male gender. Once infected, children have about a 15% probability per annum of reducing a high-risk state to a low-risk state as defined by eAg/antibody status.

Vaccines based on the antigenicity of the S Ag are highly efficacious in generating antibody response and providing protection. Protocols that involve three subcutaneous immunisations given at 0, 1 and 6 months give adequate antibody levels in 95% of individuals. In neonates, vaccination with the same dose, or half the dose for economy, at birth, 1 month, 3 months and 1 year achieves similar protection. Up to 5% of individuals will not mount an antibody response despite repeated vaccination, but it is not clear whether they all fail to develop immunity. As implied above, all neonates of HBV-positive mothers should receive a course of vaccine, irrespective of the mother's eAg/antibody status, as infants of S Ag+/e Ab+ mothers may develop fatal liver failure.

The WHO has recommended universal HBV vaccination. If such a policy was to be implemented it is highly likely that HBV would become a rare disease of children within less than 10 years, with a corresponding reduction in cirrhosis and hepatocellular carcinoma in one generation, representing one of the current great unseized opportunities of international public health.

Hepatitis C

Hepatitis C virus (HCV) was responsible for at least 90% of post-transfusion hepatitis in early US studies. Around 5% of sexual partners may become infected. Around 4–5% of infants of viraemic mothers may become infected. The risk is related to the level of maternal viraemia, with HIV-positive mothers having the highest HCV viral loads and the highest risk of transmission. HCV is also a small but significant risk for healthcare workers.

Following exposure, viraemia in HCV occurs within 7 days, with antibody positivity appearing from 21–28 days. Less than 10% of affected individuals adequately remove the virus, and the remainder progress to chronic liver disease. The rate of progression to cirrhosis is unclear, but factors such as liver iron content, alcohol consumption and other viral infections (including hepatitis A) contribute. Around 5% of adults with HCV develop cirrhosis each year. The median timescale for developing cirrhosis in HCV is probably of the order of four decades.

Hepatocellular carcinoma is a recognised complication of HCV and cirrhosis, following the latter by 5–15 years typically. Treatment is becoming rapidly more effective, including that for the more resistant genotypes I and IV. Children should be treated after the age of 5 years in order to avoid the neurotoxic effects of interferon.

Wilson's disease

This is an autosomal-recessive disorder caused by the accumulation of copper in the liver, brain, eyes, kidney and bone. The prognosis depends on the speed of diagnosis. Treatment with a low-copper diet and penicillamine is highly successful if started well before the onset of liver failure.

Drugs and the liver

Drugs are a major cause of liver dysfunction. Over 600 drug hepatopathies have been documented; common examples are given below. Drug clearance may be reduced in liver disease, and liver disease increases the risk of drug injury to the liver.

Acute/subacute hepatocellular toxicity is caused by paracetamol, aspirin, ibuprofen, iron, isoniazid, sodium valproate, carbamazepine, methotrexate and ketoconazole.

Cholestasis is caused by rifampicin, penicillins, erythromycin, oestrogens and anabolic steroids.

Progressive fibrosis is caused by azathioprine.

HIV and the liver

HIV is known to be associated with worsening of hepatitis due to other conventional causes and cholangiopathy, probably related to ascending infection with low-grade organisms such as Cryptosporidium or cytomegalovirus (CMV) infection (*see* Section 6.2.D). Hepatitis due to a conventional cause, especially CMV, may be particularly severe or progressive when associated with a low CD4 count.

Metabolic liver diseases

These are rare and difficult, if not impossible, to treat without liver transplantation or expensive diets. Advice from a specialist unit should be sought.

The management of nutrition in CLD

Malnutrition is a serious consequence of CLD. Thin limbs and a prominent abdomen are frequently seen, and malnutrition will be evident in anthropometric measurements. Triceps skinfold thickness tends to become reduced earlier in the course of progressive disease, followed by a reduction in mid upper arm circumference (MUAC). Stunting tends to occur later, unless severe rickets is present. Weight is affected by fluid balance abnormalities and organomegaly, and is therefore an insensitive indicator of nutritional state. Lean body mass, and skeletal muscle in particular, is prone to depletion as a result of progressive liver disease.

Anorexia is attributed to organomegaly or pressure effects of ascites, but may be equally due to a congested gastric mucosa or reduced gastrointestinal motility of portal hypertension or central effects of unidentified toxins. Malabsorption of long-chain fats, including those with polyunsaturated fatty acids (PUFAs), is dependent on intra-luminal bile acid concentration. Cholestasis may result in the intra-luminal bile acid concentration falling below that required for micelles to be formed. The resulting steatorrhoea creates faecal energy loss, but also risks essential fatty acid deficiency, with possible neurodevelopmental consequences, particularly in early life. Protein malabsorption may also result from functional pancreatic insufficiency with failure of protease activation by bile acids. Malabsorption may also result from bacterial overgrowth or other unspecified effects of portal hypertension; for example, congestion of the gut may cause impaired active or passive absorption.

Thus malnourished children with liver disease have high energy expenditure for their size. Target energy intake should be estimated from what the child's current weight for age should be.

Breast milk contains more PUFAs than typical formula milks. PUFAs are long-chain fats that are dependent on intraluminal bile acids for absorption, and are essential for normal cell membranes and for myelination, particularly in infancy. **Breastfeeding is therefore important in children with CLD.**

Treatment with intensive enteral feeding and **high-dose enteral or parenteral vitamins** can improve the quality of life of children who have malnutrition from their liver disease. In the absence of specialist feeds, a modular feed may be prepared using protein powder, carbohydrate polymer, MCT oil and long-chain fat oil, preferably with essential fatty acids from walnut oil or another similar source, to provide 4% of fat. Up to 4 grams/kg/day of protein, and 100–140 kcal/kg/day of energy, of which two-thirds is from carbohydrate and one third is from lipid as MCT, is an ideal target range.

Commercial liver formulas are extremely expensive, and their effect on the outcome of the liver disease is unproven. In the absence of the supplements described above, proprietary baby formula can be enriched with locally available oils and starches to give 140 kcal/kg/day, with half of the total formula energy as lipid and half as starch. Remember that if commercial formula is given at an increased concentration to increase protein intake, the electrolyte intake will increase proportionally, with a risk of sodium overload and fluid retention.

5.8 Endocrine disorders

5.8.A Diabetes

BOX 5.8.A.1 Minimum standards
- ABC resuscitation skills and equipment.
- Oxygen.
- IV 0.9% saline or Plasma-Lyte 148.
- Insulin.
- Potassium.
- Mannitol or 3% saline.
- ECG monitoring.

Diabetic ketoacidosis

Diabetic ketoacidosis (DKA) is the commonest endocrine emergency that may occur in individuals with previously diagnosed diabetes, but should be suspected in any child with:
- dehydration (diarrhoea is not the only cause)
- abdominal pain
- ketone smell on the breath
- acidosis
- acidotic breathing
- unexplained coma.

A child with DKA may die from inhalational pneumonia, hypokalaemia, severe metabolic acidosis or cerebral oedema. Cerebral oedema is unpredictable, occurs more frequently in younger children and those newly diagnosed with diabetes, and has a mortality of around 80%.

These guidelines are intended for the management of children who are more than 3% dehydrated and/or vomiting and/or drowsy and/or clinically acidotic.

Children who are 3% dehydrated or less and not clinically unwell usually tolerate oral rehydration and subcutaneous insulin.

Every unit should have a written policy for the care of children with DKA. The following guidance is adapted from that provided by the British Society for Paediatric Endocrinology and Diabetes (BSPED) (www.bsped.org.uk/clinical/docs/DKAGuideline.pdf).

Emergency management of children who are over 3% dehydrated and clinically unwell

General resuscitation: A, B, C

- **Airway:** ensure that the airway is patent, and if the child is comatose consider inserting an oropharyngeal airway. If they are comatose or suffering from recurrent vomiting, insert a nasogastric tube, aspirate and leave on open drainage.
- **Breathing:** give 100% oxygen. Give bag-and-mask ventilation if the child is apnoeic or hypoventilating.
- **Circulation:** insert an IV cannula and take blood samples (see below). Only if the child is shocked (tachycardia with poor capillary filling or hypotension) give 10 mL/kg 0.9% saline or Plasma-Lyte 148 solution as quickly as possible, and repeat as necessary up to a maximum of 30 mL/kg. Note that normal (0.9%) saline causes a hyperchloraemic acidosis because of its excess of the chloride anion. In patients who are acidotic because of diabetes, Plasma-Lyte 148 may be preferable, as it does not contain such a high concentration of chloride ions.

Confirm the diagnosis

- History: polydipsia, polyuria.
- Clinical signs: acidotic respiration, dehydration, drowsiness, abdominal pain/vomiting.
- Biochemical investigations: high blood glucose levels on finger-prick or venous blood test, presence of ketones or glucose in the urine.

Investigations

- **Weigh the child.** If this is not possible because of their clinical condition, use the most recent clinic weight as a guideline, or an estimated weight from centile charts.
- Blood glucose concentration.
- Urea and electrolytes (if plasma bicarbonate is not available, measure **arterial blood gas**).
- Packed cell volume (PCV) and full blood count.
- Blood culture.
- Urine microscopy, culture and sensitivity.
- Set up a cardiac monitor to observe T waves (hypokalaemia causes flat T waves and may cause cardiac dysrhythmias; hyperkalaemia causes peaked T waves).
- Other investigations (e.g. chest X-ray, CSF, throat swab, etc.) if indicated if the child is febrile, as there may be an underlying infection.

Assessment

Assess and record the following in the child's notes, so that comparisons can be made by others later:
- Degree of dehydration:
  - < 3%: dehydration is only just clinically detectable.
  - 3–5%: dry mucous membranes, reduced skin turgor.
  - 5–8%: as above with sunken eyes, poor capillary return.
  - > 8%: with shock – severely ill with poor perfusion, thready rapid pulse, reduced blood pressure.
- Conscious level:
  - Assess the AVPU score (**A**lert, responds to **V**oice, responds to **P**ain, **U**nresponsive).
  - Institute hourly neurological observations. If less than **A**lert on admission, or there is any subsequent deterioration, record the Glasgow Coma Scale score (*see* Section 7.3.C) and transfer the child to a

high-dependency-care unit (if available). Consider instituting cerebral oedema management.

- Full examination, looking in particular for evidence of the following:
  - **Cerebral oedema: irritability, slow pulse, high blood pressure** and papilloedema. Examine the fundi: papilloedema is a late sign.
  - Infection: look for a focus. **DKA can cause a leucocytosis but not a fever.**
  - Ileus.
- Observations to be carried out (ensure that full instructions are given to the nursing staff):
  - Strict fluid balance and urine testing of every sample for glucose.
  - Hourly capillary blood glucose measurements.
  - Twice daily weights.
  - Initially hourly or more frequent neurological observations.
- **Report immediately to the medical staff (even at night) symptoms of headache or any change in either conscious level or behaviour.**
  - Report any changes in the ECG trace, especially T-wave changes.

Management

By this stage, the circulating volume should have been restored if shock was initially present. If not, give a further 10 mL/kg of 0.9% saline or Plasma-Lyte 148 over 30 minutes. Avoid overzealous fluid replacement, as this may be a risk factor for cerebral oedema.

Estimating fluid requirements

The amount of fluid that the child needs over a 24-hour period must be calculated. It is the sum of:

estimated fluid deficit + maintenance requirements + ongoing losses.

Deficit

In DKA the deficit must be replaced more slowly than in gastroenteritis, over 48 hours rather than 24 hours. Even in very severe dehydration, use no more than 10% dehydration as the maximum in your calculations. Document the fluid balance carefully.

Determine the degree of dehydration, and **never estimate more than 10% dehydration in this situation**.

Weigh the child, or else estimate their weight from their age as follows:

$$\text{weight (kg)} = 2 \times [\text{age (years)} + 4]).$$

Use the following formula: **percentage dehydration × weight (kg) × 10 = deficit (in mL)**.

For example, a child whose weight is estimated to be 10 kg is 10% dehydrated.

Their estimated fluid loss is 10 × 10 × 10 = 1000 mL (40 mL/hour if replaced over 24 hours **or** 20 mL/hour **if replaced over 48 hours, which is safer in DKA**.

Maintenance

TABLE 5.8.A.1 Estimated maintenance fluid requirements based on child's body weight

Body weight	Volume of fluid needed per day	Volume of fluid needed per hour
First 10 kg of body weight	100 mL/kg	4 mL/kg
Second 10 kg of body weight	50 mL/kg	2 mL/kg
Subsequent kg	20 mL/kg	1 mL/kg

Ongoing losses

For each diarrhoea stool	< 2 years old: give 50–100 mL > 2 years old: give 100–200 mL
For each vomit	2 mL/kg oral rehydration solution (ORS): give small frequent volumes (e.g. 5 mL/minute in a child) via a spoon, syringe or cup
For nasogastric tube aspirates	Replace volume for volume with either ORS or 0.9% saline or Plasma-Lyte 148 containing 5% or 10% glucose

Type of fluid

Initially use 0.9% saline or Plasma-Lyte 148. Once the blood glucose concentration has fallen to 14 mmol/litre, change the fluid to 0.9% saline or Plasma-Lyte 148 containing, in addition, 5% glucose and 20 mmol KCl per 500-mL bag.

Expect the sodium concentration to rise initially as the glucose level falls and water is removed from the circulation.

Cerebral oedema may be related to a plasma sodium concentration that falls or does not show the expected rise as glucose levels fall.

Electrolytes

Bicarbonate

Bicarbonate is rarely, if ever, necessary. Continuing acidosis usually indicates insufficient resuscitation. Bicarbonate should only be considered in children who are profoundly acidotic (pH < 7.0) and shocked with circulatory failure. Its only purpose is to improve cardiac contractility in severe shock. The maximum volume of 8.4% sodium bicarbonate for half-correction of acidosis is calculated according to the following formula, and given over 60 minutes:

Volume (mL) of 8.4% sodium bicarbonate = 1/3 × weight (kg) × base deficit (mmol/litre) divided by 2.

If no **blood gas measurement** is available, do not give bicarbonate unless the child is in **profound shock**.

Potassium

- Commence potassium immediately unless anuria is suspected, or there are peaked T waves on the ECG, or the serum potassium concentration is higher than 7.0 mmol/litre.
- Potassium is mainly an intracellular ion, and there is always massive depletion of total body potassium, although initial plasma levels may be low, normal or even high. Potassium levels in blood will fall once insulin is commenced.
- Add 20 mmol KCl to every 500 mL unit of IV fluid given.
- Check urea and electrolytes 2 hours after resuscitation

is commenced and then at least 4-hourly thereafter, and alter potassium replacements accordingly (more potassium is sometimes needed).
- Use a cardiac monitor to observe frequently for T-wave changes, and alert nursing staff to any changes that might be seen, and advise them when to call for medical help.
- **If potassium-containing fluids are not available, start insulin (see below) after 1–2 hours of rehydration, and arrange transport to a unit that can provide this (if available).**

Insulin

Once fluids are running, calculation of the insulin infusion rate may be undertaken at leisure, as the blood glucose levels will already be falling. Continuous low-dose IV infusion is the preferred method.

However, **if a syringe pump is not available or not safe to use** after at least 1 hour of rehydration treatment give subcutaneous boluses of short-acting insulin 1- to 2-hourly at 0.1 unit/kg/dose. Give half the dose if the blood glucose level is falling too fast.

There is no need for an initial bolus, and some evidence that insulin should not be given during the first hour of IV fluid treatment.

If an infusion system is available and safe to use, make up a solution of 1 unit/mL of human soluble insulin (e.g. Actrapid) by adding 50 units (0.5 mL) of insulin to 49.5 mL of 0.9% saline in a syringe pump. Attach this using a Y-connector to the IV fluids that are already running. Do not add insulin directly to the fluid bags. The solution should then run at 0.1 unit/kg/hour (0.1 mL/kg/hour).

Once the blood glucose level is down to 14 mmol/litre, change to 5% glucose in 0.9% saline (add 50 mL of 50% glucose to a 500 mL bag of saline) and potassium as above. Do not reduce the insulin infusion until the pH is > 7.3 and the glucose concentration is < 14 mmol/litre, when it may safely be reduced to 0.05 mL/kg/hour.

If the blood glucose level falls below 7 mmol/litre, consider adding extra glucose to the infusion.

If the blood glucose level rises out of control, re-evaluate the patient (check whether there is sepsis or some other condition). Then:

1 Check that the insulin syringe pump is connected and working.
2 Make up a fresh solution of insulin, preferably using a new source of insulin in case the original one is denatured, and consider starting the whole protocol again.

Frequent sips of oral rehydrating fluid or nasogastric fluid up to 5 mL/kg/hour may be used as a substitute in the immediate initial period while arranging transport. Once the blood glucose level is < 14 mmol/litre, more glucose may be required (e.g. fruit juice if tolerated).

Remember that **you must have glucose ready to treat hypoglycaemia (5 mL/kg of 10% dextrose).**

Continuing management

Output

- Urinary catheterisation should be avoided, but may be useful in a critically ill child with impaired consciousness. With or without catheterisation, documentation of fluid balance, if necessary by weighing nappies, is of paramount importance.
- Measure accurately and test all urine samples for glucose and ketones.
- Record all fluid input (even oral fluids).
- If a massive diuresis continues, fluid input may need to be increased.
- If large volumes of gastric aspirate continue, replace them IV with 0.45% saline plus 10 mmol/litre KCl.

Laboratory results

Check biochemistry, blood pH and laboratory blood glucose levels 2 hours after the start of resuscitation, and at least 4-hourly thereafter.

Review the fluid composition and rate according to each set of electrolyte results. If acidosis is not correcting, resuscitation may have been inadequate, in which case consider giving more 0.9% saline or Plasma-Lyte 148. Consider sepsis as a cause of persistent acidosis. Consider antibiotic treatment.

Insulin management

Continue to give IV fluids until the child is drinking well and able to tolerate food. Do not expect ketones to have disappeared completely before changing to subcutaneous insulin. **Discontinue the insulin infusion 60 minutes after the first subcutaneous injection in order to avoid rebound hyperglycaemia.**

Cerebral oedema in DKA

Signs and symptoms of cerebral oedema

These include the following:

- headache
- irritability
- seizures
- increasing blood pressure and slowing pulse
- confusion
- reduced conscious level
- small pupils
- possible respiratory impairment.

Management

- Exclude hypoglycaemia as a cause of neurological symptoms.
- Give mannitol 500–1000 mg/kg immediately (2.5–5 mL/kg 20% mannitol over 15 minutes). Alternatively, give 3% saline 5 mL/kg over 5–10 minutes. Give this as soon as cerebral oedema is suspected.
- **Restrict IV fluids to two-thirds maintenance, and replace the deficit over 72 hours rather than 48 hours.**
- **Keep Na^+ levels > 135 mmol/litre. Keep the head in the midline and 30 degrees elevated.**
- **Avoid fever > 38.0°C.**
- Repeated doses of mannitol or strong saline (at the dose stated above, every 2–4 hours) should be used to control intracranial pressure.

Care of the newly diagnosed diabetic child

After treatment of DKA in the newly presenting but well diabetic child, the process of education and treatment should commence. It is not feasible to stabilise the child's control or to teach all aspects of diabetic care while they are an inpatient, so ideally (if resources permit) this should take place at home, although some authors advocate a prolonged initial admission for this process.

Ensure that the parents and the child (if he or she is able to do so) understand or can perform the following:

- insulin administration
- urine testing for ketones
- blood testing
- dietary measures
- other general issues.

Insulin

Draw up the specified dose of insulin correctly. As a rough guide, a new patient will need approximately 0.5 unit/kg/day.

The frequency and choice of insulin depends entirely on local resources. This may mean twice daily medium-acting insulin alone (60% in the morning, 40% in the evening), or medium-acting insulin mixed together with short-acting soluble insulin (usually in a 30% short/70% long ratio). If newer analogue fast-acting insulins are available, these may be given before every meal in an initial dose of 1 unit for every 20 grams of carbohydrate eaten, with a longer-acting insulin (40% of the total daily dose) given before bedtime.

It is very rarely possible to achieve adequate control with a single daily dose of insulin except in very small children. However, once-daily medium-acting or pre-mixed insulin should be seen as a minimum fallback position if availability of insulin is a problem. Likewise, although it is common practice to use human or genetically modified insulins, pork or beef insulin may be substituted if necessary.

Further modification of the dose will take place as an outpatient, as more insulin will be needed after the initial period and with growth and puberty.

Urine testing

Test the urine for sugar using stick tests. Clinitest tablets for reducing substances are too cumbersome for routine use, but may be used as a substitute if they are the only option. Suggest stick testing about twice daily at home. Emphasise the value of testing the first morning urine to estimate overnight control.

Test the urine for ketones using Ketostix or tablets. This only needs to be routinely done if the urine contains 3% glucose or more, and in times of intercurrent illness when the persistence of ketonuria should prompt the seeking of medical attention for incipient DKA.

The importance of accurate recording of the results in a control book, if possible, should be emphasised, to aid decision making at follow-up.

Blood testing

If resources allow, all parents should be able to test the blood glucose level, at least in an emergency, and ideally also for routine monitoring of control. The parent or carer (and also the child, if appropriate) should be taught the following:

- how to use a lancet (or automatic finger-pricking device) to draw blood from the side (**not the pulp**) of the finger
- how to ensure that an adequate sample is placed on the strip
- how to read the strip visually (a meter may be used if resources allow)
- if this method of monitoring control is chosen, the importance of providing test results at staggered times through the day (ideally one or two tests per day) should be explained; **the need for accurate recording of the values in a diary should be emphasised (ascertain the parents' literacy and numeracy levels)**
- the instantaneous nature of the result obtained and the detection of hypoglycaemia with blood testing should be highlighted, and compared with urine testing.

Diet

The parents or carers and the child should **ideally meet a specialist diabetic dietitian** and discuss the concept of carbohydrate balance and how the diet is spread through the day. The diet must be adequate for growth and nutrition, and should contain around 50% of energy as complex carbohydrate. It is not advisable to allow 'free' fatty foods, as they may accentuate later macrovascular complications.

Explain the importance of fairly close adherence to the advised diet, and that the diet may need to be revised from time to time as the child grows and their pattern of activity changes.

The parents or carers and the child should understand the influence of food intake on blood sugar levels. Diabetic carbohydrate 10-gram 'portions' are often used with analogue short-acting insulin boluses before meals (if available), but need considerable expertise to be taught effectively.

Sweet unrefined sugars should ideally only be taken before exercise or as occasional treats, although ideally the insulin dose should be varied to take this into account.

General care

- **It is essential that the parents or carers and the child (if he or she is old enough) understand how inadequate glycaemic control may predispose to micro- and macrovascular complications in the longer term. These are not uncommon findings in teenagers in Africa, due to their appalling glycaemic control in earlier childhood.**
- **It is also important that the parents or carers ensure that a supply of insulin is always available, as the commonest cause of DKA is lack of insulin at home in resource-limited environments.**
- The parents or carers and child (if appropriate) should understand how exercise, diet and insulin interact to influence blood sugar levels.
- The symptoms of hypoglycaemia should be explained. It is important that the parents or carers understand the possible signs of an attack and what can be done to terminate the 'hypo'. They should know how to use rapid-acting sweet sugary gel, non-'diet'/'lite' sugary drinks or tablets during the early stages of the attack. Ideally, a 1-mg glucagon pack (if available) should be given to each family prior to discharge, and the parents should be shown how to prepare and give the pre-packed injection in an emergency to terminate a severe hypoglycaemic attack with unconsciousness or fits. If a 'hypo' is treated, a more complex carbohydrate snack should be given to prevent immediate recurrence.
- The family should be given the address of any local support groups for individuals with diabetes and their families (if such groups exist). If possible, give the parents and child a folder containing relevant booklets on diabetes.
- The family should ideally have access to medical advice and treatment 24 hours a day if they are worried about their child's immediate health, or can be seen at the next outpatient clinic for less urgent problems.

Ideal checklist for use at discharge

- Dextrose gel: 1 box of plastic tubes or 50 grams of dextrose tablets.
- Disposable syringes and needles, ideally 0.3-mL low-volume syringes with as small a needle as can be located (down to 31-gauge are available).
- Insulin.
- GlucaGen Novo 1 mg pack.
- Glucose testing blood sticks, finger-pricking device, plus lancets **or** urine sticks.
- Control book and pen.
- Ketostix.
- Sharps disposal bin.
- Appointment at next diabetic clinic.

Outpatient care

The patient should be reviewed at regular intervals (as frequently as resources allow). Ideally, at least once a year the child should have the following reviewed:

- their knowledge of diabetes and emergency management
- growth
- blood pressure
- state of injection sites
- foot examination and discussion of foot care
- fundoscopy (at diagnosis, for cataracts; after 5 years of diabetes or in teenagers, for retinopathy)
- microalbumin/creatinine ratio in the first morning urine sample for detection of renal complications (after 5 years of diabetes or in teenagers)
- **glycosylated haemoglobin** for monitoring long-term control (ideal control is a level of < 55 mmol/mol).
- **thyroid disorders and coeliac disease are both more likely to occur in children with diabetes. Although, ideally, antithyroid antibodies and antigliadin antibodies could be checked** at the time of diagnosis of diabetes, and every 4 years thereafter, they are expensive tests and in resource-limited environments it is better to undertake a careful clinical assessment for additional thyroid or coeliac disease at annual outpatient appointments.

Transfer to adult services should take place in a planned manner, ideally at a joint handover clinic.

5.8.B The child with hypoglycaemia

BOX 5.8.B.1 Minimum standards

- Oral glucose solutions.
- IV 10% and 50% glucose.

Introduction

Hypoglycaemia is an important cause of morbidity and mortality that needs to be recognised, as the complications are potentially preventable.

Definition

Hypoglycaemia is now widely defined as a blood glucose concentration of less than 2.5 mmol/litre (45 mg/dL) at any age. The measurement should ideally be made in a laboratory with appropriate quality control. Testing with reagent strips is less accurate, particularly within the critical range.

Presentation and aetiology

Hypoglycaemia may present at any age from birth into adulthood. Symptoms are varied and rarely specific, particularly in infants. In neonates, fits and apnoeic attacks may be important clues. In infants and children the most important presentation, because of the risk of complications, is also fits and encephalopathy (*see* Table 5.8.B.1). The common causes are listed below.

In infants and children in well-resourced countries, ketotic hypoglycaemia, endocrine disorders and metabolic disorders usually predominate. By contrast, in resource-limited countries, malnutrition and infections such as malaria (and its treatment) are more common.

Treatment

Glucose dosage

There is insufficient scientific data to be definite about the quantity of glucose to give parenterally to a hypoglycaemic child. 5 mL of 10% glucose was the standard dose for a time but there is evidence that this much glucose can raise the plasma glucose to a level high enough to produce an insulin surge which then results in another hypoglycaemic episode. Of course, in a diabetic child who has become hypoglycaemic because of insufficient calories or too much insulin, this will not occur, so in these circumstances 5 mL of 10% glucose is safe.

- When testing for hypoglycaemia is not possible, treat any critically ill child presenting with suspicious symptoms such as fits, with encephalopathy, or with a condition known to be associated with hypoglycaemia, such as severe malnutrition or malaria.
- If the child is conscious and able to eat and drink, give them food or sugary fluids or glucose orally (0.5–1.0 gram/kg).
- Otherwise, give 2–5 mL/kg 10% glucose IV over 3 minutes. **Never use stronger glucose solutions IV.** Continue with 0.1 mL/kg/minute 10% glucose to maintain the blood sugar concentration in the range 5–8 mmol/litre.
- If hypoadrenalism/pituitarism is suspected, give hydrocortisone as described in Section 5.8.C.
- In hypoglycaemic children with diabetes or suspected hyperinsulinaemia, if IV access is not possible and glucagon is available, give IM 100 micrograms/kg (maximum of 1 mg as a single dose).

Longer-term management

- Provide appropriate endocrine management (*see* Section 5.8.C).
- Avoid periods of fasting. Give glucose orally when at risk during intercurrent infections, or IV if the child is comatose or vomiting, and during anaesthesia.

Diagnosis of the cause of hypoglycaemia

If the blood sugar level is less than 2.5 mmol/litre, it is important to establish a cause. Transfer 1 mL of blood into a fluoride tube, if possible also 1 mL heparinised blood, and the first urine after the hypoglycaemic episode to send for metabolic analysis, in particular for ketones.

- Is there ketosis? If so, look for signs of hypopituitarism and/or growth hormone deficiency.
- If feasible, check the cortisol growth hormone level and insulin levels in blood taken at the time of hypoglycaemia.
- If the blood lactate level is raised, consider organic acidaemia or a defect of gluconeogenesis.
- If ketosis is absent, consider hyperinsulinism (high birth weight) or disorders of fatty acid oxidation.

Prevention

As the symptoms are non-specific, measure blood glucose levels if possible in any suspected situation. If hypoglycaemia is suspected and blood glucose measurement is not possible, treat with glucose and observe the response. **If the response is clearly related to giving glucose, assume that hypoglycaemia was present.**

In the neonate, every effort should be made to avoid those factors that will exacerbate hypoglycaemia, including delayed feeding and hypothermia (*see* Section 3.4).

TABLE 5.8.B.1 Common symptoms and signs of hypoglycaemia

In childhood	In neonates
Convulsions	Convulsions
Reduced conscious level	Reduced conscious level
Anxiety	Jitteriness, tremor
Sweating, pallor	Cyanotic episodes
Palpitations	Apnoeic episodes
Headache	
Behaviour abnormalities	
Visual disturbances	
Slurred speech	
Ataxia	
Hunger	

Some causes of hypoglycaemia

Neonates

- Birth asphyxia.
- Small for gestational age.
- Preterm birth.
- Sepsis.
- Malnutrition.
- Hypothermia.
- Infant of diabetic mother.
- Liver disease, endocrine and metabolic disorders (see below).

Infants and children

Endocrine disorders

- Diabetic on treatment.
- Persistent hyperinsulinaemic hypoglycaemia of infancy (formerly nesidioblastosis) and other congenital and inherited hyperinsulinaemic syndromes.
- Islet-cell tumours.
- Hypopituitarism.
- Growth hormone deficiency.
- Adrenal insufficiency (any cause).

Metabolic disorders

- Disorders of glycogen metabolism, gluconeogenesis or fatty acid oxidation, organic acidaemias, etc.
- Ketotic hypoglycaemia ('accelerated starvation').
- Liver disease: any severe acute liver disease.
- Malnutrition.
- Infections: malaria, especially when treated with quinine.
- Any severe illness.

Poisoning

- Alcohol.
- Salicylates.
- Insulin.

Drugs

- Oral hypoglycaemic agents.

How to give glucose in suspected hypoglycaemia

If the patient is conscious, give sugary drinks or foods such as jam, candy or honey.

If the patient is unconscious:

1 Insert an IV or IO line and draw blood for emergency laboratory investigations.
2 Check blood glucose levels with a glucose monitoring stick. If low (< 2.5 mmol/litre (45 mg/dL) in a well-nourished child or < 3 mmol/litre (54 mg/dL) in a severely malnourished child) or if blood glucose cannot be measured because no stick test is available, treat as for hypoglycaemia anyway.
3 Give 2–5 mL/kg of 10% glucose solution rapidly by IV or IO injection or 2.5 mL/kg of 10% glucose in the neonate.
4 Recheck the blood glucose level after 20 minutes. If it is still low, repeat 2–5 mL/kg of 10% glucose solution. Continue if necessary with an infusion of a glucose containing fluid such as 5 mL/kg/hour of 10% glucose in 0.45% saline until the child is capable of drinking. Monitor the blood glucose until stable.
5 If venous or intra-osseous access is impossible in an unconscious patient, give sublingual sugar (*see* below for technique).
6 Feed the child as soon as they are conscious.
7 If is it not possible to feed the child without risk of aspiration, give:
   - milk or sugar solution via a nasogastric tube (to make sugar solution, dissolve 4 level teaspoons of sugar (20 grams) in a 200-mL cup of clean water)
   - IV fluids containing 5–10% glucose (dextrose).

Note: 50% glucose solution is the same as 50% dextrose solution or D50.

If only 50% glucose solution is available: dilute 1 part of 50% glucose solution to 4 parts of sterile water, or dilute 1 part of 50% glucose solution to 9 parts of 5% glucose solution. **For example, 10 mL of 50% solution with 90 mL of 5% solution gives 100 mL of an approximately 10% solution.**

Note: For the use of blood glucose stick tests, refer to the instructions on the box. Generally, the strip must be stored in its box, at 2–3°C, avoiding sunlight or high

humidity. A drop of blood should be placed on the strip (it is necessary to cover all of the reagent area). After 60 seconds, the blood should be washed off gently with drops of cold water and the colour compared with the key on the bottle or on the blood glucose reader. (The exact procedure will vary with different strips.)

Sublingual sugar (sucrose) for treatment of hypoglycaemia

Sublingual sugar may be used as an immediate 'first-aid' measure when managing hypoglycaemia in an unconscious child in situations where IV or IO administration of glucose may be impossible or delayed.

1 Give ½ to 1 teaspoonful of sugar, moistened but not dissolved with 1–2 drops of water and insert under the tongue (sublingually) and between the lower jaw and the gums (in the buccal area). Children should be monitored for early swallowing, which leads to delayed absorption, and in this case another dose of sugar should be given. If sublingual sugar is given, repeat the doses at 20-minute intervals. This is a useful technique in the community where facilities for parenteral glucose may not be available. However, note that sublingual and buccal absorption is not as effective as gastrointestinal absorption of sugar.
2 Recheck the blood glucose level after 20 minutes, and if the level is still low (< 2.5 mmol/litre or < 45 mg/dL), repeat the IV glucose (5 mL of 10% glucose/kg) or repeat the sublingual sugar.
3 Prevent further hypoglycaemia by feeding where possible. If IV fluids are being given, prevent hypoglycaemia by adding 10 mL or 20 mL of 50% glucose to 90 mL or 80 mL, respectively, of Ringer-lactate solution or 0.9% saline to give a 5% or 10% glucose solution, respectively.

5.8.C Other endocrine disorders

Adrenal crisis

BOX 5.8.C.1 Minimum standards
- ABC resuscitation skills and equipment.
- Hydrocortisone and fludrocortisone.
- IV saline 0.9%.
- IV glucose 10%.

Diagnosis

An adrenal crisis is most likely to be encountered in a neonate with congenital adrenal hyperplasia (CAH) or hypopituitarism (look for virilisation in the female with CAH, and micropenis and cryptoorchidism in the male with hypopituitarism). It may occur in older children with adrenal destruction secondary to autoimmune processes or tuberculosis.

Suspect adrenal crisis in a severely ill child with:
- acidosis
- hyponatraemia
- hypotension
- hyperkalaemia
- hypoglycaemia.

Children receiving long-term steroid therapy

Replacement steroids given as hydrocortisone up to 10 mg/m^2/day replicate natural secretion and are free of side effects if adequately monitored.

Therapeutic doses of steroids for asthma, rheumatoid arthritis, etc. will produce adrenal suppression in a manner related to the dose and duration of treatment. Short 5-day courses of prednisolone therapy will produce measurable adrenal suppression that almost never requires action. Longer courses up to 1 month should be tapered off over a 2-week period to allow recovery of the pituitary adrenal axis.

More prolonged treatment with high-dose steroids may produce profound hypoadrenalism for months after cessation of treatment. In this case, taper the steroid dose to the equivalent of 5 mg/m^2/day of prednisolone. Then convert this to an equivalent dose of hydrocortisone given in the morning (1 mg prednisolone is equivalent to approximately 3 mg hydrocortisone). Then reduce the hydrocortisone by 2.5 mg/week until the child is on approximately 6 mg/m^2/day, when it is probably safe to stop treatment after 2 weeks. **If possible, check the 9 a.m. pre-dose cortisol level and stop treatment if this exceeds 150 nmol/litre at any time.** Severe stress, infection or injury will require increased steroid cover **during the next 6 months**.

Children on physiological replacement treatment or prolonged pharmacological doses of steroids should ideally carry some warning identification for medical staff, advising against the abrupt cessation of steroids, and stating the emergency stress dose of oral (usually three times replacement dose) or parenteral treatment for operative cover or at times of illness associated with vomiting (hydrocortisone, 12.5 mg for infants, 25 mg for children, 50 mg for older children and 100 mg for adults, given as an immediate IV/IM dose and then 4- to 6-hourly IV).

Management of adrenal crisis

- Treat airway, breathing, shock and hypoglycaemia (*see* Section 5.8.B).
- Continue 0.9% saline to correct the deficit and for maintenance (*see* Section 5.8.A).
- Give hydrocortisone IV 6-hourly as follows: 12.5 mg dose for neonates and infants, 25 mg for children aged 1–5 years, 50 mg for children aged 6–12 years, and 100 mg for adolescents aged 13–18 years.
- If the diagnosis is established, continue maintenance hydrocortisone, 8–12 mg/m^2/day in three divided doses (12–15 mg/m^2/day for CAH) and, if salt loss is demonstrated in the context of CAH or adrenal destruction, fludrocortisone 150–250 micrograms/m^2/day in one dose. Infants may also require oral sodium chloride, 1 gram/10 kg/day (60 mg = 1 mmol).

Hypoglycaemia

For a discussion of neonatal hypoglycaemia, *see* Section 3.4.

Thyroid disorders

BOX 5.8.C.2 Minimum standards
- Thyroxine.
- Carbimazole.
- Propranolol.
- Iodine supplements.

Neonatal thyrotoxicosis

Mothers who have active thyrotoxicosis or who have become hypothyroid as a consequence of treatment of thyrotoxicosis may still pass thyroid-stimulating antibodies to the fetus during the last trimester. The neonate (or fetus) will show the following:

- hydrops in severe cases
- tachycardia with heart failure: **this may occur at up to 1 week post delivery**, especially if the mother is on anti-thyroid drugs
- thinness/light for dates
- diarrhoea
- hyperkinesis
- possibly craniosynostosis.

Management

- If hyperthyroidism is detected antenatally, treat the mother with low-dose carbimazole, 5–15 mg/day (use the lowest dose possible for control).
- Treat the infant with:
  - propranololol, 1 mg/kg three to four times orally daily
  - carbimazole, initially 250 micrograms/kg 3 times a day
  - aqueous iodine oral solution (5% iodine plus 10% potassium iodide), 130 mg/mL of total iodine, 1 drop 0.05–0.1 mL every 8 hours until thyroid control is achieved.
- Stimulating antibodies will clear by 3 to 6 months of age, and treatment can be stopped.

Congenital hypothyroidism

Between 1 in 2000 and 1 in 10 000 babies are born with a maldescended or absent thyroid gland. There are rarer cases of dyshormonogenesis (dominant and recessive – more common as a consequence of consanguineous relationships) associated with neonatal goitre and very rare central isolated thyroid-stimulating hormone (TSH) deficiency.

Untreated early hypothyroidism results in cretinism.

Many countries screen for this condition in the first month of life, looking for elevated TSH (except in TSH deficiency) and/or low thyroxine or free thyroxine levels. Different screening laboratories will produce different assay results.

In general, TSH in high double figures (mU/litre) is unequivocally raised and will be confirmed by a total thyroxine concentration of less than 50 nmol/litre or a free thyroxine in single figures (pmol/litre).

In resource-limited countries, X-ray of the knee or wrist to detect delayed bone age in infants and young children is helpful for diagnosis where TSH or thyroxine assays are unavailable.

An untreated affected child will develop, in the following order:

- jaundice
- constipation
- hoarse cry
- umbilical hernia
- coarse features
- mental retardation
- poor growth.

Therefore clinical awareness is important in order to identify possible cases of hypothyroidism in babies with the common symptoms of jaundice and constipation. Prolonged jaundice should lead to investigations, including those for hypothyroidism (*see* Section 3.4).

Management

Give thyroxine, 10–15 micrograms/kg once daily, titrated to maintain TSH in the normal range with normal growth and development. The adult dose is around 2–3 micrograms/kg.

Iodine deficiency

This most commonly occurs in inland mountainous areas. The clinical features vary among different ethnic groups, with deafness, mutism, mental impairment and poor growth being common, and goitre being universal. The disorder may be prevented by adding potassium iodide to cooking salt (10 mg/kg salt) or providing it as supplemented sweets and bread. Iodide as an oily suspension can be given intramuscularly every 3 years.

Acquired hypothyroidism

This is usually part of an autoimmune process (which may be familial), and may be associated with diabetes mellitus. It is much more common in older girls, who will usually have the following:

- goitre
- lethargy
- poor growth rate with excess weight gain
- pallor
- constipation
- hair loss/dry skin
- delayed puberty.

The diagnosis is confirmed by raised blood TSH levels and, if possible, demonstration of antithyroid peroxisomal antibodies.

Management

Thyroxine is given to suppress TSH to the normal range and allow normal growth and pubertal development.

Doses of thyroxine

Neonate: initially 10–15 microgram/kg once daily (maximum 50 micrograms daily) then adjusted in steps of 5 micrograms/kg every 2 weeks or as clinically indicated; usual maintenance dose 20–50 micrograms daily.

Child 1 month–2 years: initially 5 microgram/kg once daily (maximum 50 micrograms daily) then adjusted in steps of 10–25 micrograms daily every 2–4 weeks or as clinically indicated; usual maintenance dose 25–75 micrograms daily.

Child 2–12 years: initially 50 micrograms once daily then adjusted in steps of 25 micrograms daily every 2–4 weeks or as clinically indicated; usual maintenance dose 75–100 micrograms daily.

Child 12–18 years: initially 50 micrograms once daily then adjusted in steps of 25 micrograms daily every 3–4

weeks or as clinically indicated; usual maintenance dose 100–200 micrograms daily.

Thyrotoxicosis

This is much more common in older girls, often those with a family history of thyroid disease. It should be suspected if the following are present:

- fine tremor
- weight loss
- psychiatric disturbance
- exophthalmos (rare in children)
- tachycardia with a wide pulse pressure
- loose stools
- goitre with bruit.

The diagnosis is confirmed by suppressed TSH (level is undetectable) with raised thyroxine level.

Management

Treatment is with low-dose carbimazole. In neonates to children aged 12 years initially 250 micrograms/kg 3 times a day (maximum 30 mg/day) and adjusted as necessary until euthyroid. In children aged 12 to 18 years initially 10 mg 3 times a day adjusted as necessary. Carbimazole should be continued for at least 2 years, after which withdrawal should be attempted. If relapse occurs, the options include further medical therapy, surgery by an experienced thyroid surgeon, or radio-iodine in a specialised centre.

Thyroid mass

Smooth goitre

An isolated smooth goitre with or without a bruit may occur in:

- iodine deficiency
- acute and subacute thyroiditis (viral, bacterial, lymphocytic or other), which is usually tender
- ingestion of goitrogens (e.g. cabbage, kale or other brassicas)
- familial dyshormonogenesis
- idiopathic pubertal goitre
- thyrotoxicosis (Graves' disease, thyroiditis, thyroid hormone resistance)
- Hashimoto's thyroiditis.

If thyroid function is normal, no treatment is necessary; otherwise treat as described above. In iodine-deficient areas where thyroid investigations are not available, treat with oral aqueous iodine as described above.

Nodules require investigation by fine-needle aspiration and histology.

Nodular goitre

Nodular goitre may occur in:

- Hashimoto's thyroiditis
- adenoma (hot, cold, euthyroid)
- lymphoma
- non-thyroidal masses (lymph nodes, branchial cleft cyst, thyroglossal cyst)
- isolated simple cyst
- carcinoma
- histiocytosis.

Disorders of sexual development (DSD)

Uncertainty regarding a child's gender is a distressing emergency for the family.

Most of these children are well unless associated with congenital adrenal hyperplasia (CAH) and salt loss (see above) or other major congenital abnormalities.

Avoid the urge to decide the appropriate sex of rearing of the child until the results of diagnostic tests are available.

Support the parents during this difficult time.

- DSD may be the result of excess androgens in females (the commonest situation, usually secondary to CAH of the 21-hydroxylase deficiency variety), lack of androgens (or the receptor) in males, or (rarely) mixed gonadal DSD with the presence of ovarian and testicular tissue. Minimum investigations are chromosome analysis and plasma for 17-hydroxyprogesterone (**which is** elevated in the commonest form of CAH). **If a baby with a DSD becomes unwell with hypotension, hyponatraemia and hyperkalaemia, assume an adrenal crisis and treat as described above.**
- Further investigation requires highly specialised tests (i.e. blood, radiology and ultrasound, fibroblasts, laparoscopy or laparotomy). Treatment of non-CAH DSD is also complex, but can often be deferred to allow appropriate transfer of care to a specialist centre. In specialist centres there need to be close working relationships between the different specialists. It is not appropriate for surgeons to operate without involving endocrinologists in working up these patients, and **it is essential that the members of the multidisciplinary team work closely together in the management of these cases.**

Congenital adrenal hyperplasia (CAH)

Congenital adrenal hyperplasia (CAH) is an autosomal-recessive condition, and therefore is more common in consanguineous relationships. Many forms exist, as several enzymes involved in the synthesis of cortisol and aldosterone may be deficient; partial cases also occur within each subtype.

Salt-losing 21-hydroxylase deficiency is by far the commonest type. Most forms result in over-masculinisation of the female (although under-masculinisation of the male can also occur in defects near the start of the biosynthetic pathway). Salt loss occurs in several forms (see above), although the second commonest deficiency (11-beta-hydroxylase) causes salt retention and hypertension.

Females usually present as DSD (see above) and males with salt loss, which usually occurs after the first week of life (see above for acute and long-term management). In non-salt-losing forms there will be incomplete early puberty (see below).

Once the diagnosis is established, treat with mildly suppressive doses of hydrocortisone, 12–15 mg/m^2/day in three divided doses and, if salt loss is demonstrated, fludrocortisone, 150–250 micrograms/m^2/day in one dose. Infants may also require oral sodium chloride, 1 gram/10 kg/day (60 mg = 1 mmol).

Addison's disease and Cushing's syndrome

Addison's disease (hypoadrenalism)

Hypoadrenalism may present as an emergency (see above) or be suspected if there is:

- unexplained lethargy
- failure to thrive
- pigmentation of scars and skin
- vitiligo or other signs of autoimmune disease
- a strong family history of hypoadrenalism or unexplained sudden death
- hyponatraemia and hyperkalaemia
- syndrome of candidiasis and hypoparathyroidism predating the hypoadrenalism (HAM or APECED syndrome).

If confirmed by a low 9 a.m. cortisol level (< 150 nmol/litre), treat as outlined above for adrenal crisis.

Cushing's syndrome (hyperadrenalism)

Cushing's syndrome is usually the result of iatrogenic corticosteroid administration (> 12 mg/m^2/day hydrocortisone or the equivalent; see above). Over-secretion of adrenal steroids is rare. Signs of corticosteroid excess include the following:

- poor (zero) growth rate
- red cheeks
- striae
- glucose intolerance
- excess weight gain (central)
- muscle weakness
- hypertension.

Adrenal carcinoma or adenoma may produce Cushing's syndrome. There is often accompanying virilisation and an abdominal mass. The child is usually young, in contrast to the older child with Cushing's disease secondary to an ACTH-secreting pituitary adenoma.

The diagnosis is supported by a **detectable midnight cortisol level (> 50 nmol/litre) or raised urinary free cortisol excretion. The 9 a.m. cortisol level fails to be reduced to undetectable levels in response to dexamethasone 0.3 mg/m^2 given as a single dose the previous night.**

Treatment usually requires specialist surgery.

Hypogonadism and delayed puberty

- Hypogonadism may be secondary to central gonadotrophin deficiency (hypogonadotrophism: LH/FSH low) or peripheral gonadal failure (hypergonadotrophism: LH/FSH high).
- Suspect congenital central hypogonadism in a male neonate with undescended testes and micropenis (shaft length < 2.5 cm). Hypopituitarism may also be present.
- If hypogonadism remains undetected, failure of or incomplete pubertal development will occur.
- Delayed puberty is often familial, but may be induced by emotional or nutritional deprivation.
- There is delayed maturation of gonadotrophin secretion.
- Treat if the delay is severe enough to cause psychological damage.
- Give a brief course of testosterone esters (100 mg by deep IM injection (Sustanon) at 1-month intervals three times in boys) or oral oestrogen (5–10 micrograms/day for 3 months in girls). This allows puberty to be induced and also reduces the risk of later osteoporosis.
- If the hypogonadism is likely to be permanent, continue and gradually increase testosterone to 250 mg/month or oestrogen to 25–50 micrograms/day over a 2½-year period (the latter eventually as a combined oral contraceptive medication to allow withdrawal bleeding).

TABLE 5.8.C.1 Causes of delayed puberty

Low LH/FSH + low testosterone/oestrogen	High LH/FSH + low testosterone/oestrogen
Chronic ill health	Gonadal trauma/infection
Constitutional/familial	Gonadal dysgenesis or Turner's syndrome (XO)
Starvation, low body mass index	Klinefelter's syndrome (XXY)
Genetic (e.g. Kallmann's syndrome, Prader–Willi syndrome)	Some cases of DSD
Prolactinoma (rare)	Autoimmune ovarian damage
Hypopituitarism, hypothyroidism	Galactosaemia
Thalassaemia	

Precocious puberty

- In precocious puberty, early sexual maturity (at less than 8 years of age in females, or less than 10 years of age in males) is usually accompanied by a growth spurt and relatively tall stature for age.
- In central gonadotrophin activation, there is development of full puberty (i.e. breasts and pubic hair with eventual menstruation, or testicular enlargement plus pubic hair and penis development).
- In secondary cases there is excess peripheral sex steroid production/ingestion. Some aspects of puberty will be exaggerated, whereas other tissues will be normal, or may regress (e.g. large penis and pubic hair plus small hard testes in androgen excess in CAH, large breasts but no pubic hair in oestrogen-secreting tumour).
- Idiopathic central precocity is commonest in females, and may be familial.
- Male gonadotrophin activation may be a sign of a CNS tumour.
- Investigation and treatment are complex and specialised, and include suppression of gonadotrophin secretion in central precocious puberty, and surgical removal or suppression/blocking of the peripheral source of sex steroid production in peripheral causes.

Growth hormone deficiency and short stature

Growth hormone deficiency (GHD) may be idiopathic, familial, part of hypopituitarism or isolated.

In the neonatal period, isolated GHD or hypopituitarism may cause hypoglycaemia (*see* Section 3.4). After excluding or treating hypoadrenalism (*see* above), growth hormone may be required to maintain **normoglycaemia and normal growth but such treatment requires expert input**.

Growth hormone is essential for normal growth, and GHD should be suspected in the child who is:

- short in relation to their peers and in comparison with their parents
- growing slowly
- relatively heavy for their height.

Outside the neonatal period, treatment is rarely urgent. Growth hormone is administered as a subcutaneous injection. It is expensive and difficult to store.

The causes of severe short stature include the following:

- secondary to chronic ill health or under-nutrition; these patients are often thin
- secondary to chronic emotional trauma; these patients are often thin
- endocrine (hypothyroid, hypopituitary, GHD, Cushing's syndrome); these patients are often relatively heavy
- syndromic (e.g. Turner's syndrome, etc.); these patients are usually dysmorphic, but some may have few external features, so it should be suspected in all short females outside their genetic range
- disproportionate with short limbs (bony dysplasias, rickets)
- metabolic (storage disorders, osteogenesis); these patients have longer limbs than back.

Short stature in the latter three causes is extremely difficult and expensive to treat.

Hypopituitarism

In the neonate there will be hypoadrenalism with or without GHD leading to hypoglycaemia. Suspect hypopituitarism in any male neonate with cryptoorchidism and micropenis.

Onset later in life may signal an intracranial lesion such as craniopharyngioma (which may be visible as a calcified mass on plain lateral skull X-ray or CT scan; MRI scans show a cystic cavity at the base of the brain). Symptoms outside the neonatal period include the following:

- poor growth/short stature (secondary to GHD)
- lethargy
- hypotension
- hypothermia
- hypothyroidism (see above)
- hypogonadism (see above)
- visual field defects, headache and/or raised intracranial pressure if secondary to tumour.

Treatment is outlined in the sections on individual hormone deficiencies above.

Diabetes insipidus

Isolated diabetes insipidus is rare, but it can occur as part of hypopituitarism or secondary to infiltration of the posterior pituitary by tumour or destruction by infection. Suspect it in any case of:

- dehydration with dilute (colourless) urine
- polyuria and polydipsia not due to diabetes mellitus
- secondary daytime wetting without an obvious cause
- familial history.

It is important to request a fluid balance diary at home, and for carers to allow access to water alone between meals as the only fluid permitted. This will help to identify the many behavioural causes of polydipsia, and will avoid the need for awkward and unnecessary tests of urinary concentrating capacity.

Diagnosis is confirmed by the simultaneous presence of hyperosmolar serum (> 290 mOsm/litre) and dilute urine (< 300 mOsm/litre or specific gravity < 1005).

Treat by allowing free access to water and, if possible, replacement of antidiuretic hormone **with** a long-acting analogue, DDAVP, which can be given intramuscularly, by nasal spray or orally. The dose is titrated to keep **the** specific gravity **of the urine** in **the range** 1005–1010 and/or the serum osmolarity normal. Try to allow one period of diuresis before each dose is due, to prevent dangerous hyponatraemia from over-treatment.

5.9 The child or adolescent with a mental health problem

BOX 5.9.1 Minimum standards

- Knowledge, skills and tests that exclude organic medical causes.
- Effective child protection systems.
- Fluoxetine.
- Resperidone, chlorpromazine and flupenthixol.
- Supportive family therapy.

Introduction

Around 10–20% of all children have one or more mental or behavioural problems (World Health Report 2001). The rates are higher in urban areas and increase in adolescence. One in ten young people suffers from mental illness or symptoms of mental distress severe enough to cause some level of impairment, yet less than one in five receives the treatment that they need.

Prematurity, poor nutritional status, low birth weight, organic brain damage and physical handicap often bring about biological stressors. A disadvantaged socio-economic status of families contributes negatively to the mental health of children. Child development suffers where there is persistent marital discord, parental psychiatric ill health and/or a history of substance abuse. Protective factors include stable care, an adaptable and engaging personality, problem-solving abilities and a supportive network of family and friends.

The aggregate disease burden of these disorders has

not been estimated, and it is complex because many of these disorders can be precursors to much more disabling disorders during later life. Mental health disorders of childhood and adolescence are very costly to society in both human and financial terms.

Psychiatric disorders that arise in adolescence are different from those in children and similar to those in adults. The vulnerability of adolescence relates to difficulty in establishing an identity, during which there may be alienation from the parents. There is also intense emotional interaction with friends, which makes adolescents especially vulnerable to the effects of peer pressure, and issues of sexuality. Emotional disorders include anxiety states, depression, hysteria and specific phobias.

Conduct disorders occur in about the same proportion, and include conditions that range from oppositional defiant behaviour to persistent patterns of aggression and rule breaking. About 20% of the teenagers may present with a mixture of disorders.

The link between adverse family environmental factors and mental health disorders in children and adolescents is fundamental and must be explored as part of the assessment and treatment.

Acute psychiatric emergencies: suicide and deliberate self-harm

In well-resourced countries there has been a persistent rise in fatal suicide attempts, especially in young males. A history of substance abuse, conflict with the law and personal and mental illness are important factors. **The possibility of abuse within (most likely) or outside the family must be at the forefront of a search for why this occurred, as there may be other children 'at risk'.** The method of suicide depends on the means available. Males are more likely to use violent means than females. Overdoses of drugs or poison, hanging and immolation are common methods of suicide.

Suicide is extremely rare in pre-pubescent children, but the frequency rises sharply during the teenage period. Again a search for evidence of abuse must be undertaken.

Deliberate self-harm is a non-fatal act in which a child or young person deliberately ingests noxious substances in excess of therapeutic doses, or causes self-injury. It is best interpreted as a 'cry for help'. Again, the possibility of abuse must be considered in all cases.

Assessment and questions to be asked

- **Are there any indicators or clinical signs of physical or sexual abuse?**
- **Have there been any previous attempts at suicide?**
- Is there a risk of suicide or of a repeated attempt?
- Was a suicide note left?
- Was there pre-planning?
- How likely was the young person to be found?
- What was the method used?
- How lethal was the method used?
- Did the young person know how toxic the substance was?
- What quantity of the substance was taken?
- Was it impulsive in the context of a conflictual relationship?
- Was it to attract sympathy or seek attention (e.g. following a disciplinary crisis or the loss of a friend)?
- Is there a psychiatric disorder?
- What is the family and developmental history, including educational functioning?
- How well does the child solve problems and cope with difficulties?
- How effective and who are the social/parental supports, including adequacy of supervision?

It is important to clarify to the family (preferably in the presence of the child) that information given by the child is confidential.

High-risk factors

- Undiagnosed and unmanaged abuse.
- The risk of repetition is higher in the next 4 weeks after the attempt. It also increases if there is a history of previous self-harm attempts.
- Male gender.
- Lack of support, and easy access to a means of committing suicide (e.g. a firearm or drugs belonging to other family members in the home).
- Presence of depressive illness, with loss of sleep, appetite, depressed mood, agitation, and in particular continued suicidal ideas (hopelessness, inability to enjoy life, asking 'What's the point?').

Treatment

- Treatment of the medical consequences of self-harm is the priority (*see* Section 7 especially Section 7.4).
- Assessment of the child and their family should be undertaken when the child is free from the after-effects of the drug overdose/self-inflicted injury.
- It is important to take the young person's suicidal ideas seriously and not to expose them to sarcasm or ridicule in discussions. Assessment should include consideration of a mental illness and also of the family and social circumstances of the young person and the context in which the self-harm occurred.
- Nothing predicts behaviour better than past behaviour. Those with a low risk of repetition can be offered support during subsequent crises, and arrangements made to assist the child and their family in developing coping strategies. A psychologist, social worker or trained psychiatric nurse (if available) can assist the family in this way.
- **If there is abuse, the child must be protected from further harm by arranging the involvement of social services and the police (as appropriate in the setting).**
- Children at high risk of death need a major input, although inpatient facilities are generally sparse and often unavailable. Depending on resources (or lack of them) the physician needs to improvise and involve social agencies and the family (particularly the extended family if there are immediate parental problems) to provide appropriate supervision, support and treatment.
- Those with a history of substance abuse will need specific counselling.
- The presence of mental illness merits specific treatment (psychological therapies and/or medication) and intervention (see below). Issues that triggered the self-harm should be addressed if possible. Relationship difficulties should be borne in mind.

Depressive disorders

Depression is a recurring illness characterised by episodes of dysfunction. It is common, and has a lifetime prevalence in adults of 15–20%. It has been reported in 1% of preschool children, 2% of school-age children and 5–8% of adolescents; girls are twice as likely to suffer from depression as boys. The incidence is rising, or else depression is being recognised more, with each successive generation. It is detected at a younger age and there has been a parallel increase in suicide in the paediatric age group.

Sadness, unhappiness and misery are common childhood experiences (usually in reaction to adverse family circumstances), but when sadness is extreme in intensity and duration, it may be due to a depressive illness. Depression or depressive illness always needs urgent attention.

The presentation of depression varies with the age of the child. Infants and preschool children cannot express feelings of sadness in language. In this age group, depressive symptoms must be inferred from apathy, withdrawal from caregivers, delay or regression of developmental milestones, and failure to thrive that has no organic cause.

School-aged children are cognitively able to internalise family conflict, criticism or failure to achieve. They display low self-esteem and guilt, but depression is often mainly expressed in somatic complaints (headaches, stomach aches, disturbed sleep and appetite), anxiety (school phobia, excessive separation anxiety), irritability (temper tantrums and other behavioural problems) and academic decline.

Common symptoms in adolescents resemble adulthood depression, with more anger than sadness, hostility mainly towards family, sleep and appetite often normal, drug abuse, academic decline and suicide attempts. A depressed mood (dysphoria) is accompanied by loss of emotional involvement (withdrawal), feelings of guilt and unworthiness, and an inability to cope effectively. A 'depressive disorder' refers to an observable depressed mood, tearfulness, suicidal thoughts, disturbance of sleep and appetite, and a lack of energy.

When the above symptoms persist or occur despite an absence of adverse environmental causes, and functioning is impaired, a diagnosis of depressive illness can be considered. It is worth noting that around 40% of children with conduct (behaviour) disorders have associated mood disturbances, and that children presenting with depression may have other problems, such as anxiety or substance abuse.

Assessment

Assessment should include the child or adolescent and their family or other people who know the young person well. This may be impossible for the teenager who has no family, or for the older teenager who refuses to have their parents involved.

At the beginning of the assessment it is helpful to clarify the bounds of confidentiality. The parents and the child need to understand that what each of them says will not be freely shared without consent. However, it should also be made clear that there are limits to confidentiality in situations in which the law requires reporting, such as abuse, and also in situations where the child's safety is at serious risk – for example, of suicide.

Assess the degree of dysfunction and distress that the symptoms are causing the child and their family.

Assessment requires a detailed history, mental state examination, play and observation of the child–parent interaction. A full medical examination and neuropsychological testing to rule out neurological or learning disorders and to assess the child's developmental capabilities should be undertaken. Psychological assessment tests such as a strength and difficulty questionnaire may be helpful.

Risk factors

- A family history of depression predisposes to depression, and the children of depressed parents are three times more likely to develop depression themselves. Early onset in the parents is associated with a higher risk for the children.
- Family and social environmental risk factors include family conflicts, rejection, lack of communication, lack of expression of love, poor family support systems, abuse (physical, emotional or sexual), and parents who are excessively controlling.
- Adverse life events, such as the death of a parent or other loved one, parental divorce, exposure to suicide, relationship problems and academic failure can precipitate depression.
- Negative emotions such as low self-esteem, self-criticism, negative interpretation of life events and a feeling of lack of control can all contribute.
- The process of puberty can precipitate depression.

Issues in management

The diagnosis of a depressive illness (as opposed to transient sadness, which is very common) should be made **only** after careful history taking and information from the family, school and (if possible) close friends. **Almost all 'depression' in children or adolescents is related to environmental factors, and a diagnosis of depressive illness should only be made when it is certain that environmental factors are not responsible.**

In addition, and in older adolescents, **bipolar disorder** may present for the first time, and a history of symptoms of hypomania should always be undertaken. If such symptoms are elicited, a daily symptom diary may be helpful. There are specific drug treatments for bipolar disorder which include mood stabilisers, and the support of an adult psychiatrist can be very helpful.

Medical conditions that can present with depressive illness must be excluded, using appropriate investigations, in particular vitamin or mineral deficiencies (full blood count), thyroid dysfunction (TSH levels), tuberculosis (chest X-ray) and HIV infection.

If possible, address any stressful factors in the child's environment.

Management of sadness

The opportunity to discuss their difficulties with a sympathetic and helpful listener can itself be very useful to a depressed child or adolescent. The depressed child will tend to blame him- or herself, and there should be an attempt to enable the child to deal with issues without such negative feelings.

It is important to explore sensitively any factors in the child's life that may have led to the episode of self-harm, and to put the problems right as far as possible, while recognising that some situations cannot be changed.

Work to help the young person to understand him- or herself, identify feelings, change maladaptive patterns of

behaviour and improve relationships can be very helpful, and will provide useful skills for them later on in their life.

Consider the mental health of other members of the family, which may be having a significant effect on the child or adolescent. Helping the parents may help the child. Postnatal depression occurs in about 10% of mothers, and tends to recur with each pregnancy. Family therapy and support can also be very helpful.

Regular exercise (e.g. involvement in sport) can be very useful for some people with depression. It is also important to get enough sleep and to eat as healthy a diet as possible.

Formal 'talking therapies' such as cognitive–behavioural therapy can be helpful, but they require specialist training and are not widely available, even in well-resourced countries.

Management of depressive illness

It is vital that the child or adolescent is informed that their symptoms and the effects of the symptoms on their behaviour and educational function are not due to anything they have done or are doing wrong. The young person and their family need to learn how to distinguish between the normal range of feelings and those, including sadness, that suggest the onset or presence of the depressive disorder.

In more severe forms of depressive illness, particularly in adolescents, antidepressants can be helpful, but in general their use is best avoided.

Antidepressant medication

The antidepressants of first choice for adolescents aged 12–18 years are selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine, which can be effective but are expensive. They should be prescribed following baseline measurements of blood pressure and heart rate, physical examination for extrapyramidal symptoms, etc. The suggested baseline laboratory investigations are complete blood count, liver function tests, pregnancy tests for girls, and ECG. The common side effects of SSRIs are dizziness, sweating, diarrhoea, headaches, fatigue, restlessness, initial insomnia, and weight loss or gain. Uncommon side effects may include delayed micturition, blurred vision, skin rashes, etc., and should be explained to the patient and their family.

Usually fluoxetine is best tolerated if given in the morning after breakfast, but in situations in which it causes drowsiness it can be taken in the evening. Changes in symptoms do not occur for at least 3–6 weeks. Follow-up must be insisted upon while the young person is on medication.

Suicidal feelings must be explored routinely at onset and at follow-up.

Fluoxetine: the starting dose in children aged 12 to 18 years is 10 mg daily, and the dose may be increased to 20 mg daily after 1–2 weeks. There is little information about the use of fluoxetine in children under 12 years of age.

Abrupt discontinuation of SSRIs may induce withdrawal symptoms, some of which mimic a relapse of a depressive episode (e.g. tiredness, irritability and severe somatic symptoms).

Once the patient has been free of symptoms and back to normal life for at least 8 weeks, fluoxetine should be continued for 6 months, then gradually reduced and stopped over a period of 6–12 weeks. The speed of reduction should be decided with the patient, taking into consideration any symptoms of withdrawal.

Tricyclic antidepressants have major side effects, including cardiovascular complications. They are also very dangerous in overdose. Therefore they must not be used.

Monoamine oxidase inhibitors (MAOIs) must not be used because of their dangers when taken with certain foods.

Hysterical conversion disorder

This is a subgroup of somatoform disorders. It refers to loss or alteration of physical functioning without organic cause. The child presents with physical symptoms which result in disability in the absence of consistent physical signs or evidence of a physical illness. The most frequent symptoms are pseudo-seizures, loss of sensation and loss of limb function. These are common in post-pubertal female adolescents. They usually arise when the adolescent is facing a predicament that they cannot resolve. This may be related to academic, family, interpersonal, sexual, abuse, religion or societal issues.

As well as a thorough history and interview, the assessment should include a full physical examination to assess symptoms that do not correlate with known neurological pathways (e.g. a gait that is inconsistent and varying). It is important to keep an open mind about the possibility of a physical problem which has not yet manifested itself, and reconsider this regularly.

Pseudo-seizures may occur in adolescents who also have epileptic seizures, and it may be difficult to distinguish between them and provide the correct treatment. A blood test taken within 20 minutes of an episode to measure serum prolactin levels (if facilities for this are available) can be useful for differentiating between pseudo-seizures (prolactin levels are normal) and epileptic seizures (prolactin levels are raised).

Once a psychiatric disorder has been diagnosed, the emphasis should move from medical investigations to amelioration of presenting symptoms and appropriate psychological intervention. The latter should incorporate 'face-saving' formulae to allow the young person to come to terms with the absence of physical disease, but the presence of an illness which is 'real' as far as the young person is concerned. Whatever the cause, the disability and the impact on the young person's life are real, and may be more difficult to manage than a physical illness with similar symptoms. This aspect of the disorder must be carefully explained to the family as well, in case they believe that the young person is faking an illness.

Drugs and alcohol: use and abuse

Drug use and availability have changed radically in the last decade or two. The substances abused depend on availability and supply. As children get older, the proportion who have ever tried drugs increases. Which drugs are illegal and which are socially acceptable vary between countries and among different groups of people in the same country, and the use of drugs by children and adolescents is influenced by this. A child's abuse of drugs is contextual – that is, it depends on societal norms, family history, etc. Parental criminality or substance abuse increases the risk. Reliable data on drug abuse in children are scarce and not validated. However, there is increasing acceptance that the rates of drug use are increasing, particularly in inner-city areas among children who are deprived (e.g. 'street children').

Volatile substance abuse is common in children, but seldom persists into adulthood. Solvents are easily available (e.g. butane gas, lighter fuel, paint thinners, aerosols, etc.), and are most commonly abused through a plastic bag to maximise the effects.

Stimulants such as cocaine and amphetamines are taken in powder form, intranasally or injected. They produce elevation of mood, energy, a reduction in appetite and hallucinations.

Drugs may be used for pleasure, or to remove (however briefly) the pain of daily life. Many drug users live in very difficult conditions and/or have mental health problems in addition to their drug habit. Prostitution is often associated with drug use, trapping (mainly women) in a vicious cycle. There is also a strong association of substance abuse with conduct disorder. In conduct disorders there is a repetitive and persistent pattern of behaviour in which societal norms or rules are violated (e.g. fighting, bullying, cruelty to people and animals, destruction of property, stealing and deceit). Many drug abusers will take up crime to pay for their drugs.

Assessment

It is important to establish the extent, frequency and severity of drug abuse or dependence. In addition, information needs to be elicited concerning behavioural patterns, social competency, educational functioning, peer relationships and psychiatric status.

Physical examination should include a check for fresh injection marks, old scars or the physical sequelae of drug use.

Management

There are very few, if any, specialised treatment centres for children who abuse drugs. Treatment outcome will vary according to the chronicity and/or the substances abused. For example, only a limited impact is made on alcohol or marijuana abuse, whereas heroin or cocaine treatment programmes are more successful in reducing the use of these drugs.

Methadone as part of a well-controlled and structured treatment system is the most common approach to managing long-term opiate dependence. However, it is rarely available in resource-limited settings. The initial dose for children over 15 years of age is 10–20 mg daily, increasing by 10 mg/day until there are no signs of withdrawal or toxicity (the usual dose is 40–60 mg/day). Opiates can give rise to nausea and vomiting. Withdrawal symptoms include restlessness, irritability, and increased bowel activity with abdominal pain. Methadone treatment is not appropriate for those with a short history of opiate dependence.

Schizophrenia

This is a serious mental illness characterised by abnormalities of thinking, perception and emotion, usually first diagnosed in late adolescence, although rarely the onset can be seen in childhood. Consider the diagnosis if two or more of the following symptoms are present for 1 month or longer:

- delusions: beliefs which are unshakeable
- hallucinations: 80% of affected children have auditory hallucinations; visual hallucinations are more likely to be due to an organic medical disorder such as a brain tumour or poisoning
- disorganised (incoherent) speech
- grossly disorganised or catatonic behaviour
- negative symptoms (flat affect).

The onset is usually insidious. Many children have pre-existing problems with social withdrawal, disruptive behaviour, developmental delay and language problems, and then go on to develop more florid symptoms such as hallucinations. Mood disorders may present with schizophrenic-like symptoms, and making the diagnosis may be difficult.

Assessment

Any diagnosis is dependent on detailed history taking and examination, and schizophrenia is no exception. To evaluate the progress, it is important to define the baseline symptoms, functioning and problems in various aspects of the young person's life (i.e. education, family and social functioning).

Before a definitive diagnosis of schizophrenia is made, **organic medical conditions must be excluded** by the following tests. However, it has to be accepted that in resource-limited settings many of these tests will not be available: blood tests for haemoglobin, indices such as MCV (to rule out vitamin B_{12} deficiency), thyroid function, liver and renal function, heavy metals such as lead, mercury and arsenic, HIV indicators, the Wassermann reaction for syphilis, urine test for toxicology, an EEG to help to rule out temporal lobe epilepsy, and a CT scan of the brain.

Management

Children and adolescents with schizophrenia present a challenge as they are seriously ill, and often their social and educational progress is seriously disrupted. Treatment is difficult, and all management should be under the supervision of a psychiatrist (if available). Treatments aim to reduce the frequency of relapses and disability.

It is important to work closely with the family. Negative symptoms such as blunting of emotions, impoverished thinking and lack of motivation are particularly distressing to relatives. Furthermore, highly expressed emotions and negative feelings increase the risk of relapse. The family will need support and help to manage their child's symptoms. The techniques for reducing highly expressed emotions require specialist training.

Pharmacological treatment to control symptoms is the important initial management. Psycho-educational, social, cognitive and family intervention programmes are important in long-term management. Oral neuroleptics provide the patient with a sense of control. Any adverse effects will quickly become apparent, but the medication must be administered daily and the patient may not always be compliant. Depot neuroleptics provide a way of enhancing compliance.

Atypical antipsychotic drugs are now the treatment of choice (if available), as they have less extrapyramidal side effects. Risperidone can be given to children over 12 years of age, starting at 2 mg per day and increasing by 1 mg per week to a maximum daily dose of 8 mg. Side effects include postural hypotension, weight gain, hyperglycaemia and mild extrapyramidal signs.

Standard antipsychotic drugs are more likely to be available in resource-limited settings. Standard antipsychotic treatment for acute schizophrenic symptoms is usually initiated with chlorpromazine. For children aged

12–18 years, start with oral treatment with 25 mg three times a day or 75 mg at night, and then gradually increase the doses until there is control of symptoms, usually achieved with a maximum dose of 100–300 mg daily. Premature changes in drug choice should be avoided, as the response time may be 30 days or more.

Poor response may be due to an inadequate dose or poor compliance.

Depot medication is suitable for long-term treatment (flupenthixol by deep IM injection into the outer buttock or lateral thigh with a test dose of 20 mg, then after 7 days 20–40 mg repeated 3- to 4-weekly according to the response. The usual maintenance dose is 50 mg every 4 weeks to 300 mg every 2 weeks,

Side effects include extrapyramidal signs (Parkinsonism, dystonia, restlessness and tardive dyskinesia), hypotension and less commonly neuroleptic malignant syndrome (hyperthermia, fluctuating consciousness, muscle rigidity and autonomic dysfunction).

Post-traumatic stress disorder (*see* also Section 1.23)

Introduction

Nearly all children and adolescents who have experienced catastrophic situations will initially display symptoms of psychological distress, including intrusive flashbacks of the stress event, nightmares, withdrawal and inability to concentrate, among others. **Most children and adolescents will regain normal functioning once their basic survival needs are met, safety and security have been restored, and developmental opportunities have been regained, within the social, family and community context.**

Post-traumatic stress disorder (PTSD) is a relatively new diagnostic category first officially created by DSM-III in 1980. Around 25–35% of those exposed to traumatic events develop PTSD. Individual differences in response to trauma depend on the following:

- stressor severity and degree of exposure to the stressor
- exposure to previous traumatic events
- the child's perception of the event
- the child's appraisal of the threat to their survival, and the degree of human accountability
- for younger children, the response and functioning of adults, particularly close family, around them can be important.

Anxiety disorders, abnormal grief reaction, somatic complaints and impairment in educational functioning can all occur.

Diagnostic criteria

The child has experienced an event that is outside the range of normal experience and that is life-threatening to them or to those close to them. There is persistent re-experiencing of the traumatic event – that is, distressing recollections, dreams or flashbacks.

There is avoidance of the stimuli associated with the trauma, and a range of signs of physiological arousal occur, such as difficulty in sleeping, irritability or poor concentration.

In younger children, repetitive play related to the trauma may be present. They may have frightening dreams that have no obvious content, and may regress in their development.

Assessment

It must first be established that the child has experienced a traumatic event that preceded the onset of the symptoms. The traumatic event may not necessarily lead to development of PTSD. Instead, the child may develop acute stress disorder or sadness.

When assessing the child, the interviewer will need to take account of the child's maturation, and their verbal facility and functioning. Details of the traumatic event, the child's perception of the event, and their response immediately and later, should be evaluated.

The differential diagnoses include obsessive-compulsive disorder, schizophrenia and anxiety disorder. Flashbacks may need to be distinguished from intrusive and unwanted thoughts that are unrelated to the traumatic event, which occur in obsessive-compulsive disorder.

Management of trauma-affected children (*see also* Section 1.23)

If possible, reuniting the child with their parents or other close relatives and restoring normal comforting routines is helpful.

Some children will require more specialised interventions to address their suffering and help to restore their flow of development. Immediately after traumatic events, activities and opportunities that allow children to talk about or otherwise express painful experiences and feelings (e.g. by physical and artistic expression) are most beneficial if facilitated by people whom the children know and trust, and have continued contact with.

The goals of psychological treatment are reduction of symptoms, development of coping skills, and helping the individual to gain a sense of well-being and control. Education and gradually increasing goal setting help the child to relax, solve problems and gradually achieve mastery over fearful thoughts. The help of a clinically trained psychologist or psychiatrist may be needed to plan the treatment.

Trauma counselling should never be provided unless an appropriate and sustained follow-up mechanism is guaranteed.

The psychosocial well-being of adults, particularly parents and caregivers, has a direct impact on that of children, and should therefore be addressed through concurrent parent-focused psychosocial interventions. The participation of children, and adults, in decisions that affect their lives has a positive effect on their mental health, empowers them, and helps them to regain control over their own lives.

Panic attacks

These are common in children and adolescents, and can mimic physical illnesses. Hyperventilation, sometimes with tetany, is a key feature, as well as the fear of 'going crazy' or dying. The best way of controlling such attacks is to explain the physiological features of panic to the child and their family, and to teach proper breathing techniques (namely to breathe slowly at a rate normal for the child's age).

Preventive intervention

The promotion of mental health through a healthy lifestyle brought about by health education and life skills training has the potential to equip a young person for their journey through life. There is material available in the public domain on life skills training (e.g. on the WHO/UNICEF websites)

which has been used in many resource-limited and middle-income countries.

Autism and autistic spectrum disorders

This is a group of disorders with similar features, although an individual child may not display all of them, and the severity may vary. Autism becomes evident before 3 years of age, but children with other conditions that form part of the autistic spectrum may present later (e.g. at school age).

Autistic behaviour may occur as an isolated problem, or it may be a component of a number of childhood developmental disorders. It is important to consider these when assessing a child, in case intervention may help. Sensory deficits, particularly deafness, which may be hard to identify in a young child, are especially important in this respect. Children with hydrocephalus, metabolic disorders (e.g. phenylketonuria), hypothyroidism, fetal alcohol syndrome, tuberous sclerosis, neurofibromatosis, Down's syndrome and other chromosomal disorders may exhibit features of autism.

Autistic children characteristically have difficulties with the following:

- social interaction and reciprocity
- language development and communication skills
- imagination and play
- rigid thinking
- restrictive and repetitive stereotypical patterns of behaviour, activities and interests.

Social interaction

Autistic children may make little or no eye contact. They may not be able to share experiences or to understand the feelings of others, or recognise clues to their feelings from their behaviour (e.g. that people who are crying are sad).

Language and communication

Young children with autism may not point to get attention or to show another person something. They may never develop any useful language, or they may have unusual speech with abnormal intonation, jumbled words, incomprehensible sounds, or repetition of the same words again and again (echolalia).

Cognitive function

Children with autism may have global cognitive impairment or general impairment but considerable skill in some areas (e.g. numbers, art).

Rigid thinking and ritualistic behaviour

Autistic children often have very structured repetitive play (e.g. organising objects in a certain pattern). They may persist much longer than usual in putting things in their mouths, or they may hold on to objects, moving and feeling them in their hands, for long periods. Routine is very important, and they are often very upset by any disruption, which may lead to outbursts of temper.

Management

There is no cure as yet for autism. Management focuses on encouraging the child to learn as much as possible and to develop behaviour that helps him or her to live happily within the family and community.

Support for the family in caring for these children, who can be very challenging, is essential. Education for the family and community about the difficulties of autistic children, so that their behaviour is not misinterpreted as naughtiness, or caregivers criticised inappropriately, is also very important. Healthcare professionals and teachers experienced in the care of children with autism can give a great deal of assistance to families.

Vigilance for other problems, especially with hearing or vision, which if undiagnosed will add to the child's difficulties, should be maintained.

For some children with autism who have severe aggressive behaviour and only under expert supervision consider risperidone:

- **Child over 5 years and 15–20 kg:** 250 micrograms daily increased if necessary after at least 4 days to 500 micrograms daily; thereafter increased by 250 micrograms daily at 2-week intervals to maximum of 1 mg daily
- **Child over 5 years and over 20 kg:** 500 micrograms daily increased if necessary after at least 4 days to 1 mg daily; thereafter increased by 500 micrograms daily at 2-week intervals; max. daily dose 2.5 mg if under 45 kg; maximum daily dose 3 mg if over 45 kg.

Review effectiveness and side effects after 3–4 weeks; stop if no response at 6 weeks.

Asperger's syndrome

Asperger's syndrome has some features in common with autism, in that affected individuals also have difficulties with social interaction, especially in understanding the usual patterns of social behaviour of their community. They often develop very deep and detailed knowledge about subjects that interest them, and become experts who can contribute to society, but they may also become isolated if others do not share or understand their interests.

Asperger's syndrome is usually identified later than autism, often when children are at school, and are recognised as different from their peers. They may be bullied and very lonely, as they long to have friends and 'fit in', but do not have the social skills to enable them to do so.

Like autism, there is no cure for Asperger's, but teaching from as early an age as possible about appropriate behaviour can help these children. Education for their families and communities, so that they understand that the child has a condition which makes it hard for him or her to pick up social clues, and is not just being difficult, along with appreciation of any special talents, is essential. If it is acceptable to the child or adolescent, written information to give to people to explain what they find hard may be useful.

Attention deficit hyperactivity disorder (ADHD)

Children with ADHD characteristically have difficulties with the following:

- inattention
- hyperactivity
- impulsivity.

These features must be present before the age of 6–7 years, evident in more than one situation (e.g. at home and at school), and interfere with the child's social or educational functioning.

These characteristics may persist into adult life, resulting in inattentive and disorganised or impulsive risk-taking behaviour.

Inattention
Children with ADHD cannot concentrate for very long, especially on tasks they have been given which have no immediate reward (e.g. schoolwork).

Hyperactivity
These children are always on the move. Young children with ADHD may run, jump, climb, make a lot of noise and never settle to anything. School-age children and adolescents have difficulty sitting still, and may be constantly tapping their feet, wriggling and fidgeting.

Impulsivity
Children with ADHD do not think before they act. They may have accidents or get into trouble for recklessness.

Other problems
Children with ADHD can be exhausting. They are often in trouble because they are so active and may have poor relationships with other children and adults, and low self-esteem. They may sleep badly, struggling to get to sleep or waking frequently, and be poor eaters because they cannot sit still for long enough to finish a meal.

Causes
There is no known cause of ADHD. Some of the contributory factors include the following:
- genetic: parents or siblings affected
- living conditions: ADHD is more common in children from disadvantaged backgrounds
- depression in the child's mother
- these factors may all interact.

In addition to occurring alone, the features of ADHD may be seen in young people with neurological conditions such as head injuries, fetal alcohol syndrome, encephalitis and meningitis, epilepsy, hypothyroidism and some syndromes, such as fragile X syndrome, Williams' syndrome and tuberous sclerosis.

Comorbidities
Children with ADHD often have additional problems, such as mild cognitive impairment, delayed language development, poor coordination, reading difficulties and mood disorders.

Assessment
- Developmental history, especially any delay and when noted.
- Pregnancy and birth, including any exposure to drugs or alcohol.
- Family history of similar problems, maternal depression and social circumstances.
- Educational progress: both intelligent children and children with specific learning difficulties who are bored can be disruptive.
- The parents' expectations of the child and their response to his or her behaviour.
- Medical history and examination for neurological problems, including any medication being taken by the child that might affect his or her behaviour.
- Careful observation of the child in several settings, including home and school.

Management
There is no cure for ADHD, but careful management can help these children and their families a great deal.
- Look for any health problems that might be contributing to the condition and could be treated (e.g. large tonsils and adenoids preventing undisturbed sleep).
- Explain to the child and their family that they have a disorder that affects their behaviour, and that they are not just a naughty child.
- The most useful management is behavioural.
- Drugs may be helpful in severe cases.

Behavioural management
Children with ADHD do best where there are as few distractions as possible around them, and where there are clear rules about the conduct that is expected, with praise or reproof given immediately if merited. When doing tasks such as schoolwork, they are best on their own or in a small group, sitting near to the person in charge. They often have low self-esteem. Giving praise when they do well, with frequent small rewards, is very helpful.

Drugs
The most widely used drugs for ADHD are stimulants such as methylphenidate (Ritalin), which can be given to children aged over 6 years in a dose of 5 mg once or twice daily, increasing by 2.5–5 mg weekly up to a maximum daily dose of 60 mg. If methylphenidate has not made any difference after 3 weeks at full dose it should be stopped. Slow-release preparations are also available and can be given less frequently. If effect wears off in the evening (with rebound hyperactivity) a dose at bedtime may be appropriate (establish need with trial bedtime dose). Careful supervision is needed, and ideally children who require these drugs should be treated by a professional experienced in their use.

Some useful websites

Patel V, Jenkins R, Lund C, the PLoS Medicine Editors (2012) *Putting Evidence into Practice: The PLoS Medicine Series on Global Mental Health Practice*. *PLoS Medicine*, **9**, e1001226. www.plosmedicine.org/article/citationList.action;jsessionid=54EC3D8B00FC6B7057A6FD681B26F071?articleURI=info%3Adoi%2F10.1371%2Fjournal.pmed.1001226

National Institute for Health and Clinical Excellence (2005) *Depression in Children and Young People.* www.nice.org.uk/guidance/QS48

Royal College of Psychiatrists *Fact Sheets for Children and Young People*. www.rcpsych.ac.uk/healthadvice/parentsandyouthinfo.aspx

World Health Organization. *Child Mental Health Atlas.* www.who.int/mental_health/resources/Child_ado_atlas.pdf

National Institute for Health and Clinical Excellence (2006) *Methylphenidate, Atomoxetine and Dexamfetamine for Attention Deficit Hyperactivity Disorder (ADHD) in Children and Adolescents*. www.nice.org.uk/guidance/TA98

Eapen V, Graham P and Srinath S (2012) *Where There Is No Child Psychiatrist: a mental healthcare manual*. www.rcpsych.ac.uk/publications/books/rcpp/9781908020482.aspx

5.10 Nutritional disorders

5.10.A Vitamin or mineral deficiencies

BOX 5.10.A.1 Minimum standards
- Adequate diet.
- Vitamins A, B, C, D and K.
- Folic acid.
- Zinc.
- Iodine.

Vitamin A deficiency (VAD)

Significance

- Vitamin A deficiency is the single most important cause of childhood blindness in resource-limited countries.
- It makes a significant contribution to morbidity and mortality from common childhood infections, even at subclinical levels of deficiency.
- A Cochrane review indicates that regular vitamin A supplementation reduces mortality by 24%.

Prevalence

- Vitamin A deficiency is endemic in at least 60 countries worldwide, especially in Africa, South and South-East Asia, some areas of South America and the Western Pacific.
- Around 250 million preschool children are at risk.
- It causes 250 000–500 000 cases of blindness per year.

Good food sources are red palm oil, mango, pawpaw, dark green leafy vegetables, unskimmed milk, eggs and liver.

Aetiological factors

- Persistent inadequate intake of vitamin A exacerbated by insufficient consumption of dietary fat, leading to ineffective absorption.
- Frequent infections, especially measles, gastroenteritis and respiratory infections, resulting in decreased food intake, malabsorption, increased urinary loss, and increased utilisation of vitamin A by the body resulting in depletion of liver stores. The decrease in vitamin A levels in the body in turn predisposes children to infection, and so a vicious cycle is set up.
- Vitamin A deficiency is common in the context of poverty, social under-development, hostile living environments, water shortage and food scarcity, and individual factors such as lack of breastfeeding, inappropriate weaning practices and increased physiological needs during periods of rapid growth.

Clinical effects

- Night blindness (decreased ability to generate rhodopsin in the retinal rod photoreceptors essential for vision in dim light).
- Compromised integrity of epithelial surfaces due to loss of mucus-producing goblet cells, leading to 'dry eye' (conjunctival xerosis), Bitot's spots, corneal xerosis, corneal ulceration, and irreversible damage to the eye (keratomalacia).
- Depressed immunity (both innate and adaptive immunity), which results in increased susceptibility, duration and severity of common infections (e.g. acute respiratory infection, diarrhoea, measles).
- Poor growth, apathy and slow development.

TABLE 5.10.A.1 Signs of vitamin A deficiency in the eyes

Sign	Description
Night blindness	Inability to see in dim light (e.g. at dawn or dusk). Often occurs in the later part of pregnancy
Conjunctival xerosis	The conjunctiva looks dry and slightly rough instead of smooth and shiny
Bitot's spots	White foamy patches on the conjunctiva. Not always present
Active corneal lesions: At this stage the condition can worsen within a few hours and complete or partial blindness can result	
Corneal xerosis	The cornea looks dry and cloudy
Ulcers on the cornea	Often on the edge of the cornea
Keratomalacia	The cornea is cloudy and soft like jelly. Rare

Assessment of vitamin A status

There are no simple tests for vitamin A deficiency, but it is likely to affect communities where vitamin-A-rich food is scarce and infection and/or malnutrition rates are high.

- Vitamin A deficiency becomes a public health problem when the following are prevalent in the child population:
  - night blindness (> 1%)
  - Bitot's spots (> 0.5%)
  - corneal xerosis with or without ulceration (> 0.01%)
  - corneal scarring (> 0.05%).

Prevention

- Encourage the use of local foods rich in vitamin A.
  - Provide dietary education about vitamin-A-rich foods (e.g. dark green leafy vegetables, carrots, mango, papaya, eggs, orange fruits, liver, red palm oil, fatty fish).
  - Treat the siblings and mother. Mothers are especially vulnerable to vitamin A deficiency, and should be supplemented in the first month of lactation.

- Give regular supplementation every 4 to 6 months as described in Table 5.10.A.2.
- Prevent recurrent infections by recommending the use of impregnated nets, deworming, using clean water and breastfeeding.

TABLE 5.10.A.2 Vitamin A supplements to prevent vitamin A deficiency

Target group	Immunisation contact	Vitamin A dose
Infants under 6 months who are not breast fed or breast fed infants whose mothers have not received vitamin A supplements.		50 000 IU
Infants aged 6–11 months	Measles vaccine contact	100 000 IU
Children aged 12–59 months	Booster doses Special campaigns Delayed primary immunisation doses	200 000 IU every 4 to 6 months

Regular vitamin A supplementation is advised for all children in resource-limited countries. It has been shown to reduce all causes of mortality, and especially mortality from diarrhoea.

If a child has malnutrition, severe diarrhoea or measles, give one high-dose vitamin A capsule, according to Table 5.10.A.3, unless they have received a dose in the previous month.

Treatment

If there are any eye signs, give vitamin A as indicated in Table 5.10.A.3.

TABLE 5.10.A.3 Doses of vitamin A for treatment of clinical deficiency

Age	Day 1	Day 2	Two weeks later
< 6 months	50 000 IU	50 000 IU	50 000 IU
6–12 months	100 000 IU	100 000 IU	100 000 IU
> 12 months	200 000 IU	200 000 IU	200 000 IU

If there are ulcers or the eyes look soft or cloudy, instil atropine 0.1%, three times a day for 3–5 days, and a topical antibiotic. Cover the affected eye with a saline-soaked bandage.

Deep IM injection of vitamin A (retinyl palmitate) 50 000 IU for children under 2 years of age, and 100 000 IU for those over 2 years, should be given if severe stomatitis, persistent vomiting or malabsorption are present.

Vitamin B_1 deficiency: beriberi

- This may occur in areas of severe nutritional deprivation where little more than polished rice is consumed. It is uncommon in Africa, as the staple is maize or wheat, which contains vitamin B_1.
- It affects adults, children and breastfed infants of thiamine-deficient mothers.
- It is often mistaken for oedematous malnutrition (kwashiorkor), nephritis, cerebral malaria, encephalopathy or septicaemia.
- It causes wet (cardiac) or dry (neurological) beriberi:
  - cardiac failure with breathlessness, oedema and tachycardia
  - peripheral neuritis, with tingling and burning of feet, and reduced tendon reflexes
  - acute encephalopathy and coma.
- An aphonic form is characterised by a noiseless cry due to laryngeal nerve paralysis.

Beriberi is rapidly fatal.

- The initial dose is 50–100 mg thiamine hydrochloride. IM or orally. This is particularly effective in heart failure (facilities for treating anaphylaxis must be available).
- Continue with 10 mg/day for children under 2 years of age, 25 mg/day for those aged 2–12 years, and 50 mg/day for those over 12 years for 3–4 days.
- Patients with beriberi often have other B vitamin deficiencies.
- Good food sources of vitamin B_1 are pork, whole grain cereals, legumes, nuts and liver.

Nicotinic acid (niacin) deficiency: pellagra

Nicotinic acid is synthesised from the essential amino acid tryptophan, and pellagra is found where the diet is deficient in either nicotinic acid or tryptophan. It is common where maize is the staple diet, as in many parts of Africa. Maize is deficient in tryptophan, and the nicotinic acid is bound and unavailable.

Clinical features

- Dermatosis of parts of the skin exposed to sunlight, namely the neck (Casal's necklace), face and hands, usually seen in children over 5 years.
- Diarrhoea and malabsorption.
- Encephalopathy, which is rare in children.

Treatment

- Nicotinic acid:
  - 10 mg three times daily for 7 days in children under 2 years of age
  - 25 mg three times daily for 7 days in children over 2 years. In severe cases give 100 mg IV.
- Treat other B vitamin deficiencies at the same time (thiamin and riboflavin).
- Improve the diet with protein and green vegetables, peanuts, wholegrain cereals, meat, fish, chicken and liver.

Vitamin C deficiency: scurvy

This usually presents at the age of 4–10 months. Cow's milk is low in vitamin C.

- Vitamin C is needed for collagen formation (in bones, cartilage, teeth and capillary walls).
- It is important for the healing of wounds.
- It increases iron absorption.
- It is found in citrus fruits, vegetables and breast milk.

Very little vitamin C is present in cow's milk, especially if it is heated.
- Vitamin C deficiency is found in severe malnutrition and in children fed on very poor diets in institutions.

Clinical features
- Spontaneous haemorrhages, especially from gums, and defective bone, cartilage and dentine formation.
- Local tenderness and swelling of the legs (due to subperiosteal haemorrhages), which may present as irritability when the child is picked up or moved.
- Pseudo-paralysis of the limbs.
- Haemorrhagic and spongy changes in the gums.
- Petechiae and ecchymoses around the eyes.
- Microscopic haematuria may be present.
- The anterior ends of the ribs swell.
- Mild anaemia.
- Increased risk of fractures.
- Poor healing of fractures and wounds.
- Characteristic X-ray appearance: loss of trabeculae in long bones gives a ground-glass appearance, dense lines of calcification in the epiphysis next to the epiphyseal plate and calcification of subperiosteal haemorrhages.

Treatment
- **By mouth**
  - Child 1 month–4 years 125–250 mg daily in 1–2 divided doses
  - Child 4–12 years 250–500 mg daily in 1–2 divided doses
  - Child 12–18 years 500 mg–1 g daily in 1–2 divided doses.
- A subsequent improvement in diet is needed, with plenty of fresh fruit and vegetables.

Vitamin D_3 deficiency: rickets

Vitamin D deficiency causes the following:
- rickets (failure of mineralisation of growing bone)
- hypocalcaemic tetany in infancy
- osteomalacia in adults.

Nutritional rickets is most prevalent in North Africa, the Middle East and Pakistan. Asian and Afro-Caribbean children are also at risk in the UK and other countries where there is limited sunshine. Vitamin D deficiency is unusual in African children over 18 months, as at this age they can walk and therefore go out into the sunshine. Older children in Africa with rickets must be investigated for causes of rickets other than vitamin D deficiency, such as dietary calcium deficiency or inherited forms of hypophosphataemic rickets.

Biochemistry
- Vitamin D increases Ca^{2+} absorption from the gut, reabsorption of Ca^{2+} from the kidney, and a phosphate diuresis.
- Vitamin D deficiency reduces Ca^{2+} and increases parathyroid hormone (which increases phosphate loss by the kidney), resulting in low Ca^{2+} and low phosphate levels. Subsequently there is a rise in alkaline phosphatase and then the X-ray features of rickets occur.

Aetiology
- Prolonged breastfeeding, especially if the mother is vitamin D deficient.
- Lack of vitamin-D-containing foods such as oily fish, eggs, butter and margarine.
- Lack of sunlight exposure (UV light) (black- and brown-skinned children living indoors or in countries where there is little sunlight are particularly at risk).
- An infant's diet contains only small amounts of vitamin D, so fortification of foods and vitamin D supplementation is recommended.
- If a child presents with rickets and has normal exposure to sunlight, consider a hypocalcaemic diet (reported in South Africa and Nigeria). Cereals can bind calcium and prevent its absorption.
- Rarely, there is a metabolic disorder such as familial hypophosphataemic rickets. Where consanguinity is common, renal tubular disorders can produce this.
- Vitamin D deficiency also occurs in chronic renal and liver failure.

Clinical features
- 1,25-Dihydroxyvitamin D crosses the placenta, and the neonate generally has sufficient levels for the first few months of life.
- Disturbance of the normal growth of the epiphyseal plate leads to the formation of inadequately calcified new bone at the diaphysis edge of the plate (so-called osteoid tissue). The proliferating zone on the epiphyseal side of the plate enlarges excessively, producing a swelling of the plate. Osteoid tissue may also form subperiosteally. There is also demineralisation of the skeleton. The following features result from these abnormalities:
  - epiphyseal swelling (especially distal radii at the wrists, and also the ankles and knees)
  - craniotabes (soft areas of the skull bones, especially of the occiput, which when pressed gently are easily depressed)
  - rickety rosary (enlarged costochondral junctions)
  - delayed fontanelle closure
  - curvature of the shafts of the tibia and femur (may occur in severe cases)
  - bossing of the frontal and parietal skull bones due to osteoid formation
  - pigeon chest (pectus carinatum)
  - Harrison's sulci
  - deformities of the thoracic and lumbar spine can produce kyphoscoliosis and lumbar lordosis
  - pelvic bone deformities in female children can lead to subsequent birthing difficulties due to damage to the inlet and outlet of the birth canal
  - delayed dentition
  - delayed gross motor development with generalised muscle weakness and hypotonia
  - growth retardation
  - occasionally, especially in infants, symptoms of hypocalcaemia.

Diagnosis
- Very elevated plasma alkaline phosphatase activity.
- Usually normal, but possibly slightly low, plasma calcium levels.
- Very low plasma phosphate levels.

- Lowered plasma levels of 25-hydroxyvitamin D_3, but often this cannot be tested for.
- The best sites to radiologically assess for rickets are those where there is rapid bone growth, namely the wrists and knees.
  - Typical X-ray appearance: cupping and fraying of the distal ends of the long bones, such as the ulna and radius.
  - There is widening of the metaphyseal plate due to osteoid formation.
  - The periosteum may be raised.
  - There may be abnormal curvature of bones and generalised under-calcification.

Prevention measures

- Exposure to sunlight and foods such as egg yolk, milk and fortified margarine.
- Vitamin D_2 (ergocalciferol) supplementation, 400–600 IU daily.

Treatment

- Vitamin D_3 (colecalciferol) or vitamin D_2 (ergocalciferol) by mouth daily for 4 weeks: child aged 1–6 months 3000 IU, 6 months–12 years 6000 IU and 12–18 years 10 000 IU.
- If hypocalcaemia is present, calcium supplements may be added in the early stages of treatment.

Vitamin K deficiency

- Vitamin K is a cofactor for the hepatic synthesis of clotting factors (prothrombin, and factors VII, IX and X).
- Sources are green leafy vegetables, meat, liver, cheese, and synthesis by gut flora.
- Deficiency may occur as a result of the lack of bile salts and the malabsorption of fats after the use of broad-spectrum antibiotics, or in the breastfed newborn whose gut is not yet colonised with bacteria and therefore does not produce vitamin K.
- Treat bleeding due to vitamin K deficiency with 250–300 microgram/kg (max 10 mg) IV; neonates 1 mg. Repeat doses every 8 hours if needed.
- Prevent haemorrhagic disease of the newborn by giving 1 mg vitamin K to all newborn infants either orally or IM (preterm 400 microgram/kg maximum dose 1 mg).

Folic acid deficiency

- The most important issue here is that women who are deficient in folic acid at the time of conception and in early pregnancy are at increased risk of having a baby with a neural tube defect (spina bifida or anencephaly).
- Relative deficiency occurs in haemolytic anaemias and in preterm infants (*see* Section 3.3 and Section 5.11.C).
- Deficiency occurs in malabsorption syndromes such as coeliac disease and blind loop syndromes.
- Anticonvulsants such as phenytoin may interfere with the metabolism of folic acid.
- Consequences of folic acid deficiency include the following:
  - fetal abnormalities
  - megaloblastic anaemia, neutropenia and thrombocytopenia.
- Sources of folic acid include green leafy vegetables, oranges and other fruit, legumes, nuts, liver and yeast.

Treatment

- All women who are anticipating pregnancy should be taking an additional 400 micrograms of folic acid per day before and throughout pregnancy.
- To treat deficiency, give infants 500 micrograms/kg once daily and children over 1 year of age 5 mg once daily.
- Treat for up to 4 months and exclude concomitant vitamin B_{12} deficiency, which if untreated could result in neuropathy.
- For haemolytic anaemia, treat with 2.5–5 mg orally once a day for children aged 1 month to 12 years, and 10 mg once a day for those over 12 years of age.
- Neonates 50 micrograms once daily or 500 micrograms once weekly.
- Give preterm infants 100–200 micrograms orally per day.

Iodine deficiency

Iodine deficiency in pregnancy causes maternal hypothyroidism and cretinism in the newborn.

- It is one of the commonest causes of disability worldwide.
- Clinical features of cretinism range from mild neuromuscular incoordination and cognitive deficit to severe mental retardation, spasticity and deafness, and severe stunting of growth.
- Iodine deficiency is endemic in mountainous regions far from the sea (e.g. the Andes, the Himalayas, Central Africa, Papua New Guinea) and areas where iodine is eluted from the soil by repeated flooding (e.g. Bangladesh).
- The prognosis is poor even after early recognition and treatment with thyroid hormone.
- Prevention is by salt iodination or a single oral dose of iodine in pregnancy.

Zinc deficiency

- Zinc is an essential trace element required for maintaining cells, bone growth and immune function (it scavenges for free radicals).
- Deficiency often occurs in children living in resource-limited settings, and arises from either insufficient intake of zinc-containing foods or insufficient absorption.
- Foods high in zinc are of animal origin, such as meats, fish and dairy products.
- Dietary fibre and phytates found in cereals and legumes bind zinc and reduce its absorption.
- Zinc deficiency is difficult to diagnose, as serum zinc levels do not reflect total body zinc levels.
- Zinc deficiency is associated with stunting of growth, impaired immunity and increased risk and severity of diarrhoea and respiratory infections.
- Zinc deficiency is a feature of the rare disease acrodermatitis enteropathica, in which children present with peri-oral and peri-anal rashes.

Therapeutic zinc supplementation is now recommended as an adjunct to oral rehydration therapy for treatment of diarrhoea. Routinely giving 10 mg per day to children under 6 months of age and 20 mg per day to those over 6 months of age for 10–14 days can reduce diarrhoea duration and severity and the likelihood of subsequent infections for 2 to 3 months.

Zinc supplements of 2 mg/kg/day should be an essential component of the mineral mix used in the management of severe malnutrition.

Useful website

World Health Organization (1997) *Vitamin A Supplements: a guide to their use in the treatment and prevention of vitamin A deficiency and xerophthalmia*, 2nd edn. http://whqlibdoc.who.int/publications/1997/9241545062.pdf

5.10.B Severe malnutrition

BOX 5.10.B.1 Minimum standards

- Scales (accurate to 5 gram), metre length board, MUAC tapes, care charts.
- ReSoMal.
- Vitamin and mineral mixtures.
- Antibiotics.
- IV 10% glucose.
- Antihelmintic drugs.
- F-75 and F-100 feeds.
- Barrier skin cream.
- Sources of heat (blankets, hat, warm room, clothes).

Introduction

Severe acute malnutrition (SAM) is characterised by oedema or wasting, often with anorexia and infection. The main immediate causes of death are infections, septic shock, hypoglycaemia, electrolyte imbalance, dehydration, hypothermia, cardiac failure and severe anaemia. Every physiological and metabolic function is impaired, so the children affected are extremely fragile, similar to the premature neonate.

In 2009 the WHO and UNICEF defined SAM for children aged 6–60 months as follows:

1 using new weight for length/height charts (see procedures) a cut-off of below minus 3 standard deviations
2 **and** the mid upper arm circumference (MUAC) less than 115 mm.

Two clinical pictures are seen, with much overlap between them.

- Marasmus (wasting) affects all ages, but young infants are particularly at risk. It is usually due to insufficient intake of growth nutrients after breastfeeding stops. It can also be due to chronic illness. The baby is extremely thin, with loss of subcutaneous fat, resulting in skin wrinkles and folds. Weight for length or height is less than 70% of the median (*see* Section 9), or the MUAC is less than 115 mm.
- Kwashiorkor (oedematous malnutrition) usually occurs in children aged 2–4 years. It is an acute illness that suddenly appears over a few days. It is thought to be due to a deficit in the antioxidant nutrients. It presents with sodium retention and oedema of various degrees (from pedal to generalised), and skin lesions that are like severe sunburn in a fair-skinned person. There is fatty liver, with low circulating levels of all hepatic export proteins. The hair may be de-pigmented (this has no relation to the prognosis, and should be ignored clinically), and the hair pulls out very easily and painlessly (which **is** related to the prognosis).

In severe malnutrition, biochemical abnormalities include the following:

- low urea
- severe hypoproteinaemia
- hypokalaemia and hypophosphataemia
- hypomagnesaemia
- hypoglycaemia (see below)
- anaemia (frequently present).

Principles of treatment

Early identification and treatment is important, and children are often missed on the general admission wards or in outpatients because they are not measured. Screening using MUAC is helpful for identifying children if length measurement is not easily performed, or weight for height is not charted.

Treatment is much more successful if standard treatment protocols are followed than if clinical judgements are made on individual patients. This is because the illness itself changes the clinical presentation, signs and symptoms of common complications.

Inpatient versus outpatient community management of acute malnutrition (CMAM)

Traditionally, care has been provided for all children in inpatient hospital units, ideally in a defined malnutrition ward. However, carers are less likely to be prepared to attend these until the child is unwell, so patients tend to present late. They also want the child to be discharged as soon as they are clinically stable, so often leave before nutritional deficits have been restored and the child has recovered. This predisposes to higher post-discharge mortality, which is rarely identified by the inpatient programme.

There has been a change to management of the malnourished child who is not unwell, through CMAM programmes. This is sometimes referred to as community-based therapeutic care (CTC). These programmes separate children into those with complications or severe oedema (complicated malnutrition), and those with uncomplicated malnutrition, Children with uncomplicated malnutrition have a reasonable appetite, and on formal testing are able to eat a portion of ready-to-use therapeutic food (RUTF). Children with fever, poor appetite, diarrhoea or dehydration, or who are not fully alert or have generalised oedema are identified and referred to inpatient care (a stabilisation centre), where initial management is delivered.

If a CMAM programme is operating in your area, children with complicated malnutrition will be sent to the hospital, and you may be able to direct those with uncomplicated malnutrition to the CMAM programme after hospital

admission for an illness, or if they present with complicated malnutrition, once they are stabilised and on phase II feeds (see later).

This subsection will deal with the care of children managed in an inpatient hospital unit.

Inpatient management

The inpatient treatment of severe malnutrition is divided into two phases, which are separated by a transition phase.

Phase I (initial treatment)

Specific objectives: return of normal homeostasis and treatment of complications.

- The immediate treatment of life-threatening complications: hypoglycaemia, hypothermia, heart failure, septic shock, infections and infestations, severe dehydration and very severe anaemia.
- The prevention of hypoglycaemia and hypothermia.
- Nutritional treatment based on a maintenance diet (total 100 kcal/kg/day), divided into frequent meals (eight meals per 24 hours).

Transition phase: the diet is gradually increased over 4–5 days.

Phase II (rehabilitation or catch-up growth)

Specific objectives: promotion of rapid weight gain (10–20 g/kg/day) and preparation for discharge.

- A nutritional treatment based on a high energy intake (160–200 kcal/kg/day) divided into six meals a day.
- Emotional and physical stimulation.

The treatment in phase II can be given as ready-to-use therapeutic food (RUTF) in the community, or through an Outpatient Therapeutic Programme (OTP), either administered through a hospital clinic, or preferably in community-based clinics. If RUTF or an equivalent (such as a high-energy biscuit) is not available, children continue on F-100 until nutritional cure is achieved. This is usually defined as achieving 85% of median weight for height.

Ongoing nutritional support

After discharge from this therapeutic programme, it is good practice to link the child to a supplementary feeding programme, which gives a food ration to the family for up to 4 months following discharge. This is a means of ensuring food security for the vulnerable child. Programmes with this safety-net provision often discharge children at 80% of median weight for height.

Admission criteria

- Weight for height less than 70% of the median.
- Oedema (exclude nephritic syndrome and other clinical conditions).
- MUAC of less than 110 mm if the child is over 65 cm in length.

Assessment of nutritional status and recovery

For practical procedures relating to nutrition measurement, *see* Section 9.

Discharge criteria

These depend upon the quality of the follow-up services. If adequate follow-up services and a Supplementary Food Programme (SFP) are available, the discharge criteria are as follows:

- weight for height of more than 80% of the median for 3 days (85% if there is no SFP)
- **and** no oedema for 10 days
- **and** no medical complications.

Medical and nutritional history and examination

The pro-forma history and examination sheet (see Appendix, Section 9) should be filled in by the admitting physician or an experienced nurse.

Key points in the history

- Recent intake of foods and fluids.
- Usual diet before current illness.
- Whether breastfeeding or not.
- Duration and frequency of diarrhoea and vomiting.
- Type of diarrhoea (watery/bloody).
- Appetite.
- Family circumstances.
- Previous attempts at treatment, local drugs and/or traditional medicines given.
- History of chronic cough or contact with TB.
- History of contact with measles.
- Potential HIV infection (including mother's status and whether parents are alive).

Key points on examination

- Oedema.
- Dehydration (this is very difficult to diagnose, and impossible in the oedematous child).
- Shock (often gives the appearance of dehydration in a child with oedema).
- Severe palmar pallor.
- Eye signs for vitamin A deficiency (dry eyes, Bitot's spots, corneal ulceration, keratomalacia) (*see* Section 5.10.A).
- Signs of local infection (ear, throat, skin, pneumonia).
- Signs of HIV (adenopathy, oral candida, chronic ear discharge) (*see* Section 6.2.D).
- Fever.
- Hypothermia (oral temperature < 35.5°C, axillary temperature < 35°C).
- Mouth ulcers, *Candida* or other oral problems.
- Skin changes of kwashiorkor (hypo- or hyperpigmentation, desquamation, ulceration, exudative lesions resembling burns, often with secondary infections such as *Candida*).

Children with vitamin A deficiency are likely to be photophobic and will keep their eyes tightly closed. Examine their eyes carefully to prevent corneal rupture.

Laboratory tests

Laboratory tests are not needed to guide or monitor treatment. Electrolytes and haemoglobin are difficult to interpret and can easily be misleading. If haemoglobin is measured this should be done on admission only, and a transfusion should be given at this time if essential. The patient should not be given a blood transfusion after the first 48 hours

following admission. The haemoglobin level nearly always falls after admission due to haemodilution with expansion of the circulation during mobilisation of oedema and export of sodium from inside the cells in marasmus. At this time, with expansion of the circulation, there is such a grave danger of precipitating heart failure that a transfusion should rarely be given, even for very severe anaemia.

In endemic areas, a malaria smear or rapid test is useful if malaria treatment is not given as part of the routine management of all severely malnourished children.

In regions where HIV is prevalent, HIV testing (serology using two tests in children over 1 year of age, or serology and PCR for children under 1 year) is informative for ongoing care, initiating co-trimoxazole prophylaxis, and determining eligibility for antiretroviral (ARV) therapy. The mother of a seropositive child is invariably HIV infected, and mothers of seropositive children should be offered an HIV test. Services vary, but would normally include counselling prior to voluntary HIV testing. Where testing is routinely offered, uptake is usually high. CD4 counts are not usually required for the initial management of severe acute malnutrition, as this follows the standard protocols, but may be relevant when considering initiating ARV therapy (*see* Section 6.2.D).

Details of treatment

In Phase I (initial phase) the aim is to restore nutritional imbalances and metabolic function and treat complications. Phase II (catch-up growth) is a period of rapid weight gain. There is a 'transition phase' between these phases.

TABLE 5.10.B.1 Phases of malnutrition treatment

Phases of treatment		
Phase 1 (1–7 days)	**Transition phase (3–4 days)**	**Phase 2 (usually 14–21 days)**
Treat dehydration		Correct nutrient deficiencies
Treat hypoglycaemia		
Treat hypothermia		
Treat infection	Treat helminths	
Do not give iron	Do not give iron	Correct iron deficiency
Correct electrolyte problems		
Diet is maintenance intake	Diet is moderate intake	Diet is high intake
Stimulate the child	Stimulate the child	Stimulate the child
		Provide physical activities
		Prepare for discharge

- There are **routine measures** that are systematically implemented for all malnourished children, and additional routine treatments that are often included.
- **Specific treatments:** these include emergency management of life-threatening complications and of specific diseases.
- **General points:** on admission, severely malnourished children should be separated from those with infections and kept in a warm room (25–30°C) without draughts. Washing should be minimal and when possible with warm water, and the child immediately dried. The mother should be encouraged to stay with her child.

Intravenous infusion and blood transfusion

Intravenous infusions are to be avoided whenever possible in all severely malnourished children. The risk of precipitating heart failure is very high because of their atrophic heart muscle and high intracellular sodium and electrolyte imbalance.

- The only indication for IV infusion in severely malnourished children is unconsciousness due to circulatory collapse or shock. This is a condition which is difficult to diagnose.
- The only indication for blood transfusion is when anaemia is present on admission and is life-threatening.
- Cannulas should not have IV fluids running after the prescribed treatment has been given. If flushed for IV treatment, they should be removed when not required.

Nasogastric tube feeding is recommended in cases of:

- anorexia with an intake of less than 70 kcal/kg (70% of phase I feed prescribed)
- severe dehydration with inability to drink
- inability to drink and eat because of weakness or clouded consciousness
- painful or severe mouth lesions (herpes, cancrum oris)
- repeated, very frequent vomiting.

Try to not tube-feed for more than 3–4 days. Always explain the reason to the mother.

Try to breastfeed or feed by mouth every time, and top up by nasogastric tube.

Dehydration with severe malnutrition

Dehydration from diarrhoea is common in severely wasted children (with marasmus) on admission. The treatment of dehydration is not the same as in the non-malnourished child (with the exception of cholera).

This section does not apply to mild diarrhoea occurring during transition from one phase to another, which is a common event.

Signs of dehydration in malnutrition

The normal signs used to assess dehydration are all unreliable in severe malnutrition.

Assume that all children with acute watery diarrhoea have some dehydration.

The interpretation of the signs relies on the history. The specific signs are as follows:

- history and observation of frequent **watery** diarrhoea
- history of recent sinking of the eyes; the eyes appear 'staring'
- history of not passing urine for 12 hours
- history and observation of thirst.

Reduced skin turgor and sunken eyes (that are long-standing symptoms) are features of malnutrition itself. It is not possible to adequately determine the degree of dehydration in the severely malnourished child.

The appearance of dehydration in children without watery diarrhoea or in those with oedema can be caused by a toxic shock with dilatation of the blood vessels. These patients should not be treated as if they have dehydration, but as cases of septic shock (see later).

Note that low blood volume can occur with oedema.

Oral treatment of dehydration in malnutrition

Standard WHO oral rehydration solutions (ORS) have too high a sodium content and too low a potassium content for children with severe malnutrition.

ReSoMal (rehydration solution for malnutrition; see below) is a special solution for this situation.

TABLE 5.10.B.2 Composition comparison of ReSoMal, standard WHO ORS and reduced-osmolarity WHO ORS

Composition	ReSoMal (mmol/litre)	Standard ORS (mmol/litre)	Reduced-osmolarity ORS (mmol/litre)
Glucose	125	111	75
Sodium	45	90	75
Potassium	40	20	20
Chloride	70	80	65
Citrate	7	10	10
Magnesium	3	–	–
Zinc	0.3	–	–
Copper	0.045	–	–
Osmolarity (mOsm/litre)	300	311	245

Children with watery diarrhoea in an adequate clinical state

At admission, give one dose of ReSoMal orally or by nasogastric tube and start to feed the child with the phase I diet. Feed smaller amounts more frequently if they are vomiting. Further ReSoMal can be given after each stool or vomit.

- Give a 50-mL dose for children less than 2 years or less than 85 cm in length.
- Give 100 mL for children over 2 years or over 85 cm in length.

Children with watery diarrhoea in a poor clinical state

Start rehydration with ReSoMal immediately. Give 10 mL/kg/hour for the first 2 hours, and then 5 mL/kg/hour until rehydration is complete.

This rate is slower than for normally nourished and dehydrated children.

Completed rehydration

The rehydration is completed when the child is alert, no longer thirsty, and has passed urine. There should be less sunken eyes and fontanelle and improved skin turgor. (**Note that loss of sunken eyes in a severely wasted patient or the worsening of oedema can be a sign of over-hydration.**)

The diet should now be given.

Monitoring

ReSoMal at 70 mL/kg weight per day is usually enough to restore hydration. However, be careful, as **rehydration can quickly lead to fluid overloading, causing cardiac failure or sudden death**. Malnourished children do not excrete excess sodium well. The clinical state of the child should be reassessed every 30 minutes during the first 2 hours, and then every hour. The best way to monitor the child is by regularly measuring their weight; this gives 'fluid balance' directly and accurately, without having to measure any stool or vomit. The ReSoMal should be stopped immediately if:

- the body weight increases by 10% or more
- the respiratory rate or pulse rate increase
- the jugular vein becomes engorged
- oedema appears or the eyelids become puffy
- the liver enlarges by more than 2 cm (mark its position on the skin with marker pen at the onset of rehydration).

Note: It is common for malnourished children to pass many small unformed stools. This must not be confused with profuse watery stools, and does not require fluid replacement.

Feeding and rehydration

- Breastfeeding should continue during rehydration.
- Phase I diet should start immediately when the child is alert.
- If the child has had severe dehydration, feeding should start as soon as the child is alert and the severe dehydration has been treated (2–3 hours).

Rehydration solutions

If no commercial ReSoMal is available, a solution can be made. (Note that this is double the quantity of water normally used, i.e. 2 litres, so the solution is effectively half strength.)

To 2 litres of boiled filtered water add:

- 1 sachet of ORS (3.5 grams sodium chloride, 2.9 grams trisodium citrate dihydrate, 1.5 grams potassium chloride, 20 grams glucose)
- 50 grams of sugar
- 40 mL of combined mineral mix* (or commercial CMV if available).

* See below for the recipe for the electrolyte/mineral solution. If this cannot be made up, use 45 mL of potassium chloride solution (100 grams of KCl in 1 litre of water) instead.

Formula for concentrated electrolyte/mineral solution

This is used in the preparation of starter and catch-up feeding formulas and ReSoMal. Sachets containing premixed electrolytes and minerals are produced by some manufacturers. If these are not available or affordable, prepare the solution (2500 mL) using the ingredients shown in Table 5.10.B.3.

TABLE 5.10.B.3 Electrolyte and mineral mixture

Constituent	Grams	Concentration/20 mL
Potassium chloride (KCl)	224	24 mmol
Tripotassium citrate	81	2 mmol
Magnesium chloride	76	3 mmol
Zinc acetate	8.2	300 micromol
Copper sulphate	1.4	45 micromol

Water: make up to 2500 mL.

If available, also add selenium (0.028 grams of sodium selenate) and iodine (0.012 grams of potassium iodide) per 2500 mL.

- Dissolve the ingredients in cooled boiled water.
- Store the solution in sterilised bottles in the fridge to slow down deterioration. Discard if it turns cloudy.
- Make fresh solution each month.
- Add 20 mL of the concentrated electrolyte/mineral solution to each 1000 mL of milk feed.

If it is not possible to prepare this electrolyte/mineral solution, and pre-mixed sachets are not available, give potassium, magnesium and zinc separately. Make a 10% stock solution of potassium chloride (100 grams in 1 litre of water) and a 1.5% solution of zinc acetate (15 grams in 1 litre of water).

Emergency IV treatment of severe dehydration with shock in severe malnutrition

IV infusion should be administered only in the case of circulatory collapse severe enough to reduce consciousness. **Alert children should never be given an infusion.**

The main signs are as follows:

- cold hands and feet with increased capillary refill time > 3 seconds
- weak or absent radial pulse
- diminished consciousness.

Severe dehydration and septic shock are difficult to differentiate in children with severe malnutrition. They both present with signs of hypovolaemic shock. The following points help to differentiate them:

- Eyelid retraction associated with a history of diarrhoea is a sign of severe dehydration. The child with septic shock has eyelids that droop.
- If the child is unconscious (or asleep) without having the eyelids together (a sign of excess adrenaline), either dehydration or hypoglycaemia is present.
- Superficial veins are always constricted in severe dehydration, but may be dilated in septic shock.

Treatment protocol for life-threatening dehydration with shock in severe malnutrition

Immediate treatment should be given as follows:

1 Give 15 mL/kg IV over 1 hour. The recommended solution is Ringer-lactate or Hartmann's solution, each with 5% glucose.
2 At the same time, insert a nasogastric tube and give ReSoMal at 10 mL/kg per hour.
3 Monitor carefully for signs of over-hydration, reassessing respiratory rate and heart rate every 15 minutes.
   - **If after 1 hour the child is improving but still severely dehydrated**, continue nasogastric ReSoMal 10 mL/kg/hour for up to 5 hours.
   - If after 1 hour the child has not improved (i.e. radial pulse is still weak), assume that they have septic shock and treat it accordingly (*see* below for treatment of septic shock). Since hypoalbuminaemia is likely also to be present, 4.5% albumin 5–15 mL/kg IV over 1 hour may also be helpful in intractable shock but this approach requires urgent research.

Electrolyte problems in SAM

All severely malnourished children have deficiencies of potassium and magnesium that may take 2 weeks or more to correct. Oedema is partly a result of these deficiencies. **Do not treat oedema with a diuretic.** Excess body sodium exists even though the plasma sodium levels may be low. **Giving high sodium loads could kill the child.**

Treatment

- Give extra potassium (3–4 mmol/kg daily).
- Give extra magnesium (0.4–0.6 mmol/kg daily).
- The extra potassium and magnesium are present in commercial F-75 and F-100 feeds, but if making from ingredients locally should be added to the feeds during their preparation. *See* Table 5.10.B.3 for a recipe for a combined electrolyte/mineral solution. Add 20 mL of this solution to 2.5 litres of feed to supply the extra potassium and magnesium required.
- Prepare food without adding salt.

Infections in SAM: treatment and prevention

All malnourished children must be assumed to have an infection. Because of the lack of an inflammatory response, clinical signs of infection may be entirely absent in a malnourished child with severe systemic infection. If untreated, this may cause mortality, morbidity and poor weight gain.

All children with severe acute malnutrition should routinely be given broad-spectrum antibiotics.

Protocol for treatment

Specific infections

Children with specific infections should receive the appropriate antibiotic according to local guidelines.

No specific infection and no suspected septic shock

The principle is to have a first-line treatment and a second-line treatment.

- **First-line treatment** is routinely given on admission to all severely malnourished children **without** complications such as septic shock, hypothermia, hypoglycaemia or a specific infection (skin, eyes). This is usually oral amoxicillin or co-trimoxazole.
- **Second-line treatment** is given after 48 hours to children who do not respond to the first-line treatment, and to all children with complications. This usually includes a parenteral antibiotic, although absorption of oral ciprofloxacin and chloramphenicol is excellent, so these can

be used orally once the child is stabilised. Some units routinely give metronidazole 7.5 mg/kg orally 8-hourly for 7 days in addition to the above.

The choice of the antibiotics used in first-line and second-line treatment is based on local guidelines, which are ideally informed by local resistance patterns. Factors such as route of administration, availability and cost of the drugs are all relevant. It should be a broad-spectrum antimicrobial agent, such gentamicin 7.5 mg/kg IV once daily for 7 days, **in combination** with either ampicillin (50 mg/kg 6-hourly for 2 days IV) then oral amoxicillin (15 mg/kg/dose 8-hourly for 5 days) **or** ciprofloxacin (10 mg/kg 12-hourly IV or orally for 7 days). If the child fails to improve after 48 hours, add chloramphenicol 25 mg/kg 8-hourly (IV or oral) or ceftriaxone 100 mg/kg daily IV (or IM if this is not possible). These doses are correct for children over 1 year of age, but all doses should be checked against local guidelines, and for infants.

Septic shock: recognition

Septic shock is a very common cause of deaths in these patients. The signs are as follows:

- clouding of consciousness
- rapid respiratory rate:
  - 50 breaths/minute for children aged 2–12 months
  - 40 breaths/minute for children aged 12 months to 5 years
- rapid pulse rate
- cold hands and feet with visible subcutaneous veins and prolonged capillary refill time > 3 seconds
- signs of dehydration but without a history of watery diarrhoea
- hypothermia or hypoglycaemia
- poor or absent bowel sounds
- an abdominal splash when the child is shaken.

It can be very difficult to distinguish between severe dehydration and septic shock.

Suspected septic shock: treatment

- A broad-spectrum IV antibiotic treatment (ceftriaxone) is started immediately.
- Warm the child to prevent or treat hypothermia (see hypothermia below).
- Feeding and fluid maintenance should be undertaken by nasogastric tube or orally.
- Close monitoring of the vital signs (pulse, respiration and conscious level) is essential.

Circulatory collapse

- Give high-flow oxygen through a face mask with reservoir.
- Give IV infusion as described in the case of circulatory collapse due to severe dehydration. However, as soon as the radial pulse becomes strong and the child regains consciousness, discontinue the infusion and start the diet orally or by nasogastric tube.

Hypothermia: prevention and treatment

Malnourished children have a low metabolic rate. The thermoneutral temperature is 28–32°C. At 24°C they can become hypothermic. Those with infection or extensive skin lesions are at particular risk. A hypothermic malnourished child should always be assumed to have septicaemia.

Signs

The signs of hypothermia are a core temperature (oral) < 35.5°C (with a low-reading thermometer). If the axillary temperature is < 35°C or does not register, assume hypothermia.

Routine prevention

- Cover all children with clothes and blankets. They should wear a warm hat (most heat is lost from the head).
- Ensure that the mother sleeps alongside her child. **Do not leave a child alone in bed at night.**
- Keep the ward doors and windows closed to avoid draughts.
- Avoid wet nappies, clothes or bedding.
- Do not wash very ill children. Others can be washed quickly, ideally with warm water, and dried immediately.
- Make sure that the child is fed, so that metabolic heat can be produced. Ensure that feeds occur during the night.
- **Avoid medical examinations which leave the child feeling cold.**

Emergency treatment of hypothermia

- Immediately place the child on the mother's bare chest or abdomen (skin to skin) and cover both of them. Give the mother a hot drink to increase her skin blood flow.
- If no adult is available, clothe the child thoroughly (including the head) and put them near a lamp or radiant heater.
- Immediately treat for hypoglycaemia (see below) and then start normal feeds.
- Give second-line antibiotics.
- Monitor the temperature every 60 minutes until it is normal (> 36.5°C).

Hypoglycaemia: prevention and treatment

Severely malnourished children easily develop hypoglycaemia. This is associated with serious infection. If available, test blood glucose levels (< 2.5 mmol/litre), or if they are not measurable assume that hypoglycaemia is present.

Signs

The main signs of hypoglycaemia are as follows:

- lethargy, limpness, loss of consciousness or convulsions
- drowsiness/unconsciousness with the eyelids partly open, or retraction of the eyelids
- low body temperature
- convulsions.

Sweating and pallor do not usually occur in this situation.

Routine prevention

- Give frequent small feeds, day and night.
- Feeding should start while the child is being admitted.
- Treat any infections.

Emergency treatment

If hypoglycaemia is suspected:

- **If the child can drink:** give therapeutic milk or 50 mL of glucose 10%, or 50 mL of drinking water plus 10 grams of sugar (one teaspoon of sugar in 3.5 tablespoons of clean water). Follow this with the first feed as soon as possible. If achievable, divide the first feed into four and

give half-hourly. If not, give whole feeds every 2 hours during the day and night for at least the first day.
- **If the child is unconscious or has convulsions:** give 5 mL/kg body weight of glucose 10% IV or by the intra-osseous (IO) route, or if neither of these routes is possible give 5 mL/kg of glucose 10% or sugar solution as described above by nasogastric tube.

Continue frequent feeding to avoid a recurrence.

Give second-line antibiotics.

If there are convulsions other causes must be excluded, including cerebral malaria, meningitis, encephalitis, thiamine deficiency and hypernatraemic/hyponatraemic dehydration (especially in hot dry climates).

If blood glucose levels are available and are low, repeat the finger or heel prick after 60 minutes.

Congestive heart failure

This is a common and dangerous complication that usually occurs several days after admission. The heart muscle is atrophic (effectively there is a cardiomyopathy). During early recovery from severe malnutrition, sodium can be mobilised from the tissues before the kidney recovers sufficiently to excrete the excess. All blood transfusions must be done as soon as possible (in the first 2 days after admission), and should be rarely indicated.

Heart failure is usually caused by inappropriate treatment, including the following:
- misdiagnosis of dehydration with consequent inappropriate 'rehydration'
- very severe anaemia
- overload due to blood transfusion
- a high-sodium diet, using conventional oral rehydration solution, or excess ReSoMal
- inappropriate treatment that involves 're-feeding diarrhoea' with rehydration solutions.

Signs

Excess weight gain is the most reliable sign, and daily weights should be taken for all malnourished children. Differentiate pneumonia and heart failure by weighing the child. If their weight has increased, particularly if by more than 5%, consider heart failure. If they have lost weight, consider pneumonia.

First sign: fast breathing:
- 50 breaths/minute for children aged 2–12 months
- 40 breaths/minute for children aged 12 months to 5 years.

Later signs:
- lung crepitations
- respiratory distress
- rapid pulse rate
- engorgement of the jugular vein
- cold hands and feet
- cyanosis or hypoxaemia diagnosed by pulse oximetry if available (SaO_2 < 94% in air at sea level)
- liver enlarged by > 2 cm from baseline.

Emergency treatment of congestive cardiac failure

- **Give high-flow oxygen.**
- Stop all oral intake and IV fluid.
- The treatment of heart failure takes precedence over feeding of the child.
- No fluid at all should be given until the cardiac function improves, even if it takes 24–48 hours.
- Give a diuretic IV, usually furosemide (1 mg/kg). This is the only situation in which diuretics should be used: **diuretics should never be given to reduce oedema in malnourished children.**

Measles: prevention and treatment

Measles is especially dangerous in severe malnutrition.

Routine prevention

All children over 6 months of age who are admitted with malnutrition should be vaccinated against measles. This is often done weekly, but if measles is being transmitted locally, it should be done on admission. A second dose of vaccine in a previously immunised child is not harmful. A second dose should be given once recovered or at the normal time, where the prior vaccination state is uncertain or the child was not vaccinated before admission.

Treatment of measles

If a case of measles is admitted:
- Isolate the individual and any suspected cases.
- Review the vaccination status of all patients in the ward, and ensure that all are immunised.
- Give two doses of vitamin A separated by 1 day.
- Treat for measles (*see* Section 6.2.E) as well as for malnutrition.

Micronutrient deficiencies

All children with acute malnutrition will have these deficiencies. Commercial F-100 and RUTFs contains all of the required micronutrients in the correct amounts.

If not using these, give a daily multivitamin supplement, and add a mineral mix to the feeds. This should contain potassium, zinc, copper, magnesium and ideally selenium. Premixed sachets are available, or a solution can be made. It is important to **avoid** adding iron to milk-based feeds during the first 2 weeks, and until the child is gaining weight (RUTFs contain iron within the food, and this is safe to use for stable children and in CMAM programmes). After 2 weeks, iron is added to the F-100 feeds. In goitrous regions, potassium iodide should be added to the mineral mixture (12 mg/2500 mL), or else the child should be given Lugol's iodine, 5–10 drops per day.

Vitamin A: prevention and treatment

Routine preventive treatment

Oral vitamin A is particularly important for the severely malnourished child, and one dose should be given routinely to each child admitted with malnutrition.

TABLE 5.10.B.4 Vitamin A dosage: preventive treatment

Weight	Dose at admission
< 6 kg	50 000 IU once
6–10 kg	100 000 IU once
> 10 kg	200 000 IU once

Treatment of xerophthalmia

If a child shows signs of vitamin A deficiency (xerophthalmia) or has measles, three doses of vitamin A treatment should be given.

TABLE 5.10.B.5 Vitamin A dosage in xerophthalmia

Weight	Dose on day 1	Dose on day 2	Dose on day 3
< 6 kg	50 000 IU	50 000 IU	50 000 IU
6–10 kg	100 000 IU	100 000 IU	100 000 IU
> 10 kg	200 000 IU	200 000 IU	200 000 IU

If the eyes show signs of inflammation or ulceration, give the following additional care to the affected eye(s) to prevent corneal rupture and extrusion of the lens:

- Instil chloramphenicol or tetracycline eye drops, 2- to 3-hourly as required for 7–10 days.
- Instil atropine eye drops, one drop three times daily for 3–5 days.
- Cover with sterile saline-soaked eye pads.
- Bandage the eye(s).

Note that **children with vitamin A deficiency are likely to be photophobic and have their eyes closed. It is important to examine their eyes very gently to prevent corneal rupture**.

Treatment of anaemia

The majority of malnourished children have anaemia. This is due to the many deficiencies they have (iron, folic acid, riboflavin, pyridoxine, ascorbic acid, vitamin E, copper) and their inability to metabolise iron. **Iron should not be given until 2 weeks after the start of treatment.**

Routine treatment

Folic acid

Give 5 mg of folic acid on the day of admission, then 1 mg/day thereafter (in F-100 already).

Iron

Iron should never be given during Phase I or during the transition phase. In malnourished patients, iron is not properly metabolised and is therefore dangerous. The free iron enhances the production of free radicals that can damage cell walls. Excess free iron encourages systemic infection.

Oral iron supplementation should start 14 days after admission. This is best added to the F-100 milk diet at a dose of one crushed tablet of ferrous sulphate (200 mg) to 2 litres of therapeutic milk. Alternatively, it can be given as ferrous sulphate 3 mg/kg/day orally, which should be continued until anaemia has resolved clinically, or ideally on blood test. It is present in adequate amount in RUTF.

Emergency treatment of very severe anaemia

Blood transfusion in malnourished children is potentially dangerous because it can precipitate heart failure. There are only two indications for considering blood transfusion, namely:

- the child with a haemoglobin concentration of < 4 grams/100 mL, especially if in shock
- the child with signs of heart failure due to anaemia (at immediate risk of death).

Give 10 mL/kg body weight of packed cells (or whole blood) slowly by partial **exchange** transfusion. Ideally, and if this can be achieved, use a carefully and continuously observed cannula in an artery or central vein. It is also possible in a vein in the antecubital fossa. First 2.5 mL/kg of anaemic blood is removed and then when 5 mL/kg of appropriately screened and cross-matched blood has been transfused, 2.5 mL/kg is again taken and the cycle is repeated. The child is closely monitored for signs of congestive heart failure.

If partial exchange is not possible and heart failure is present, give 10 mL/kg, ideally as packed cells, otherwise as whole blood. Transfuse over 4 hours and give IV furosemide 1 mg/kg at the start of the transfusion. Monitor carefully for worsening heart failure.

Intestinal parasites

Routine treatment

Routine deworming treatment is given to all children over 1 year of age, but only in phase II or the transition phase.

For children over 1 year of age, give mebendazole 100 mg (1 tablet) twice daily for 3 days. Some countries use albendazole 200 mg (for children aged 12–24 months) or 400 mg (for those over 24 months of age) once.

Dermatosis of kwashiorkor

Shedding of the skin in scales or sheets, desquamation, exfoliation, cracking of the skin surface, and ulceration of the genital or perianal areas are all common.

There can be widespread weeping skin lesions that resemble burns.

Zinc deficiency is usual in this situation, and oral zinc supplements improve the skin (give 2 mg/kg/day of elemental zinc).

Treatment

- Leave the exposed area open to dry during the day.
- Apply barrier cream (zinc and castor oil ointment) or petroleum jelly or tulle gras to the raw areas, and gentian violet or nystatin cream to the skin sores twice a day.
- These children should be on broad-spectrum antibiotics.
- Do not use plastic pants or disposable nappies for these children.

Continuing diarrhoea

See also Section 5.12.B.

Diarrhoea should subside during the first week of treatment. In the rehabilitation phase, loose or poorly formed stools are normal and do not need treatment provided that weight is increasing.

Treatment

Giardiasis

Giardiasis and mucosal damage are common causes of continuing diarrhoea. Where possible, examine the stools by microscopy.

If cysts or trophozoites of *Giardia lamblia* are found, give metronidazole (7.5 mg/kg 8-hourly for 7 days). If not

detected but clinically *Giardia* is possible, give metronidazole anyway.

Lactose intolerance

Diarrhoea is only rarely due to lactose intolerance. Only treat for lactose intolerance if the continuing diarrhoea is preventing general improvement. Starter F-75 is a low-lactose feed. In exceptional cases:

- Substitute milk feeds with yoghurt or a lactose-free infant formula.
- Reintroduce milk feeds gradually in the rehabilitation phase.

Osmotic diarrhoea

This may be suspected if the diarrhoea worsens substantially with hyperosmolar F-75, and ceases when the sugar content and osmolarity are reduced. In these cases:

- Use a lower osmolar cereal-based starter F-75 (for the recipe, *see* Table 5.10.B.7) or, if available, use a commercially prepared isotonic starter F-75.
- Introduce catch-up F-100 gradually.

Malaria: treatment and prevention

In endemic areas, all malnourished children should have a rapid malaria smear or rapid test on admission. Where this is not possible, all malnourished children should receive antimalarial treatment according to local guidelines for the area. The parasitaemia is usually much lower than in normal children. In initially smear-negative children, there can be a recrudescence during nutritional replacement treatment, so consider malaria in children who develop fever.

Children and mothers should sleep under impregnated nets in the wards.

Tuberculosis

In patients treated for malnutrition, tuberculosis (TB) can be a cause of failure to gain weight. In malnourished children, the diagnosis of tuberculosis is particularly difficult and misdiagnosis is common.

How to diagnose pulmonary TB

The signs of TB in malnourished children are often not specific (e.g. anorexia, failure to thrive). Asymmetric chest signs or asymmetric lymph nodes are usually TB. Pneumonia in malnourished children affects both lungs, and HIV gives symmetrical lymphadenopathy.

Consider TB as a possible diagnosis in children who fail to gain weight during admission.

Sputum is rarely available. The Mantoux test can be negative in malnutrition. Undertake a chest X-ray if possible. A family history is often helpful. BCG offers protection against TB, but does not protect completely against infection.

Treatment (*see* Section 6.1.N)

Children with TB should not be isolated, for the following reasons:

- Young children are not a source of transmission (as it is rarely a cavitating disease).
- Treatment quickly eliminates the risk of transmission.
- An isolated child is stigmatised and neglected in resource-limited settings.

Usually paediatric TB is acquired from a sputum-positive adult, so the TB infected carer is a much higher infection risk to the ward. Take note of the carer on the ward with cough, as they should have a chest X-ray.

Malnutrition and AIDS

Basically, the initial stabilisation phase and nutritional treatment of HIV-infected patients is the same as for any other severely malnourished patient (*see* Section 6.2.D). They follow the same dietary and initial medical treatments. Many HIV-positive patients will respond well to the nutritional treatment and gain weight.

However, in units where HIV is prevalent, and particularly where there are programmes that offer additional nutritional support, co-trimoxazole, ARV treatment, PMTCT, and counselling on future pregnancies, there are excellent reasons why a carer would choose to have their child identified during admission as infected with HIV. Moreover, where this is routinely offered, such a policy is not found to be stigmatising.

The presentation of HIV-infected children is similar to that of the uninfected, so cannot be easily identified clinically, although there are some conditions that are more common. HIV-infected children are less likely to present with kwashiorkor than with marasmus. They are more likely to have oral candida, discharging ears, lymphadenopathy, chronic cough, persistent diarrhoea and dermatosis. They may have a family member with HIV, or be orphaned. They may present in infancy, while still breastfeeding, which is an uncommon time for presentation with severe acute malnutrition otherwise.

HIV testing should follow counselling, and be voluntary. It is usually done using two rapid ELISA serological tests. In infants under 1 year of age, serology reflects maternal status rather than infection in the infant. To diagnose infection in infants, a PCR test is required. All children identified as infected with HIV (or where PCR is not available as having indeterminate status) should be commenced on prophylactic co-trimoxazole. This has been shown to reduce long-term mortality.

In an HIV-infected infant, or one possibly infected with HIV and presenting with malnutrition, it is not sensible to stop breastfeeding during admission, as this will deprive the infant of an important source of nutrition. For children who are PCR negative, but exposed to HIV, the decision is less clear, although it will depend on the mother's likely viral load (check whether she is on ARV treatment), the food security of the family, the mother's ability to provide an alternate breast milk substitute, and her choice. There will usually be guidelines depending on local factors.

If the HIV-infected child is not responding well to malnutrition treatment, this may be because of unidentified infection. Non-typhoidal salmonella (NTS) is more common, as are organisms resistant to commonly used antibiotics. TB is a recognised co-infection, although it may be difficult to identify. Some children do not start gaining weight until ARV drugs are started.

It is not known when it is best to initiate ARV therapy in severe acute malnutrition, although it is generally accepted that children should be on phase II feeds. Some children do not meet the criteria for treatment clinically if they respond well to nutritional support with rapid weight gain. CD4 testing is helpful for determining who would benefit, as not

all HIV-infected children have severe immunodeficiency, because HIV can be related to malnutrition through food insecurity as well as illness. However, long-term follow-up of infected malnourished children has identified them as being at high risk of mortality, suggesting that earlier ARV treatment might be of greater help in reducing this.

On discharge it is important to ensure that the child is linked into HIV and nutrition support programmes which the family can access, that carers are aware of the ongoing needs of the child, and that the wider family is offered HIV testing.

Dietary treatment of severe malnutrition

Dietary treatment in Phase I

Objectives

The aim of this phase is progressive restoration of the electrolyte, metabolic and physiological balance by the frequent feeding of special formula milk.

Principles

Severely malnourished children are usually anorexic, and have thin bowel walls, damaged metabolism, and too much sodium in their bodies. Initially they require a low-salt and low-protein diet and are unable to tolerate large amounts of food because their **capacity is reduced**. Therefore initially a diet high in carbohydrate with low levels of sodium and iron and very modest protein content is given. This diet leads to restoration of metabolic and physiological function, but is insufficient for weight gain.

- Feeding should start quickly after admission.
- It should be divided into many small meals to stay within the absorptive and metabolic capacity of the child and to prevent hypoglycaemia and hypothermia.
- The child should be encouraged to eat, but not be forced to do so. Feeding a malnourished child requires time and patience. Use a cup, bowl, spoon or syringe to feed very weak children. If the child takes less than 70% of the prescribed diet, they should be fed by a nasogastric tube.
- Always continue breastfeeding, and encourage the mother to breastfeed. After the breastfeed give the scheduled amounts of starter formula first (see below).

The following guidelines are also useful:

- Give frequent small feeds of low osmolarity and low lactose content.
- Night feeds are essential.
- Give oral or nasogastric feeds (never parenteral preparations).
- Give 100 kcal/kg/day.
- Protein: give 1–1.5 grams/kg/day.
- Liquid: give 130 mL/kg/day to all children, whether or not oedema is present.

TABLE 5.10.B.6 A recommended schedule

Days	Frequency	Volume/kg/feed	Volume/kg/day
1–2	2-hourly	11 mL	130 mL
3–5	3-hourly	16 mL	130 mL
6 onwards	4-hourly	22 mL	130 mL

TABLE 5.10.B.7 Volumes of F-75 per feed

Child's weight (kg)	2-hourly (mL/feed)	3-hourly (mL/feed)	4-hourly (mL/feed)
2.0	20	30	45
2.2	25	35	50
2.4	25	40	55
2.6	30	45	55
2.8	30	45	60
3.0	35	50	65
3.2	35	55	70
3.4	35	55	75
3.6	40	60	80
3.8	40	60	85
4.0	45	65	90
4.2	45	70	90
4.4	50	70	95
4.6	50	75	100
4.8	55	80	105
5.0	55	80	110
5.2	55	85	115
5.4	60	90	120
5.6	60	90	125
5.8	65	95	130
6.0	65	100	130
6.2	70	100	135
6.4	70	105	140
6.6	75	110	145
6.8	75	110	150
7.0	75	115	155
7.2	80	120	160
7.4	80	120	160
7.6	85	125	165
7.8	85	130	170
8.0	90	130	175
8.2	90	135	180
8.4	90	140	185
8.6	95	140	190
8.8	95	145	195
9.0	100	145	200
9.2	100	150	200
9.4	105	155	205
9.6	105	155	210
9.8	110	160	215
10.0	110	160	220

Mix the milk, sugar, oil and electrolyte/mineral solution to a paste, and then slowly add the warm boiled water. Make up to 1000 mL. If available, use an electric blender or hand whisk.

What food to give

The special milk for phase I is called F-75. If it is not available, F-100 should be diluted to the same calorie strength as F-75 and given in its place. Alternatively, it can be made from ingredients using the recipe in Table 5.10.B.7 above.

TABLE 5.10.B.8 Homemade recipes for re-feeding formulas F-75 and F-100

	F-75[ab] (starter)	F-75[c] (starter: cereal-based)	F-100[d] (catch-up)
Dried skimmed milk (grams)	25	25	80
Sugar (grams)	100	70	50
Cereal flour (grams)	–	35	–
Vegetable oil (grams)	27	27	60
Electrolyte/mineral solution (mL)	20	20	20
Water: make up to (mL)	1000	1000	1000
Contents per 100 mL			
Energy (kcal)	75	75	100
Protein (grams)	0.9	1.1	2.9
Lactose (grams)	1.3	1.3	4.2
Potassium (mmol)	4.0	4.2	6.3
Sodium (mmol)	0.6	0.6	1.9
Magnesium (mmol)	0.43	0.46	0.73
Zinc (mg)	2.0	2.0	2.3
Copper (mg)	0.25	0.25	0.25
% energy from protein	5	6	12
% energy from fat	32	32	53
Osmolality (mOsm/litre)	413	334	419

[a] A comparable starter formula can be made from 35 grams of whole dried milk, 100 grams of sugar, 20 grams of oil, 20 mL of electrolyte/mineral solution, and water to make 1000 mL. If using fresh cow's milk, take 300 mL of milk, 100 grams of sugar, 20 mL of oil, 20 mL of electrolyte/mineral solution, and water to make 1000 mL.

[b] Isotonic versions of F-75 (280 mOsmol/litre) are available commercially, in which maltodextrins replace some of the sugar, and in which all of the extra nutrients (potassium, magnesium and micronutrients) are incorporated. These are of lower osmolarity and therefore less likely to cause osmotic diarrhoea.

[c] Cook for 4 minutes. This may be helpful for children with dysentery or persistent diarrhoea.

[d] A comparable catch-up formula can be made from 110 grams of whole dried milk, 50 grams of sugar, 30 grams of oil, 20 mL of electrolyte/mineral solution, and water to make 1000 mL. If using fresh cow's milk, take 880 mL of milk, 75 grams of sugar, 20 mL of oil, 20 mL of electrolyte/mineral solution, and water to make 1000 mL.

F-75 contains:

- 75 kcal/100 mL
- 0.9 grams of protein/100 mL (around 5% of kcal provided by protein)
- 2 grams of fat/100 mL (around 32% of kcal provided by fat)
- 13 grams of carbohydrate/100 mL (around 62% of kcal provided by carbohydrates).

What quantity of food to give

Give 100 kcal/kg/day. The daily number of kcal should be divided by the number of meals given during the day (usually eight meals per day).

F-75: 133 mL = 100 kcal.

Example

A child of 6 kg should receive a diet of 100 kcal/kg/day. The child will be given eight meals of F-75.

Number of kcal/day: 100 kcal × 6 kg = 600 kcal. Quantity of F-75 per day: 800 mL (798 exactly). Quantity per meal: 800/8 = 100 mL.

Do not exceed 100 kcal/kg/day in this initial phase. Diarrhoea should gradually decrease and oedematous children should **lose weight** as the oedema disappears. If diarrhoea continues, see above.

Dietary treatment in the transition phase (for 48 hours)

What food to give

In the transition phase, full-strength F-100 is given in the same volume that was calculated for F-75 in phase I. There is no other change made in the transition phase. F-100 contains:

- 100 kcal/100 mL
- around 2.6 grams of protein/100 mL (10% of kcal provided by protein)
- around 5.6 grams of fat/100 mL (50% of kcal provided by fat)
- around 9.8 grams of carbohydrate (40% of kcal provided by carbohydrate).

There are two forms of F-100.

Commercial F-100

This therapeutic milk is prepared in a sachet. All that the nurse has to do is open the packet and dilute the contents in 2 litres of potable (boiled) water. The commercial F-100 has a lower osmolarity to reduce 're-feeding' diarrhoea in the severely malnourished children.

Home-made F-100

This can be made from ingredients using the recipe shown in Table 5.10.B.8 above.

Dietary treatment in phase II

Objectives

The aim is catch-up growth of the child with rapid weight gain (10–20 g/kg/day). Usually the appetite has returned.

Principles

The child has re-established their physiological balance and should get enough food to gain weight as quickly as possible. They are given a high-energy diet with normal protein content.

- The intake is increased in quantity (to about 200 kcal/kg/day).
- Reduce meal frequency from eight to six meals per day.
- There should be no limit on the quantity of food given. The child is allowed to eat as much as they want, but must never be forced to eat.
- Breastfeeding continues. Breast milk must always be offered **before** the high-energy food is given.
- Aim for weight gain of more than 10 grams/kg/day.
- Remain alert for heart failure.

What food to give

The basic diet is composed of F-100 meals. However, when the child is gaining weight quickly, other foods can be introduced – for example:

- enriched porridges (1 mL contains 1 kcal/gram) as one to two meals a day
- enriched biscuits (useful for overnight feeding if phase II is conducted in a day-care centre) or RUTF (see below)
- local meal: composed of the usual food eaten in the area; this should be enriched in the pot with the addition of oil and CMV and sometimes DSM.

Quantity of food to give

Dispense and offer 200 kcal/kg of F-100 per kg of body weight per day.

Example of calculation

A child who weighs 9 kg should receive 200 kcal × 9 = 1800 kcal per day. The child will receive six meals per day, and each meal should provide 1800 kcal/6 = 300 kcal.

The diet is composed of six meals of F-100. The enriched porridge or family meal is given **in addition** if the child wishes to take it.

- F-100 (1 mL of F-100 = 1 kcal): the child should receive 300 mL of F-100 per meal.

Older children and adolescents, when they are gaining weight rapidly, often do not want the milk and demand 'solid food'. This usually slows the rate of recovery. The solid food should always be enriched.

When developing local recipes the weight gain should be compared with that of children taking F-100 alone. If the weight gain is similar, the recipe for the porridge is adequate.

Ready-to-use therapeutic foods (RUTFs)

RUTFs have been developed to provide the same nutritional content as F-100, but in a peanut-butter-type paste that is not susceptible to pathogens growing in it, due to its low water content. These are usually based on a mix of groundnuts, vegetable oil, dry skimmed milk, sugar and micronutrient mix. If this is available, children can be introduced to this when on phase II feeds, and if they have a good appetite, could be followed up after 1–2 weeks in an outpatient- or community-based malnutrition programme. This is referred to as an Outpatient Therapeutic Programme (OTP), CMAM or CTC (see Further Reading at the end of this subsection).

Individual child monitoring

Phase I

A daily medical and nutritional round of all the children in phase I should be done. The children should be carefully monitored every day for:

- oedema
- weight
- appetite: how the child is eating and the quantity eaten
- clinical state: consciousness, diarrhoea, vomiting, skin, etc.
- behaviour: apathetic, alert, crying, etc.
- temperature
- liver size, heart rate and heart sounds.

This information should be recorded every day on an individual chart.

When to pass to the transition phase

Children usually remain in phase I for 1–7 days. The child can pass to the transition phase when:

- they regain appetite
- they are lively and interested
- serious medical complications are under control
- oedema is decreasing (although it may be still present).

If after 5–7 days the child is not ready for the transition phase, they should be completely re-examined and investigated.

After 2 days in the transition phase without experiencing any problem, the child is ready to move to phase II. Oedema should be significantly improved, and the child must be stable, before progressing to phase II.

Phase II

The monitoring in phase II includes the following:

- a daily round by the nurse, who checks the general state of the child, including whether there is oedema, nausea or vomiting, and how the child is eating
- a physician round undertaken weekly if the child is stable
- measurement of the child's weight twice a week if they are well
- measurement of their height monthly or in each OTP clinic review.

This information should be recorded on the individual chart.

If a child develops a complication in phase II, such as re-feeding diarrhoea or vomiting that requires passage of a nasogastric tube, rehydration solutions, transfusion, etc., they should be returned to phase I and subsequently the transition phase again. The above treatments must never be given to children while in phase II and taking very large amounts of F-100 diet.

When the child can be discharged

Children remain in phase II until they meet the criteria for recovery. The average total length of stay is around 4 weeks

in traditional inpatient care, and longer if very severe complicated malnutrition, HIV, TB, or underlying disease or disability is present.

Figure 5.10.B.1 shows an example of a typical growth recovery chart.

When the child has reached their target weight and is in a good clinical state, they will be either referred to a supplementary feeding programme or sent directly home with arrangements made for follow-up. Children with long-term illness should be transferred to an appropriate community service.

Failure to gain weight

If the child fails to gain weight they should be investigated. Weight gain is defined as poor if it is less than 5 grams/kg/day, moderate if it is 5–10 grams/kg/day, and good if it exceeds 10 grams/kg/day. The following are the most common reasons for failure to gain weight:

- Food prescription or food preparation (kitchen) is incorrect and the child has not received the right quantity of the right food.
- The child does not eat the amount of food prescribed (e.g. because they dislike the food, or the food is being eaten by other people).
- Suspect hidden acute infections (e.g. urinary tract infection, acute respiratory infection, otitis media, mouth candidiasis, giardiasis).
- There are chronic hidden infections (tuberculosis, HIV).
- Re-examine, do stool and urine microscopy, and take a chest X-ray.
- Look for poor feeding techniques, and check that night feeds are occurring.

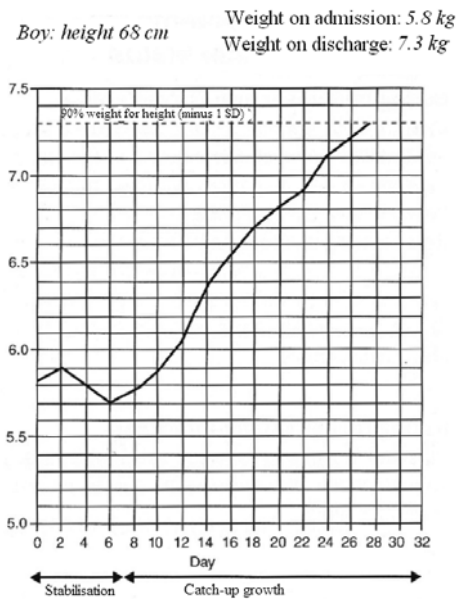

FIGURE 5.10.B.1 Weight catch-up chart for a boy weighing 5.8 kg on admission to hospital.

Emotional and physical stimulation

The severely malnourished child is nearly always psychosocially deprived. The illness itself makes the child unresponsive, and so they do not cry or complain. Because mothers use a cry as the signal to give attention, these children do not receive the attention they need to stimulate them. The neglect is not wilful on the part of the mother, but rather it is a failure of the two-way communication between the mother and her child.

Because they do not cry or complain, these children are often also neglected by nurses and staff. This greatly compounds the problems associated with being in a strange environment. It is essential to stimulate these children, particularly the unresponsive ones. The ward should be made as much like home as possible and children should sleep alongside their mothers.

- **In phase I** it is essential that the mother (or other carer) is present, feeds the child, comforts them, holds them, plays with them, and talks and sings to them.
- **In phase II** it is important to stimulate the child to move, and to play with other children. A play area should always be present. Staff should be identified who have a responsibility for providing (local) toys and encouraging play.

The daily organisation of the activities

To organise the treatment of malnourished children, a schedule of activities (e.g. care, distribution of meals) must be established. An example is given below.

TABLE 5.10.B.9 Daily organisation of activities

Time (24-hour clock)	Children in phase I and transition phase	Children in phase II (day care)
02.00	Milk distribution	
05.00	Milk distribution	
07.00	Team changeover (day shift)	
07.30	Temperatures	Arrival of children
08.00	Milk distribution and drugs	Milk distribution and drugs
09.00	Weight, oedema assessment	Weight, oedema assessment
09.30	Mother's meal	Medical round
10.00	Medical round	Milk distribution
11.00	Milk distribution	Mother's meal
12.00		Milk distribution and drugs
13.00	Dressings	Dressings
14.00	Milk distribution and drugs	
15.00		Porridge distribution
16.00	Mother's meal	Mother's meal
17.00	Milk distribution	Milk distribution
18.00	Medical round	Departure home with porridge and enriched biscuits for the night
19.00	Team changeover (night shift)	
20.00	Milk distribution and drugs	
21.00	Close windows, wrap child	
23.00	Milk distribution	

Inappropriate practices

- Too much sodium, energy and protein given during phase I of treatment.
- No distinction made between phases I and II.
- Failure to monitor food intake.
- Lack of feeding at night.
- Lack of blankets and hats.
- No daily schedule organised.
- Diuretic given to treat oedema.
- Anaemia treated from time of admission with iron supplements.
- Intravenous fluids given for indications other than circulatory collapse.
- Use of high-sodium diet and standard oral rehydration solution.
- Routine antibiotics not given.
- No vitamin A given.
- No measles vaccine given.

Problems with the management of severe malnutrition

A high level of care is needed. The treatment of a severely malnourished child requires intensive protocol-based care, like that for a premature neonate, with close monitoring, some complex medical care (severe or chronic infections), a diet well enriched in nutrients (F-100, etc.), and an emotionally stimulating, rich and physically warm environment.

The resources are almost always limited. The limited financial resources lead to difficulty in obtaining therapeutic milks and other fortified food, drugs and materials.

However, if staff follow the protocols advocated by the WHO, and described above, outcomes can improve. Staff need to be confident that they can follow the guidelines approved for their unit, and if they are unable to do so, be able to address these deficits in care provision. Nursing staff are often better at following the guidelines than doctors, who may try to individualise treatment as they would for other children. The recording charts, weight charts and pro forma are tools that greatly help in the management of these children.

Analysis has shown that the main reasons for death are inappropriate medical interventions, such as fluid overload from ORS, blood transfusion, and the use of diuretics in oedema. Another reason is failure to adhere to the guidelines, due to either a lack of resources, or a lack of understanding of the differences in the care needs of this group of children. A significant and often unrecognised cause of death and relapse is inadequate discharge planning, or premature discharge.

However, perhaps the greatest problem is posed by the limited human resources on the malnutrition ward, with an insufficient number of skilled personnel, and constant movement of staff as soon as they are trained. The greatest resource that a unit can have is a motivated, trained and experienced staff, who have the basic resources to deliver the care described in this subsection.

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5.11 Haematological disorders

5.11.A Anaemia

BOX 5.11.A.1 Minimum standards
- Haemoglobin estimation facility.
- Blood transfusion.
- Drugs:
  - Haematinic agents: iron, folic acid.
  - Antihelmintic drugs: mebendazole, albendazole, pyrantel.
  - Antimalarial drugs.

Introduction

Definition of anaemia

Table 5.11.A.1 gives the World Health Organization (WHO) definition of haemoglobin concentrations below which anaemia is present at sea level.

TABLE 5.11.A.1 Lower limit of normal haemoglobin concentrations

Age of child	Haemoglobin concentration (grams/dL)	Haematocrit (%)
6 months to 4 years	11	33
5–11 years	11.5	34
12–14 years	12	36

The problem of anaemia

- It is widespread in disadvantaged countries.
- It is common in young children under 5 years of age.
- More than one cause of anaemia is usually found in each anaemic child.
- Genetic causes of anaemia are common.
- It has significant deleterious effects on growth, health and development.

Main causes of childhood anaemia in resource-limited settings

- Low birth weight:
  - results in low iron and folate stores (0–2 years age group).
- Dietary:
  - diets tend to be low in iron
  - delayed weaning
  - poor maternal iron intake in breastfed infants
  - weaning on to non-fortified cow's milk.
- Infections:
  - malaria (haemolysis)
  - hookworm (*Ancylostoma duodenale* and *Necator americanus*) (*see* Section 6.3.C)
  - whipworm (*Trichuris* species)
  - congenital infection (CMV, rubella)
  - HIV.
- Genetic:
  - haemoglobinopathies (HbSS, thalassaemias)
  - glucose-6-phosphate dehydrogenase deficiency.
- Malignancy:
  - leukaemia
  - other types of malignancy.

The child with iron-deficiency anaemia

Clinical features of anaemia

- Often asymptomatic until haemoglobin concentration is < 8 grams/dL.
- Breathless on exertion when haemoglobin concentration is < 6 grams/dL.
- Pallor:
  - nail beds (the best site)
  - palmar creases
  - mucous membranes.
- Suboptimal growth, delayed puberty.
- Congestive heart failure.

Investigations

The tests in **bold** listed below should **always be done before a transfusion** (to exclude causes other than iron deficiency):

- **Haemoglobin concentration** (cyanmethaemoglobin method or **HemoCue B**).
- Haematocrit or PCV (microcentrifuge).
- **Blood film**:
  - **malarial parasites**
  - red blood cells: hypochromia, microcytosis, anisocytosis target cells (iron deficiency, thalassaemia)
  - sickle cells
  - macrocytes (folate, vitamin B_{12} deficiency)
  - white blood cells: hypersegmented neutrophils (folate, vitamin B_{12} deficiency).
- Mean corpuscular volume (MCV) and reticulocyte count as the two principal criteria for the initial classification of anaemia.
- **Haemoglobin electrophoresis:** sickle cell, thalassaemia.
- Stool test: parasitic ova, blood.

Management of anaemia

- Establish the diagnosis, cause and severity of iron-deficiency anaemia.
- Treat malaria (oral route) (*see* malaria guidelines in Section 6.3.A.d).
- Give empirical antihelmintic therapy in endemic areas (*see* Section 6.3.C).
- Give haematinics:

– folic acid: up to 5 years of age, 2.5 mg once daily; above 5 years, 5 mg once daily
– iron (*see* Table 5.11.A.2).

Iron medication

TABLE 5.11.A.2 Dosage of iron medications for iron-deficiency anaemia in childhood

Age or weight (6 mg/kg elemental iron)	Ferrous sulphate 200 mg (60 mg/kg elemental iron)	Ferrous fumarate 60 mg per 5 mL (12 mg elemental iron/mL)
2–4 months (4–6 kg)	–	2 mL
4–12 months (6–10 kg)	–	2.5 mL
1–3 years (10–14 kg)	½ tablet	4 mL
3–5 years (14–19 kg)	½ tablet	5.5 mL
> 5 years (> 19 kg)	1 tablet	–

- Preterm infants should start prophylactic iron (5 mg/day) from 4–6 weeks of age until mixed feeding is established.
- Treatment with iron injections may increase mortality (meningitis) and morbidity (respiratory infections, malaria) in infants.

Antihelmintic drugs (see Section 6.3.C)

- Albendazole (the drug of choice if available):
  – 400 mg as a single dose (200 mg if child is less than 2 years of age).
- Mebendazole (most effective against hookworm and whipworm):
  – For children over 1 year of age, 250 mg as a single dose (or 500 mg if the child is over 2 years). May be repeated after 2 or 3 weeks.

Blood transfusion (see also Section 1.7)

Only undertake this if it is essential.

- Warm the blood first under the mother's clothing, in contact with the skin, especially if it is to be given to an infant.
- Do not use blood that has been stored for more than 35 days at 2–6°C or out of the fridge for more than 2 hours, or that is visibly spoiled (plasma must not be pink, and red cells must not be purple or black), or from a bag that is open or leaking.
- Check that the blood is the correct group and that the patient's name and number are identical on both label and form.
- Use a needle/catheter that is 22 gauge or larger, to prevent clotting.
- If there are signs of heart failure, give l mg/kg of furosemide IV at the start of transfusion unless hypovolaemic shock is also present.
- Record the baseline temperature and pulse rate.
- Each transfused unit must be completely used within 4 hours of removal from the fridge.
- Ideally, in infants or those with heart failure, control the flow with an in-line burette.
- Record observations every 30 minutes, looking for heart failure (shortness of breath) and transfusion reactions (fever and malaise).
- Record the quantities given.

Indications for transfusion

- Severe anaemia (haemoglobin concentration < 4 grams/dL).
- Impending or overt cardiac failure if the haemoglobin concentration is < 6 grams/dL.
- Hyperparasitaemia in malaria if the haemoglobin concentration is < 6 grams/dL.
- Children in congestive cardiac failure due to severe anaemia (consider partial exchange).
- Acute severe blood loss with shock that is unresponsive to 40 mL/kg of volume resuscitation given in 10 mL/kg aliquots, or where massive haemorrhage is continuing.

Volume of transfusion

- Use packed red cells where possible.
- Give whole blood: 20 mL/kg or:
  – required volume (mL) = weight (kg) × 4 × desired rise in haemoglobin (grams/dL) **or**
- Packed red cells: 10–15 mL/kg **or**
  – required volume (mL) = weight (kg) × 3 × desired rise in haemoglobin (grams/dL).
- In all cases, rate = 5–10 mL/kg/hour (usually over 3–4 hours unless shocked).
- Consider giving furosemide 1 mg/kg IV immediately in advance of transfusion to avoid precipitating cardiac failure (unless there is hypovolaemic shock) in cases of very severe anaemia.

Treatment of severely anaemic child with septic shock

The first priority will still be to call for help, and manage the airway, followed by breathing and then the circulation.

Call for help.

Airway

Assess the airway by the simple technique of asking the child 'Are you all right?'

Any vocalisation, such as a reply or crying, indicates an open airway and some ventilation. In the absence of a response, formally open the airway with a head tilt/chin lift or a jaw thrust manoeuvre (*see* Section 1.12), and assess the breathing by looking, listening and feeling for its presence.

Breathing

All children with suspected shock must receive high-flow oxygen.

If possible, this should be given through a mask with a reservoir to achieve the higher concentrations. In the absence of spontaneous breathing, give assisted ventilation with a bag-mask (*see* Section 1.13).

Circulation

Intravenous access with a short wide-bore venous cannula, or placement of **an intra-osseous line** (*see* Section 8.4.B), is vital. Severely anaemic children cannot tolerate rapid boluses of fluid as they are likely to be in heart failure and may also be malnourished. The fluid they need most is blood. When transfusing severely anaemic children we usually give packed cells, but in **suspected septic shock**, fresh whole blood has the following advantages:

- It increases oxygen-carrying capacity.
- Plasma content improves circulating volume better than crystalloids.
- Clotting factors and platelets are beneficial in septic shock.

While awaiting the blood, which should be transfused at 20 mL/kg, give 10 mL/kg of Hartmann's solution or Ringer-lactate solution, and then reassess the child. If fresh whole blood is not available, give stored blood, but it should be packed, or if the child is in heart failure, consider partial exchange transfusion. Give antibiotics IV. A third-generation cephalosporin or a combination of gentamicin and a penicillin would be advisable. Flucloxacillin should be added if *Staphylococcus* is suspected (e.g. if there are boils or a known abscess). In suspected intra-abdominal sepsis, metronidazole should be added to cover anaerobic organisms.

Transfusion reactions

See Section 1.7.

Prevention of iron-deficiency anaemia

- Improve iron intake in infants:
  - breastfeeding for at least 6 months
  - give breastfeeding mothers iron
  - include vitamin-C-rich foods (citrus fruit juices) and/or meat, fish, beans and leafy vegetables by 6 months with cereals
  - low-birth-weight babies should receive oral iron 2 mg/kg daily from the age of 4 weeks, for 6 months.
- Prevent infections:
  - diarrhoea (breast milk)
  - measles (vaccination)
  - prevention and prompt treatment of malaria
  - routine deworming of children under 5 years every 3–6 months
  - malaria prophylaxis in sickle-cell patients.

5.11.B Sickle-cell disease

BOX 5.11.B.1 Minimum standards

- Facility for haemoglobin estimation and electrophoresis.
- Analgesia: paracetamol, NSAIDs, opiates.
- Blood transfusion.
- Oxygen.
- Penicillin prophylaxis.
- Pneumococcal (PCV and Pneumovax), hepatitis B and *Haemophilus influenzae* vaccines.
- Oral rehydration solution (ORS).
- Antimalarial drugs.
- Iron chelation: desferrioxamine, deferasirox or deferiprone.

Introduction

Genetic basis

Sickle-cell disease is a recessively inherited disorder of haemoglobin synthesis. It occurs due to a point mutation at position 6 on chromosome 11 resulting in the substitution of valine for glutamic acid on the beta-globin chain. Those affected inherit two copies of the altered beta-globin gene and are therefore homozygous for HbS (HbSS). Alternatively, a single HbS may be inherited with another beta-chain mutation such as beta thalassaemia (HbSB+ or HBSB^{o}) or HbC (HbSC).

A child who inherits two of the same trait genes, one from each parent, will be born with the disease. However, a child of two carriers has only a 25% chance of receiving two trait genes and developing the disease, and a 50% chance of being a carrier. Most carriers lead completely normal healthy lives.

The HbS mutation is common. It is estimated that up to 5% of the world population are healthy carriers of sickle gene, and this can rise to 25% in West Africans. Although the HbS mutation is most common in Africa, it occurs widely across many groups. It is estimated that each year 300 000 children are born with homozygous sickle-cell disease worldwide.

Prognosis

In well-resourced countries, the life expectancy of individuals with sickle-cell disease has been continuously improving, and historic data suggest that it is now well beyond the fifth decade of life, with the overwhelming majority of children surviving into adulthood. The pattern of the disease and its complications is also changing in well-resourced countries, with a shift from being a fatal paediatric illness to a chronic disease associated with episodic painful crises and progressive deterioration and organ damage in later life.

However, in resource-limited countries, sickle-cell disease is still associated with a very high mortality and morbidity, particularly during childhood. Sickle-cell disease remains a major cause of mortality in children under 5 years of age, with estimates as high as 50–90% in some rural areas of Africa. The major causes of death are infection, especially malaria and invasive pneumococcal infection, and severe profound anaemia. For those who live with the condition, sickle-cell disease is the cause of a great burden of suffering for those affected and their families.

Pathogenesis

The clinical manifestations of sickle-cell disease are due to vaso-occlusion and chronic haemolysis, often in response to triggers such as illness, hypoxia or dehydration.

The presence of abnormal HbS leads to the production of a haemoglobin tetramer ($\alpha 2/\beta S2$) that is poorly soluble when deoxygenated, and polymerises readily into a rope-like fibre within the red blood cell. This leads to red cell distortion into the classic sickle shape, a reduction in red cell deformability, and red cell destruction through haemolysis, with consequent shortening of the red cell lifespan, and anaemia.

Vaso-occlusive episodes occur when blood vessels become clogged with sickle cells, causing pain, tissue oxygen deprivation and organ damage alongside altered cell adhesion and abnormal erythrocyte–endothelium

interaction. In addition to vaso-occlusion, there is a chronic intravascular haemolysis leading to a compensated anaemia with functional nitric oxide (NO) dysregulation with chronic vascular endothelial damage. This means that polymerisation alone does not account for the pathophysiology of sickle-cell disease. Changes in red cell membrane structure and function, disordered cell volume control, and increased adherence to vascular endothelium also play an important role.

Clinical presentations

In children, the most common presentation of sickle-cell disease is with an acute crisis, usually as a painful episode. More recently, as more countries adopt a newborn screening programme, children may be diagnosed with sickle-cell disease before their first crisis.

Presentation includes the following:

- newborn screening
- a painful vaso-occlusive crisis
- infection and overwhelming sepsis
- severe anaemia
- acute chest syndrome (ACS)
- stroke.

Newborn screening programmes

The goal of any newborn screening programme for sickle-cell disease is to identify affected children as early as possible and thus reduce the morbidity and mortality of sickle-cell disease, especially from bacterial infections, through the early introduction of antibiotic prophylaxis. In well-resourced countries, the preferred option is the universal screening programme rather than selective screening of high-risk infants only.

Methodology of newborn screening

The methodology of screening can vary, but in principle involves the collection of a dried neonatal blood spot sample for transport and testing by haemoglobin electrophoresis, thin-layer isoelectric focusing, or HPLC. A second confirmatory test may be taken 1–2 weeks later for repeat testing by isoelectric focusing, HPLC, PCR techniques or DNA analysis by a reference laboratory. The tests used must have the capability to distinguish between HbF, HbS, HbA and HbC. As several of the sickle-cell disease syndromes can have similar results on electrophoresis or isoelectric focusing, examining the peripheral blood smear remains useful.

- Haemoglobin electrophoresis is the standard method for separating HbS from other haemoglobin variants.
- Thin-layer isoelectric focusing is a more complicated technique, which can distinguish some haemoglobins not seen on standard electrophoresis, as the bands are more sharply seen.
- High-performance liquid chromatography (HPLC) is a very precise and fully automated technique for identification and quantification of haemoglobins.
- Sickle solubility test. A positive sickle solubility test will detect the presence of HbS but will not identify whether the person is a carrier or has sickle-cell disease.

Results and patterns in the newborn period

Finding	Pattern	Interpretation
HbF and HbA	FA	Normal baby
HbF, HbA and HbS	FAS	Sickle-cell trait
HbF, HbS and HbA	FSA	Sickle-cell beta^{+} thalassaemia
HbF and HbA	FS	Sickle-cell disease (HbSS or HbS beta^{0} thalassaemia)

In countries with limited resources, the combination of haemoglobin electrophoresis and a sickle solubility test will confirm the diagnosis of sickle-cell disease for most older children once the beta-chain production is fully developed beyond the newborn period.

Diagnosis

- Haemoglobin electrophoresis demonstrates the absence of HbA and either HbS (SS) or HbS and another haemoglobin such as HbC (SC).
- A positive sickle solubility test denotes the presence of sickle haemoglobin, but does not indicate whether the person is a carrier (Hb AS) or Hb SS.
- A full blood count shows severe (SS) to mild anaemia (SC).
- Examination of the peripheral blood shows sickled erythrocytes.

General principles of the management of an acute sickle crisis

Most children do not develop symptomatic disease in the first few months of life until adult haemoglobin production is established. The principles of managing any acute crisis are based on searching for, and actively treating, any precipitants (*see* Table 5.11.B.1). Any child presenting with an acute crisis should be considered at risk of sudden and life-threatening deterioration, and clinicians are advised to have an anticipatory approach.

Crisis precipitants include the following:

- infection
- dehydration
- extremes of temperature.

TABLE 5.11.B.1 Precipitants of sickle crises

Problem/precipitant	Approach
Fever and/or evidence of infection Child should be considered functionally asplenic and immunocompromised	Treatment dose of appropriate antibiotics
	Use of appropriate antimalarial drugs
	Use of antipyretic drugs
Dehydration	Rehydration
Extremes of temperature and cold	Warmth and rest

Clinicians should be alert to signs suggesting the possibility of a sudden acute deterioration during a crisis. The following **trigger list may be helpful for identifying children at increased risk of sudden or rapid deterioration:**

- uncontrolled pain despite strong opiate analgesia
- increasing pallor, breathlessness or exhaustion
- marked fever (> 38°C)
- significant tachycardia, tachypnoea or hypotension

TABLE 5.11.B.2 Management of an uncomplicated acute painful episode

Treatment	Comment
Antibiotics and antimalarial drugs (see later)	Any fever should prompt the search for infection and active treatment. Oral antibiotic dosages should be administered at higher dose as per the immunocompromised child
Hydration	Dehydration occurs readily in children with sickle-cell disease, due to impairment of renal concentrating power. Fluids should be given at 150% maintenance (orally or IV)
Analgesia	Assess pain using an age-appropriate visual analogue scale (VAS) (see below). Use the VAS to assess response to analgesia with the goal of minimal pain allowing successful mobilisation. Manage pain with prompt administration of the most appropriate choice and dose from the analgesic ladder. Take into account previous drugs and dosages given at home. Children in severe pain may need early use of opiates orally or IV. **Do not use pethidine**
Severe anaemia	Consider transfusion if the haemoglobin concentration is very low (e.g. < 5 grams/dL) or has fallen by > 2 grams/dL from a known baseline level, or the child is clearly clinically compromised
Oxygen	Provide oxygen if the saturations in air are below 95%. Falling saturations in air or a rising oxygen requirement should prompt re-evaluation and the search for an emerging complication of the crisis

- chest pain with or without signs of consolidation
- desaturation in air or a rising oxygen requirement to maintain saturations above 94%
- abdominal pain with or without distension
- severe diarrhoea and vomiting
- sudden profound pallor with or without jaundice
- parents reporting an enlarged spleen
- any abnormal neurological signs, including painless loss of function, headache and fitting.

The acute painful sickle episode

- This is also referred to as a painful or vaso-occlusive crisis, and is the most common presentation of sickle-cell disease in childhood, resulting from blockage of small vessels. The mainstay of treatment is effective and prompt pain control (*see* Section 1.15), alongside management of any precipitants.
- Approximately 40% of children with sickle-cell disease will have an episode of 'hand–foot syndrome' or dactylitis during early childhood, and this number rises to 50% of children under 2 years old who go on to develop symptomatic disease. Typically children present with vaso-occlusion and infarction of the metacarpals or metatarsals, which is evident as an overlying soft tissue reaction with swelling, redness and marked tenderness affecting either one or all of the hands and feet.
- By later childhood the most common sites of bony sickle-related pain include the long bones, thighs, hips, spine, ribs, shoulders and upper humerus, as well as the bones of the cranium, joints and muscles.

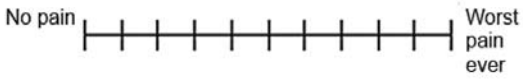

FIGURE 5.11.B.1 Visual analogue scale.

Hydration and fluids in sickle-cell disease

Dehydration occurs readily in children with sickle-cell disease, due to impairment of renal concentrating power.

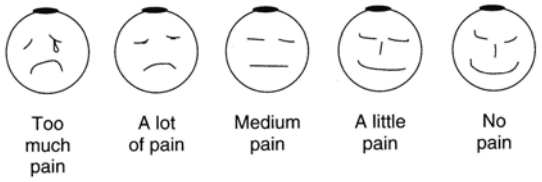

FIGURE 5.11.B.2 Faces scale.

Diarrhoea and vomiting are thus of particular concern. Rehydration calculations are therefore based on the assumption that children with sickle-cell disease have a higher fluid requirement than unaffected children.

Fluids can be delivered by the oral, nasogastric or IV route (or a combination of these) and titrated against clinical response. Generally it is safe to start with hyperhydration (150% of normal), although this may be reduced to normal hydration in children who are less unwell.

TABLE 5.11.B.3 Fluids in sickle-cell crises

Body weight (kg)	Fluids (mL/kg/day)
First 10 kg	150
11–20 kg	75
Subsequent kg over 20	30

Infection

Infection is a common precipitating factor in painful or other types of sickle crises. All children with sickle-cell disease (regardless of type) should be considered to be immunocompromised.

Bacteria

Patients with sickle-cell disease are immunodeficient due to functional asplenia.

Functional asplenia occurs irrespective of spleen size in sickle-cell disease well before the age of 1 year in the majority of sufferers. Clinicians should therefore consider all patients to have increased susceptibility to infection,

TABLE 5.11.B.4 Antibiotic choices in sickle-cell crises

Drug	Rationale and comment
Augmentin	Good activity against *Pneumococcus* *Haemophilus* resistance is low Suitable for use with clarithromycin for pneumonia Does not mask *Salmonella* osteomyelitis
Clarithromycin	Good activity against *Haemophilus* Pneumococcal resistance is low Suitable for use with augmentin for pneumonia Does not mask *Salmonella* osteomyelitis
Cefuroxime	Suitable for severe pneumonia with or without clarithromycin Masks *Salmonella* osteomyelitis
Ceftriaxone and other third-generation cephalosporins	For suspected sepsis First-line treatment for suspected osteomyelitis (with clindamycin) Second-line treatment for *Yersinia* if there is glucose-6-phosphate dehydrogenase (G6PD) deficiency
Ciprofloxacin	For use in patients on desferrioxamine with suspected *Yersinia* infection **Stop iron chelation if suspected**

particularly with the encapsulated organisms listed below, all of which can cause life-threatening sepsis:

- *Pneumococcus*
- *Salmonella* species
- *Haemophilus.*

Any suspected bacterial infection should be managed with prompt institution of IV antibiotics to cover these organisms. Suggested choices are listed in Table 5.11.B 4 (note that these may vary according to region and local sensitivities).

Persistent localised bone pain, swelling or fever should raise suspicion of osteomyelitis, which may require surgical treatment, and 6 weeks of antibiotic therapy

Specific infections

Osteomyelitis

This infection can be very difficult to distinguish from vaso-occlusive bone pain, which is commonly associated with localised swelling and joint effusions. Osteomyelitis should be considered in any child with persistent and localised pain who is systemically unwell.

The diagnosis of osteomyelitis in sickle-cell disease is more likely in the presence of:

- swinging pyrexia (fevers may not be persistent)
- severe systemic upset
- unusual swelling or pain
- positive blood cultures.

Few if any investigations are absolutely conclusive in making the diagnosis. Treatment is complex and may involve surgical intervention (rare) and a prolonged course of IV antibiotics (6 weeks). The oral route can be used to complete a course of antibiotics once the child is systemically well (i.e. fevers have settled) and any tests such as CRP have returned to normal. Antibiotic choices are broad, but may include the following:

- first line: IV ceftriaxone and clindamycin (consider flucloxacillin if no clindamycin available).
- second line: IV clindamycin.
- alternatives: meropenem, imipenem or ciprofloxacin.

Malaria

Studies confirm that sickle-cell trait (HbAS) is protective against severe complicated malaria, including cerebral malaria and severe anaemia related to malaria in children.

By contrast, malarial infection in homozygous sickle-cell disease (HbSS) can be rapidly fatal, and requires prompt recognition and urgent treatment. Although children with sickle-cell disease are not at greater risk of complicated malaria infection, once infected they have a higher mortality, especially related to severe anaemia. In addition to drug treatment, transfusion may be required.

Prevention should be emphasised (*see* Section 6.3.A.d).

Meningitis

Bacterial meningitis is more common in children with sickle-cell disease than in unaffected children, especially in the youngest age groups. The most frequent infecting organism is pneumococcus. Clinicians should maintain a high index of suspicion for this complication and treat it empirically.

Gastroenteritis/diarrhoea

Severe diarrhoea may precipitate sickling and crisis, including stroke. Hydration must therefore be maintained vigorously using ORS or IV fluid where necessary. Education relating to hand hygiene, clean water and prompt treatment should be given.

Children who are systemically unwell with a diarrhoeal illness may also be at higher risk of sepsis related to Gram-negative infection, and may require IV antibiotic treatment in addition to vigorous rehydration under such circumstances.

Children with diarrhoea who are also on the iron chelation medication desferrioxamine are at high risk of *Yersinia* or *Klebsiella* infection, and require prompt treatment with ciprofloxacin, alongside discontinuation of the desferrioxamine until they recover.

Viral infection

Children with sickle-cell disease are at particular risk of profound anaemia secondary to parvovirus B19 infection, which may trigger an aplastic crisis.

Children with sickle-cell disease should also be protected from blood-borne viral infection, specifically HIV and hepatitis B infection. Routine immunisation against HBV must be undertaken in view of the probability that a child with sickle-cell disease may at some stage be a recipient of blood products or be started on a long-term transfusion programme.

Severe anaemia in sickle-cell disease

Children with sickle-cell disease are known to have a compensated anaemia, but are also at risk of events that may precipitate a sudden and potentially fatal drop in their haemoglobin levels. The main conditions to consider are as follows:

- acute sequestration events
- aplastic crisis
- infection with malaria.

Acute sequestration events

Sequestration events are characterised by pooling of red cells in an organ, most commonly the spleen, lungs and liver, and are associated with a sudden and potentially life-threatening fall in haemoglobin level, with shock and collapse alongside rapid (and often painful) expansion of the organ affected.

Sequestration events are often precipitated by infection or sepsis that requires vigorous antibiotic treatment. There is a high mortality. Any child who appears to be deteriorating during an acute painful crisis should be re-examined to exclude undiagnosed sequestration.

Treatment includes administration of antibiotics to manage any precipitating infection, and blood transfusion in children with cardiovascular compromise, or who have a haemoglobin level of < 5 grams/dL, or where there has been a sharp fall in haemoglobin level by > 2 grams/dL.

Urgent blood transfusion in children with sickle-cell disease is not uncommon, but does carry some risks. Clinicians should be cautious about over-transfusing beyond a target of 8 grams/dL (usually a maximum of 20 mL/kg) or at a higher rate than 5 mL/kg/hour, due to the risks of hyperviscosity associated with a sudden increase in haematocrit.

Aplastic crisis

Transient red cell aplasia caused by parvovirus B19 (with an associated reticulocytopenia) can lead to a sudden severe worsening of the patient's anaemia. Ask about any recent viral prodromal illness, but classical erythema infectiosum ('slapped cheek syndrome') is uncommon. Second infections with parvovirus are extremely rare, as immunity to parvovirus is lifelong. Review other family members with sickle-cell disease, because they too may be infected with parvovirus.

The differential diagnosis of a sudden fall in haemoglobin level includes sequestration crisis, and therefore abdominal palpation is mandatory in any acutely anaemic child to exclude this diagnosis.

Treatment includes use of blood transfusion in children who are cardiovascularly compromised, if the haemoglobin level is < 5 grams/dL, or if there has been a sharp fall in haemoglobin level by > 2 grams/dL.

See above for the risks of urgent blood transfusion.

Acute chest syndrome (ACS)

This is a major cause of morbidity and mortality in sickle-cell disease. It is strictly defined by evidence of new pulmonary infiltrates involving at least one complete lung segment consistent with the presence of alveolar consolidation, but excluding atelectasis. Clinically, patients have chest pain, a temperature of more than 38.5°C, tachypnoea, wheezing, or cough usually associated with arterial desaturation.

It is important to recognise that patients can be in the process of developing ACS and be severely ill before these strict criteria are met. Signs of lung consolidation, usually bilateral, generally start at the bases, but may be unilateral and impossible to distinguish from infection.

Chest X-ray signs may lag or be misleading. Early treatment may prevent further deterioration, so **prompt action on clinical suspicion is essential**.

Acute sickle chest syndrome is likely to be multifactorial in origin, with infection, thrombosis of pulmonary arteries and fat embolism all resulting in potentially similar clinical patterns. The diagnosis of this potentially life-threatening crisis must therefore be considered if there is a combination of desaturation in air, tachypnoea, pain and a high fever.

Management of ACS

- Anticipatory clinical approach.
- Effective analgesia to prevent basal atelectasis.
- Careful observations, including regular pulse oximetry.
- Chest X-ray:
  - upper lobe consolidation without basal changes suggests pneumonia rather than ACS.
- Start dual IV antibiotics: treat pneumonia aggressively as it is often clinically indistinguishable.
- High-flow oxygen.
- Hyperhydration.
- Arterial gases in air if the oxygen requirement is rising.
- CPAP (if available) and saturations falling to the low 90s in air.
- Exchange transfusion (if available) if PaO_2 in air is < 8 kPa or the child is deteriorating.
- May require ventilation.
- There is no role for diuretics.

Neurological involvement in sickle-cell disease

Sickle-cell disease is associated with several central nervous system complications and events, as outlined below. The most significant event is stroke, mainly infarction. The treatment approach is outlined in the next section.

Neurological complications of sickle-cell disease

- Infection: meningitis and malaria.
- Stroke: ischaemic stroke, subarachnoid haemorrhage and transient ischaemic attacks (TIAs).
- Silent infarcts.
- Convulsions.
- Neurocognitive decline: reduction in IQ, attention deficits.

Stroke in sickle-cell disease

Stroke is a potentially devastating complication of sickle-cell disease, most commonly occurring in (but not limited to) individuals with homozygous disease (HbSS). The

most common event is infarctive stroke, but haemorrhagic stroke can also occur with increasing frequency as children progress towards adulthood. Stroke can occur in any age group, but is most common in children under 10 years.

Predictive factors for stroke include a history of transient ischaemic attacks, a recent episode of acute chest syndrome, hypertension, or a low haemoglobin F percentage and/or low baseline haemoglobin levels. Any child with sickle-cell disease can have a stroke (even if they are apparently not 'high risk').

Precipitating factors for stroke include a recent history of fever, infection, dehydration and acute chest syndrome. However, some children will have a stroke without any identifiable precipitating event or risk factor.

Symptoms and signs of stroke can be broad, and range from the 'classic' presentation of a focal neurological deficit such as a hemiplegia (painless loss of function) to behavioural changes, severe headache, altered consciousness, convulsions or coma.

Historic data from the USA suggest that 11% of children with sickle-cell disease have a stroke episode by the age of 20 years. More recent data from well-resourced countries speculate that this figure is coming down with the advent of transcranial Doppler (TCD) screening to identify children at high risk of stroke and the aggressive use of regular long-term blood transfusion programmes as a primary prevention strategy.

Stroke is a major cause of mortality and morbidity in sickle-cell disease. On the long-term transfusion programme the risk of stroke falls to approximately 10%.

Treatment of acute stroke

Prompt treatment of an ischaemic stroke can potentially arrest a stroke in evolution. Children with a suspected stroke require:

- rehydration with fluids
- antibiotic treatment of any suspected infection, including malaria or meningitis
- treatment of any convulsions (*see* Section 5.16.D and E)
- exchange transfusion to reduce the circulating sickle percentage as rapidly as possible to less than 25%; this procedure is usually performed in a staged manner over 24–48 hours
- there is no role for aspirin in stroke related to sickle-cell disease.

In the absence of accessible exchange transfusion, it may be reasonable to consider a cautious top-up blood transfusion to maximise oxygen-carrying capacity and reduce the HbS percentage through a dilutional effect. Extreme care must be taken to avoid over-transfusion and the risk associated with increasing blood viscosity thus further contributing to the stroke. In either situation, the haematocrit should not exceed 0.4.

Most children make a good motor recovery from an initial stroke, but may be left with intellectual defects. If untreated, most of these children will suffer a second cerebrovascular accident, usually within 2–3 years of the first episode, as a result of which many of them will die and most will be seriously impaired. Transient ischaemic attacks may presage a more major event.

Secondary prevention of stroke

Because of the risk of a subsequent stroke, all children should be considered for the long-term transfusion programme to reduce their recurrence risk (although the risk is never fully eradicated). Most children require a top-up transfusion every 4 weeks for life, and this is a heavy burden for patients and their families.

The treatment goals of secondary prevention of stroke using the transfusion programme are as follows:

- to reduce and then maintain the pre-transfusion HbS% at below 30%
- to maintain the pre-transfusion haemoglobin level in the range 9–9.5 grams/dL
- in order to achieve these goals, the post-transfusion target is usually set no higher than 12.5 grams/dL
- to monitor and treat iron overload.

Note that there is no role for co-administration of desferrioxamine during transfusions.

Risks of the long-term transfusion programme include the following:

- transmission of bloodborne viral infection
- allo-immunisation to foreign red cell antigens
- iron overload.

In more well-resourced settings, some children may be able to receive alternatives to long-term top-up transfusions as outlined above. These alternatives include the use of manual or automated **exchange transfusions** to maintain a low HbS% without incurring iron overload states. These children may be able to go for longer periods between blood transfusions, although the risk of exposure to blood does not change.

Unfortunately, recent trials have indicated that there is little role for drugs such as hydroxyurea as an effective alternative to transfusion in the primary or secondary prevention of stroke.

Transcranial Doppler (TCD) and primary prevention of stroke

The use of annual TCD monitoring in more well-resourced countries is having a significant impact on the reduction of the incidence of stroke events in children with no prior apparent risk of stroke, and is now a routine screening tool in sickle-cell disease care.

Children are identified as at high risk of stroke if the recorded velocities on TCD persistently exceed 200 cm/second. The stroke risk can be significantly reduced from 40% in high-risk patients through the use of the long-term transfusion programme as outlined above. Unfortunately, once started, there is little evidence as to whether transfusions could ever be discontinued, as the data suggest that once transfusions are stopped the original stroke risk rapidly returns.

In areas where access to TCD machines and trained technicians may be limited, use of TCD may not be possible, particularly when weighing up the risks and benefits of the long-term transfusion programme.

Prevention programmes

Iron overload and transfusions

Children who are exposed to multiple and regular blood transfusions are likely to develop iron overload. The most widely available iron-chelating agent is desferrioxamine (Desferal), which is administered as a subcutaneous dose

around 20–30 mg/kg over slow subcutaneous infusion (8–12 hours) for 5–7 nights per week. Many children become non-compliant with this regimen, and newer medications are available as outlined below.

TABLE 5.11.B.5 Drug treatments to reduce iron loading (iron chelation)

Drug	Advantages	Disadvantages
Desferrioxamine	Well-understood safety profile through long-term use Cheap	Relatively poor iron chelation properties Poor patient compliance Risk of *Yersinia* infection
Deferiprone	Oral administration Effective chelation agent	Requires close monitoring due to risk of sudden unexpected neutropenia and risk of overwhelming infection
Deferasirox (Exjade)	Oral once-daily administration Well tolerated Highly effective iron chelation	Expensive Long-term safety profile not yet fully understood Common side effects are deranged urea and electrolytes and gastrointestinal upset Requires some monitoring

Note: *see* Section 5.11.C for doses of newer iron chelation treatments

Prevention of infection

Prevention of infection is the mainstay of reducing mortality and morbidity in sickle-cell disease.

- All children should receive immunisation against *Pneumococcus, Haemophilus influenzae*, meningococcus and hepatitis B, in addition to any standard immunisation schedule.
- Pneumococcal immunisation should be as broad as possible, including pneumococcal conjugate vaccine **and** Pneumovax. Pneumovax should be given from the age of 2 years, every 5 years for life.
- All children should receive prophylactic penicillin V (erythromycin or clarithromycin can be used as an alternative):
  - age up to 1 year: penicillin 62.5 mg twice a day
  - age up to 5 years: penicillin 125 mg twice a day
  - age 5 years or over: penicillin 250 mg twice a day into adulthood.
- All children should be protected from malaria infection (*see* Section 6.3.A.d).
- Families should be counselled about prevention, risks and signs of infection, so that they can seek prompt treatment.

Prevention of crises

- Maintain good fluid intake, especially during gastroenteritis or other infections.
- Folic acid:
  - age up to 1 year: 1 mg daily
  - age up to 5 years: 2.5 mg daily
  - age 5 years or over: 5 mg daily into adulthood.
- Families should be taught how to feel their child's abdomen in order to identify the onset of a sequestration crisis.
- Hydroxyurea (hydroxycarbamide) may raise baseline haemoglobin levels by promoting fetal haemoglobin (HbF) production. This may reduce the frequency and severity of crises in children. However, it is myelosuppressive and should be used with caution and only where facilities for monitoring blood counts exist and the dose can be monitored carefully.

Splenectomy (and surgery) in sickle-cell disease

Splenectomy is not routinely undertaken in children with sickle-cell disease, although it does have a role in allowing the baseline haemoglobin to rise by approximately 2 grams/dL in children with evidence of hypersplenism.

Splenectomy may also be indicated in children who have had an episode of life-threatening splenic sequestration.

As with all surgical procedures in sickle-cell disease, careful risk assessment should be undertaken before a planned procedure involving a general anaesthetic, due to the risk of post-operative sickling secondary to hypoxaemia and cold. Current advice suggests that children with sickle-cell disease undergoing moderate- or low-risk surgical procedures should be considered for a pre-operative transfusion to bring their haemoglobin level up towards (but not higher than) 10 grams/dL, to maximise oxygen-carrying capacity.

Growth

Growth failure and delayed puberty are common in children with sickle-cell disease, especially in those with hypersplenism or who have had multiple acute sickle crises. Weight tends to be affected more than height, and malnutrition is a major factor in determining whether children achieve their full growth potential.

Puberty may be delayed because of hypersplenism or malnutrition because of the hyper-metabolic state and inadequate nutrition.

Dietary advice, treatment of any chronic infections and possibly splenectomy (if hypersplenism is present) may be helpful. Occasionally, children may benefit from temporary use of the monthly transfusion programme to assist them into puberty.

Priapism

Priapism is a serious but under-reported complication of sickle-cell disease. If untreated, it can lead to fibrosis of the corpus cavernosa and impotence, a risk which appears to be lower in pre-pubertal boys. The duration of an episode predicts the overall outcome. Therefore prompt recognition and management are essential.

Patients typically present with an erect painful penis, which may be precipitated by a painful sickle crisis, fever, dehydration, use of recreational drugs, or sexual activity.

Acute fulminant priapism is characterised by a prolonged and sustained episode, more than 4 hours in

duration. In stuttering priapism, episodes are repetitive and may be individually brief. Patients may have a combination of both of these events.

Treatment of acute priapism is still the subject of much debate. Current best practice suggests the initial use of warm baths, exercise, hydration and gentle sedation while preparing for a more definitive intervention. Subsequent definitive treatment choices include aspiration of blood from the corpus cavernosum followed by surgical washout using saline (irrigation) or adrenergic agonists, which can be performed under conscious sedation. The goal is rapid detumescence within 4–12 hours of the procedure. Ideally, treatment should start within 2 hours of an episode. After 12 hours the patient may require surgical intervention to achieve detumescence. Exchange transfusion (the target haemoglobin concentration is approximately 10 grams/dL, with a haematocrit no higher than 0.4) may be required.

There is still considerable debate about the best treatment options for stuttering priapism, and this is the subject of an ongoing international trial (PISCES). Currently patients with stuttering priapism can be advised to try gentle exercise and warm baths. A preventative approach may be needed, and the following options are available:

- Pseudoephedrine at 30 mg/kg/day, increasing to 60 mg/kg four times a day:
  - alternatively give etilefrine 0.25 mg/kg twice a day
  - both of these drugs are part of the ongoing PISCES trial (2011).
- Hydroxyurea at 10–30 mg/kg/day.
- Use of the long-term transfusion programme.

Other problems

- Around 30% of SS children suffer from **sleep-related upper airways obstruction** with consequent hypoxaemia. Nocturnal hypoxaemia has been increasingly identified as a risk factor for acute chest syndrome (and possibly an independent risk factor for stroke) in children with sickle-cell disease, and marked improvement can occur after adeno-tonsillectomy. Treatment is as indicated for other children with upper airways obstruction (*see* Section 5.1.D).
- Chronic pain resulting from damage caused by acute vaso-occlusive crises occurs, and other pain secondary to the haemolytic process can occur.
- Avascular necrosis of the hip or shoulder can occur as young as 6 years, although it is uncommon before adolescence. The initial presentation may be with the acute vaso-occlusive crisis, but once disintegration of the femoral head occurs, the pain is of a chronic osteoarthritic type, and should be managed as such.
- Leg ulcers that can become seriously infected are common, and their prevalence rises with age. Appropriate antibiotics such as erythromycin and flucloxacillin, wound cleaning and protection together with rest and elevation of the leg are helpful. Compression stockings may also be of benefit.
- Children develop a renal tubular concentrating defect by the age of 2 years. During adolescence, proteinuria, the nephrotic syndrome or chronic renal failure may develop.
- Renal papillary necrosis may produce haematuria, urinary tract infection and renal colic. Rarely the haematuria is severe and blood transfusion is required. Renal colic is treated with copious fluids and adequate analgesia.
- Many patients are chronically jaundiced with exacerbations. There is no treatment, and reassurance should be given that this rarely represents liver failure.
- Gallstones are common, due to pigment from haemolysis. The pain can mimic an acute painful crisis. Treatment is surgical. Antibiotic treatment of cholecystitis with amoxicillin and metronidazole may be required.

5.11.C Haemolytic anaemias

BOX 5.11.C.1 Minimum standards

- Folic acid.
- Screened blood for transfusion.
- Splenectomy.
- Iron chelation therapy: desferrioxamine.
- Pneumococcal vaccine/penicillin.
- Meningococcal vaccine.
- *Haemophilus influenzae* type B (HiB) vaccine.

Definition

Haemolytic anaemias are disorders characterised by a reduction in the lifespan of red blood cells, and may be congenital or acquired.

Clinical features of haemolytic anaemia

These include **pallor, jaundice, splenomegaly** and **gallstones.**

The degree of splenomegaly can be a useful clue to the cause of haemolytic anaemia.

TABLE 5.11.C.1 The differences between congenital and acquired haemolytic anaemia

Congenital	Acquired
Haemoglobin defects: sickle-cell disease, thalassaemia	Infection: malaria, visceral leishmaniasis
Red cell enzyme defects: G6PD, pyruvate kinase deficiency	Alloimmune: haemolytic disease of the newborn, transfusion reactions
Red cell membrane defects: spherocytosis, elliptocytosis	Red cell fragmentation: haemolytic–uraemic syndrome
	Autoimmune infection (e.g. EBV, CMV, HIV, mycoplasma), malignancies (lymphomas, leukaemias), immune deficiencies
	Drugs
	Burns

TABLE 5.11.C.2 Degree of splenomegaly in haemolytic anaemias

With minor splenomegaly	With marked splenomegaly
G6PD deficiency	Sickle-cell disease
Autoimmune haemolytic anaemia	Beta-thalassaemia major
Haemolytic–uraemic syndrome	Hb E beta-thalassaemia
Beta-thalassaemia minor	Hereditary spherocytosis
Hb H alpha-thalassaemia syndrome	Hyper-reactive malarial splenomegaly (tropical splenomegaly)
	Visceral leishmaniasis (kala-azar)

Laboratory features of haemolytic anaemias: general

These include low haemoglobin, increased reticulocyte count, raised and predominantly unconjugated bilirubin, pink plasma after centrifuging of blood (due to free haemoglobin) in severe cases, reduced haptoglobin, and increased urinary urobilinogen.

Hereditary haemolytic anaemias

Red cell membrane defects (dominant inheritance)

Spherocytosis

This is the most common haemolytic anaemia due to a membrane defect. It may present at any time from birth to old age, and varies in severity from patients with haemoglobin concentrations of 4–5 grams/dL to asymptomatic individuals with normal haemoglobin levels. Acute haemolytic or aplastic crises may be triggered by viral infections. These usually last for 10–14 days, but may result in sudden severe anaemia requiring transfusion.

Diagnosis

- Along with a positive family history, the clinical features are mild jaundice, pallor and splenomegaly. Gallstones may occur in children.
- Laboratory features: blood film shows spherocytes, increased osmotic fragility of red cells, increased reticulocytes, negative antiglobulin (Coombs') test.

Treatment

- Folic acid 1 month–12 years 2.5–5 mg daily; 12–18 years 5–10 mg daily.
- Severely anaemic and symptomatic moderately anaemic children may benefit from splenectomy if the facilities available make this a low-risk procedure.
  - **Splenectomy carries a major risk of lifelong increased vulnerability to infection with capsulated bacteria such as pneumococci, meningococci and *Haemophilus influenzae* type B. The risks and benefits need to be weighed up very carefully before splenectomy is undertaken.**
  - Delay splenectomy until after the age of 5–10 years if possible.
- Administration of **pneumococcal, meningococcal and HiB vaccine** prior to splenectomy, and lifelong prophylactic oral **penicillin** thereafter (under 12 months of age, 62.5 mg twice daily; 1–5 years 125 mg twice daily; over 5 years 250 mg twice daily).

Elliptocytosis

This condition is less common than spherocytosis. It is rare in European populations, but is seen more often in West Africa. In South-East Asia there is a variant, South-East Asian ovalocytosis (SAO), which causes oval-shaped red cells and neonatal hyperbilirubinaemia, but little haemolysis later in life.

Diagnosis

- Blood film shows 25–90% of oval, elliptical or rod-shaped red blood cells.
- Homozygotes tend to have severe haemolytic anaemia from infancy.

Treatment

This is the same as for spherocytosis.

Stomatocytosis

Hereditary stomatocytosis is rare, but it can be acquired in several conditions, especially liver disease. The hereditary form may cause neonatal oedema and ascites which resolves spontaneously.

Diagnosis

Blood film shows erythrocytes with a central mouth-like slit (stomatocytes).

Treatment

This is the same as for spherocytosis, but **splenectomy is ineffective and may be harmful**, leading to a thrombotic tendency.

Metabolic defects

Glucose-6-phosphate dehydrogenase deficiency (G6PD) (X-linked)

There are two types of normal G6PD enzymes (types A and B). Worldwide, there may be 100 million people with diminished red cell G6PD activity. G6PD A deficiency is common in black children, and their G6PD function is reduced to about 10% of normal. G6PD B deficiency (G6PD Mediterranean) is less common, and the enzyme activity is reduced to 1–3%; this and the Chinese variant of G6PD deficiency are the more severe forms of the disease.

Clinical features

Severe enzyme deficiency causes chronic haemolytic anaemia and jaundice.

Haemoglobinuria may occur with less than 10% enzyme activity, and severe episodes of haemolysis occur with oxidant stress:

- favism due to ingestion of the fava broad bean or inhalation of its pollen
- oxidant drugs such as antimalarial drugs, sulphonamides, high-dose aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), quinidine, quinine, nitrofurantoin, phenacetin and vitamin K analogues
- other chemicals, such as those in mothballs, can also trigger an episode.

Diagnosis
- Blood film shows 'blister' and 'bite' cells. Heinz bodies may be seen on unstained blood film.
- Enzyme assay (if available) is needed to make the diagnosis (but this may be normal if reticulocyte numbers are raised). It may be necessary to wait several weeks after an acute episode before measuring enzyme levels.

Treatment
- Avoid drugs that cause oxidant stress (i.e. chloroquine, primaquine, sulphonamides, nitrofurantoin, quinolones, dapsone, high-dose aspirin, phenacetin) or fava beans. If primaquine is necessary, this can be given weekly for 8 weeks.
- Patients usually recover spontaneously once the precipitating factors have been removed.
- Transfusion may be necessary if there is severe haemolysis.

Pyruvate kinase deficiency (autosomal recessive)
This is the second commonest enzyme defect of the glycolytic pathway, and affects mainly northern Europeans.

Clinical features
These are very variable.
- Neonates may have severe haemolysis and present with early jaundice (within 48 hours), anaemia and hyperbilirubinaemia.
- In older children, haemolysis is variable and may be asymptomatic or lead to poor growth, delayed puberty and the skeletal changes associated with chronic haemolysis, such as maxillary prominence and frontal bossing and an increased tendency to long bone fractures.

Diagnosis
- Blood film shows increased reticulocytes, Heinz bodies and mild macrocytosis.
- Enzyme assay for pyruvate kinase.

Treatment
- Folic acid (250 micrograms/kg once daily).
- Splenectomy (only if the facilities available make this a low-risk procedure).
- Transfusion if there is severe anaemia or an aplastic crisis.

Haemoglobin defects
- Abnormal variants: sickle (*see* Section 5.11.B), Hb C, Hb E, Hb D, etc.
- Defective synthesis: thalassaemias.
- Beta-thalassaemia major (autosomal recessive).

Beta-thalassaemia major
In this condition there is a complete or almost complete absence of the beta-globin chain synthesis. There is a high incidence of the beta-thalassaemia gene (1–15%) in southern Europe, the Middle East, India, Pakistan and South-East Asia.

Clinical features
- Anaemia, which becomes obvious by 3 months.
- Weakness and tiredness.
- Failure to thrive, intermittent fever and poor feeding.
- Cardiac failure may develop.
- Infections and splenomegaly.
- Stunted growth with skeletal changes (e.g. frontal bossing, maxillary hyperplasia, increased tendency to fractures).
- Increased skin pigmentation.
- Delayed puberty.

Diagnosis
- Blood film shows microcytosis, anisocytosis, and hypochromic and nucleated red cells.
- Haemoglobin electrophoresis: Hb F increased (10–90%), Hb A absent, Hb A_2 can be reduced, normal or occasionally elevated.
- Serum iron and ferritin levels are increased.
- Reticulocyte numbers are often lower than expected for the degree of anaemia.

Management of beta-thalassaemia major
Management is by regular blood transfusion and iron chelation therapy to reduce iron deposition in tissues, especially the heart, liver and endocrine glands (transfusion haemosiderosis).

Blood transfusion
- Monitor haemoglobin levels, growth and development, and **transfuse when the child stops developing or when the haemoglobin concentration is less than 7 grams/dL in the absence of infection**.
- **Blood should be ABO, rhesus (Dd, Cc, Ee) and Kell matched and filtered to avoid allo-immunisation and transfusion reactions.**
- Immunise against hepatitis B prior to transfusion.
- Transfuse 20 mL/kg of filtered red cell concentrate over 2–3 hours.
- To monitor, calculate the transfused red cell concentrate in mL/kg yearly. If blood consumption is > 300 mL/kg, investigate the cause.
- Increased blood consumption may be due to large spleen, large liver, autoimmune haemolytic anaemia or multiple allo-antibodies.
- To prevent bone deformities, osteoporosis and extramedullary haematopoiesis, **aim for a pre-transfusion level of not less than 9 grams/dL**.
- Pre-transfusion haemoglobin is mandatory. Post-transfusion haemoglobin is optional.
- As a rule, the haemoglobin level drops by 1 gram/week in splenectomised children, whereas in non-splenectomised patients it drops by 1.5 grams/week.
- Monitor serum ferritin levels (normal range is 7–200 micrograms/litre in children over 5 months old).

Iron chelation
- To avoid damage to the endocrine glands, liver and heart, iron chelation should be started when the **serum ferritin level is around 1000 micrograms/litre.**
  1. Desferrioxamine infusion IV or subcutaneous given slowly over 10–12 hours. The initial dose should not exceed 30 mg/kg desferrioxamine in 10 mL of water for injection, followed by maintenance doses of 20–50 mg/kg each over 10–12 hours on 3–7 nights a week.

     Too much desferrioxamine can cause growth,

hearing and eyesight problems. Give 100–200 mg vitamin C orally at the same time as desferrioxamine. This enhances iron excretion in the urine, but it should be given separately from food as it also enhances iron absorption from food. Desferrioxamine should not be given to children with cardiac dysfunction.

2. Oral chelation (Deferiprone or Deferasirox) may be used when desferrioxamine is not available or not tolerated. These drugs are much more acceptable to children than desferroxamine as they are oral rather than a long overnight infusion but they have significant side effects.

- Deferiprone by mouth: child 6–18 years 25 mg/kg 3 times daily (maximum 40 mg/kg daily).
- Deferasirox by mouth: child 2–18 years initially 10–30 mg/kg once daily according to serum-ferritin concentration. For maintenance, consult product literature.
- The most serious side effect is neutropenia.
- Monitor the neutrophil count every 2 weeks.
- If the neutrophil count is less than 1.0×10^9/litre, stop iron chelation and monitor recovery.
- If infection is present, the neutrophil count is less than 0.5×10^9/litre and there are symptoms, take blood cultures and treat with a broad-spectrum antibiotic to prevent septicaemia.
- Other side effects are joint pain, nausea, fluctuating liver enzymes and zinc deficiency.

Monitoring treatment

- Measure height and weight, plot height velocity and watch for delayed puberty.
- To avoid psychological trauma and ensure the development of secondary sexual characteristics, treat if no signs of sexual development have occurred by 16 years of age (*see* Section 5.8.C).
- Check the following at least twice yearly: serum ferritin (iron overload), liver function tests, calcium, phosphate, alkaline phosphatase (hypoparathyroidism, tetany).
- Undertake yearly screening for HCV and HIV infection.
- If HCV is positive, assess viraemia (serotype) if possible, perform a liver biopsy and give interferon with or without ribavirin to avoid cirrhosis and hepatoma.
- If HIV-positive, continue transfusions and give the latest available antiviral treatment.
- All blood donors should be tested for HCV and HIV.

Acquired haemolytic anaemia

Immune mediated

- Haemolytic transfusion reaction.
- Haemolytic disease of the newborn (*see* Section 3.4).
- Hypersplenism.
- Secondary to infection: EBV, CMV, *Mycoplasma*, rarely HIV.
- Secondary to malignancies: lymphomas, leukaemias.
- Secondary to autoimmune diseases: SLE, rheumatoid arthritis.

Diagnosis

- Anaemia with increased reticulocytes.
- Splenomegaly.
- Positive direct Coombs' test.

Management

- Most secondary cases (70–80%) are transient, lasting about 3 months.
- Infants and older children may develop the chronic form.
- Treatment may not be needed if the symptoms are not severe.
- Transfusion may be necessary if there is severe haemolysis.
- Steroids: prednisolone 2 mg/kg/day (up to 6 mg/kg/day in severe cases) can be given if treatment is needed until the rate of haemolysis declines, and then stopped gradually.

Malaria

See Section 6.3.A.d.

Secondary to organ disease

Renal failure (*see* Section 5.6.C).

Liver disease (*see* Section 5.7.B).

Burns

See Section 7.3.I.b.

Miscellaneous

- Chemicals and drugs.
- Toxins (e.g. *Haemophilus influenzae* type B, staphylococcal, streptococcal, clostridial).
- Venoms (e.g. cobra, viper, rattlesnake, bee, wasp, yellow jacket).

Reference

British Committee for Standards in Haematology. www.bcshguidelines.com (up-to-date guidelines on spherocytosis and infection risk in people who have had splenectomy).

5.11.D Blood clotting disorders

BOX 5.11.D.1 Minimum standards
- Regional/national centre.
- Prednisolone.
- Immunisation; hepatitis B.
- Blood clotting products.
- Desmopressin and tranexamic acid.

Factor deficiencies

The incidence of haemophilia is similar worldwide, at around 1 in 5000–10 000 male births. Major advances have been made in both separating haemophilia A (factor VIII deficiency) and haemophilia B (factor IX deficiency) and delivering safe therapeutic intervention with replacement therapy. However, this is only available to the 20% of haemophiliacs who live in well-resourced countries. For those in resource-limited countries, severe haemophilia continues to be a personal and social disaster, with affected boys becoming progressively crippled during childhood from spontaneous painful intractable haemorrhages into muscles and joints. These boys commonly die in childhood or early adulthood. Severe deficiencies of the other coagulation factors (X, XI, VII, V, XIII, fibrinogen and von Willebrand factor) are also associated with severe and sometimes life-threatening or fatal haemorrhage.

- The largest barrier to providing replacement therapy is its high cost.
- There are also non-financial barriers, including insufficient knowledge even among the medical community, lack of a proper healthcare structure, and low levels of literacy.
- In the last decade the WHO and the World Federation of Haemophilia (WFH) have made considerable progress in setting up programmes in resource-limited countries.
- The WHO has identified the following as core components:
  - training of care providers and the establishing of care centres
  - identification and registration of people with haemophilia
  - improving social awareness of haemophilia
  - prevention of haemophilia
  - providing safe therapeutic products
  - developing a programme of comprehensive care.

How can delivery of haemophilia care be implemented in resource-limited countries?

- National haemophilia societies are crucial. In addition to supporting affected families, they can lobby for support from the healthcare budget.
- The WHO and WFH have visiting teams that have contributed to education and improvement through these national groups. They include international haemophilia training fellowships, workshops and twinning programmes, in order to transfer knowledge and diagnostic expertise to these embryo services.
- It is important that those planning healthcare fully appreciate that provision of laboratory diagnostic services for haemophilia and the development of safe blood transfusion services to provide safe replacement therapy will benefit a wide range of medical services.

How should the service be built and structured?

- At least one national centre should be created where the laboratory, scientific and medical expertise exists to make an accurate diagnosis, which will then allow the appropriate counselling, including genetic counselling, of the patient's family (similar to a national centre for cancer therapy with links to centres in well-resourced countries: *see* Section 5.14). With advances in molecular biology, carriers of haemophilia can currently be identified and antenatal diagnosis provided so that a choice can be made to prevent the birth of haemophiliac boys, particularly if treatment is not available.
- National registers should be set up for service planning.
- A clinical service involving paediatricians, dentists, orthopaedic surgeons and adult physicians needs to be set up. Safe replacement therapy, probably initially derived from donated plasma, should be developed.
- Donor screening and product treatment to remove the risk of at least HIV and hepatitis B and C infection must be provided.
- Haemophiliacs should be vaccinated at an early age against hepatitis B.

What treatment should be given in the absence of replacement therapy?

Spontaneous haemorrhages into muscles and joints can be extremely painful and will lead to progressive crippling deformities. The acute episode must be managed with bed rest. For bleeds such as those in the knees, splinting with a back slab to restrict movement may help. Analgesia for the pain is also required (*see* Section 1.15). Opiates may be needed to obtain adequate pain relief. Bleeding with loss of first dentition may be severe enough to warrant blood transfusion.

In mild to moderate cases, desmopressin (DDAVP) can be helpful.

- **By intravenous infusion over 20 minutes:** Child 1 month–18 years 300 nanograms/kg as a single dose immediately before surgery or after trauma; may be repeated at intervals of 12 hours if no tachycardia.
- **Intranasally:** Child 1–18 years 4 micrograms/kg as a single dose. For pre-operative use, give 2 hours before procedure.

Avoid drugs that impair haemostasis, such as aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) (e.g. ibuprofen).

Platelet deficiencies: idiopathic thrombocytopenic purpura (ITP)

- Isolated thrombocytopenia usually follows a viral infection 1–3 weeks previously.
- Boys and girls are equally affected, and the peak incidence is in those aged 2–4 years.

- There is a 90% probability of complete remission, but those presenting over the age of 10 years are more likely to have chronic ITP.
- ITP that persists for 6 months is defined as chronic.
- Children with chronic ITP are more likely to have an underlying cause (e.g. autoimmune disease).
- Bleeding manifestations include petechiae, purpura, epistaxes, haematuria, gastrointestinal haemorrhage and (rarely) intracerebral haemorrhage. The child has no hepatosplenomegaly and is usually well.
- Other causes of thrombocytopenia must be excluded. If there is any doubt, a bone-marrow aspirate will show normal haematopoiesis with increased numbers of megakaryocytes in ITP.

Management

- Treatment is based on symptoms, **not platelet count**, and many patients require no treatment.
- Petechiae on the head and neck, and gastrointestinal and oral bleeding, are indicators for prednisolone (1–2 mg/kg/day after food in two divided doses for no more than 14 days or 4 mg/kg for no more than 4 days; reduce over 5 days and stop irrespective of the platelet count if the patient is asymptomatic). Prednisolone does not alter the course of the disease. The time to remission is very variable.
- Tranexamic acid can be useful in the treatment of mucosal bleeding. Give 10 mg/kg IV slowly over 10 minutes in children 6–18 years (maximum 1 gram) followed by 25 milligrams/kg orally (maximum 1.5 gram) three times daily for 2–8 days.
- Hormonal treatment can benefit girls with menorrhagia. In addition Tranexamic acid 1 gram orally 3 times daily for up to 4 days can help (initiate when menstruation starts).
- Chronic ITP with serious bleeding into the gastrointestinal tract or brain may require splenectomy. However, in resource-limited countries there is a high risk of infection following splenectomy, and long-term penicillin prophylaxis and pneumococcal vaccination are required.

Reference

Grainger JD, Rees JL, Reeves M *et al.* (2012) Changing trends in the UK management of childhood ITP. *Archives of Disease in Childhood*, **97**, 8–11.

5.12 Gastrointestinal disorders

5.12.A Acute diarrhoea

BOX 5.12.A.1 Minimum standards

- Reduced-osmolarity ORS.
- ReSoMal for children with severe malnutrition.
- IV fluids: Hartmann's or Ringer-lactate solution with glucose 5% or 10% to prevent hypoglycaemia.
- Potassium: oral and IV.
- ABC resuscitation for shock.
- Antibiotics: co-trimoxazole, amoxicillin, nalidixic acid, ciprofloxacin, cefotaxime, chloramphenicol, erythromycin, metronidazole, tetracycline, vancomycin, doxycycline.

Important issues

- Shock management, rehydration therapy and continued feeding are key strategies.
- Antibiotics are **not** given routinely, but they are indicated in bloody diarrhoea (probable *Shigella* infection) and suspected cholera.
- Antidiarrhoeal drugs and anti-emetics should never be given and can be dangerous in children.
- Zinc supplementation speeds recovery and helps to prevent further episodes.

Introduction

Diarrhoeal diseases are a leading cause of childhood morbidity and mortality in resource-limited countries. In 2001, an estimated 1.5 million children under 5 years of age died from diarrhoea, 80% of them in the first 2 years of life. Around 50% of these deaths are due to watery diarrhoea and occur either because of lack of access to oral rehydration solution (ORS) or because of incorrect case management. About one-third of deaths are caused by persistent diarrhoea and the remainder (approximately 15%) are caused by dysentery.

This section is primarily aimed at the management of the infant and child under 5 years as they are the most seriously affected. There are particular problems in managing children with severe co-morbidities: these include significant malnutrition and anaemia (Hb below 6 G/dL *see* Sections 5.10.B and 5.11.A). In these children, assessment is more difficult and there is likely to be an abnormal response to a fluid load because of poor cardiac function. Modifications to the management plans for these children largely involve slower shock management and rehydration, the careful use of blood transfusion and diuretics and very frequent re-assessment.

ORS has been a simple and effective solution, reducing morbidity and mortality in diarrhoeal illness. The new low-osmolarity ORS reduces by 33% the need for supplemental

IV fluid therapy after initial rehydration compared with the previous standard WHO ORS solution. The new ORS also reduces the incidence of vomiting by 30% and stool volume by 20%.

In addition, zinc supplementation has been shown to significantly reduce the severity and duration of diarrhoea.

Definition

Diarrhoea is the passage of loose or watery stools, usually at least three times in a 24-hour period. However, it is the consistency of the stools rather than the number that is most important. Mothers usually know when their children have diarrhoea, and may provide useful working definitions in local situations. The volume of fluid lost through the stools in 24 hours can range from 5 mL/kg (near normal) to 200 mL/kg, or more. Dehydration occurs when these losses are not replaced adequately and a deficit of water and electrolytes develops. The concentrations and amounts of electrolytes lost also vary. The total body sodium deficit in young children with severe dehydration due to diarrhoea is usually about 70–110 millimoles/litre of water deficit. Potassium and chloride losses are in a similar range.

The most common causes of diarrhoea are rotavirus, enterotoxigenic *E. coli* (ETEC) and, during epidemics, *Vibrio cholerae* O1 or O139.

Classification of diarrhoea

- **Acute watery diarrhoea** (including cholera): this lasts from several hours to days. The main danger is dehydration, and malnutrition also occurs if feeding is not continued. If there is a current epidemic, cholera is likely and causes severe dehydration with a positive stool culture for *Vibrio cholerae* O1 or O139.
- **Acute bloody diarrhoea**, or dysentery (blood is mixed in with stool): the main dangers are intestinal damage, sepsis and malnutrition. Other complications, including dehydration, may also occur.
- **Persistent diarrhoea:** this is defined as passage of three or more loose watery stools in a 24-hour period, which lasts for 14 days or longer. The main danger is malnutrition and serious non-intestinal infection; dehydration may also occur (*see* Section 5.12.B).
- **Diarrhoea with severe malnutrition** (marasmus or kwashiorkor): the main dangers are severe systemic infection, dehydration, heart failure and vitamin and mineral deficiency (*see* Section 5.10.A).
- **Diarrhoea associated with a recent course of broad-spectrum oral antibiotics.**

Assessment of the child with diarrhoea

- Fever, vomiting and loose stools are the common symptoms of acute gastroenteritis.
- If possible, rule out other serious illness (e.g. meningitis, malaria, bacterial sepsis).
- Assess for degree of dehydration, bloody diarrhoea, persistent diarrhoea, malnutrition and serious non-intestinal infections.

History

Specific points to enquire about in the history include the following:

- duration of diarrhoea
- presence of blood in the stool
- local knowledge or reports of a cholera epidemic
- recent use of antibiotics
- the presence of fever, cough or other important problems (e.g. convulsions, measles)
- usual feeding practices
- the type and amount of fluids (including breast milk) and food taken during the illness
- drugs or other remedies taken
- immunisation history.

Physical examination

First assess the patient for shock and treat this urgently as a priority if it is present. Children with shock will have reduced consciousness, a high and increasing heart rate, weak pulse, poor skin circulation time with prolonged capillary refill time (> 3 seconds), and low or even unmeasurable blood pressure.

Children with shock require immediate resuscitation (ABC), including high concentrations of oxygen (if available) and an IV bolus of 10–20 mL/kg of either Ringer-lactate or Hartmann's solution given as rapidly as possible (*see* Section 5.5.B). If IV access is not possible (often the veins are collapsed), consider the intra-osseous route (*see* Section 8.4.B). If shock is not relieved by 20 mL/kg, give another bolus of 10–20 mL/kg, but watch very carefully for fluid overload and in particular pulmonary oedema (this is most likely if the patient is also severely anaemic and will be shown by increasing breathlessness, crepitations may be heard).

The examination includes measurement of vital signs together with clinical correlation. The degree of dehydration is graded according to signs and symptoms that reflect the amount of fluid lost (*see* Table 5.12.A.2). Infants with acute diarrhoea are more apt to dehydrate than are older children, because they have a higher body surface area to weight ratio, have a higher metabolic rate, and are dependent on others for fluid. Although the most accurate assessment of fluid status is acute weight change, the patient's premorbid weight is often not known.

In severe dehydration, prolonged skin retraction time and decreased perfusion are more reliably predictive of dehydration than a sunken fontanelle or the absence of tears. A good correlation has been reported between capillary refill time and fluid deficit. However, fever, ambient temperature and age can affect capillary refill time as well. **In severe dehydration, shock and death soon follow if rehydration is not started quickly.**

Children with some dehydration or severe dehydration should be weighed without clothing when estimating their fluid requirements. If weighing is not possible, the child's age may be used to estimate their weight:

- Weight = (age in years + 4) × 2 for children less than 10 years old.
- For an infant up to 1 year old, birth weight doubles by 5 months and triples by 1 year.

Treatment should never be delayed because facilities for weighing are not rapidly available.

In addition:

- Look for an abdominal mass or abdominal distension.
- In an infant less than 1 week old, diarrhoea is sometimes a sign of neonatal sepsis (*see* Section 3.4). In an infant, blood in the stool may be due to an intussusception (*see* Section 5.19).

Remember other diagnoses, including typhoid, antibiotic-associated colitis and (rarely) inflammatory bowel disease (*see* Section 5.12.D).

Investigations

Laboratory investigations are rarely needed at the outset. Serum electrolytes, especially sodium or potassium concentrations, are useful in severe dehydration and for monitoring progress, if available. Stool cultures should be undertaken if at all possible in dysentery (bloody diarrhoea), but are not needed to initiate treatment in the usual case of acute watery diarrhoea. Stool microscopy can be useful for diagnosing *Giardia lamblia, Cryptosporidium* and amoebic dysentery.

Principles of case management

There are five essential elements of the management of all children with diarrhoea:

- **Resuscitation from shock, if present:** Give IV boluses of Hartmann's solution or Ringer-lactate solution. This needs to be done rapidly (caution is required in malnutrition and anaemia; *see* Section 5.10.B). Improvement in conscious level is a good indicator of response to circulatory shock treatment.
- **Rehydration therapy:** this should be done more slowly, so as not to cause rapid metabolic change.
- **Maintenance therapy:** this is to replicate the normal fluid needs and any ongoing extra losses.
- **Zinc supplementation.**
- **Continued feeding.**

Calculating fluid requirements

WHO Plans A to C for gastroenteritis in children (*see* Appendix to this section) include estimates of total fluid requirements, and assume that most children will be drinking by 4 hours into treatment and thus able to 'self-regulate'. For patients for whom this is not the case, fluid management can be undertaken using the following guidelines.

Estimating fluid requirements

The amount of fluid that the child needs over a 24-hour period needs to be calculated. It is the sum of:

estimated fluid deficit + maintenance requirements + ongoing losses.

Deficit

If an accurate recent pre-illness weight is available, subtract the current weight to estimate lost fluid (1 kg = 1 litre of fluid).

For example, a child who weighed 9.2 kg is seen with diarrhoea and weighs 8.3 kg:

estimated fluid loss is (9.2 – 8.3) kg = 0.9 kg = 900 mL deficit, i.e. 10% dehydrated.

If no recent weight is available, or the recorded weight is considered to be unreliable, assess the degree of dehydration as described in Table 5.12.A.2.

Weigh the child (or estimate their weight from their age as follows: weight (kg) = 2 × [age (years) + 4]) if over one year.

Then use the following formula: percentage dehydration × weight (kg) × 10 = deficit (in mL).

For example, a child whose weight is estimated to be 10 kg is 10% dehydrated.

Their estimated fluid loss is 10 × 10 × 10 = 1000 mL (40 mL/hour if replaced over 24 hours).

Maintenance

TABLE 5.12.A.1 Estimated maintenance fluid requirements based on body weight for a child

Body weight	Fluid needed per day	Fluid needed per hour
First 10 kg of body weight	100 mL/kg	4 mL/kg
Second 10 kg of body weight	50 mL/kg	2 mL/kg
Subsequent kg	20 mL/kg	1 mL/kg

Ongoing losses

For each diarrhoeal stool:

- < 2 years of age: give 50–100 mL or 10 mL/kg
- ≥ 2 years of age: give 100–200 mL or a cup or small glass if drinking or tolerating NG fluid.

For each vomit: use 2 mL/kg ORS, and give small frequent volumes (e.g. 5 mL/minute in a child) via a spoon, syringe or cup. Gradually increase the amount given and closely supervise this.

For nasogastric tube aspirates: replace volume for volume with either ORS or Ringer-lactate solution with 5% or 10% glucose **or** Hartmann's solution with 5% or 10% glucose.

Signs of over-hydration

- Oedematous (puffy) eyelids.
- Heart failure (especially in severe malnutrition), chronic malnutrition or protein-losing enteropathy: look for tachycardia, tachypnea, crepitations at the lung bases, hepatomegaly or gallop rhythm (*see* Section 5.4.B).
- A chest X-ray may be helpful in showing pulmonary plethora or oedema.

Stop giving ORS, but give breast milk or plain water, and food.

Do not give a diuretic unless there is pulmonary oedema (lung crepitations), in which case give furosemide 1 mg/kg IV.

Treatment phases in dehydration with shock

In the shock phase, the circulating volume must be improved sufficiently to perfuse vital organs, this will be identified by an improvement in conscious level, falling heart rate and stronger pulse volume.

- In the rehydration phase, the fluid deficit should be replaced and clinical hydration achieved.
- In the maintenance phase, adequate dietary and fluid intake should be maintained.
- In all phases, excess fluid losses must be replaced continuously.

TABLE 5.12.A.2 Estimated degrees of dehydration with symptoms, signs and treatment

Degree of dehydration with diarrhoea	Symptoms and signs present	Treatment
No dehydration	None Increased thirst	• Treat at home with extra fluids. WHO Treatment Plan A (see below) • Breastfeeding or standard diet must continue • Warn mother about danger signs of some or severe dehydration and when to return • Zinc supplements
Some dehydration (5–9% fluid deficit)	Two or more of the following signs: • Restless and irritable • Sunken eyes • Drinks eagerly/thirsty • Loss of skin turgor; tents when pinched and goes back slowly Any one additional sign of severe dehydration below	• Treat with WHO Treatment Plan B in hospital for at least 24 hours (if feasible) • Give ORS or ReSoMal if there is malnutrition • Breastfeeding or standard feeding to continue • Zinc supplements
Severe dehydration (10% or greater)	Two or more of the following signs • Prostration • Sunken eyes • Loss of skin turgor; tents when pinched and goes back very slowly (≥ 2 seconds) • Not able to drink or drinks poorly In addition may show: • Rapid deep breathing from acidosis • Lack of urine output	• WHO Treatment Plan C • Rapid IV rehydration, giving ORS while IV cannula is put in place • Test for and treat any hypoglycaemia • Breastfeeding or standard feeding as soon as possible • Zinc supplements
Shock	As above with: • High and increasing heart rate; weak pulse volume • Poor skin circulation time (cool and poorly perfused extremities) with prolonged capillary refill time (> 3 seconds) • Low or even unmeasurable blood pressure • Very reduced conscious level or coma	• Urgent IV or intra-osseous access • Urgent IV/intra-osseous fluid bolus of 10 mL/kg Ringer-lactate or Hartmann's solution • Repeat 10 mL/kg boluses if remains shocked, up to a total of 40 mL/kg, then beware of fluid overload • Then rehydrate more slowly • Use NG or oral ORS/breast milk as soon as tolerated

A child's fluid deficit can be estimated as follows:
- Mild or no signs of dehydration: < 5% fluid deficit; < 50 mL/kg.
- Some dehydration: 5–10% fluid deficit; 50–100 mL/kg.
- Severe dehydration: > 10% fluid deficit; > 100 mL/kg.

Rehydration therapy is based on degree of dehydration.

Treatment with low-osmolarity ORS

The formula for standard ORS and the latest low-osmolarity ORS recommended by the WHO and UNICEF is given in Table 5.12.A.3. The quantities shown are for preparation of 1 litre of ORS, by adding one sachet of oral rehydration salts to 1 litre of clean water.

When prepared and given correctly, ORS provides sufficient water and electrolytes to correct the deficits associated with acute diarrhoea. Potassium is provided to replace the large potassium losses associated with acute diarrhoea, especially in infants, thus preventing serious hypokalaemia. Citrate (or bicarbonate) is provided to prevent or correct base deficit acidosis. Glucose is essential because, as it is absorbed, it promotes the absorption of sodium and water in the small intestine. This is true irrespective of the cause of the diarrhoea. Without glucose, ORS solution would be ineffective.

Healthcare workers and mothers criticised standard ORS because it did not reduce stool output or the duration of diarrhoea. Reduced-osmolarity ORS is as effective as standard ORS for preventing and treating diarrhoea, but it also reduces stool output/volume by 25%, reduces vomiting by almost 30%, and reduces the need for supplemental IV rehydration by 33%. This means that there is less need for hospital care, less disruption of breastfeeding, less use of needles and, where IV treatment is not available, less risk of dying from acute diarrhoea.

It is as effective as standard ORS in the treatment of cholera in adults, but may produce transient hyponatraemia. In children it appears to be as effective as standard ORS in cholera, but careful observations for hyponatraemia should be undertaken if possible.

Use ReSoMal instead of low-osmolarity ORS in

TABLE 5.12.A.3 Composition by weight of WHO/UNICEF oral rehydration salts to be dissolved in boiled water to produce 1 litre

Ingredient	Original standard ORS (grams/litre clean water)	New and recommended low-osmolarity ORS (grams/litre clean water)
Sodium chloride	3.5	2.6
Trisodium citrate dihydrate	2.9	2.9
Potassium chloride	1.5	1.5
Glucose anhydrous	20	13.5

TABLE 5.12.A.4 Resulting molar concentration of components of standard and reduced-osmolarity WHO oral rehydration solutions

ORS	Standard osmolarity (mEq/litre)	Reduced osmolarity (mEq/litre)
Glucose	111	75
Sodium	90	75
Chloride	80	65
Potassium	20	20
Citrate	10	10
Osmolarity	311* mOsm/litre	245 mOsm/litre

* Hyperosmolar with respect to plasma osmolality (normal = 276–295 mOsm/litre).

If using bicarbonate ORS there are 30 mmol/litre of bicarbonate instead of citrate.

children with severe malnutrition, as this product is specifically designed for such children.

Zinc supplementation

Zinc is an important micronutrient for children's overall health and development. It is lost in greater quantity during diarrhoea. Replacing the lost zinc is therefore important both for helping the child to recover and for keeping them healthy in the coming months. It has been shown that zinc supplements given during an episode of diarrhoea reduce the duration and severity of the episode, and lower the incidence of diarrhoea in the following 2–3 months. For these reasons, all patients with diarrhoea should be given zinc supplements as soon as possible after the diarrhoea has started. **Give 10 mg/kg for infants less than 6 months old and 20 mg/kg for older infants and children for 14 days.**

Treatments for different degrees of dehydration with/without shock

Dehydration does not neatly fit into discrete categories, although texts such as this one and the WHO publications show practicality in this way for clarity and guidance. Similarly, it can be very difficult to distinguish severe dehydration from dehydration with shock, and the two 'categories' overlap. The essential point to understand is that each severely ill patient must be reassessed frequently to ascertain whether the treatment protocol is having the desired effect of reversing the life-threatening signs of fluid loss. Look for the following:

- increasing awareness and response to stimuli
- gradually strengthening pulse with a decreasing rate (however, a slow weak pulse is a pre-terminal sign).

Children severely dehydrated with shock: shock treatment phase

Children with shock will have a high and increasing heart rate, weak pulse, poor skin circulation time with prolonged capillary refill time (> 3 seconds), depressed conscious level, and low or even unmeasurable blood pressure.

These children require immediate resuscitation (ABC) and emergency treatment (*see also* Section 5.5.B).

Airway (if patient has a reduced conscious level)

- Use an opening manoeuvre if the airway is not open or if it is partially obstructed. Then keep the airway open. If there is immediate improvement but the airway closes without active opening support, consider using airway adjuncts to support the airway.
- Suction if necessary, but not routinely.
- If the child is deeply unconscious (P or less on the AVPU scale), the airway may need to be secured by intubation using experienced senior help (if available).

Breathing

- Give 100% oxygen (mask with reservoir and flow rate of at least 6 litres/minute) regardless of SpO_2 (this increases oxygen delivery as well as improving tissue oxygenation).
- For inadequate ventilation or depressed conscious level (as indicated by the AVPU score) with hypoventilation, respiration should be supported with oxygen via a **bag and mask**, and experienced senior help summoned (if available).

Circulation

- Obtain vascular access to give boluses quickly. Insert an IV cannula and if facilities available send blood for a full blood count, urea and electrolytes blood glucose, cross-matching (if anaemic) and clotting. If peripheral veins are difficult to access an intra-osseous infusion (e.g. EZIO) is rapid and effective. In the absence of IO equipment, the **external jugular vein** or **long saphenous vein cut-down** are good alternatives (*see* Section 8.B for circulatory procedures). If a skilled operator is available, an internal jugular vein central line is ideal, once an initial rapid infusion has been given, if the patient is very severely shocked and likely to need ongoing high dependency care, as it can also allow CVP measurements (if available).
- Give an initial **rapid** bolus of 10 mL/kg of Ringer-lactate or Hartmann's solution and reassess. **Do not use 5% glucose or 0.18% saline/4% glucose solutions for resuscitation, as these can cause hyponatraemia and cerebral oedema.** Boluses should be manually pushed in using a 20- to 50-mL syringe (utilising a three-way tap and link to an IV giving set).
- The re-assessment after the first bolus allows the clinician to ascertain whether the child has any contraindications to large volume resuscitation. Assess for:
  - malnutrition (this should be obvious: *see* Section 5.10.B) severe anaemia or cardiac problem. **Rapid fluid infusion can be fatal in malnutrition, severe anaemia or cardiac problems. Stop the rapid infusion and proceed more slowly with reference to Sections 5.10.B malnutrition, 5.11.A anaemia and 5.4.B heart failure and consider a blood transfusion.**
- Further 10 mL/kg boluses with reassessment will usually be required if shock continues. In a child with shock from severe dehydration caused by diarrhoea, it would be very unusual to need more than 30–40 mL/kg to improve the child's circulation. Reconsider the diagnosis. For example:
  - surgical abdominal pathology (e.g. intussusception or volvulus) (*see* Section 5.19)
  - additional pathology e.g septicaemia (*see* Section 5.5.C)
  - ongoing severe diarrhoea, particularly if there is a cholera epidemic.

- Once a **total** of 40 mL/kg of boluses have been given IV, complications such as pulmonary oedema may occur. If available, expert help (including CVP monitoring and facilities for positive pressure ventilation) is essential. If expert help is not available and there is ongoing severe diarrhoea, continue with fluid resuscitation until there is some improvement in conscious level.
- If a blood glucose shows hypoglycaemia (< 2.5 mmol.L) or glucose stick test has not been available, give a dose of 5 mL/kg of 10% glucose IV to any child who still has a depressed conscious level, as hypoglycaemia may be contributing to this problem. Increased alertness confirms hypoglycaemia (and see below).
- Keep the patient warm, but do not overheat them as this will cause peripheral vasodilatation and reduce the blood supply to vital centres. Hypothermia will exacerbate poor peripheral perfusion, acidosis and coagulation abnormalities.
- Elevate the legs (raise the foot of the bed).
- Give a 10 mL/kg bolus of fresh blood as soon as possible if severe anaemia is present, but watch for circulatory overload.
- Consider using broad-spectrum IV antibiotics.
- Monitor urine output.
- If the child has a reduced level of consciousness or has a convulsion, particularly if they are an infant or young child, hypoglycaemia may be present. Always measure the blood glucose level in this situation. However, if blood glucose measurement is not possible, always treat as for presumed hypoglycaemia and, in addition to the IV fluids given above, give 5 mL/kg of 10% glucose IV or, if there is no IV access, by intra-osseous needle.

As shock is being treated, reassess the child's vital signs: alertness, pulse, respiratory rate etc. after each bolus and at least every 15–30 minutes until signs of shock are improving. Increased alertness, lower pulse and respiratory rate are encouraging signs, but the easiest and most sensitive to recognise is the degree of responsiveness.

Children severely dehydrated with shock: rehydration phase

The best route for rehydration is the oral or nasogastric one, but in children who were sick enough to require rapid IV boluses, further IV fluid is likely to be needed initially.

At this stage, also, there is a need to again consider hypoglycaemia (which may have been identified earlier on stick testing). See below.

Fluid requirement for replacing in the rehydration phase

Fluid requirement falls into the three categories mentioned above:

1 Correction of deficit
   - Weigh the child again or estimate the weight as above
   - Re-assess the clinical signs of dehydration as shown in Table 5.12.A.2 and estimate the percentage of dehydration: fluid deficit in mL = weight in kg × % dehydrated × 10
   - e.g. a 6 kg child with a 5% dehydration will have 6 × 5 × 10 = 300 mL deficit.

2 Replacement of ongoing losses
   - For each diarrhoeal stool: < 2 years of age: give 50–100 mL or 10 mL/kg and ≥ 2 years of age: give 100–200 mL
   - For each vomit: use 2 mL/kg ORS
   - For nasogastric tube aspirates: replace volume for volume
   - e.g. a 6 kg child of 7 months with 5 loose watery stools will need another 300 mL as replacement.

3 Maintenance fluids (*see* Table 5.12.A.5).

TABLE 5.12.A.5 IV maintenance fluids

Weight	Total fluid in 24 hours	Fluid/ hour
First 10 kg of body weight	100 mL/kg	4 mL/kg
Second 10 kg of body weight	50 mL/kg	2 mL/kg
Subsequent kg	20 mL/kg	1 mL/kg

The 6 kg child will need 600 mL in 24 hours for maintenance

Total fluid in 6 kg child with 5 loose watery stools who is 5% dehydrated is 300 + 300 + 600 mL = 1200 in 24 hours. The IV would be set to run at 50 mL/hr. initially. Adjustments to the volume will have to be made in the presence of further large watery stools or vomits or nasogastric aspirate. If available, a check on the plasma electrolytes is very useful at least daily to monitor response to treatment and to guide further therapy. Clinical observations should be done at least hourly and include looking for evidence of urine output.

Choice of IV fluid

As described before, a solution such as **Ringers's lactate or Hartman's** solution is preferable to Normal (0.9%) Saline as it contains less chloride and contains potassium which is vital in diarrhoea treatment. If N saline must be used, add 10 mmol of potassium chloride to each 500 mL bag **once urine has been passed**. If Ringers's lactate or Hartman's solution are being used, add 5mmol to each 500 mL bag **once urine has been passed**.

There is an advantage in managing these children with a urinary catheter as urine volume measurement is a useful guide to fluid need in the absence of cardiac failure but its use must be weighed against the risk of infection.

There is always a possibility of hypoglycaemia as the child is not eating (see below) so for this reason, add glucose to the infusion fluid.

To make a 5% solution of dextrose in Ringers's lactate, Hartman's solution or N saline, remove 50 mL from the 500 mL bag and replace with 50 mL of 50% dextrose

To make a 10% solution of dextrose in Ringers's lactate, Hartman's solution or N saline, remove 100 mL from the 500 mL bag and replace with 100 mL of 50% dextrose.

Start the rehydration fluid regime, review the child's vital signs at least hourly, including assessing urine output and looking for signs of fluid overload, such as puffy face or limbs or increased breathlessness. Also review if there is any change reported by the mother. Once the child is regaining a degree of responsiveness and has a gag reflex, consider introducing oral or nasogastric (enteral) fluids to replace the IV route.

Re-introduction of enteral fluid

Re-assess the child's dehydration status by checking skin pinch, level of consciousness, and ability to drink, at least

every hour, in order to confirm that hydration is improving. Sunken eyes recover more slowly than other signs, and are less useful for monitoring.

As has been mentioned earlier, enteral fluid is the safest way to rehydrate the child. Enteral rehydration can be achieved when:

- The child is conscious enough to be fed by a nasogastric tube without aspiration i.e there is a gag reflex present OR
- The child is conscious enough to take sufficient fluid orally
  AND
- The child is not vomiting a significant volume of the fluid

The enteral rehydration fluid should be reduced osmolarity ORS (or ReSoMal if malnutrition is present). ORS should be introduced while the IV infusion is still running and the IV fluid volume reduced accordingly. Allow the child to breast feed whenever they want.

Once volumes approaching those required (see WHO Plan B in the Appendix to this section) are reached, the IV infusion can be discontinued and WHO Plan B rehydration continued alone.

All the WHO Plans for rehydration with details on prevention fluids, home fluids and advice for parents can be found in the Appendix to this section (see below).

Hypoglycaemia in diarrhoea (blood glucose < 2.5 mmol/L or < 45 mg/dL)

If the child has a reduced level of consciousness or has a convulsion, particularly if they are an infant, hypoglycaemia may be present. Always measure the blood glucose level in this situation. However, if blood glucose measurement is not possible, always treat as for presumed hypoglycaemia. Give 2–5 mL/kg of 10% glucose IV or, if there is no IV access, by intra-osseous needle. If there is no circulatory access, while further attempts are made to access the circulation, any hypoglycaemia can be temporarily managed as below, if there are sufficient staff.

Sublingual sugar (sucrose) for treatment of hypoglycaemia

- Sublingual sugar may be used as an immediate 'first-aid' measure for managing hypoglycaemia in an unconscious child in situations where IV administration of glucose may be impossible or delayed.
- Give 1 teaspoonful of sugar, moistened with 1–2 drops of water, under the tongue. More frequent repeated doses are needed to prevent relapse. Children should be monitored for early swallowing, which leads to delayed absorption, and in this case another dose of sugar should be given. If sublingual sugar is given, repeat doses at 20-minute intervals.
- Recheck the blood glucose concentration in 20 minutes, and if the level is low (< 2.5 mmol/litre or < 45 mg/dL) repeat the sublingual sugar.
- Clearly, once an IV or IO access has been established, glucose can be given into the circulation if necessary.

Electrolyte disturbances in dehydration from diarrhoeal illnesses

Knowledge of the levels of serum electrolytes rarely changes the management of children with diarrhoea. Indeed, these values are often misinterpreted, leading to inappropriate treatment. The disorders described below are usually adequately treated by oral rehydration therapy (ORT).

Hypernatraemia

Some children with diarrhoea develop hypernatraemic dehydration, especially when given drinks that are hypertonic due to their sugar content (e.g. soft drinks, commercial fruit drinks) or salt. These draw water from the child's tissues and blood into the bowel, causing the concentration of sodium in extracellular fluid to rise. If the solute in the drink is not fully absorbed, the water remains in the bowel, causing osmotic diarrhoea.

Children with hypernatraemic dehydration (serum Na^+ > 150 mmol/litre) have thirst that is out of proportion to other signs of dehydration. Their most serious problem is convulsions, which usually occur when the serum sodium concentration exceeds 165 mmol/litre, and especially when intravenous therapy is given. Seizures are much less likely to occur when hypernatraemia is treated with ORS, which usually causes the serum Na^+ concentration to become normal within 24 hours.

It is absolutely essential that intravenous rehydration does not lower the serum Na^+ too rapidly. Intravenous glucose solutions (5% glucose or 0.18% saline/4% glucose) are particularly dangerous and can result in cerebral oedema, which is usually fatal or permanently disabling.

Hyponatraemia

Children with diarrhoea who drink mostly water, or watery drinks that contain little salt, may develop hyponatraemia (serum Na^+ < 130 mmol/litre). Hyponatraemia is especially common in children with shigellosis and in severely malnourished children with oedema. It is occasionally associated with lethargy and (less often) with seizures. ORS is safe and effective therapy for nearly all children with hyponatraemia. An exception is children with oedema, for whom ORS may provide too much sodium. ReSoMal (*see* Section 5.10.B) may be helpful here.

Hypokalaemia

Inadequate replacement of potassium losses during diarrhoea can lead to potassium depletion and hypokalaemia (serum K^+ < 3 mmol/litre), especially in children with malnutrition. This can cause muscle weakness, paralytic ileus, impaired kidney function and cardiac arrhythmias. Hypokalaemia is worsened when base (bicarbonate or lactate) is given to treat acidosis without simultaneously providing potassium. Hypokalaemia can be prevented, and the potassium deficit corrected, by using ORS for rehydration therapy and by giving foods rich in potassium during diarrhoea and after it has stopped (e.g. bananas, coconut water, dark green leafy vegetables).

It is also essential to check blood potassium levels, especially if the child has not passed urine, prior to replacing potassium IV, in order to avoid complications of hyperkalaemia secondary to pre-renal failure.

If it is necessary to give potassium intravenously (e.g. if serum K^+ is < 2.0 mmol/litre or there are ECG signs of hypokalaemia, namely ST depression, T-wave reduction and prominent U waves), great care must be taken. In acute depletion, an infusion at the rate of 0.2 mmol/kg/hour can be used and the serum K^+ level checked after 3 hours. The potassium for injection **must** be diluted before use and thoroughly mixed before being given. **The maximum**

concentration of potassium that can be given through a peripheral vein is 40 mmol/litre. The maximum infusion rate of potassium is 0.5 mmol/kg/hour. The recommended concentration is 20 mmol/litre.

Note: The injectable form of KCl usually contains 1.5 grams (i.e. 20 mmol of potassium in 10 mL), and can be given orally. The daily potassium requirement is 2.5–3.5 mmol/kg.

Supportive treatments

Dietary therapy

During diarrhoea, a decrease in food intake, lack of nutrient absorption and increased nutrient requirements combine to cause weight loss and failure to grow. In turn, malnutrition can make the diarrhoea more severe, more prolonged and more frequent, compared with diarrhoea in non-malnourished children. Therefore give nutrient-rich foods during the diarrhoea and when the child is recovering.

- Breastfed infants: continue feeding on demand.
- Bottle-fed infants: administer full-strength formulas immediately after rehydration (no longer than 4 hours). Lactose intolerance may develop and cause an exacerbation of diarrhoea with a lactose-containing formula. If this happens, temporarily reduce or remove lactose from the diet.
- Older children: continue their usual diet during diarrhoea. Recommended foods include starches, cereals, yoghurt, fruits and vegetables. Foods high in simple sugars and fats should be avoided. Excess fluid losses via vomiting or diarrhoea must be replaced with ORS (see above).

Zinc treatment

Zinc is an important micronutrient which is lost in diarrhoeal illnesses. Replacement speeds recovery and reduces severity as well as reducing the frequency of diarrhoeal illnesses in the ensuing 2 to 3 months.

Dose under 6 months of age 10 mg (½ tablet) daily for 10–14 days; dose over 6 months of age 20 mg (1 tablet) daily for 10–14 days.

Drug therapy: use of antimicrobial and 'anti-diarrhoeal' drugs

Antimicrobial drugs should not be used routinely. This is because, except as noted below, it is not possible to distinguish clinically episodes that might respond, such as diarrhoea caused by enterotoxigenic *E. coli*, from those caused by agents unresponsive to antimicrobials, such as rotavirus or *Cryptosporidium*. Moreover, even for potentially responsive infections, selecting an effective antimicrobial drug requires knowledge of the likely sensitivity of the causative agent, and such information is usually unavailable. In addition, use of antimicrobials adds to the cost of treatment, risks adverse reactions and enhances the development of resistant bacteria.

Antimicrobial drugs are reliably helpful only for children with bloody diarrhoea (probable shigellosis), suspected cholera with severe dehydration, and serious non-intestinal bacterial infections such as pneumonia. Antiprotozoal drugs are rarely indicated except as described below when a definite diagnosis is available.

Antimicrobial drugs for acute diarrhoea

Neonates

Diarrhoea and vomiting may be a symptom of septicaemia. If septicaemia is suspected, parenteral antibiotics are required (*see* Section 3.4).

Bloody diarrhoea

- **Bacterial causes:** *Campylobacter jejuni*, *Shigella sonnei*, *Shigella flexneri* and *Shigella dysenteriae*, and less commonly *Salmonella*, *E. coli* 0157:117 and *Aeromonas*.
- May be accompanied by abdominal pain and rectal prolapse.
- As culture facilities may not be available, sick toxic children with bloody diarrhoea should be treated for shigella dysentery.
- Children with diarrhoea and blood in stool (dysentery) should be treated with ciprofloxacin as first-line treatment and ceftriaxone as second-line treatment if they are severely ill and local antimicrobial sensitivity is not known. Where local antimicrobial sensitivity is known, local guidelines should be followed:
  - ciprofloxacin: 20 mg/kg/dose twice daily for 5 days
  - ceftriaxone: 80 mg/kg IV or IM once daily for 5 days.
- Mild infections due to *Shigella sonnei* are usually self-limiting. *Shigella* in resource-limited countries is commonly resistant to co-trimoxazole and ampicillin. Nalidixic acid, ciprofloxacin, ceftriaxone **or the antibiotic of choice for the area** should be used for a 5-day course.
- In infants and young children, exclude surgical causes (e.g. intussusception) (*see* Section 5.19).

Salmonella

If non-typhoidal *Salmonella* is suspected in infants under 1 year of age or in immunocompromised children, blood cultures should be undertaken. If these are positive or the infant is toxic, an appropriate parenteral antibiotic should be given (e.g. chloramphenicol, ceftriaxone or ciprofloxacin) for 7–10 days. Be alert for pneumonia or metastatic abscesses in bone, brain or elsewhere. Otherwise *Salmonella* gastroenteritis is not treated with antibiotics.

Systemic *Salmonella* infection is common in malnutrition, HIV infection, sickle-cell disease and schistosomiasis.

Campylobacter jejuni (and also *Shigella* and *Salmonella*) may cause severe abdominal pain, mimicking a surgical emergency. Otherwise the disease is self-limiting and does not require antibiotics. If treatment is considered appropriate, erythromycin (12.5 mg/kg four times daily) for 5 days is the antibiotic of choice.

Other causes of diarrhoea that warrant antimicrobial treatment

- **Amoebic dysentery:** this is diagnosed by microscopy of fresh warm stool. Treatment is with metronidazole 10 mg/kg three times daily (maximum dose 2 grams) for 5–7 days.
- **Cholera:** this is usually only diagnosed during epidemics. If the child has severe watery diarrhoea, suspect cholera or enterotoxigenic *E. coli* (only diagnosed by specialist laboratories). Treatment for cholera is with tetracycline 12.5 mg/kg four times a day for 3 days in children aged over 8 years. The alternative for young children is chloramphenicol 25 mg/kg 8-hourly for 3 days. In addition to rehydration, give an antibiotic to which local

strains of *Vibrio cholerae* are sensitive. These include tetracycline, doxycycline, co-trimoxazole, erythromycin and chloramphenicol.

- **Giardiasis:** this is diagnosed by microscopy of stool, and is usually self-limiting or asymptomatic. If symptomatic in a malnourished child or the disease is prolonged, it is justified to treat with metronidazole for 5 days (as for amoebic dysentery). Tinidazole is an alternative (50–75 mg/kg once only (maximum dose 2 grams), a second dose may be given if necessary).
- *Clostridium difficile* usually occurs after a course of antibiotics for some other illness, and is associated with antibiotic-associated pseudomembranous colitis (there is a danger of bowel perforation). Antibiotics, especially clindamycin, may alter the flora of the gastrointestinal tract and allow overgrowth of *C. difficile*. The latter produces a toxin which causes damage to the gut mucosa, resulting in pseudomembranous colitis. Confirmation is by culture of *C. difficile* in the faeces. Treatment is with oral vancomycin for 7–10 days, which clears *C. difficile* from the gut. The doses are orally:
  - **Child 1 month–5 years:** 5 mg/kg 4 times daily for 10–14 days (increased up to 10 mg/kg 4 times daily if infection fails to respond or is life threatening)
  - **Child 5–12 years:** 62.5 mg 4 times daily for 10–14 days (increased up to 250 mg 4 times daily if infection fails to respond or is life threatening)
  - **Child 12–18 years:** 125 mg 4 times daily for 10–14 days (increased up to 500 mg 4 times daily if infection fails to respond or is life threatening).

Symptomatic drugs

'Antidiarrhoeal' drugs and anti-emetics have no practical benefits for children with acute or persistent diarrhoea. They do not prevent dehydration or improve nutritional status, which should be the main objectives of treatment. Some, like loperamide, have dangerous and sometimes fatal side effects. These drugs should never be given to children under 5 years of age.

Treatment of rectal prolapse

Gently push back any tissue that has come out of the anus using a surgical glove or wet cloth, or if it is oedematous and cannot be reduced, warm compresses of magnesium sulphate may reduce the oedema.

Haemolytic–uraemic syndrome

If laboratory tests are not available, suspect this syndrome when purpura, pallor, altered level of consciousness and low or absent urine output are present. If laboratory tests are available, blood smear shows fragmented red cells and decreased or absent platelets. There will be an increase in blood urea and creatinine levels (*see* Section 5.6.A).

Appendix

WHO Treatment Plan A: home therapy to prevent dehydration and malnutrition

Children with no signs of dehydration need extra fluids and salt to replace their losses of water and electrolytes due to diarrhoea. If these are not given, signs of dehydration may develop.

Mothers should be taught how to prevent dehydration at home by giving the child more fluid than usual, how to prevent malnutrition by continuing to feed the child, and why these actions are important. They should also know what signs indicate that the child should be taken to a health worker. *These steps are summarised in the four rules of Treatment Plan A.*

Rule 1: Give the child more fluids than usual, to prevent dehydration

What fluids to give

Many countries have designated recommended home fluids. *Wherever possible, these should include at least one fluid that normally contains salt* (see below). Plain clean water should also be given. Other fluids should be recommended that are frequently given to children in the area, that mothers consider acceptable for children with diarrhoea, and that mothers would be likely to give in increased amounts when advised to do so.

Suitable fluids

Most fluids that a child normally takes can be used. It is helpful to divide suitable fluids into two groups:

Fluids that normally contain salt, such as:

- ORS solution
- salted drinks (e.g. salted rice water or a salted yoghurt drink)
- vegetable or chicken soup with salt.

Insert

Teaching mothers to add salt (about 3 g/L) to an unsalted drink or soup during diarrhoea is also possible, but requires a sustained educational effort.

A home made solution containg 3 g/L of table salt (one level teaspoon) and 18g/l of common sugar (sucrose) is effective but is not generally recommended because the recipe is often forgotten, the ingredients may not be available or too little may be given.

Fluids that do not contain salt, such as:

- plain water
- water in which a cereal has been cooked (e.g. unsalted rice water)
- unsalted soup
- yoghurt drinks without salt
- green coconut water
- weak tea (unsweetened)
- unsweetened fresh fruit juice.

Unsuitable fluids

A few fluids are potentially dangerous and should be avoided during diarrhoea. Especially important are drinks sweetened with sugar, which can cause osmotic diarrhoea and hypernatraemia. Some examples are:

- commercial carbonated beverages
- commercial fruit juices
- sweetened tea.

Other fluids to avoid are those with stimulant, diuretic or purgative effects, for example

- coffee
- some medicinal teas or infusions.

How much fluid to give

The general rule is: give as much fluid as the child or adult

wants until the diarrhoea stops. As a guide, after each loose stool, give:

- children under 2 years of age: 50–100 mL (a quarter to half a large cup) of fluid
- children aged 2 up to 10 years: 100–200 mL (a half to one large cup)
- older children and adults: as much fluid as they want.

Insert

Rule 2: Give supplemental zinc (10–20 mg) to the child every day for 10 to 14 days

Zinc can be given as a syrup or as dispersible tablets, whichever formulation is available and affordable. By giving zinc as soon as diarrhoea starts, the duration and severity of the episode as well as the risk of hydration will be reduced. By continuing zinc supplementation for 10–14 days, the zinc lost during diarrhoea is fully replaced and the risk of the child having new episodes of diarrhoea in the following 2 to 3 months is reduced.

Rule 3: Continue to feed the child, to prevent malnutrition

The infant's usual diet should be continued during diarrhoea and increased afterwards. Food should never be withheld, and the child's usual foods should not be diluted. Breastfeeding should always be continued. The aim is to give as much nutrient-rich food as the child will accept. Most children with watery diarrhoea regain their appetite after dehydration is corrected, whereas those with bloody diarrhoea often eat poorly until the illness resolves. These children should be encouraged to resume normal feeding as soon as possible.

When food is given, sufficient nutrients are usually absorbed to support continued growth and weight gain. Continued feeding also speeds the recovery of normal intestinal function, including the ability to digest and absorb various nutrients. In contrast, children whose food is restricted or diluted lose weight, have diarrhoea of longer duration, and recover intestinal function more slowly.

What foods to give

This depends on the child's age, food preferences and pre-illness feeding pattern; cultural practices are also important. In general, foods suitable for a child with diarrhoea are the same as those required by healthy children. Specific recommendations are given below.

Milk

- Infants of any age who are breastfed should be allowed to breastfeed as often and as long as they want. Infants will often breastfeed more than usual; this should be encouraged.
- Infants who are not breastfed should be given their usual milk feed (or formula) at least every three hours, if possible by cup. Special commercial formulas advertised for use in diarrhoea are expensive and unnecessary; they should not be given routinely. Clinically significant milk intolerance is rarely a problem.
- Infants below six months of age who take breast milk and other foods should receive increased breastfeeding. As the child recovers and the supply of breast milk increases, other foods should be decreased (if fluids other than breastmilk are given, use a cup, not a bottle). This usually takes about 1 week. If possible, infants of this age should become **exclusively** breastfed.

There is no value in routinely testing the stools of infants for pH or reducing substances. Such tests are oversensitive, often indicating impaired absorption of lactose when it is not clinically important. It is more important to monitor the child's clinical response (i.e. weight gain, general improvement). Milk intolerance is only clinically important when milk feeding causes a prompt increase in stool volume and a return or worsening of the signs of dehydration, often with loss of weight.

Other foods

If the child is at least 6 months old or is already taking soft foods, he or she should be given cereals, vegetables and other foods, in addition to milk. If the child is over 6 months old and such foods are not yet being given, they should be started during the diarrhoea episode or soon after it stops.

Recommended foods should be culturally acceptable, readily available, have a high content of energy and provide adequate amounts of essential micronutrients. They should be well cooked, and mashed or ground to make them easy to digest; fermented foods are also easy to digest. Milk should be mixed with a cereal. If possible, 5–10 mL of vegetable oil should be added to each serving of cereal. (Most staple foods do not provide enough calories per unit weight for infants and young children. This is improved by adding some vegetable oil.) Meat, fish or egg should be given, if available. Foods rich in potassium, such as bananas, green coconut water and fresh fruit juice, are beneficial.

How much food and how often

Offer the child food every three or four hours (six times a day). Frequent small feedings are tolerated better than less frequent large ones.

After the diarrhoea stops, continue giving the same energy-rich foods and provide one more meal than usual each day for at least 2 weeks. If the child is malnourished, extra meals should be given until the child has regained normal weight for height.

Rule 4: Take the child to a healthcare worker if there are signs of dehydration or other problems

The mother should take her child to a healthcare worker if the child:

- starts to pass many watery stools
- has repeated vomiting
- becomes very thirsty
- is eating or drinking poorly
- develops a fever
- has blood in the stool
- does not get better in 3 days.

WHO Treatment Plan B: oral rehydration therapy for children with some dehydration

Children with some dehydration should receive oral rehydration therapy with ORS in a healthcare facility following the treatment plan described below.

Children with some dehydration should also receive zinc supplementation as described above.

TABLE 5.12.A.6 Guidelines for treating children with some dehydration: approximate amount of ORS to give in the first 4 hours

Age	< 4 months	4–11 months	12–23 months	2–4 years	5–14 years	15 years or older
Weight (kg)	< 5	5–7.9	8–10.9	11–15.9	16–29.9	30 kg or more
Volume (mL)	200–400	400–600	600–800	800–1200	1200–2200	2200–4000

How much ORS is needed?

Use Table 5.12.A.6 to estimate the amount of ORS needed for rehydration. If the child's weight is known, this should be used to determine the approximate amount of solution needed. The amount may also be estimated by multiplying the child's weight in kg by 75 mL. If the child's weight is not known, select the approximate amount according to the child's age.

The *exact* amount of solution required will depend on the child's dehydration status. Children with more marked signs of dehydration, or who continue to pass frequent watery stools, will require more solution than those with less marked signs or who are not passing frequent stools. *If the child wants more than the estimated amount of ORS, and there are no signs of over-hydration, give more.*

Oedematous (puffy) eyelids are a sign of *over-hydration*. They may be a sign of chronic malnutrition. If this occurs, stop giving ORS, but give breast milk or plain water, and food. Do not give a diuretic. When the oedema has gone, resume giving ORS or home fluids according to Treatment Plan A.

How to give ORS

A family member should be taught to prepare and give ORS. The solution should be given to infants and young children using a clean spoon or cup. Feeding bottles should *not* be used. For babies, a dropper or syringe (without the needle) can be used to put small amounts of solution into the mouth.

Children under 2 years of age should be offered a teaspoonful every 1 to 2 minutes. Older children (and adults) may take frequent sips directly from the cup.

Vomiting often occurs during the first hour or two of treatment, especially when children drink the solution too quickly, but this rarely prevents successful oral rehydration, as most of the fluid is absorbed. After this time vomiting usually stops. If the child vomits, wait 5–10 minutes and then start giving ORS again, but more slowly (e.g. a spoonful every 2–3 minutes).

Monitoring the progress of oral rehydration therapy

Check the child from time to time during rehydration to ensure that ORS is being taken satisfactorily and that signs of dehydration are not worsening. If at any time the child develops signs of severe dehydration, switch to WHO Treatment Plan C.

After 4 hours, reassess the child fully, following the guidelines in Table 5.12.A.2. Then decide what treatment to give next:

- If signs of *severe dehydration* have appeared, intravenous (IV) therapy should be started following Treatment Plan C. This is very unusual, however, occurring only in children who drink ORS poorly and pass large watery stools frequently during the rehydration period.
- If the child still has signs indicating *some dehydration*, continue oral rehydration therapy by repeating Treatment Plan B. At the same time start to offer food, milk and other fluids, as described in Treatment Plan A (see above), and continue to reassess the child frequently.

If there are *no signs of dehydration*, the child should be considered fully rehydrated. When rehydration is complete:

- the skin pinch is normal
- thirst has subsided
- urine is passed
- the child becomes quiet, is no longer irritable and often falls asleep.

Teach the mother how to treat her child at home with ORS and food following Treatment Plan A. Give the mother enough ORS sachets for 2 days. Also teach her the signs that mean she should bring her child back.

- Use the patient's age only when you do not know their weight. The approximate amount of ORS required (in mL) can also be calculated by multiplying the patient's weight in kg by 75.
- If the patient wants more ORS than is shown above, give more.
- Encourage the mother to continue breastfeeding her child.
- For infants under 6 months who are not breast fed, if using the old WHO ORS solution containing 90 mmol/L of sodium also give 100–200 mL clean water during this period. However, if using the new reduced (low) osmolality ORS solution containing 75 mmol/L of sodium, this is not necessary.

Note: During the initial stages of therapy, while still dehydrated, adults can consume up to 750 mL per hour, if necessary, and children up to 20 mL/kg body weight/hour.

Meeting normal fluid needs

While treatment to replace the existing water and electrolyte deficit is in progress, the child's normal daily fluid requirements must also be met. This can be done as follows:

- **Breastfed infants:** continue to breastfeed as often and for as long as the infant wants, even *during* oral rehydration.
- **Non-breastfed infants** under 6 months of age: if using the old WHO ORS solution containing 90 mmol/L of sodium also give 100–200 mLs clean water during this period. However, if using the new reduced (low) osmolality ORS solution containing 75 mmol/L of sodium, this is not necessary.
- **Older children:** throughout rehydration and maintenance therapy, offer as much plain boiled water to drink as they wish, in addition to ORS.

If oral rehydration therapy must be interrupted

If the mother and child must leave hospital before rehydration with ORS is completed:

- Show the mother how much ORS solution to give to finish the 4-hour treatment at home.

- Give her enough ORS packets to complete the 4-hour treatment and to continue oral rehydration for two more days, as shown in Treatment Plan A.
- Show her how to prepare ORS solution.
- Teach her the four rules in Treatment Plan A for treating her child at home.

When oral rehydration fails

With the previous ORS, signs of dehydration would persist or reappear in about 5% of children. With the new reduced (low) osmolality ORS it is estimated that such treatment 'failures' will be reduced to 3% or less. The usual causes for these 'failures' are:

- continuing rapid stool loss (more than 15–20 mL/kg/hour), as occurs in some children with cholera
- insufficient intake of ORS due to fatigue or lethargy
- frequent severe vomiting.

Such children should be given ORS by nasogastric (NG) tube or Ringer Lactate Solution intravenously (IV) (75 mLs/kg in four hours) usually in hospital. After confirming that the signs of dehydration have improved, it is usually possible to resume ORT successfully.

Rarely, oral rehydration therapy should not be given. This is true for children with:

- abdominal distension with paralytic ileus, usually caused by opiate drugs (e.g. codeine, loperamide) and hypokalaemia
- glucose malabsorption (indicated by a marked increase in stool output, failure of the signs of dehydration to improve, and a large amount of glucose in the stool).

In these situations, rehydration should be given IV until the diarrhoea subsides; nasogastric therapy should *not* be used.

Giving zinc

Begin to give supplemental zinc, as in Treatment plan A, as soon as the child is able to eat, following the four hour rehydration period.

Giving food

Except for breast milk, food should not be given during the initial 4-hour rehydration period. However, children who are continued on Treatment Plan B for longer than 4 hours should be given some food every 3–4 hours as described in Treatment Plan A. All children older than 6 months of age should be given some food before being sent home. This helps to emphasise to mothers the importance of continued feeding during diarrhoea.

WHO Treatment Plan C: intravenous rehydration therapy for patients with severe dehydration

The preferred treatment for children with severe dehydration is initial rapid intravenous rehydration following Treatment Plan C. If possible, the child should be admitted to hospital. Guidelines for IV rehydration are given in Table 5.12.A.7.

Children who can drink, even poorly, should be given ORS by mouth until the IV drip is running. In addition, all children should receive some ORS solution (about 5 mL/kg/hr) when they can drink without difficulty, which is usually within 3–4 hours for infants and 1–2 hours for older patients. This provides additional base and potassium which may not be adequately supplied by the IV fluid.

Monitoring the progress of intravenous rehydration

Patients should be reassessed every 15–30 minutes until a strong radial pulse is present. If it is not, the intravenous drip should be given more rapidly.

When the planned amount of intravenous fluid has been given (after 3 hours for older patients, or 6 hours for infants), the child's hydration status should be reassessed fully as in Table 5.12.A.2.

Look and feel for all the signs of dehydration

- If signs of *severe* dehydration are still present, **repeat** the intravenous fluid infusion as outlined in Treatment Plan C. This is very unusual, however, occurring only in children who pass large watery stools frequently during the rehydration period.
- If the child is improving (able to drink) but still shows signs of *some dehydration*, **discontinue** the intravenous infusion and give ORS for 4 hours, as specified in Treatment Plan B.
- If there are *no signs of dehydration*, follow Treatment Plan A. If possible, observe the child for at least six hours before discharge while the mother gives the child ORS, to confirm that she is able to maintain the child's hydration. Remember that the child will require therapy with ORS until the diarrhoea stops.

If the child cannot remain at the treatment centre, teach the mother how to give treatment at home following Treatment Plan A, give her enough ORS packets for two days and teach her the signs that mean she should bring her child back.

What to do if intravenous therapy is not available

- If IV therapy is not available at the facility, but can be given nearby (i.e. within 30 minutes), send the child immediately for intravenous treatment. If the child can drink, give the mother some ORS and show her how to give it to her child during the journey.
- If IV therapy is not available nearby, healthcare workers who have been trained can give ORS by NG tube, at a rate of 20 mL/kg body weight per hour for 6 hours (total of 120 mL/kg body weight). If the abdomen becomes

TABLE 5.12.A.7 Guidelines for intravenous treatment of children with severe dehydration

Start IV fluids immediately. If the patient can drink give ORS by mouth until the drip is set up. Give 100 mLs/kg of Ringers Lactate Solution[a] divided as follows		
Age	**First give 30 mL/kg in:**	**Then give 70 mL/kg in:**
Infants under 12 months	1 hour[b]	5 hours
Older	30 minutes[b]	Over 2.5 hours

Reassess the patient every 1–2 hours. If hydration is not improving, give the IV drip more rapidly. After six hours (infants) or three hours (older patients), evaluate the patient using the assessment chart. Then choose the appropriate Treatment Plan (A, B or C) to continue treatment

a. If Ringers Lactate Solution is not available, normal saline may be used

b. Repeat once if radial pulse is still very weak or not detectable

swollen, ORS should be given more slowly until the abdomen becomes less distended.
- If NG treatment is not possible but the child can drink, ORS should be given by mouth at a rate of 20 mL/kg body weight per hour for 6 hours (total of 120 mL/kg body weight). If this rate is too fast, the child may vomit repeatedly. In this case, give ORS more slowly until the vomiting subsides.
- Children receiving NG or oral therapy should be reassessed at least every hour. If the signs of dehydration do not improve after 3 hours, the child must be taken immediately to the nearest facility where intravenous therapy is available. Otherwise, if rehydration is progressing satisfactorily, the child should be reassessed after 6 hours and a decision on further treatment made as described above for those given IV therapy.
- If neither NG nor oral therapy is possible, the child should be taken *immediately* to the nearest facility where IV or NG therapy is available.

Further reading

World Health Organization (2005) *The Treatment of Diarrhoea: a manual for physicians and other senior health workers*, 4th revision. http://whqlibdoc.who.int/publications/2005/9241593180.pdf

World Health Organization and UNICEF (2013) *Ending Preventable Child Deaths from Pneumonia and Diarrhoea by 2025: the integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD)*. http://apps.who.int/iris/bitstream/10665/79200/1/9789241505239_eng.pdf

5.12.B Post-infectious prolonged or persistent diarrhoea

BOX 5.12.B.1 Minimum standards
- Low-osmolality ORS and ReSoMal in severely malnourished children.
- Ringer-lactate or Hartmann's solution with potassium: oral and IV.
- Antibiotics: amoxicillin, gentamicin.
- Vitamin A and zinc.
- Electrolyte and mineral mix.
- Folic acid.

Introduction

Epidemiology

- Diarrhoeal episodes that start acutely and last for 7–14 days are usually labelled as prolonged diarrhoea, and may be associated with greater morbidity and more severe nutritional consequences.
- Persistent diarrhoea is commonly defined as diarrhoea that starts acutely, but lasts for more than 14 days and is associated with growth faltering.
- Most cases are thus post-infectious in origin, and other disorders such as inflammatory bowel disease and coeliac disease are therefore excluded.
- Around 4–20% of all episodes of diarrhoea in resource-limited countries become prolonged, with associated case-fatality rates that may exceed 50% in severe cases.
- In parts of sub-Saharan Africa, the association of persistent diarrhoea with HIV infection is often the terminal event.

Risk factors for prolonged and persistent diarrhoea

Appropriate case management of acute diarrhoea is key to the prevention of prolonged episodes.

Specific pathogens: although some studies have identified an association between persistent diarrhoea and infections with organisms such as entero-aggregative *E. coli* or *Cryptosporidium*, this is by no means pathognomonic, nor is there a particular pattern of small bowel microbial colonisation or overgrowth seen in most cases. In HIV-endemic parts of Africa an association of persistent diarrhoea with cryptosporidiosis is well recognised, but may represent a manifestation of immunodeficiency. Evidence from Bangladesh does suggest that recurrent bouts of infection with bacterial pathogens such as *Shigella* lead to prolongation of the duration of successive diarrhoeal episodes, and thus there is a link between prolonged and persistent diarrhoea as an epidemiological continuum.

Malnutrition: persistent diarrhoea is commonly seen in association with significant malnutrition, and the relationship may be bidirectional. It is widely recognised that diarrhoeal episodes, especially if invasive, may become prolonged in malnourished children. The recent evidence of micronutrient deficiencies, especially of zinc and vitamin A in malnourished children with persistent diarrhoea, may indicate impaired immunological mechanisms for clearing infections, as well as ineffective mucosal repair mechanisms.

Dietary risk factors: although many children with persistent diarrhoea are lactose-intolerant, there is no role of specific dietary allergies in inducing and perpetuating enteropathy of malnutrition or post-infectious prolonged diarrhoea. Several studies have highlighted the high risk of prolonged diarrhoea with lactation failure and early introduction of artificial feeds in resource-limited countries.

Inappropriate management of acute diarrhoea: the association of prolongation of diarrhoea with food deprivation and inappropriately prolonged administration of parenteral fluids is well recognised. Unnecessary food withdrawal, and replacement of luminal nutrients, especially breast milk, with non-nutritive agents is prolonging the mucosal injury after diarrhoea. In particular, blanket administration of antibiotics and **any administration of antimotility agents must be avoided**. Optimal management of acute diarrhoea episodes with ORS, zinc and appropriate diets is a key factor in reducing the risk of recurrence and prolongation of diarrhoeal episodes.

Principles of management of persistent diarrhoea

In general, the management of persistent diarrhoea in malnourished children (*see* Figure 5.12.B.1) represents a blend of the principles of management of acute diarrhoea and malnutrition (*see* Section 5.12.A and Section 5.10.B).

Associated malnutrition may be quite severe in affected children, necessitating appropriate and rapid nutritional rehabilitation, sometimes in hospital. Given the chronicity of the disorder, prolonged hospitalisation may be quite problematic in resource-limited countries, and whenever possible the importance of ambulatory or home-based therapy must be emphasised.

The following represent the basic principles of management of persistent diarrhoea, and a suggested therapeutic approach is shown in Figure 5.12.B.1.

Rapid resuscitation and stabilisation

- Most children with persistent diarrhoea and associated malnutrition are not severely dehydrated, and oral rehydration is adequate.
- However, acute exacerbations and associated vomiting may require brief periods of intravenous rehydration with Ringer-lactate solution.
- Acute electrolyte imbalance such as hypokalaemia and severe acidosis may require correction (*see* Section 5.6.A).
- Associated systemic infections (bacteraemia, pneumonia and urinary tract infections) are well recognised in severely malnourished children with persistent diarrhoea, and are a frequent cause of early mortality. These must be screened for at admission. In severely ill children requiring hospitalisation, it may be best to cover with intravenous antibiotics at admission (usually ampicillin, IV 25 mg/kg three times daily up to a maximum of 4 grams/day, and gentamicin, IV 7.5 mg/kg once daily) while awaiting cultures. In other instances with suspected severe pneumonia, oral amoxicillin will suffice.
- It should be emphasised that there is little role for oral antibiotics in persistent diarrhoea, as in most cases the original bacterial infection that triggered the prolonged diarrhoea has disappeared by the time the child presents.

Oral rehydration therapy

This is the preferred mode of rehydration and replacement of ongoing losses. Although in general the standard low-osmolality WHO oral rehydration solution (containing 75 mmol/litre of Na^+) is adequate, some evidence indicates that the hypo-osmolar rehydration fluid ReSoMal (containing 45 mmol/litre of Na^+) as well as cereal-based oral rehydration fluids may be advantageous in severely malnourished children. In general, replacing each stool with about 50–100 mL of ORS or ReSoMal is safe.

Enteral feeding and diet selection

- Most children with persistent diarrhoea are not lactose intolerant, although administration of a lactose load exceeding 5 grams/kg/day is associated with higher rates of stooling and treatment failure. In general,

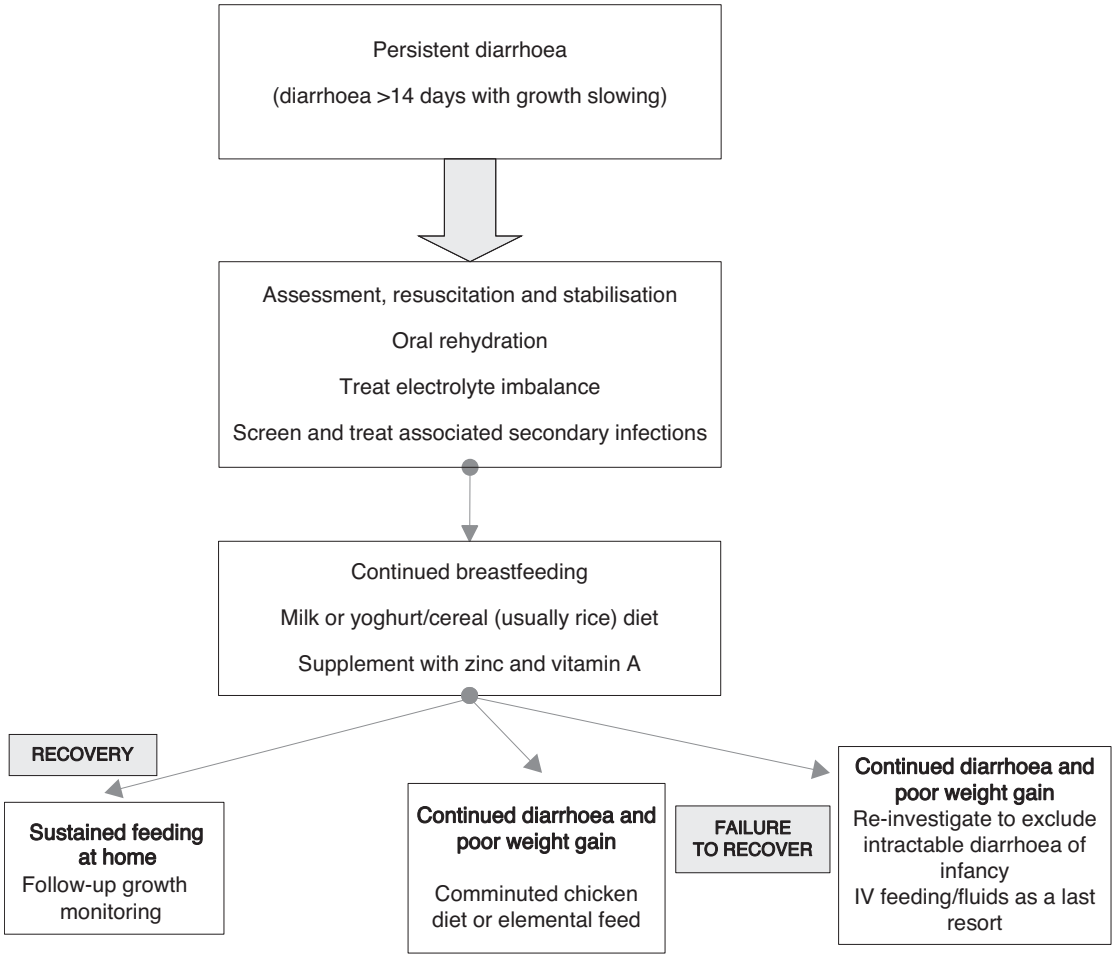

FIGURE 5.12.B.1 Management of persistent diarrhoea in malnourished children.

therefore, withdrawal of milk and replacement with specialised (and expensive) lactose-free formulations is unnecessary.
- Alternative strategies for reducing the lactose load in malnourished children with persistent diarrhoea include reducing the overall amount of milk intake, addition of lactose-free milk to cereals, and replacement of milk with fermented milk products such as yoghurt. These measures have now been extensively evaluated in successive studies of the management of persistent diarrhoea in South Asia, and found to be extremely effective.
- It is rare to find persistent diarrhoea in breastfed infants, and **it must be emphasised that breastfeeding must not be stopped under any circumstances**.
- Rarely, when dietary intolerance precludes the administration of cow's-milk-based formulations or milk, it may be necessary to administer specialised milk-free diets such as a comminuted or blenderised chicken-based diet or an elemental formulation. However, the latter may be almost unaffordable in most resource-limited countries. A choice of enteral diets and formulations is given in Table 5.12.B.2. It must be emphasised that this is extremely rare, and most infants will recover with the approach outlined above.
- The usual energy density of any diet used for the therapy of persistent diarrhoea should be around 1 kcal/gram, aiming to provide an energy intake of at least 110 kcal/kg/day and a protein intake of 2–3 grams/kg/day (in meals given six times daily). Nasogastric feeding may be required during the first 2–3 days of care, particularly while infection is being treated.
- There should be at least 3 successive days of increasing weight before a response can be verified.
- Dietary failure is shown by an increase in stool frequency (> 10 watery stools/day) or a failure to establish a daily weight gain within 7 days.
- In selected circumstances when adequate intake of energy-dense food is problematic, the addition of amylase to the diet through germination techniques which increase the endogenous amylase content of foods may be helpful. The ready-to-use therapeutic foods (RUTFs) can be used in moderate amounts in children with severe malnutrition and persistent diarrhoea, and the diets below also offer a suitable alternative.

TABLE 5.12.B.2 Suggested composition of selected diets in children with persistent diarrhoea

Component	Khitchri (rice-lentils) (per 100 grams)	Home made version of F-75 diet (WHO) (per 1000 mL)	Comminuted chicken (per 100 grams)	Semi-elemental diet (per 100 mL)
Protein	Mung lentils, 30 grams	Dried skimmed milk, 25 grams	Protein, 8 grams	Protein, 2.25 grams (hydrolysed)
Fat	Oil, 2 grams	Vegetable oil, 27 grams	Fat, 4 grams	Fat, 1.65 grams (medium-chain triglycerides)
Minerals and micronutrients	Salt (to taste)	Vitamin mix, 140 mg Mineral mix, 20 mL	Electrolytes (sodium, 0.4 mmol; potassium, 1.3 mmol; calcium, 0.2 mmol; phosphorus, 1.5 mmol)	Electrolytes (sodium, 1.9 mmol; potassium, 2.3 mmol; calcium, 1.8 mmol)
Carbohydrate	Rice, 60 grams	Cereal flour, 35 grams Sugar, 70 grams		Caloreen, 5 grams

First diet: a starch-based reduced milk concentration (low-lactose) diet

The diet should contain at least 70 kcal/100 grams, provide milk or yoghurt as a source of animal protein, but no more than 3.7 grams of lactose/kg body weight/day, and should provide at least 10% of calories as protein. The following example provides 83 kcal/100 grams, 3.7 grams of lactose/kg body weight/day and 11% of calories as protein:
- full-fat dried milk: 11 grams (or whole liquid milk: 85 mL)
- rice: 15 grams
- vegetable oil: 3.5 grams
- cane sugar: 3 grams
- water to make up to 200 mL.

Of the children who do not improve on this first diet, more than 50% will improve when given the second diet, from which the milk has been totally removed and starch (cereals) partly replaced with glucose or sucrose.

Second diet: a no-milk (lactose-free) diet with reduced cereal (starch)

The second diet should contain at least 70 kcal/100 grams, and provide at least 10% of calories as protein (egg or chicken). The following example provides 75 kcal/100 grams:
- whole egg: 64 grams
- rice: 3 grams
- vegetable oil: 4 grams
- glucose: 3 grams
- water to make up to 200 mL.

Finely ground, cooked chicken (12 grams) can be used in place of egg to give a diet that provides 70 kcal/100 grams.

Of the children who do not improve on the first diet, more than 50% will improve when given the second diet, from which milk has been totally removed and starch (cereals) partly replaced with glucose or sucrose.

Micronutrient supplementation

Most malnourished children with persistent diarrhoea have associated deficiencies of micronutrients, including zinc, iron and vitamin A. This may be a consequence of poor intake and continued enteral losses. It is therefore important to ensure that all children with persistent diarrhoea and malnutrition receive an initial dose of vitamin A orally, or if that is not possible by deep intramuscular injection (< 6 months of age, 50 000 units; 6–12 months, 100 000 units; > 1 year, 200 000 units). They should also receive a daily intake of the following for the next 2 weeks:
- a multivitamin supplement

- folic acid, 250 micrograms/kg on day 1, then 75 micrograms/kg/day
- zinc, 3–5 mg/kg/day.
- copper, 0.3 mg/kg/day
- magnesium, 0.2 mmol/kg/day.

Although the association of significant anaemia with persistent diarrhoea is well recognised, iron replacement therapy should not be initiated until recovery from diarrhoea has started (ferrous sulphate 18 mg/kg/day, or 6 mg/kg/day of elemental iron in two divided doses).

Follow-up and nutritional rehabilitation

Given the high rates of relapse in most children with persistent diarrhoea, it is important to address the underlying risk factors and institute preventive measures. These include appropriate feeding (breastfeeding, complementary feeding) and close attention to environmental hygiene and sanitation. This poses a considerable challenge in communities deprived of basic necessities such as clean water and sewage disposal.

By the time they return home, children should be receiving a diet that provides at least 110 kcal/kg/day (including milk and fresh fruit and well-cooked vegetables).

Further reading

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5.12.C Constipation

BOX 5.12.C.1 Minimum standards

- Movicol – osmotic laxative – softens
- Lactulose – osmotic laxative – softens
- Docusate sodium – softener and weak stimulant
- Senna or sodium picosulphate-stimulant laxative
- Glycerine suppositories – lubricant and rectal stimulant
- Small volume of phosphate enema (e.g. fleet enema)
- Sodium citrate enema (e.g. Micralax enema).

Introduction

Definition

Constipation is defined as difficulty with, delay in or pain on defecation.

Normal defecation patterns

- Breastfed babies average three stools per day and formula-fed babies two stools per day. However, the range of normal stool frequency in breastfed babies is very wide, from one stool every few days to a stool with every feed.
- Children average one stool per day after 3 years, but the normal range is from once on alternate days to three times daily.

Pathophysiology

Most children with constipation have no underlying medical cause. An episode of constipation can be triggered by inadequate food or fluid intake, an intercurrent illness, or excessive intake of cow's milk.

Constipation cycle

The child passes a hard painful stool. On subsequent occasions they try to withhold the stool in order to avoid experiencing pain (faecal holding). The stool remains in the rectum, becoming harder still, and so causing even more pain when it is eventually passed.

If this cycle is allowed to continue, eventually the rectum may become enlarged, resulting in a 'megarectum'. The child by this stage has lost the normal urge to defecate, and the large rectal mass of stool holds open the anal sphincter, which leads to soiling with liquid faeces. This is involuntary and should not be confused with encopresis, which occurs when the child voluntarily passes normal stools in unacceptable places.

Diagnosis

Diagnosis can usually be made by taking a good history.

- On examination of the abdomen, faecal masses may be palpable. These are often in the left and right iliac fossae, but sometimes suprapubically. On inspection of the anus, anal tags and fissure may be seen in chronic constipation.
- On rectal examination, hard impacted faeces may be felt. Rectal examination is usually not necessary. If there is an anal fissure, rectal examination should be done with topical lignocaine jelly (1%) and terminated if it is too painful.
- Abdominal X-ray is not a useful examination for diagnosis of constipation.

Pathological causes

The vast majority of constipation is idiopathic, but there are a few uncommon causes that are important not to miss.

Hirschsprung's disease

Suspect this when there is infancy-onset constipation and a delay of more than 48 hours in passing meconium at birth. In more advanced cases there will be abdominal distension and sometimes failure to thrive and vomiting. There may be alternating constipation and diarrhoea and surprisingly little soiling for the degree of constipation. On rectal examination an explosive gush of faeces occurs when the examining finger is withdrawn.

Anal lesions that cause pain or create an obstruction

These include anal fissures, perianal skin infections and (rarely) congenital anterior anus and anal stenosis. One cause of painful anal lesions is sexual abuse, a rare but important cause which should not be missed.

Endocrine conditions

Hypothyroidism, renal tubular acidosis, diabetes insipidus and hypercalcaemia can be associated with constipation. There should be a high level of suspicion for a metabolic or endocrine cause if constipation and failure to thrive coexist.

Neurogenic constipation

Spinal cord lesions involving sensation in the rectum will cause neurogenic constipation. These can be excluded by a normal neurological and spinal examination.

Management of idiopathic constipation

Parental understanding of the aetiology and sequence of events in developing chronic constipation is crucial to successful physical and psychological management (*see* Figure 5.12.C.1). Each and every element of this flow diagram should be addressed and treated if management is to be completely successful.

Explanation

A careful and thorough explanation of the problem should be given to the parent and child. Emphasise that soiling is not deliberate, and that the child needs support, not condemnation. Assess the need for psychological as well as physical treatment.

Evacuation of hard impacted faeces

1 To soften and lubricate the retained faeces, initially give a softener. This could be a macrogol such as Movicol or another softening laxative such as docusate sodium. The dose will vary according to age.
2 Alongside the softener, in order to expel the retained mass, give a stimulant laxative (e.g. sodium picosulphate).
3 If sodium picosulphate is not available, a large dose of senna can be tried, but may need to be used for longer.
4 Only if the above fails give suppositories (glycerine) once daily (infant, 1 gram; child < 12 years, 2 grams; child > 12 years, 4 grams).
5 If the oral and suppository methods are unsuccessful, if excessive abdominal pain develops and/or there is vomiting, stimulant enemas will be required. Phosphate enemas should not be used in children under 2 years of age. For children aged 2–10 years give 60 mL (half a phosphate enema) and for those over 10 years of age give 120 mL (full enema). If phosphate enemas are not available, a small-volume sodium citrate enema (micro-enema) can be used. However, the use of enemas can add to the child's fear of defecation. **The child should never be forcibly held down to receive an enema.** Give enemas **once a day** in the morning. Most children need two or three enemas to clear a faecal mass.
6 If these measures fail, the child should undergo manual evacuation of faecal mass under general anaesthetic, **but only if this is available and can be done safely.**

Maintenance laxatives to keep the stool soft, defecation pain-free and overcome faecal holding

- Softening agents such as Movicol or docusate sodium to keep the stool soft.
- Stimulant laxatives, usually senna or sodium picosulphate, to expel the soft stool. The aim is to produce

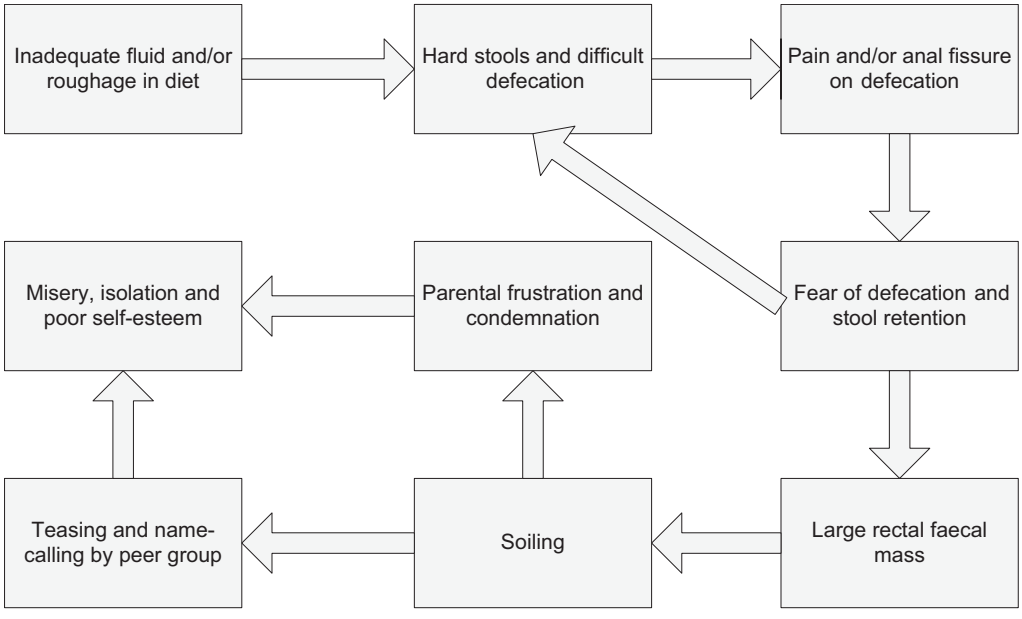

FIGURE 5.12.C.1 Sequence of events in faecal soiling.

loose stools initially and then subsequently reduce the dose to produce at least one soft stool per day. Often large doses will be required initially to overcome the child's faecal holding.

Behaviour changes

- Encourage increased fluid intake and a high-roughage diet (fruit, vegetables and cereals).
- Give positive praise and encouragement for regular toileting, and for passage of stool into the toilet.

Length of treatment

Children are likely to require several months of stimulant laxatives until their fear of defecation resolves, and often months to years of continuous or intermittent treatment with softening laxatives. A general rule of thumb is that the child will need laxatives for the same length of time that they were constipated before treatment started.

5.12.D Inflammatory bowel disease

BOX 5.12.D.1 Minimum standards

- Aminosalicylates.
- Prednisolone.
- Methylprednisolone.
- Corticosteroid enemas.
- Blood transfusion.
- Polymeric diet.
- Metronidazole.

Introduction

Inflammatory bowel disease (IBD) is uncommon in children in resource-limited countries, where abdominal tuberculosis is more common. However, in the UK about 18% of children with IBD are non-white, of whom most are of either Indian or Caribbean origin. Although IBD may present in younger children, the mean age in the UK is approximately 12 years. Crohn's disease is more than twice as common as ulcerative colitis. A family history is common.

Diagnosis

- Clinical symptoms of ulcerative colitis are almost invariably bloody diarrhoea with predefecation abdominal pain and tenesmus. Crohn's disease may have a wide variety of symptoms, especially extra-intestinal ones. Iron-deficiency anaemia is common in both.
- The interval between onset of symptoms and diagnosis is often over 6 months in Crohn's disease, and may be 2–3 months in ulcerative colitis. Denial of symptoms is common, especially in adolescents.

Investigations

- Growth parameters and investigations are a guide to the severity and duration of disease and the nutritional state of the child.
- Examination of the mouth and anus is essential.
- Stool examination is essential to exclude bacterial and parasitological causes of diarrhoea, especially before corticosteroids are prescribed.
- Normal investigations: acute-phase reactants (erythrocyte sedimentation rate or C-reactive protein), haemoglobin, platelet count, albumin; do not exclude ulcerative colitis, but normal blood tests would be very unusual in Crohn's disease.
- Children with ulcerative colitis often have little or no weight loss or growth failure.
- Children with Crohn's disease and severe involvement of the colon may present similarly to those with ulcerative colitis, but generally have larger haematological changes.

TABLE 5.12.D.1 Comparison between Crohn's disease and ulcerative colitis

Feature	Ulcerative colitis	Crohn's disease
Pathology	Mucosal disease	Transmural disease, skin lesions, strictures, fistulae
Site	Recto-colonic (rectum always involved). In children over 70% have a pancolitis	Panenteric disease is common in children: small bowel and colon, 50%; colon, 35%; ileum, 6%; upper gastrointestinal tract, 50%
Common presenting symptoms	Diarrhoea mixed with blood/mucus Pain (lower abdominal) Often no or little weight loss	Pain in the right iliac fossa Diarrhoea with or without blood Growth failure and weight loss Peri-anal and oral disease
Extra-intestinal features (finger clubbing, arthritis, skin disorders, fever)	Uncommon	Common

General investigations

Stool

- Blood, mucus.
- Microscopy for *Entamoeba histolytica*, *Schistosoma*, *Trichuris trichiura*, *Giardia lamblia.*
- Culture for bacteria.

Full blood count
- Haemoglobin level decreased.
- White blood cell count increased.
- Platelet count increased.

Acute-phase reactants
- Erythrocyte sedimentation rate raised.
- C-reactive protein raised.

Chemical pathology
- Electrolytes (if diarrhoea severe).
- Ferritin (may be spuriously raised – acute-phase reactant).
- Albumin level low.

Specific investigations

Specific investigations depend on the availability of paediatric gastrointestinal facilities.
- Sigmoidoscopy is essential.
- Flexible endoscopy of the lower and upper gastrointestinal tract should ideally be undertaken.
- Barium enema (double contrast) is required in colitis **only** if colonoscopy is not available.
- Normal macroscopic appearance of the lower or upper gut **does not exclude IBD**. **Histology is essential.**
- 'Indeterminate colitis' is a term used to describe patients whose histology is not typical of ulcerative colitis or Crohn's disease. They are usually treated initially as having ulcerative colitis.

TABLE 5.12.D.2 Specific investigations for Crohn's disease and ulcerative colitis

Feature	Ulcerative colitis	Crohn's disease
Endoscopy*	Proctoscopy Sigmoidoscopy Colonoscopy	Lower gut Upper gut*
Radiological studies	Barium enema† (double contrast)	Barium meal and follow-through
White blood cell scan (technetium labelled)‡	Screening	Screening

* Depending on availability.

† Only required if colonoscopy is unavailable.

‡ Only available in well-resourced countries.

Management of ulcerative colitis

- Initial management depends on severity.
- Follow-up: parents and older children should be taught so that they understand how to recognise and treat any relapse promptly.

Management of active colitis (*see* Table 5.12.D.3)

- **Mild disease:** less than four motions per day, intermittent blood, normal acute-phase reactants, no toxicity:
  - Aminosalicylates.
  - Mesalazine (1 g rectally) or corticosteroid (20 mg) enema until the bleeding stops, and then given alternate nights for 1 week.
  - Corticosteroids given orally if there is no response within 2 weeks.
- **Moderate disease:** four to six motions per day, moderate blood, slight toxicity, anaemia and raised acute-phase reactants:
  - As above plus oral steroids immediately. If there is a poor response, treat as for severe disease.
- **Severe disease:** more than six bloody motions per day, nocturnal stools, toxicity, fever, anaemia and hypoalbuminaemia:
  - Intravenous pulse methylprednisolone or hydrocortisone dose for 3–5 days.
  - Antibiotics (e.g. metronidazole) (benefit is not proven).
  - Intravenous fluids and correction of electrolyte deficits.
  - Blood transfusion if required.
  - Intravenous cyclosporine (500 micrograms–1 mg/kg aged 3–18 years) or oral cyclosporine (2 mg/kg twice daily maximum 5 mg/kg aged 2–18 years) may be of value if there is no response to intravenous corticosteroids.
- **Toxic dilation:** if there is no response to intensive therapy by 12–24 hours, perform colectomy.

Relapse

Prompt commencement of rectal mesalazine or a corticosteroid enema is essential. If there is no response, give a course of oral corticosteroids.

Maintenance

- Aminosalicylic acid preparations are generally given lifelong. Mesalazine 10 mg/kg 2–3 times daily 5–12 years, 2 G once daily 12–18 years.
- If relapses occur when corticosteroids are reduced, give azathioprine for up to 3–5 years.

TABLE 5.12.D.3 Drug dosages for ulcerative colitis

Corticosteroids	
Prednisolone:	2 mg/kg/day (maximum 40 mg) for 3 weeks, then reduce by 5 mg/week
Methylprednisolone:	IV 1–1.5 mg/kg/day (maximum 60 mg)
Hydrocortisone:	IV 4 mg/kg 6-hourly
Prednisolone enema or foam (20 mg in 100 mL):	50–100 mL at night
Aminosalicylates	
Sulphasalazine: (tablets 10 mg and 50 mg)	10 mg/kg 4- to 6-hourly for acute episodes. Decrease the dose by half for maintenance as soon as possible. Urine and tears will turn orange. Report sore throat
Mesalazine: (oral tablets 500 mg)	Under 40 kg body weight aged 5–12 years give 10 mg/kg 2–3 times daily; over 40 kg body weight aged 12–18 years, give 2 G once daily
Mesalazine: rectal	Aged 12–18 years, 1 gram daily
Metronidazole: (orally)	7.5 mg/kg three times daily
Azathioprine: (orally)	1.5–2.5 mg/kg once daily

- Regular monitoring of the blood count (every 1 to 2 months) is important.

Indicators for colectomy

- Toxic megacolon (see above), intractable disease and growth failure.
- The risk of cancer relates to the extent of disease and its duration. Good maintenance therapy is important for prevention. Two-yearly colonoscopy should be considered in those with pancolitis for 10 years after the commencement of disease.
- Colectomy and ileostomy would be the usual operation in resource-limited settings, and are curative symptomatically, but the patient then has the ileostomy for life.

Management of Crohn's disease

- The key to management is to maintain growth and nutrition and control symptoms.
- Most children will have recurrent relapses.
- Many will require surgery at some stage.
- Nutritional treatment and support are essential.

Polymeric diet

A polymeric diet can be any liquid nutritional preparation that is nutritionally complete. Examples would include PaediaSure/Ensure (Abbott Nutrition), Modulen IBD/Resource Junior (Nestle) and Alicalm/Fortini (Nutricia). Polymeric diet is effective in producing 70% remission in small bowel disease and 50% remission in colonic disease. The advantages over corticosteroids are the positive effect on growth and lack of side effects. The diet is given for 6 weeks, usually orally, during which time no other food is given (but the child can drink water), and then the normal diet is re-introduced.

Maintenance therapy with polymeric diet can also be used.

Drug therapy

See Table 5.12.D.3 for drug dosages in ulcerative colitis.

- Prednisolone 2 mg/kg/day (maximum 40 mg/day) is effective in small and large bowel disease. Continue this dose for 3 weeks, then reduce it by 5 mg/week and then stop. If required to maintain remission, alternate-day therapy may have fewer side effects.
- Mesalazine but not sulphasalazine can be effective for maintaining remission in ileal as well as colonic disease (dose is aged 5–12 years 10–15 mg/kg orally 2–3 times daily, aged 12–18 years 2 G once daily).
- Azathioprine is effective in long-term maintenance and has steroid-sparing effects. It may be useful for healing perianal fistulae. It takes many months to act, and it should be continued for at least 4 years. Blood counts should be undertaken every 1–2 months.
- Metronidazole may be effective in controlling perianal disease and fistulae. It may also reduce small bowel overgrowth. Ciprofloxacin is an alternative.
- Infliximab is a very expensive monoclonal antibody that inhibits tumour necrosis factor alpha (TNFα). It is used in severe Crohn's disease that is not responding to conventional treatment. It is administered IV at intervals. Because of its immunosuppressive effects there are real dangers from infection, especially **latent TB**. Other side effects include anaphylaxis, lymphoma and possibly demyelinating disorders.

Surgery

Indications for surgery include failure of medical therapy, intestinal obstruction and growth failure. Strictureplasty may be an effective method of avoiding excision of bowel when strictures are present.

Follow-up and support for IBD

Patients and their families require long-term understanding and support. Psychological therapy may be helpful in some cases.

5.12.E Upper gastroenterological disorders

Introduction

Upper gastrointestinal disorders are not common complaints in the population presenting to hospitals in resource-limited countries. It may be that symptoms are under-reported or overlooked because of more common problems, such as gastroenteritis, persistent diarrhoea, intestinal helminths and malnutrition. However, certain life-threatening conditions do occur, including obstruction of the oesophagus due to a foreign body, strictures due to caustic soda poisoning, haematemesis due to peptic ulcer or portal hypertension, and volvulus due to malrotation.

In well-resourced communities, particularly **where facilities for upper gastrointestinal paediatric endoscopy** are available, similar symptoms to those that occur in well-resourced countries present. These include recurrent abdominal pain, epigastric and substernal pain, recurrent/persistent vomiting, dyspepsia and water-brash/heartburn.

Gastro-oesophageal reflux

TABLE 5.12.E.1 Gastro-oesophageal reflux

Symptoms	Complications
Vomiting (regurgitation)	*In Infants*
Water-brash/heartburn	Apnoea
Nausea	Life-threatening event
Epigastric/retrosternal pain	*All ages*
	Failure to thrive*
	Aspiration pneumonia
	Haematemesis
	Anaemia
	Oesophageal stricture

*Particularly in children with cerebral palsy.

Gastro-oesophageal reflux (GOR) is a normal physiological condition in infants, children and adults. If GOR is associated with complications (as below) then it is termed gastro-oesophageal reflux disease (GORD). GORD is common in children with cerebral palsy.

Note: Sandifer–Sutcliffe syndrome is dystonic posturing associated with GOR.

Diagnosis

Often no investigations are needed and a diagnosis can be made by taking a good clinical history. The following investigations are helpful if they are needed and available:

- **Barium swallow:** This is often the only diagnostic facility available in resource-limited countries. It is a much less sensitive method for diagnosing reflux than pH monitoring, but will detect associated or other conditions such as oesophageal stricture, hiatus hernia, diaphragmatic hernia and malrotation.
- **Endoscopy and biopsy** (particularly looking for oesophagitis).
- pH monitoring: this grades the frequency and duration of exposure of the lower oesophagus to acid (pH < 4.0).

Management

- Simple GOR in the thriving child: reassurance is all that is needed.
- Excessive regurgitation causing failure to thrive in an infant, or mild symptoms of oesophagitis: treatment by thickening feeds with Carobel (Cow & Gate) or an alginate preparation (e.g. Gaviscon) can be tried.
- Moderate to severe GOR with oesophagitis: H_2-receptor antagonists, such as ranitidine (2–4 mg/kg twice daily, maximum 150 mg twice daily) or the proton pump inhibitor, omeprazole (700 micrograms to 3 mg/kg once daily) should be given. Motility stimulants such as domperidone (200–400 micrograms/kg every 4–8 hours) may be effective, particularly in children with cerebral palsy. However, proof of their efficacy is lacking.
- Surgery: Nissen fundoplication would be considered if, despite medical management, there **was** severe oesophagitis, failure to thrive or aspiration pneumonia. It is sometimes required in children with cerebral palsy and GOR.

Helicobacter pylori

Helicobacter pylori is a ubiquitous bacterium that commonly infects the stomach (especially the antrum) of children in resource-limited countries from an early age. Child-to-child transmission is important. In developed countries up to 40–60% of adults are infected, probably mainly during childhood. Conditions associated with *H. pylori* include the following:

- **Chronic gastritis:** often asymptomatic; not a major cause of abdominal pain in children.
- **Duodenal ulcer:** *H. pylori* has a strong association with duodenal ulcer and must be eradicated to ensure healing.

Diagnosis

Testing for *H. pylori* should only be undertaken if the child has symptoms of ulcer dyspepsia. Diagnostic tests (outlined below) are rarely available as routine in resource-limited countries.

- Serology: this is good for epidemiological studies, but has reduced sensitivity in children under 7 years of age.
- Urea breath test (13C-UBT): this is sensitive and specific, especially in children over 6 years of age.
- Faecal antigen testing: this is sensitive and specific in both children and adults.
- Endoscopy: histological demonstration and culture of *H. pylori*.

Management

Selection of optimal antibacterial agents is difficult because of the development of resistance.

Suggested regimen

1 Omeprazole
   - Aged < 2 years 700 micrograms/kg to 3 mg/kg once daily up to a maximum of 20 mg.
   - Aged > 2 years, body weight 10–20 kg, give 10 mg once daily up to maximum 20 mg once daily.
   - Aged > 2 years, body weight > 20 kg, give 20 mg once daily up to a maximum of 40 mg once daily.
2 **plus** antibiotics, such as amoxicillin (< 1 year, 62.5 mg; 1–4 years, 125 mg; 5–12 years, 250 mg; > 12 years, 250–500 mg, three times daily)
3 **plus** clarithromycin (7.5 mg/kg twice daily) **or** metronidazole (7.5 mg/kg three times daily).

Treatment should be continued for 1–2 weeks. Strict compliance in order to avoid the development of resistance is imperative.

Duodenal ulcer

Duodenal ulcers are uncommon in children, but can be life-threatening due to haematemesis, melaena and perforation.

There is often a family history. Common symptoms include epigastric pain that typically:

- is worsened by fasting
- is improved by eating or antacids
- causes **nocturnal waking**.

Diagnosis

- **Endoscopy, including biopsy for *H. pylori*, is the optimal method.**
- Barium swallow: this is less sensitive for diagnosing acute ulceration and better at detecting scarring.

Management

- Unless facilities to diagnose *H. pylori* are available, all children should be treated for eradication of presumed *H. pylori.*
- Give H_2 antagonists or a proton pump inhibitor for 6–8 weeks: ranitidine 2–4 mg/kg twice daily (maximum 150 mg twice daily); omeprazole 10 mg for 10–20 kg (can increase to 20 mg) and 20 mg for > 20 kg once daily (can increase to 40 mg).

5.12.F Gastrointestinal bleeding

BOX 5.12.F.1 Minimum standards
- Full blood count.
- Stool examination, microscopy and culture, parasite identification.
- Ultrasound.
- Barium X-ray studies.
- Gastroscopy.
- Colonoscopy.

Introduction

- The causes of bleeding from the gastrointestinal tract are many, and relate to the age of the child. A good history and clinical examination are essential and will indicate specific investigations.
- In haematemesis, it is important to exclude swallowed blood due to disorders of the nose and mouth.
- In children the commonest cause of fresh rectal bleeding is an anal fissure.
- Melaena has to be differentiated from dark stools associated with medication (e.g. iron preparations) and colouring from foods.
- A large bleed from the upper gastrointestinal tract may present as red blood at the anus because of rapid transit.

TABLE 5.12.F.1 Causes of gastrointestinal haemorrhage

Site of bleeding	Clinical features/further information
Upper gut	
Poisoning with or treatment with salicylates	'Coffee-ground' vomit
Mallory–Weiss syndrome	
Oesophagitis, gastro-oesophageal reflux	*See* Section 5.12.E
Portal hypertension, oesophageal varices	*See* Section 5.7.B (liver disease) *See* Section 6.3.C.c (schistosomiasis)
Midgut	
Intussusception, volvulus	Infants (*see* Section 3.4 and 5.19)
Meckel's diverticulum	Often symptomless
Colorectal	
Infection (e.g. shigellosis, amoebiasis)	*See* Section 5.12.A and Section 6.3.B
Inflammatory bowel disease	Abdominal pain, diarrhoea, weight loss *See* Section 5.12.D
Milk protein intolerance	*See* Section 5.12.G
Polyps (single, multiple, Peutz–Jeghers syndrome)	Blood separate from normal stool
Anus	
Fissure	Infants, constipation, tags (*see* Section 5.12.C)
Crohn's disease	*See* Section 5.12.D
Miscellaneous	
Necrotising enterocolitis (*see* Section 3.4), Henoch–Schönlein purpura (*see* Section 5.13), AIDS (*see* Section 6.2.D)	
Any coagulation or blood malignancy disorder (*see* Section 5.11.D and Section 5.14)	

Investigations

The investigations chosen will depend on the suspected site of bleeding and the clinical features.

See appropriate sections as indicated in the tables above.

It is important to consider the following:

- Stool:
  - Direct observation: blood, mucus.
  - Microscopy: *Cryptosporidium*, *Salmonella*, *E. coli*, *Shigella*, *Campylobacter*, ova, cysts and parasites.
  - Faecal occult blood.
- Full blood count, grouping and cross-matching.
- Serum ferritin and iron levels.
- Isotope scan: diagnosis of Meckel's diverticulum (30% false negative).
- Barium studies: diagnosis of malrotation.
- Ultrasound: diagnosis of intussusception.
- Upper endoscopy: diagnosis and treatment of oesophageal, gastric and/or duodenal bleeding.
- Colonoscopy: diagnosis and treatment of colitis and/or polyps.

TABLE 5.12.F.2 Features of gastrointestinal bleeding

History/examination	Looking for:
History	
Acute/chronic, amount of blood	Severity
Endemic area	Schistosomiasis
Haematemesis	Upper gastrointestinal disorder
Nose and mouth lesions	Swallowed blood
Site of any pain	Upper or lower gastrointestinal tract
Stool: Hard/loose Blood mixed in stool Blood around or separate	 Constipation/diarrhoea Inflammation/infection Anal fissure/polyp
Inflammatory bowel disease, family history	*See* Section 5.12.D
Bleeding tendency	Clotting disorder, malignancy
Examination	
Nose and mouth lesions	Swallowed blood
Pallor, capillary refill, blood pressure	Anaemia, shock
Petechiae, telangiectasia	Thrombocytopenia, hereditary telangiectasia
Abdomen	Tenderness, hepatosplenomegaly
Anus	Fissure, tags, infection

5.12.G Malabsorption, including coeliac disease

Malabsorption

Malabsorption is an abnormality in absorption of food nutrients from the gastrointestinal tract.

Common causes of malabsorption and resultant failure to thrive in resource-limited countries include recurrent respiratory infection, persistent diarrhoea and HIV infection. None of these require bowel investigation. The main emphasis is on nutritional rehabilitation which regenerates the small bowel atrophy and the immune system (see management of persistent diarrhoea and severe malnutrition in Sections 5.12.B and 5.10.B, respectively). Only a limited response to nutritional support is expected in HIV infection, depending generally on the stage of disease and the response to antiretroviral (ARV) drugs.

Types of malabsorption

- **Selective:** as seen in lactose intolerance.
- **Partial:** as observed in Crohn's disease and HIV infection.
- **Total:** as seen in coeliac disease.

Pathophysiology

The gastrointestinal tract functions to digest and absorb nutrients (fat, carbohydrate, protein and fibre), micronutrients (vitamins and trace minerals), water and electrolytes. This is dependent on the proper processing of food by mechanical (chewing and gastric churning) and enzymatic (gastric, pancreatic, biliary or intestinal) means. The final products of digestion are then absorbed through the intestinal epithelial cells.

Malabsorption constitutes the pathological breakdown of the normal physiological sequence of digestion (i.e. intraluminal process), absorption (i.e. mucosal process) and transport (post-mucosal events) of nutrients.

Clinical features

Symptoms can be intestinal or extra-intestinal, and include the following:

- diarrhoea/steatorrhoea: watery, diurnal and nocturnal, bulky, frequent stools
- bloating
- flatulence
- abdominal discomfort/cramping abdominal pain
- growth retardation
- weight loss
- failure to thrive
- delayed puberty
- swelling or oedema from loss of protein
- anaemia (vitamin B_{12}, folic acid and iron deficiency)
- fatigue
- weakness
- muscle cramp
- osteomalacia and osteoporosis
- bleeding tendencies.

Diagnosis

Investigation is guided by symptoms and signs. Since a range of different conditions can produce malabsorption, it is necessary to look for each of these specifically. Tests are also needed to detect the systemic effects of deficiency of the malabsorbed nutrients (e.g. anaemia with vitamin B_{12} malabsorption).

Investigations may include the following:

- full blood count and blood film
- C-reactive protein and erythrocyte sedimentation rate
- serum albumin
- serum iron, ferritin and total iron-binding capacity (TIBC)
- serum folic acid
- serum cholesterol or triglyceride
- serum calcium, phosphate and alkaline phosphatase
- prothrombin time and activated partial thromboplastin time
- blood chemistry (electrolytes, glucose, HCO_3^-, urea and creatinine)
- serum zinc levels
- stool studies, including cultures.

TABLE 5.12 G.1 Common causes of malabsorption

	Common causes of malabsorption
Due to infective agents	Intestinal tuberculosis
	HIV-related malabsorption
	Tropical sprue
	Traveller's diarrhoea
	Parasites, such as *Giardia lamblia*, fish tapeworm, roundworm, hookworm (*Ancylostoma duodenale* and *Necator americanus*)
Due to structural defects	Blind loops
	Inflammatory bowel diseases (e.g. Crohn's disease)
	Intestinal hurry from surgical procedures (e.g. post-gastrectomy, gastro-jejunostomy)
	Fistulae, diverticulae and strictures
	Short bowel syndrome
Due to mucosal abnormality	Coeliac disease
	Cow's milk intolerance
	Soya milk intolerance
Due to enzyme deficiencies	Lactose intolerance (constitutional, secondary or rarely congenital)
	Sucrose intolerance
Due to digestive failure	Pancreatic insufficiencies
	Cystic fibrosis
	Chronic pancreatitis
	Bile salt malabsorption
	Terminal ileal disease
	Obstructive jaundice
	Bacterial overgrowth
Due to systemic diseases	Coeliac disease
	Hypothyroidism and hyperthyroidism
	Addison's disease
	Diabetes mellitus
	Hyperparathyroidism and hypoparathyroidism
	Malnutrition

Serological studies

The following specific tests are carried out to determine the underlying cause:

- IgA anti-transglutaminase antibodies
- IgA anti-endomysial antibodies.

Radiological studies

- Barium meal and follow-through.
- Barium enema.
- CT of the abdomen.

Specialised tests (if available)

- Biopsy of small bowel.
- Colonoscopy can be helpful in colonic and ileal disease.
- Endoscopic retrograde cholangiopancreatography (ERCP) will show pancreatic and biliary structural abnormalities.
- Glucose hydrogen breath test for bacterial overgrowth.
- Lactose hydrogen breath test for lactose intolerance.
- Magnetic resonance cholangiopancreatography (MRCP).

Management

Treatment is directed largely towards management of the underlying cause. In severe nutritional deficiency, hospital admission may be required for total parenteral nutrition (TPN). Subsequently, advice and support from a dietitian is vital.

Coeliac disease

BOX 5.12.G.1 Minimum standards

- Gluten-free diet.
- Full blood count and film.

Coeliac disease is an autoimmune disorder of the small intestine in genetically predisposed people of all ages from middle infancy onwards. It is caused by a reaction to gliadin, a gluten protein found in wheat and similar cereals. Therefore it is common among populations whose diet contains substantial amounts of wheat. Apart from people of European origin, in whom it commonly manifests, it is also frequently seen in North Africa, the Middle East, and the north of the Indian subcontinent where wheat is a staple diet. Other populations at increased risk for coeliac disease include children with Down's syndrome and Turner syndrome, type 1 diabetes and autoimmune thyroid disease, including both hyperthyroidism and hypothyroidism.

Pathophysiology

Upon exposure to gliadin, the enzyme tissue transglutaminase (tTG) modifies the immune system to cross-react with the small-bowel villous lining, causing an inflammatory reaction. This leads to villous atrophy, which interferes with the absorption of nutrients, minerals and the fat-soluble vitamins A, D, E and K.

Coeliac disease appears to be polyfactorial. Almost all people with coeliac disease have either the HLA-DQ2 or the HLA-DQ8 allele. However, additional factors are needed for coeliac disease to manifest besides the HLA risk alleles. Furthermore, around 5% of those people who do develop coeliac disease may not have typical HLA-DQ2 or HLA-DQ8 alleles.

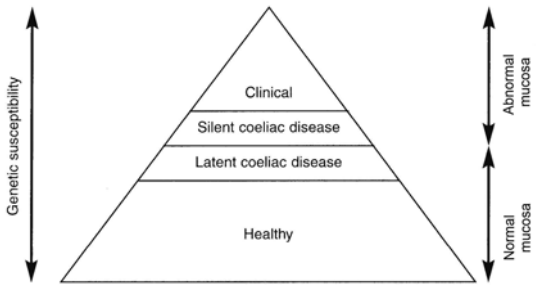

FIGURE 5.12.G.1 The spectrum of coeliac disease. Latent coeliac disease: positive anti-endomysial antibodies, normal small bowel, but risk of developing disease.

Clinical features

Clinical features may range from severe to almost non-existent. Severe coeliac disease in young children leads to the characteristic symptoms of pale, loose and greasy stools (steatorrhoea) with weight loss or failure to gain weight. Adolescents and older children with milder coeliac disease may have symptoms that are much more subtle and occur in other organs rather than in the bowel itself.

TABLE 5.12.G.2 Clinical features of coeliac disease

Under 2 years of age	Over 2 years of age
Steatorrhoea	Short stature
Vomiting	Delayed puberty
Abdominal distension	Iron-resistant anaemia
Irritability	Rickets/osteomalacia
Anorexia	Behaviour problems
Growth failure	*With or without the gut disorders that occur in younger children*

Diagnosis

The diagnosis of coeliac disease is based on two types of testing.

Serological blood tests

These are the first-line investigation and include the following:

- **IgA anti-tissue transglutaminase (tTG) antibodies:** this test is reported to have a high sensitivity (99%) and specificity (over 90%) for identifying coeliac disease. Therefore it should be done first. It is also an easier test to perform. An equivocal result on tTG testing should be followed by antibodies to endomysium.
- **IgA anti-endomysial antibodies:** this test has a sensitivity and specificity of 90% and 99%, respectively, for detecting coeliac disease.

It is important that the total serum IgA level is also checked, as coeliac patients with IgA deficiency may be unable to produce the antibodies on which these tests depend ('false-negative'). In such patients, IgG antibodies against transglutaminase (IgG-tTG) or IgG anti-gliadin antibodies (IgG-AGA) may be helpful in reaching a diagnosis.

Dudeno-jejunal biopsies

Because of the implications of a diagnosis of coeliac disease, guidelines recommend that a positive serological blood test may still be followed by a dudeno-jejunal biopsy. Similarly, a negative serology may still be followed by a recommendation for a biopsy if clinical suspicion remains high. Tissue biopsy is still considered the gold standard in the diagnosis of coeliac disease.

For this purpose, biopsies can be obtained using metal capsules attached to a suction device. The capsule is swallowed and allowed to pass into the small intestine. After X-ray verification of its position, suction is applied to collect part of the intestinal wall inside the capsule. Commonly used capsule systems are the Watson capsule and the Crosby–Kugler capsule. This method has now been largely replaced by fibre-optic endoscopy, which carries a higher sensitivity and a lower frequency of errors.

TABLE 5.12.G.3 Investigations for malabsorption

General	Specific
Full blood count plus film	Immunoglobulins IgA and IgG
Serum iron and ferritin	IgA tTG antibodies
Folate (red blood cell)	IgA anti-endomysial antibodies
Vitamin B_{12} levels	IgA anti-gliadin (AGA)
Serum albumin	Small bowel biopsy: • Villous atrophy • Hyperplasia of crypts • Increased inflammatory cells
Hydrogen breath test	
Serum calcium, phosphate and alkaline phosphatase	
Serum T_4 and TSH	

There are several ways in which these tests can be used to assist in diagnosing coeliac disease. However, all tests become invalid if the patient is already taking a gluten-free diet. Intestinal damage begins to heal within weeks of gluten being removed from the diet, and antibody levels decline over a period of months. In such cases it may be necessary to perform a re-challenge with gluten-containing food over 2–6 weeks before repeating the investigations.

A histology compatible with coeliac disease on a gluten-containing diet, followed by a clinical improvement (i.e. gain in weight and height and resolution of symptoms) once the gluten is removed from the diet is often enough to establish the diagnosis. Most guidelines do not recommend a repeat biopsy unless there is no improvement in the symptoms on the gluten-free diet. In some cases a deliberate gluten challenge, followed by biopsy, may be conducted to confirm or refute the diagnosis. A normal biopsy and normal serology after the challenge indicates that the diagnosis may have been incorrect.

In resource-limited countries where facilities for biopsies may not exist, the same model can be used with serological tests. A positive serological test on a gluten-containing diet will revert to normal with clinical improvement once the patient is on a gluten-free diet.

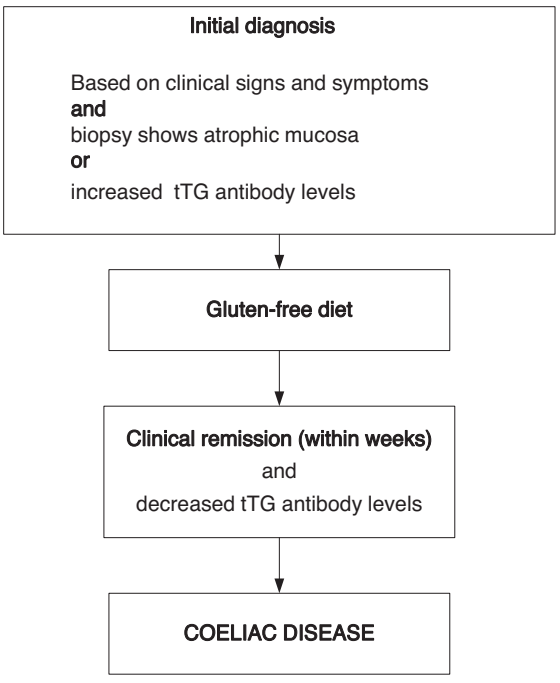

FIGURE 5.12.G.2 Diagnosis of coeliac disease.

BOX 5.12.G.2 Gluten challenge

Do a gluten challenge if:

- the diagnosis is in doubt
- there is a possibility of another diagnosis, especially in children under 2 years of age (e.g. milk protein intolerance, persistent diarrhoea, giardiasis)
- the response to a gluten-free diet is not clear-cut
- the subject is asymptomatic (e.g. first-degree relatives).

Note: Gluten challenge should preferably be undertaken when the child is over 6 years old and before puberty, to reduce the effects on dentition and growth.

Treatment

At present, the only effective treatment is a lifelong gluten-free diet. Strict compliance allows the intestines to heal, with resolution of symptoms in most cases. Early intervention and good compliance can eliminate the heightened risk of intestinal cancer and in some cases sterility.

Dietitian input can be helpful in ensuring that the patient is aware of which foods contain gluten, which foods are safe, and how to have a balanced diet despite the limitations. The diet can be cumbersome, and failure to comply may cause relapse.

The commonly implicated cereals include wheat (and its subspecies, such as spelt, semolina and durum), barley, rye and oats.

Other cereals, such as maize (corn), millet, sorghum, teff and rice, are safe for patients to consume. Similarly, non-cereal foods such as fruits, vegetables and foods derived from animal sources (i.e. milk, fish, poultry and other meat) can be used.

Further reading

Steele R (2011) Diagnosis and management of coeliac disease in children. *Postgraduate Medical Journal*, **87**, 19–25.

European Society for Pediatric Gastroenterology, Hepatology, and Nutrition Guidelines for the Diagnosis of Coeliac Disease: http://espghan.med.up.pt/position_papers/Guidelines_on_coeliac_disease.pdf

5.13 Rheumatology

BOX 5.13.1 Minimum standards

- Penicillin.
- Aspirin.
- Prednisolone.
- Haloperidol, diazepam and lorazepam.
- Anti-endocarditis measures.
- IV gamma globulin if at all possible.
- Non-steroidal anti-inflammatory drugs (NSAIDs).
- Sulphasalazine.
- Ocular steroids and mydriatics.
- Intra-articular steroids.
- Physiotherapy and family support.

Introduction

Making a diagnosis of a rheumatic disease in a child relies primarily on clinical skill and experience, as there are few diagnostic laboratory tests. Although these diseases are rare in children, symptoms that raise the possibility of rheumatic disease are common. Rheumatic symptoms may be relatively specific, such as joint swelling, or relatively non-specific, such as fever, lethargy, pallor, anorexia, failure to thrive, muscle weakness, musculoskeletal pain, rash, headache and abdominal pain. The interpretation of these clinical features requires a meticulous approach to characterising the nature of each feature and considering the overall pattern of all the clinical features in the individual patient. The aims of this section are to assist in the recognition of common patterns of clinical features, and to provide guidance for appropriate treatment and monitoring of rheumatic disease in children.

pGALS (paediatric Gait, Arms, Legs and Spine) is a simple quick approach to joint examination and helps to discern abnormal from normal joints; this is especially useful in the context of non-specific features such as limp or fever. pGALS includes incorporates a series of simple manoeuvres to assess all joints quickly (takes approximately 2–3 minutes). It has been validated in school-aged children (although can be performed in younger children) and has been shown to be effective when performed by non-specialists in detecting significant joint abnormalities in acute paediatric practice (including in Africa). The interpretation of pGALS requires knowledge of normal musculoskeletal development and the clinical context to facilitate a differential diagnosis (www.arthritisresearchuk.org/health-professionals-and-students/video-resources/pgals.aspx).

Rheumatic fever

Rheumatic fever is an abnormal immune response to group A streptococcal infection in genetically susceptible individuals. It is most common between the ages of 6 and 16 years. Symptoms of acute rheumatic fever follow streptococcal pharyngitis after a latent period of approximately 3 weeks. The disease usually presents with joint pain, but may have an insidious onset, especially if carditis is the predominant feature. There is no definitive test, and diagnosis depends on recognition of clinical signs known as the Jones criteria.

TABLE 5.13.A.1 Jones criteria for diagnosis of rheumatic fever

Major criteria	Minor criteria
Carditis	Previous history of rheumatic fever
Migratory large-joint polyarthritis	Fever
Erythema marginatum	Arthralgia
Subcutaneous nodules	First-degree heart block
Chorea (onset 2–6 months after pharyngitis)	Elevated acute-phase reactants (ESR and CRP)

ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

Diagnosis: Jones criteria

The diagnosis in an individual is made by the **Jones criteria** (revised by the WHO in 2003) on the basis of the presence of either **two major criteria** (which include polyarthritis, erythema marginatum rash, subcutaneous nodules, carditis and chorea) or **one major criterion and two minor criteria** (minor criteria include persistent fever, arthralgia, raised ESR or CRP, persistent leukocytosis, abnormal ECG except if carditis is the major feature, and previous episode of rheumatic fever). Each combination must also include evidence of streptococcal infection, usually a rising titre of antistreptolysin O.

- Evidence of **streptococcal infection** (usually a pharyngitis secondary to group A beta-haemolytic streptococcus) with positive throat swab culture or, preferably, a positive serology for recent streptococcal infection. This is usually accompanied by a prolonged fever and followed by other clinical features after a 2- to 3-week period.
- **Arthritis** of the large joints. This is a reactive arthritis (rather than a septic arthritis), often affecting many joints, and it is migratory in nature. It usually responds dramatically to aspirin, up to 120 mg/kg/day in four to six divided doses by mouth after food, but do not exceed 75–80 mg/kg/day if facilities for assay of salicylate levels are not available. Alternatively, use non-steroidal anti-inflammatory drugs (NSAIDs; see below). The presence of joint pain without swelling (i.e. arthralgia alone) may still indicate rheumatic fever in the presence of the other clinical features compatible with a diagnosis of acute rheumatic fever.
- **Rash and subcutaneous nodules:** erythema marginatum is an uncommon feature. It has a 'snake-like' appearance, usually over the trunk, and occurs early in the disease, is usually transient, and disappears within a few hours. Subcutaneous nodules are not uncommon, occurring over bony prominences such as the elbows and knees.
- **Carditis:** this may range from a tachycardia with a prolonged PR interval seen on the ECG through to myocarditis with a systolic apical mitral murmur, pericarditis or cardiac failure. Cardiac inflammation may involve the endocardium (valvulitis mostly affecting the mitral and aortic valve), the myocardium (impaired cardiac function) or the pericardium in severe cases (pericarditis). Examination may reveal a pericardial friction rub, an apical pansystolic murmur from mitral regurgitation, or an early diastolic decrescendo murmur from aortic regurgitation. As the valves heal they may scar and fibrose. **Mitral regurgitation, mitral stenosis** and **aortic regurgitation** are the commonest long-term consequences of acute rheumatic fever.
- **Chorea** is an involuntary movement disorder, often of the face, tongue and upper limbs. It may appear as dysarthria or clumsiness, and is associated with emotional lability. It is a late manifestation of acute rheumatic fever, and is more common in girls.

The disease may be prevented by detecting group A streptococcus in cases of pharyngitis (throat swab or rapid antigen test) and treating with penicillin (see below).

Treatment

Management of acute rheumatic fever

- Eradicate streptococcal infection (give oral penicillin V 10–12.5 mg/kg/dose (maximum dose 500 mg) three times a day for 10 days).
- Commence aspirin 90–120 mg/kg a day in four divided doses after food. Monitor serum salicylate levels (the optimal level is 15–25 mg/dL). Reduce the dose to two-thirds of the original dose when there is a clinical response.
- When the CRP and ESR decrease to normal levels, taper the aspirin dose over 2 weeks.
- Give prednisolone 2 mg/kg/day (maximum 60 mg/day) in place of aspirin if there is moderate to severe carditis or pericarditis.
- If prednisolone is given, continue treatment for 3 weeks, and then taper the dose over a further 2–3 weeks. As the prednisolone dose starts to taper, commence aspirin 50 mg/kg/day in four divided doses and stop aspirin 1 week after prednisolone is stopped.
- Treat heart failure as described in Section 5.4.B.
- Urgent valve replacement is sometimes required.

The requirement for bed rest during the acute attack is controversial; it is also very difficult to enforce on young children.

For arthralgia, give aspirin as described above or an NSAID (e.g. ibuprofen 30–60 mg/kg daily up to a maximum of 2.4 G in three to four divided doses after food). Naproxen at 20 mg/kg/day in two divided doses appears be a better alternative.

Treatment of streptococcal infection with IM benzylpenicillin (1.2 million units as a single injection, often given as 0.6 million units in each thigh) or a 10-day course of oral penicillin at high dose (12.5 mg/kg four times a day). Once there has been one episode of rheumatic fever a recurrence is likely. The recurrence risk is minimised by giving long-term penicillin prophylaxis, preferably for life. This is usually given as intramuscular injections of 1.2 million units of benzathine penicillin every 3 weeks (this drug must not be given IV). If oral penicillin is required, the highest dose generally recommended is 250 mg twice daily for all ages, as doses of oral penicillin in children below the age of 5 years need not be given because rheumatic fever does not occur in this age group. For patients who are allergic to penicillin, erythromycin in the same doses can be used.

For acute carditis, prednisolone given orally (2 mg/kg/day) for 2–3 weeks or by intravenous infusion is effective.

Chorea may respond to haloperidol, 12.5–25 micrograms/kg twice daily (maximum 10 mg a day). Extrapyramidal side effects may occur. Chorea usually becomes less of a problem within a few weeks.

Vasculitis in children

Vasculitis in childhood may be primary, including Henoch–Schönlein purpura, Kawasaki disease and the rare vasculitides, or secondary to multisystem connective tissue diseases, including juvenile dermatomyositis and systemic lupus erythematosus (SLE). In all of these diseases, skin manifestations are usually prominent, but the combination with other clinical features helps to ascertain the diagnosis.

Henoch–Schönlein purpura (HSP)

Presentation

- **Purpuric rash:** a palpable purpuric rash is most commonly seen over the buttocks and around the ankles and legs. The purpura occurs in crops and may range from small petechiae-like lesions to large ulcerating ecchymoses. Oedema and urticaria may precede the purpura, particularly at the ankles, scrotum and face.
- **Gastrointestinal pain:** abdominal pain is a prominent feature early in the disease, and is often accompanied by vomiting. Occasionally, frank gastrointestinal haemorrhage may occur.
- **Arthritis:** this typically affects the large joints of the lower limb, especially the ankles. Ankle swelling may be difficult to interpret in the presence of tissue oedema. The joint pain is usually transient. Arthritis in HSP is never erosive.
- **Renal disease:** haematuria and proteinuria are common manifestations of the disease, but are usually only detected on dipstick urine analysis. A small proportion of children (1–3%) may develop renal failure secondary to severe glomerulonephritis. Clinically significant renal disease is uncommon below 5 years of age.

Treatment

Henoch–Schönlein purpura is usually a self-limiting disease, requiring supportive care and symptomatic treatment with simple analgesia only. If the abdominal pain is severe, prednisolone (1–2 mg/kg/day) for 1 week may be helpful.

Kawasaki disease

Kawasaki disease is characterised by a combination of most of the following features in a young child (usually less than 5 years old) who is extremely irritable.

- **Fever:** an irregular spiking fever that persists for 1–3 weeks despite antibiotics is characteristic during onset.
- **Skin involvement:** rash is variable and polymorphic, ranging from diffuse erythema of the trunk and face to minimal macular lesions on the limbs. The rash in Kawasaki disease is never vesicular. Tissue oedema of the dorsal surfaces of the hands, feet and perineum is characteristic. These changes are followed within days to weeks by desquamation, usually of the finger and toe tips (periungual desquamation), but occasionally more widespread.
- **Mucositis and conjunctivitis:** inflammation of the mucous membranes of the mouth and eyes results in a characteristic appearance of red eyes (conjunctival 'injection' rather than conjunctivitis) and red swollen cracked lips.
- **Lymphadenopathy:** this usually affects the cervical lymph nodes, often unilaterally.
- **Cardiac disease:** myocarditis with heart failure or pericarditis is a rare but serious complication of Kawasaki disease. Coronary artery aneurysms may be present from early in the disease process. Clinical manifestations are relatively non-specific, but the two-dimensional echocardiography appearances are diagnostic of the condition. However, echocardiography may be completely normal in Kawasaki disease.
- It is important to exclude infections (e.g. measles, adenovirus or streptococci), as they may present in a similar manner, despite having distinct clinical characteristics.

Kawasaki disease is a rheumatological emergency. Delays in recognition and treatment of this condition can result in the development of coronary artery abnormalities with disastrous long-term consequences, including fatalities.

Treatment

- Hospitalisation and monitoring of cardiac status.
- Aspirin, 50–75 mg/kg/day in 4 divided doses after food until the acute inflammatory phase of the disease settles, then 1–10 mg/kg/day (usually 3–5 mg/kg/day) (antiplatelet doses).
- Intravenous gamma globulin 2 grams/kg immediately on diagnosis, if available. **Every effort must be made to procure intravenous gamma globulin for the treatment of these children, as this is the only effective therapy for Kawasaki disease.** This treatment reduces the likelihood of coronary artery aneurysms if given as early as possible during the illness (several inexpensive brands of intravenous gamma globulin are now available in resource-limited countries).
- Corticosteroids (e.g. prednisolone 1–2 mg/kg/day) may have a role in controlling the acute inflammation of Kawasaki disease, but are generally not recommended.
- Follow-up clinical examination and echocardiography (if available) is recommended at 6–8 weeks, as coronary artery aneurysms may appear after the initial presentation.

Juvenile idiopathic arthritis

Juvenile idiopathic arthritis is one of the more common physically disabling chronic diseases of children. The most prominent clinical features include joint swelling, restriction of joint movement, joint pain and tenderness at the joint margins, muscle wasting and any of the features mentioned below. The most common mistake is to diagnose arthritis in the absence of objective evidence of persistent joint swelling.

Diagnosis of juvenile idiopathic arthritis

All of the following four criteria are required:

1. The presence of arthritis, defined by swelling of a peripheral joint. Loss of joint range of movement and pain on movement are sufficient for the definition of arthritis involving the hip or spine (in the absence of other causes for the pain).
2. Persistence of arthritis for more than 6 weeks.
3. Onset of arthritis before the child's 16th birthday.
4. The absence of any known cause for the arthritis.

Classification and differential diagnosis

There are a variety of different forms of juvenile idiopathic arthritis that are important to consider when advising on the prognosis and most appropriate treatment of the illness.

- **Arthritis affecting only a few joints:** oligo-arthritis

carries the best prognosis; 30% of these children may have arthritis in adulthood.
- **Arthritis affecting many joints:** polyarthritis is likely to persist into adulthood in 40% of cases.
- **Arthritis affecting few or many joints with prominent extra-articular features:**
  - **Systemic arthritis:** with fever, rash, and enlargement of the liver, spleen and lymph nodes, Pericarditis and macrophage activation syndrome are life-threatening complications. Macrophage activation syndrome presents with persistent fever, encephalopathy, liver failure and clotting abnormalities and low platelet counts. The persistence of arthritis with this illness carries the worst prognosis: over 50% of these children have arthritis as adults.
  - **Psoriatic arthritis:** often associated with a psoriatic rash, nail pitting and a family history of psoriasis. This has a similar outcome to polyarthritis.
  - **Enthesitis-related arthritis:** the clinical manifestations of enthesitis include pain, tenderness and occasionally swelling localised to the exact site of tendon insertion. Other features include back pain, red painful eyes and urethritis. There is a 60% risk of development of ankylosing spondylitis in adulthood.

Monitoring for complications and disease progress in juvenile idiopathic arthritis

There are several important complications of juvenile idiopathic arthritis, including joint failure, chronic anterior uveitis and local growth disorders, as well as the general complications of chronic inflammatory disease in children, such as anaemia, fatigue, delayed puberty and growth failure. Three of these complications, namely joint failure, chronic anterior uveitis and growth disorders, will be discussed in more detail.

Joint failure

- Inability to walk without pain and stiffness.
- Inability to write or perform activities of self-care without pain and stiffness.
- The integrity of joint cartilage and bone density is affected from the onset of the disease.
- If the inflammation remains poorly controlled, destruction of cartilage, joint space narrowing and erosion of bone will result in permanent loss of joint function.

Differential diagnosis of juvenile idiopathic arthritis

- Transient arthritides: irritable hip, reactive arthritis.
- **Septic arthritis** and **osteomyelitis**, including immunodeficiency.
- **Acute lymphoblastic leukaemia, neuroblastoma, lymphoma** and **local neoplasia.**
- Bleeding diatheses: haemophilia.
- Haemoglobinopathies: thalassaemia, sickle-cell crisis.
- Epiphyseal disorders: dysplasia, avascular necrosis, osteonecrosis, slipped upper femoral epiphysis.
- Metabolic and endocrine disorders.
- **Traumatic joint disease, including non-accidental injury**.
- Hypermobility and inherited connective tissue diseases.
- Systemic connective tissue diseases, including systemic lupus erythematosus, dermatomyositis and vasculitis.
- Idiopathic musculoskeletal pain syndromes.

TABLE 5.13.A.2 Important sites of joint contracture

Joint affected	Type of contracture	Consequence of contracture
Tibio-talar gait	Plantar flexion	Circumduction or high-deformity stepping
Knee	Flexion	Quadriceps wasting, limping gait
Hip	Flexion	Limited 'swing-phase' gait
Wrist	Flexion	Poor writing
Neck	Flexion	Poor neck rotation

- Arthritis of inflammatory bowel disease.

Note: diseases shown in bold type in the above list are emergencies, and require prompt expert management.

Initial minimal set of investigations for differential diagnosis

- Full blood count, including white blood cell differential and platelet counts.
- Plain radiographs of affected joints.
- Synovial fluid aspiration, microscopy and culture.
- Blood culture.

Eye disease

- Chronic anterior uveitis is typically insidious and asymptomatic: all children with juvenile idiopathic arthritis (but especially those with oligo-arthritis) should undergo slit-lamp eye examination to detect cells in the anterior chamber and protein 'flare'. **Delay in the diagnosis can lead to blindness.**
- Inflammation is treated with ocular topical corticosteroids (hydrocortisone 1% eye drops or ointment 0.5%) three times daily and mydriatics (3 minutes after hydrocortisone) (atropine 0.5% eye drops or 1% ointment).
- Severe chronic anterior uveitis may require systemic treatment with corticosteroids or methotrexate.

Growth disorders

- Generalised growth failure may be due to inadequate energy intake (chronic inflammatory disease increases energy demands) or the adverse effects of medication. It is usually treated with dietary energy supplements.
- Local growth disturbance: bony overgrowth of the knee with an increase in leg length, sometimes with a valgus knee deformity. Arthritis of the small joints of the hands is likely to cause premature fusion of the epiphyses and reduced growth of the affected fingers.

Treatment of juvenile idiopathic arthritis

- The first priority is to exclude the differential diagnoses, especially the emergencies of septic arthritis, acute lymphoblastic leukaemia or other malignancies, and non-accidental injury. Septic arthritis will require large doses of intravenous antibiotics (*see* Section 5.17).
- The effective treatment of juvenile idiopathic arthritis usually requires a team of trained healthcare professionals, including therapists and medical staff.
- Education of the patient and family is important, especially concerning the risks and benefits of all treatment and the natural history of the disease.
- Physiotherapy, hydrotherapy and occupational therapy

work together to maintain joint function and muscle bulk, correct joint deformities and rehabilitate affected joints.
- Drug treatment should begin as soon as the diagnosis is made, with the following:
  - **Non-steroidal anti-inflammatory drugs (NSAIDs):** Give ibuprofen up to 60 mg/kg/day up to a maximum of 2.4 g in three or four divided doses after food. Naproxen at 20 mg/kg/day in two divided doses is possibly a better alternative. Avoid using more than one NSAID at a time.
  - Intra-articular corticosteroids: Strict aseptic conditions, no-touch technique, appropriate sedation, and local or general anaesthetic must be given. Triamcinolone hexacetonide is the most effective steroid, at a dose of 1 mg/kg/large joint (e.g. knee, hip or shoulder) or 0.5 mg/kg/small joint (e.g. ankle, wrist or elbow). This technique requires an experienced operator.

For children with polyarthritis or systemic arthritis, in addition to the above, the following should be considered:
- **Methotrexate:** Begin with 500 micrograms/kg/week (up to 15 mg/week) starting dose, given orally 1 hour before food, and increased if necessary by 2.5 mg every month until 1.0 mg/kg/week (maximum 30 mg/week). Alternative dosage is 10–15 mg/m^2 once weekly starting dose and increased if necessary to a maximum dose of 25 mg/m^2 once weekly (*see* Section 9 for chart showing how to calculate m^2 from weight). The drug may be given by subcutaneous injection in severe cases. The patient should be monitored monthly for cytopenia (with full blood counts) and liver function abnormalities. Administration is sometimes accompanied by nausea, a side effect that can be improved with folic acid 1 mg once daily (not on the day of methotrexate treatment, but beginning the day after the methotrexate dose).
- **Intravenous methylprednisolone:** This may be needed for severe disease flares or for complications such as pericarditis. Give 30 mg/kg/dose (maximum dose of 1 gram) once a day for 3 days by slow intravenous infusion over a 2- to 3-hour period. Blood pressure monitoring for acute hypertension during the administration of this medication should take place every 30 minutes.
- **Sulphasalazine:** Begin with 12.5 mg/kg/day for the first week, increasing by 12.5 mg/kg/day each week until the maximum dose of 50 mg/kg/day in two divided doses is reached, or until adverse drug reactions occur. These may include a rash, nausea, abdominal pain and pancytopenia. Monitoring with 2- to 3-monthly full blood counts is a sensible precaution.
- More recently, a new group of drugs have been developed which appear to slow the progress of disease in some patients. They work by opposing tumour necrosis factor alpha, which contributes to cell damage, and are immunosuppressants. They include etanercept and infliximab. These drugs are currently very expensive.

Paediatric systemic lupus erythematous (SLE)

Pattern of clinical features in SLE

There is a malar rash and erythema of the hard palate with hair loss in a child with multiple constitutional symptoms.

Childhood SLE tends to be more severe than its adult counterpart, with a higher frequency of renal, neurological and haematological involvement. The clinical features are varied and wide-ranging (it has surpassed syphilis as the great imitator of signs and symptoms), but the more common presentations include the following:
- **Non-specific constitutional symptoms:** fever, fatigue and weight loss.
- **Skin rash:** malar erythema or discoid rash with photosensitivity. Erythema of the hard palate is common and specific. Occasionally oral or nasal ulcerations occur.
- **Haematological cytopenias:** anaemia, thrombocytopenia, lymphopenia and leukopenia.
- **Arthritis:** painful non-erosive arthralgias and overt arthritis.
- **Renal disease:** commonly nephrotic syndrome (proteinuria > 0.5 grams/day) with cellular casts. This is occasionally the sole presentation in paediatric SLE.
- **Neurological disease:** ranging from seizures to psychosis to chorea.
- **Endocrine abnormalities:** diabetes, autoimmune thyroid dysfunction, delayed menarche, lowered male virility, and reduced growth and bone mass.
- **Positive immunoserology (where available):** antinuclear antibody, anti-double-stranded DNA antibodies, antiphospholipid, anticardiolipin and lupus anti-coagulant antibodies.

Treatments

- The first step is to rule out other conditions which can mimic SLE, such as infection, malignancy, post-streptococcal nephritis, other rheumatic diseases and drug-induced lupus-like syndromes.
- For mild musculoskeletal disease, NSAIDs (e.g. ibuprofen 20–40 mg/kg/day in three daily doses) are effective.
- For rapid control of acute moderate-to-severe disease, glucocorticoids (e.g. prednisone up to 2 mg/kg per day) are useful, tapering rapidly to the lowest tolerated dose.
- Hydroxychloroquine (5–7 mg/kg/day) is now a standard adjunctive therapy for limiting joint, skin and constitutional symptoms.
- Immunosuppressive agents (e.g. azathioprine, cyclophosphamide, mycophenolate mofetil) are useful additions in moderate to severe disease.
- Other general health measures that need to be considered include the following:
  - Bone health: weight-bearing exercises with calcium and vitamin D supplementation.
  - Cardiovascular health: education on modifiable risk factors for atherosclerosis, together with advice on reducing weight, smoking and cholesterol.
  - Health education (regarding vaccination, sun protection, dietary advice, exercise and reproductive health) and psychological support.
- Routine 2- to 3-month follow-up is necessary to monitor for complications. This should involve full blood count, renal and liver profiles, ESR, urinalysis, and urine:protein creatinine ratio, together with complement and anti-dsDNA antibody levels.

Juvenile dermatomyositis (JDM)

Pattern of clinical features in JDM

There is erythema over the face, shawl area, knuckles

and knees, associated with proximal muscle weakness (which may be subtle).

Juvenile dermatomyositis is the most common inflammatory myopathy of childhood, and the diagnosis is based on the following criteria:

- **Muscle weakness:** a symmetrical, usually progressive weakness affecting proximal muscles.
- **Skin rash:** erythematous rashes occurring over the face or extremities, heliotrope rash over the eyelids, and Gottron's papules over extensor joint surfaces. More severe complications include skin ulceration and calcinosis at pressure points, causing functional disabilities. Capillary loop abnormalities seen proximal to the cuticles with an auroscope are a very characteristic sign if present.
- **Laboratory evidence of muscle disease:** this can include increased activity of muscle enzymes in the blood (creatine kinase, lactate dehydrogenase, transaminases), or results from more invasive tests, such as muscle biopsy or electromyography (if available).

Treatment

- High-dose corticosteroids are the standard treatment, namely early IV methylprednisolone 30 mg/kg per day (maximum 1 gram daily) with or without low-dose daily oral corticosteroid (500 micrograms/kg per day).
- It can be useful to add methotrexate (15 mg/m^2/week orally or subcutaneously) as a steroid-sparing agent and intravenous immunoglobulin in resistant cases (where available).
- Skin disease may also be helped by routine photoprotective agents and topical corticosteroids or tacrolimus.
- Physiotherapy and aerobic exercise are helpful for improving function and strength.

TABLE 5.13.A.3 Differential diagnosis of childhood idiopathic inflammatory myopathies

Weakness alone	Weakness with or without rash	Rash alone
Muscular dystrophies (e.g. Duchenne's, limb-girdle)	Viruses (enterovirus, influenza, coxsackie, echovirus, polio)	Psoriasis
Metabolic myopathies (e.g. glycogen- or lipid-storage disorders)	Bacterial (*Staphylococcus*, *Streptococcus*, Lyme disease)	Eczema
Endocrine myopathies (hypothyroidism, hyperthyroidism, Cushing's syndrome, diabetes mellitus)	Parasitic (toxoplasmosis, trichinosis)	Allergy
Drug-induced myopathies (e.g. glucocorticoids, hydroxychloroquine, growth hormone)	Other rheumatic conditions (SLE, mixed connective tissue disease, scleroderma, juvenile idiopathic arthritis, vasculitis)	
Neurological (myasthenia gravis, spinal muscular atrophy)	Other inflammatory conditions (coeliac disease, inflammatory bowel disease)	

5.14 Cancer in children

BOX 5.14.1 Minimum standards

- Local enthusiastic clinical lead.
- Supporting team of doctors and nurses.
- Basic diagnostic pathology and imaging (X-ray and ultrasound).
- Centre with provision for some chemotherapy and surgery.
- Access to antibiotics.
- Access to blood products.
- Access to palliative care drugs (*see* Section 1.16).

Ideal extra requirements

- Imaging with computed tomography (CT) scan.
- Access to radiotherapy.
- Indwelling long-term vascular access.

Introduction

- **More than 85% of all newly diagnosed children with cancer and 95% of deaths in children with cancer occur in low- and middle-income countries.**
- With an increasing global population, principally in resource-limited countries, the number of children will continue to increase both in terms of absolute numbers and proportionally in these countries.
- As malnutrition and infection decline, particularly in young children, the worldwide contribution to mortality from cancer will increase.
- **Only a limited proportion of all children with cancer in resource-limited countries receive curative therapy, and most do not even receive any form of palliative care.**
- **A child diagnosed with cancer who lives in one of the poorest countries has an 80% probability of dying, compared with less than 30% in the most well-resourced countries (*see* Figure 5.14.1).**

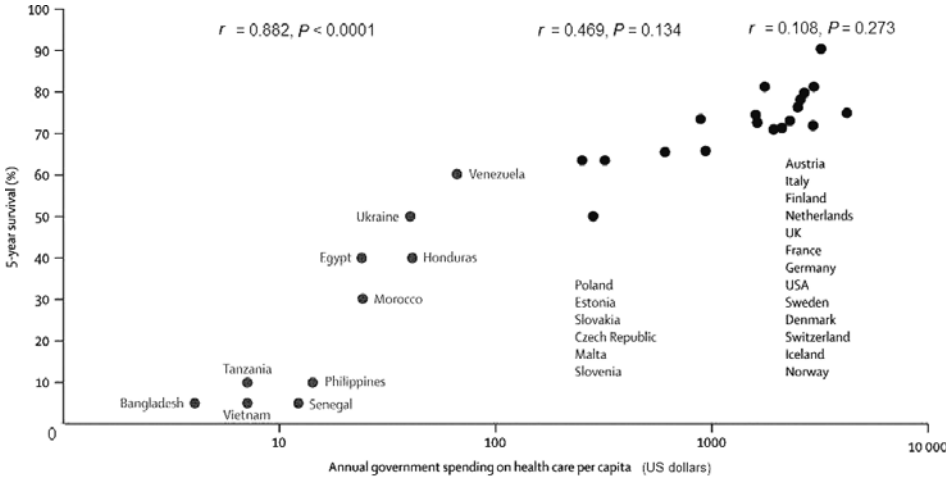

FIGURE 5.14.1 Correlation between annual government healthcare expenditure (US$) per capita and childhood cancer survival (From Ribeiro RC, Steliarova-Foucher E, Magrath I *et al.* (2008) Baseline status of paediatric oncology care in ten low-income or mid-income countries receiving My Child Matters support: a descriptive study. *Lancet Oncology.* **9**: 721–9.). Reproduced with permission from Macdonald S, Magill-Cuerden J (ed.) *Mayes' Midwifery: a textbook for midwives.* Elsevier Health Sciences; 2010. © Elsevier

Epidemiology

Globally, the reported incidence rate of cancer in children (aged < 15 years) ranges from 80 to 150 per million per year. Boys are around 20% more likely to develop cancer overall than girls. However, there are some differences between resource-limited and resource-rich countries. **The incidence rates in children from low- and middle-income countries are towards the lower end of the range, which may partly be due to both under-diagnosis and under-reporting. The ratio of boys to girls registered with childhood cancer increases with decreasing gross domestic product and with increasing infant mortality, suggesting a gender bias in diagnosing and registering cases in some resource-limited countries.**

There are clear variations in the incidence of different childhood cancers around the world – for example, a reported excess of retinoblastoma in India, Pakistan and sub-Saharan Africa. It is likely that some of this 'excess' is due to better diagnosis and recognition of retinoblastoma, which once at an advanced stage is easy to identify. On the other hand, the incidence of brain tumours and neuroblastoma is generally lower in resource-limited settings, and this may be due to varying levels of case ascertainment. In many countries, most noticeably those in sub-Saharan Africa, the HIV pandemic has been associated with a significant increase in cancers such as Kaposi's sarcoma and other tumours.

The cause of the majority of childhood cancers is unknown. Most cancers probably result from the interaction of environmental factors with a genetic predisposition. For example, African Burkitt lymphoma is related to infection with the Epstein–Barr virus (EBV) very early in life, with persistence of induced genetic rearrangements within B lymphocytes. However, the widespread use of medicinal plants which may increase the likelihood of cell transformation by EBV, chronic malnutrition that induces immunosuppression, and frequent infections that cause B-cell proliferation are all likely aetiological factors.

Problems of treating children with cancer in resource-limited countries

The problems listed below are not exclusive to resource-limited countries, and not mutually exclusive (i.e. many factors interact, compounding the difficulties in treating cancer).

- **Poverty:** national, regional, local and personal. This is often associated with low government expenditure on healthcare, absence of social care, and lack of insurance for medical illnesses.
- **Lack of suitable treatment centres and training programmes.** Existing centres lack trained staff and resources.
- **Lack of trained staff**, especially nurses, but also lack of surgeons, pathologists and paediatricians (especially paediatric oncologists).
- **Healthcare professional resources**
  Staff morale problems (*see* Section 1.1)
  Low morale may be due to low wages, overwork and dirty crowded conditions, compounded by too many patients and by becoming accustomed to low patient survival rates. Solutions may include better training and remuneration, better working and living conditions, and making staff feel valued.

  It is important that all healthcare professionals recognise that nursing care is fundamental. Nurse bonus schemes for work effectively performed can be helpful (e.g. IV antibiotics and chemotherapy correctly administered for all patients).

  Nurses often rotate every few months between departments. Try to ensure that, for paediatric oncology, a cohort of nurses remains permanently on the ward, as much of the work is very specialised (e.g. chemotherapy administration).

Paediatric oncologists

An effective service needs good leadership in a major centre. This can develop the service through training and the development of fellowship programmes. There can be support from overseas experts, perhaps with

'twinning' of hospitals from a well-resourced country to share decision making on complex cases and to supply visiting experts. Much useful work can be done in oncology with email and web conferencing to facilitate knowledge sharing in both directions. As there is an increase in the number of trained and training staff, round-the-clock expertise in paediatric oncology can be achieved with the development of on-call rotas.

- **Late presentation**
  - Patients' families are often very poor.
  - They may present to traditional healers first, leading to a delay in diagnosis and referral.
  - They often cannot afford transport.
- **High cost of treatment**
  - Expensive cytotoxic agents, counterfeit medications, quality control problems, cold chain difficulties (e.g. asparaginase is an enzyme and must be kept cool), restrictions (e.g. on oral morphine).
  - Cost of diagnostic imaging and pathology.
  - Cost of supportive care: antibiotics and other antimicrobials, blood products.
  - Cost of caring for critically ill children: high-dependency/intensive care, postoperative care.
- There is a need for multiple support networks and institutions to develop the paediatric oncology service in the face of the poverty that causes the above problems. These will include individuals and their families, non-governmental organisations (NGOs), corporate business, public social responsibilities, twinning, and public private–partnership. Government involvement is vital.
- **Inadequate provision of analgesics and other drugs**
  - For all patients, and especially where cure is not possible, palliative care is a vital part of oncology treatment. Analgesics play a large part in supportive care and procedural sedation and analgesia, as well as in palliative care. The lack of these drugs is often coupled with a poor understanding and awareness of pain management in healthcare professionals.
- **There is often an interrupted supply and insufficient quality control of all drugs.**
- **Comorbidities**
  - There is often a high prevalence of co-infections, malaria, anaemia, helminths and malnutrition which can confound the diagnosis and cause decreasing tolerance of cytotoxic therapy.
- **Untimely and inappropriate cessation of treatment (i.e. abandonment of treatment)**
  - A lack of education and knowledge about uncommon diseases among families, communities and healthcare workers leads to a lack of understanding of the need for treatment.
  - There is then a lack of financial and social support as treatment is lengthy and the parent has to stay with the child in hospital. This makes it difficult to look after other children at home, and to work, leading to loss of employment.
  - Traditional beliefs include unrealistic preconceptions about cancer and reliance on traditional medicines. In Swahili, 'the never healing sore' refers to the fact that there is no expectation of cure, and therefore no point in treatment.
  - Adolescents frequently treated on adult wards.
  - Patients may be left on wards for months because of a lack of diagnostic facilities (e.g. children with brain tumours or osteosarcomas). It is important to search the wards for such patients and to alert colleagues to refer children to an oncologist where the diagnosis is unknown.
- **Impact on family structure**
  - The loss of parental income may result in disruption and potential disintegration of the family, and at the very least to a change in family roles, especially where both parents need to work to maintain the family income.

Management of children with cancer in resource-limited countries

The following principles and practices should guide the management of children with cancer in resource-limited settings.

- Engage in twinning – that is, developing a link between a treatment centre in a resource-limited country and one in a resource-rich country, with the objective of sharing professional and technological expertise along with other resources.
- Initially, target curative treatment for cancers that are common and have a relatively good prognosis. When curative treatment is not an option or is not offered, it is essential to provide palliative care to reduce suffering. **Both curative and palliative care must be seen as active forms of therapy.**
- If curative treatments are to be undertaken, then whenever possible they should be given in a specialist children's cancer centre (see below). There is potential for greatly increasing suffering by only offering 'half treatment' of cancer for children. It has to be done fully and professionally, or alternatively the child must be given palliative care (*see* Section 1.16).
- Adapt treatment protocols in accordance with local infrastructure and facilities, maintaining a balance between treatment response and cure on the one hand and treatment toxicity and mortality on the other.
- Take steps to ensure compliance with and completion of treatment. Anticipate abandonment of treatment, and address the causes, which vary from country to country.
- Maintain a database of patients using free resources such as POND4kids (www.pond4kids.org).
- Engage in the education and training of healthcare professionals, including nurses and doctors, by using free resources such as cure4kids (www.cure4kids.org) as well as conducting in-house workshops.
- Aim to be part of regional, national and international collaborative groups to derive benefit from shared expertise and uniformity of treatment and supportive care.
- Develop parent support groups and provide resources for food, lodging and transport.

In countries where there is an improving infrastructure, the following cancers may have a good or reasonable chance of cure:

- **Standard-risk acute lymphoblastic leukaemia:** children aged 2–10 years, with a white blood cell count of $< 50 \times 10^9$/litre, may have a reasonable chance of cure with induction chemotherapy (vincristine, prednisolone, asparaginase) followed by maintenance chemotherapy as described below without the use of intensification

modules. However, **CNS-directed therapy with cranial radiotherapy plus limited intrathecal methotrexate or intrathecal methotrexate throughout therapy is required in all cases**.

- **Hodgkin's disease:** chlorambucil, vinblastine, procarbazine, prednisolone (ChlVPP) or mustine, vinblastine, procarbazine, prednisolone (MVPP) – six to eight courses.
- **Burkitt's lymphoma:** single-agent cyclophosphamide with intrathecal methotrexate and hydrocortisone. Alternatively, cyclophosphamide, vincristine, methotrexate, prednisolone (COMP) chemotherapy with intrathecal methotrexate and hydrocortisone.
- **Non-Burkitt/non-Hodgkin's lymphoma:** early stage – surgery plus COMP or cyclophosphamide, Adriamycin, vincristine, prednisolone (CHOP).
- **Brain tumours:**
  - Resectable low-grade gliomas: surgery alone.
  - Medulloblastoma and ependymoma (resectable/non-metastatic): surgery followed by **radiotherapy**.
- **Retinoblastoma:** enucleation (radiotherapy in some cases).
- **Neuroblastoma** (stage I and II): surgery alone.
- **Wilms' tumour:**
  - Stage I: surgery plus 10 doses of vincristine (at weekly intervals).
  - Stage II (and possibly stage III): surgery plus vincristine/actinomycin for 6 months.
- **Resectable embryonal rhabdomyosarcoma** (certain sites): surgery plus vincristine/actinomycin D (four courses).
- **Germ-cell tumours:**
  - **Mature and immature teratoma:** surgery alone.
  - **Malignant germ-cell tumours (stage I):** surgery alone.

Specialist cancer centres or units

Establishment

- Specialist cancer centres or units, and the use of standard treatment protocols (discussed below), have both been fundamental to the ever-improving survival of children with cancer in resource-rich countries.
- Cancer is a relatively rare disease and its treatment is usually complex.
- Management requires a dedicated and experienced multidisciplinary team.
- **Every country should aim to have at least one adequately equipped and funded centre, and then develop shared care or a satellite centre.**

Advantages of a specialist children's cancer centre or unit

- Development of medical, nursing and paramedical expertise.
- Improved supportive care, including pain relief for children.
- Facilities to protect cancer patients from other children suffering from contagious diseases.
- Opportunities for training and retention of staff, leading ultimately to accreditation as a principal care centre in paediatric oncology.
- Improved support, education and counselling of affected children and their families.
- Stimulus for the development of similar units in the same part of the world.
- Improved opportunities for research, including the development of treatment protocols relevant to the particular region or country.
- Development of links with national and international oncology units and organisations.

Requirements of a specialist children's cancer centre or unit

- Dedicated paediatric oncologist(s) and nursing staff supported by nutritionists, psychologists and social care workers.
- General surgeon and neurosurgeon trained in paediatric surgery.
- Access to radiotherapy and services of a radiotherapist.
- Blood and platelet banking facilities.
- Pathologist with experience of paediatric tumours with adequate histology and cytology facilities (immunohistochemistry is desirable; this can be in a centralised laboratory if it provides a service for more than one centre or country).
- Haematology, biochemistry and microbiology laboratories with good quality control.
- Diagnostic imaging: X-ray, ultrasound; CT imaging is desirable, especially for brain tumours. Families may have to pay for these, which is often a limiting factor that determines whether a child is diagnosed and treated properly. Fine-needle aspiration is important, as are lumbar punctures performed under appropriate analgesia and sedation.
- It is vital to have good supportive care, including regular supplies of medication, good stock-keeping and drug ordering (ensure that drugs are not stolen and sold on the 'black market'), IV fluid management systems to avoid tumour lysis syndrome, and good post-operative care.
- Adequate bed capacity. Most units are constantly overcrowded, with two patients per bed, and as units develop it is essential to build the capacity to cope with increasing numbers of patients.
- Computer facilities with Internet connections (for emailing to the link centre, Medline searches, patient database).
- Active involvement in auditing practice and participating in research.

Above all, there must be a keenness of all staff to work together to learn and make the unit successful.

Centre or unit database

All centres or units should keep a record of treatment, including details of patient demographics, diagnosis, treatment, side effects and survival. This will aid the identification of specific problems, the development of more effective treatment protocols for treatment and supportive care, and overall healthcare planning and development. The availability of free online and electronic resources such as POND4kids (www.pond4kids.org) makes this feasible.

Links with other centres or units and organisations

Provision should be made for communication and transportation for patients from remote areas. Satellite or shared-care centres can be developed by linking with

healthcare facilities in other areas so that appropriate care can be continued (e.g. district hospitals).

Links with centres or units in resource-rich countries (twinning)

Links with an established unit in resource-rich countries can have the following advantages:

- sharing information and experience on how to raise awareness of cancer and reduce delays in diagnosis
- helping to speed up diagnosis and make it more precise
- development of locally affordable supportive, palliative and curative care guidelines
- helping to train and retain staff
- helping to create patient data registration
- help to develop long-term sustainability
- providing support and advice for difficult problems (e.g. by email or web conferencing)
- pathology samples can be couriered for more complex testing (e.g. for immunophenotyping, special staining, VMMA, etc.)
- research collaboration.

In addition, links with international organisations are to be encouraged – for example, with the International Society of Paediatric Oncology (SIOP).

Principles of the curative treatment of children with cancer as undertaken in a specialised unit or centre

Diagnosis

- A complete history and examination.
- Investigations to confirm histology, determine the extent of the tumour (staging) and identify any tumour-related toxicity (e.g. disturbance of renal, liver and/or bone-marrow function).

Imaging

- To define the dimensions of the primary tumour and to determine the degree of tumour spread (staging).
- Good plain posterior–anterior and lateral chest X-rays are generally adequate for chest imaging, while **CT scan of the chest may be more definitive if it is available**.
- Ultrasonography affords good visualisation of the abdomen and pelvis, although **CT of the abdomen and pelvis may have advantages over ultrasonography in some patients**.
- Intravenous urography and cavagrams may also be useful in patients with abdominal tumours.
- For the brain, CT scanning is a necessary part of investigation and management. **MRI of the brain has advantages over CT**, but the availability of this technique is very limited.
- **Nuclear imaging can further assist in accurate staging (e.g. technetium bone scan for bone and soft tissue sarcomas, and metaiodobenzylguanidine (MIBG) scan for neuroblastomas).**

Biochemical markers

These are useful in the diagnosis of a limited number of tumours (e.g. urinary catecholamines in neuroblastoma, and serum alpha-fetoprotein in hepatoblastoma and germ-cell tumours).

Pathology

- Good histopathology is essential for the individual, and is the only way to compile accurate incidence figures and survival data and to identify favourable histological subgroups.
- Close involvement of the pathologist is needed before biopsy or surgery so that the surgeon can obtain an optimal specimen in the right fixative.

Multidisciplinary team meetings

Following initial clinical assessment and investigation, all children with cancer should ideally be discussed at regular multidisciplinary team meetings that may include the oncologist, radiologist, surgeon and radiotherapist. Such discussions are also recommended at the time of significant events during treatment (e.g. progression or relapse). This ensures that the child benefits from the collective knowledge of the treating team and there is consistency in treatment. However, this can be difficult as staff will be very busy and may require extra funding.

Treatment protocols

- Each unit should use a standard protocol for each tumour type, with the necessary variations for tumour stage.
- Protocols should be based on established and effective protocols used by national and international groups.
- Protocols may require modification based on the resources, drug availability, cost and the level of supportive care that can be provided by the unit.
- Such protocols are currently being developed by the SIOP Paediatric Oncology in Developing Countries (PODC) Graduated Intensity Treatment Guidelines Working Group. The first such protocol for acute lymphoblastic leukaemia was recently published.

Chemotherapy

- Late diagnosed childhood malignant tumours are almost always disseminated, requiring treatment with systemic chemotherapy.
- Cytotoxic drugs prevent cell division by a variety of mechanisms.
- Although occasionally single-agent therapy is given (e.g. for stage I Wilms' tumour), the great majority of treatment protocols employ a combination of drugs used synergistically to produce maximal cell kill with acceptable toxicity, and to prevent tumour cell resistance.

Surgery

- This is important both for obtaining diagnostic material, and as local therapy to reduce tumour bulk. Surgeons should be specially trained and have experience in oncology.
- It is preferable for surgeons to have received specific training in operating on children and in tumour surgery.
- Operating facilities must be of high quality to reduce the risk of infection.
- There must be adequate support from blood transfusion services.
- Several treatment protocols use pre-operative chemotherapy, which may reduce tumour size, and thus reduce peri-operative risks.

Radiotherapy

- Radiotherapy is used to treat regional tumour extension, including nodal disease, and as part of local tumour control to eradicate local residual microscopic (or sometimes macroscopic) disease following surgery.
- It has a particular role to play in certain brain tumours, and may also be used as curative therapy in early-stage Hodgkin's disease.
- It is also frequently used in the management of bone and soft tissue sarcomas and in the prevention of overt central nervous system disease in acute lymphoblastic leukaemia.
- Megavoltage machines have advantages over the older orthovoltage therapy in giving a more controllable beam and avoiding damage to skin and overlying tissues when administered to deep tissues.
- The whole of the original tumour volume is generally irradiated, plus a safety margin (usually 1–2 cm) of surrounding normal tissue.
- The combination of chemotherapy and radiotherapy can increase late local effects and should be avoided whenever possible.

Procedures

Bone-marrow aspiration

- This is needed in the diagnosis of leukaemia and lymphoma, and also to identify any bone-marrow infiltration with solid tumours such as neuroblastoma.
- **It is a painful procedure and must be done under analgesia and sedation (e.g. ketamine 2 mg/kg) (*see* Section 1.15 and Section 1.24) along with infiltration of the skin and subcutaneous tissues down to periosteal level with a local anaesthetic.**
- Aspiration is preferably performed from the posterior iliac crest, but can also be taken from the anterior crest.

Lumbar puncture

- This is needed in the diagnosis of malignant meningitis, especially with leukaemia and lymphoma, but also in certain brain tumours (e.g. medulloblastoma) and other solid tumours, particularly those affecting the head and neck.
- **Lumbar puncture is a painful procedure, and in children should be done under analgesia and sedation along with local anaesthetic wherever possible (especially if multiple lumbar punctures are needed).**

Venous access

- Venepuncture for administration of chemotherapy and blood sampling is painful and especially difficult in the young child (analgesia and sedative cover may be needed).
- Repeated venepuncture results in loss of venous access due to venous thrombosis, and may significantly compromise therapy.
- Several agents, especially vinca alkaloids, are extremely damaging to tissues when extravasated.
- Short-term percutaneous placement of medium-length or long lines under local anaesthetic may provide an alternative means of venous access.
- **The placement of a long-term central venous catheter (e.g. Broviac line, Hickman line) (if available) can be considered in children receiving intravenous chemotherapy. It should be placed by an experienced surgeon, and its use is associated with an increased risk of infection, particularly from skin organisms such as staphylococci.**

Psychological support

Cancer and its treatment are frightening experiences for many patients, and every attempt should be made to reduce the child's fears. An explanation of the diagnosis and treatment, including the likely outcome, should be given in clear understandable terms to the child's family and also to the affected child or young adult wherever appropriate. Such information is best delivered over more than one conversation, allowing the family to understand it and come back to ask questions.

All aspects of treatment and associated side effects should be clearly explained, including details of supportive care, such as infection control, the **importance of seeking a healthcare worker if a fever develops**, mouth care, pain relief, care of lines, and procedures, such as surgery, bone-marrow aspirate and lumbar puncture. These conversations need to continue throughout treatment, thus establishing a relationship with the child and their family. The family must always be fully involved in the patient's care (e.g. by donating blood when it is needed). Parents want their child's doctor to focus on a potential cure and relief of symptoms, and then they can have faith in the doctor and derive hope for the future.

Side effects of the disease and/or its treatment

TABLE 5.14.1 General side effects of chemotherapy

Acute effects
Bone-marrow suppression • Infection • Bleeding • Anaemia
Nausea and vomiting
Mucositis
Alopecia
Fatigue and cachexia
Tumour lysis syndrome
Late effects
Infertility
Secondary malignancy

TABLE 5.14.2 Specific side effects of chemotherapy

Neurotoxicity	Vincristine (muscle weakness due to peripheral neuropathy, constipation, rarely encephalopathy)
Cardiomyopathy	Doxorubicin/daunorubicin
Respiratory system	Bleomycin
Urinary tract	Cisplatin (renal), ifosfamide (renal and bladder), cyclophosphamide (bladder)
Liver	Thioguanine, actinomycin D
Hearing	Cisplatin

Infection

- Neutropenia, both at diagnosis in leukaemia and following most chemotherapy, produces a risk of significant

bacterial and fungal sepsis derived from the patient's own flora when the neutrophil count is < 1.0×10^9/litre, and particularly when it is < 0.2×10^9/litre.
- The greatest risk is from Gram-negative bowel organisms such as *E. coli, Proteus, Klebsiella* and *Pseudomonas.*
- Gram-positive organisms from the skin and mucosal surfaces, especially staphylococci, may also cause significant morbidity.
- Life-saving measures include identification of those at risk, close observation, and the empirical administration of intravenous antibiotics to patients with a neutrophil count of < 1.0×10^9/litre who develop fever (e.g. > 38°C for 2 hours or > 38.5°C on one occasion).
- The antibiotic regimen should be determined by each centre depending on the prevailing flora and the cost and availability of antibiotics.
- First-line therapy for febrile neutropenia should generally be with a combination of a broad-spectrum beta-lactam antibiotic and an aminoglycoside.
- If the temperature fails to remit, or if Gram-positive organisms are isolated, therapy with vancomycin or teicoplanin is recommended.
- For microbiologically proven septicaemia, antibiotics should be given for 5–7 days, the choice of drug depending on the antibiotic sensitivity of the isolated organism.
- Newer very broad-spectrum antibiotics, such as the carbapenems and quinolones, are best avoided as they are expensive and may promote fungal colonisation and bacterial resistance if commonly or repeatedly used.
- If systemic fungal infection is proven or suspected (e.g. if fever fails to remit after 4–5 days of antibiotics), then intravenous amphotericin, despite its renal toxicity, is still the drug of choice and is widely available. Newer lipid-based formulations of amphotericin are less toxic but very expensive.
- *Pneumocystis carinii* pneumonia, especially in patients with leukaemia, requires prophylaxis with co-trimoxazole (calculated as a dose of 150 mg/m^2/day of trimethoprim given twice a week).
- Viral infections are generally tolerated, but chickenpox and measles cause life-threatening infections in immunosuppressed patients. Whenever possible, children must be isolated from direct contact with these infections. **Immunoglobulin therapy, including zoster immune globulin, may be life-saving but is rarely available.**
- High-dose aciclovir is the treatment of choice for zoster infections, but is expensive and not yet widely available globally.

Bleeding and anaemia

- Adequate blood banking facilities with availability of blood component therapy such as packed red blood cells and platelets (*see* Section 1.7) are a fundamental part of therapy. Red blood cell transfusion should be reserved for symptomatic anaemia, or when the haemoglobin falls to a very low level (e.g. < 6 grams/dL).
- Platelets should be reserved for patients with florid petechiae or overt bleeding, or to cover procedures such as lumbar puncture, when a platelet count of > 40 × 10^9/litre is essential.
- Prophylactic platelet transfusions in response to specific platelet counts are not recommended.
- In the presence of fever, bleeding may occur at higher platelet counts than would normally be expected.

Nausea and vomiting

- Nausea and vomiting are a very unpleasant side effect of chemotherapy and can lead to poor compliance with therapy and additional complications, such as metabolic disturbance, dehydration and oesophageal tears.
- Chemotherapeutic agents vary in their potential to produce vomiting, from very low (e.g. vincristine and etoposide) to very high (e.g. cisplatin). Anti-emetic therapy should be given wherever possible, preferably prophylactically, but certainly to patients with established retching and vomiting.

Anti-emetic agents

- **Metoclopramide:** this is effective in high dose, but a greater risk of extrapyramidal side effects exists in children. Give 100 micrograms/kg for 1/12 to 1 year, 1–3 years 1 mg, 3–5 years 2 mg, twice daily and 5–9 years 2.5 mg, 9–18 years 5 mg thrice daily orally or slowly (over 2 minutes) by IV injection. Over 60 kg children can have 10 mg three times daily. **Avoid the IM route.**
- **Chlorpromazine:** orally or IV (the IV route can cause severe hypotension), child 1–12 years 500 micrograms/kg every 4–6 hours, maximum 75 mg daily. For 12–18 years 25–50 mg every 3–4 hours until vomiting stops.
- **Prochlorperazine:** orally or IV slowly over 10 minutes, 250 micrograms/kg 1–12 years every 8–12 hours (only if the child weighs over 10 kg or is over 1 year of age). 12–18 years 5–10 mg three times daily.

The following drugs are generally available but have a high incidence of side effects, including drowsiness. They may be more effective when combined with steroids.
- **Benzodiazepines:** the main effect is sedation and amnesia. These drugs are useful for anticipatory nausea.
- **Steroids:** the main effect is in combination with other agents (prednisolone 0.5 mg/kg every 12 hours).
- **$5HT_3$ antagonists (e.g. ondansetron): these are the most effective anti-emetics, especially when combined with steroids. However, they are expensive.**

Ondansetron dosage

Six months–18 years either 5 mg/m^2 or 150 micrograms/kg (max single dose 8 mg) IV before chemotherapy then repeated every 4 hours for two further doses, then give orally. Oral dose < 10 kg = 2 mg 12 hourly, > 10 kg = 4 mg 12 hourly for up to 5 days.

Oral mucositis

- This is a common side effect of many cytotoxic agents and also radiotherapy.
- **Scrupulous simple oral hygiene should be maintained. This can be achieved by regular thorough tooth brushing two to three times a day together with use of a mouthwash such as chlorhexidine if available.**
- Oral fluconazole and oral acyclovir may be of benefit in oral mucositis with secondary infection from candida and herpes infection, respectively.

Alopecia

This is inevitable with most chemotherapy, but usually entirely reversible on completion of treatment. Some children are not upset by the appearance of alopecia, but for those who are distressed by it, a light but attractive head covering may be acceptable.

Nutrition

Maintenance of adequate nutrition is essential. 'Cancer wasting' or cachexia is a well-recognised complication of paediatric tumours, and is subsequently associated with a decreased tolerance of chemotherapy and its side effects, and possibly an increase in cancer mortality.

Poor nutritional status may result from any of the following:

- stress
- pain
- increased metabolism (due to tumour or infection)
- anorexia
- altered sense of taste and smell
- chemotherapy-induced nausea and mucositis (e.g. stomatitis, oesophagitis)
- radiotherapy-induced mucositis and dry mouth (xerostomia)
- surgery-induced pain, bowel obstruction and appetite suppression.

In addition to this, an unacceptably high number of children in resource-limited countries who do not have cancer are malnourished. The effect of cancer and its treatment can be even more deleterious for such children.

Each child should have a nutritional assessment, including measurement of height or length, weight, mid upper arm circumference and triceps fold thickness (using callipers). Height and weight should be plotted on a standard percentile chart (*see* Section 9).

Nutritional support should be given to children who consistently show a decrease across percentile lines. It may also be indicated in children with baseline malnourished status. A high-calorie diet with adequate protein should be given to all children with cancer, supplemented if necessary with specific additives to provide additional calories and protein.

If sufficient food cannot be taken orally, enteral feeding via a nasogastric tube (particularly overnight) should be considered. Total parenteral nutrition should be avoided, as it is expensive and associated with a high risk of complications, including infection and metabolic disturbance.

Tumour lysis syndrome (TLS)

This is a life-threatening complication that occurs when the rapid lysis of tumour cells, usually resulting from chemotherapy, leads to the release of excessive quantities of cellular contents into the systemic circulation, resulting in a metabolic disturbance characterised by the following:

- hyperkalaemia
- hyperphosphataemia
- hyperuricaemia
- hypocalcaemia.

This metabolic derangement may lead to acute oliguric renal failure and cardiac arrhythmias.

TLS can occur spontaneously in tumours with a very high proliferative rate, as well as following initiation of treatment. It can be classified as laboratory TLS (with no clinical manifestations) or clinical TLS (with life-threatening clinical abnormalities).

Management of TLS

- Most importantly, anticipate and recognise patients who are at high risk of tumour lysis, i.e. those with leukaemia and lymphoma (particularly T-cell or Burkitt's phenotype, and those with a high white cell count > 50×10^9/litre, hepatosplenomegaly or mediastinal mass, or high LDH).
- Intravenous hydration with potassium-free fluids, at least 2.5–3.0 litres/m^2/day, should be commenced prior to treatment and then continued for the first few days of treatment. Ensure that there is adequate urine output (≥ 1 mL/kg/hour).
- Regular allopurinol, 100 mg/m^2 dose every 8 hours, should be commenced prior to treatment and then continued for the first few days of treatment.
- Clinical and laboratory monitoring should be undertaken, including daily weight, input and output review, and assessment of blood biochemistry, with measurement of uric acid levels up to four times a day if needed.

Infertility

- This mainly occurs in males and is a consequence of specific cytotoxic agents, especially the alkylating agents such as cyclophosphamide, or radiation to the gonads. Girls may suffer from ovarian failure causing a premature menopause after certain therapies.
- Families should receive counselling about infertility, and hormonal treatment may be offered.
- Sperm storage for adolescent boys before the start of treatment can be considered if this service is available.

Second tumours

- Chemotherapy results in a small but important risk of second tumours, especially acute myeloid leukaemia.
- This is particularly associated with alkylating agents such as cyclophosphamide (especially if used with radiotherapy), anthracyclines and topoisomerase-2 inhibitors (e.g. etoposide).

Treatment of individual tumour types

A detailed discussion of the presentation and management of every type of tumour is beyond the scope of this book.

Acute lymphoblastic leukaemia (ALL)

Approximately one-third of all children under 15 years of age with cancer have acute leukaemia, and 75–80% of these have acute lymphoblastic leukaemia, making it the most common childhood cancer in well-resourced countries.

Presentation

- Myelosuppression.
- Anaemia, infection (which can be life-threatening) and thrombocytopenia (bruising, bleeding, petechiae).
- Lymphadenopathy and hepatosplenomegaly.
- Bone pain and limp.

Diagnosis

- Full blood count.
- Blood film can be diagnostic for patients with very high white cell counts.
- Bone-marrow aspirates (these are always required).

- Morphology (e.g. FAB system), cytochemistry and immunocytochemistry (if available).
- Lumbar puncture: CSF cell count and cytospin for lymphoblasts.
- Chest X-ray (T-cell leukaemia).
- Ultrasound scan of the abdomen for assessment of the liver, spleen and kidneys.

Treatment

Rapid tumour lysis, which can sometimes be spontaneous, is a major risk, particularly for patients with high white cell counts leading to biochemical disturbances. **Intravenous fluids, allopurinol and close monitoring of renal function are required at the start of treatment.** The treatment of acute lymphoblastic leukaemia is divided into a number of phases, as described below.

Induction

The aim is to get the patient into remission (defined as the presence of < 5% blasts in bone marrow). Four weeks of oral prednisolone or dexamethasone with weekly vincristine injections will result in a 90% remission rate, *although the addition of a third drug, asparaginase (9–12 doses every 48 hours), is associated with improved long-term survival. If asparaginase is not available or is too expensive, anthracyclines (e.g. doxorubicin) can be substituted.*

CNS-directed therapy

This is needed in all patients to prevent CNS relapse. Standard therapy is to give five to six doses of intrathecal methotrexate together with cranial irradiation (18 Gy). For standard-risk (not high-risk) patients, irradiation can be replaced with intrathecal methotrexate at regular intervals throughout the treatment period, although some units may find radiotherapy easier to administer than repeated lumbar punctures.

Intensification therapy

The administration of periods of more intensive therapy (e.g. with drugs such as cyclophosphamide, daunorubicin and cytosine) has been associated with increased survival, although this treatment carries the risk of severe myelosuppression and should be used with caution unless a high level of supportive care is in place.

Continuation (maintenance) therapy

This essential part of treatment generally lasts for 2 to 3 years. Most regimens employ daily oral mercaptopurine and weekly oral methotrexate with vincristine and a short course of steroid given every month.

Prognosis

With current therapy in specialised centres one can expect at least 50% of standard-risk patients (i.e. those with a white cell count at diagnosis of < 50 × 10^9/litre, and aged 2–10 years) to survive.

Acute myeloid leukaemia (AML)

This accounts for 15–20% of acute leukaemias in children.

Presentation

The presentation is the same as for acute lymphoblastic leukaemia, with more likelihood of tissue infiltration:

- gum hypertrophy: monocytic leukaemia
- skin involvement: myeloblastic leukaemia
- disseminated intravascular coagulation: promyelocytic leukaemia.

Diagnosis

See above section on acute lymphoblastic leukaemia.

Treatment

This is less successful than for acute lymphoblastic leukaemia. *Induction therapy is based on 8–10 days of intensive chemotherapy with drugs such as daunorubicin, etoposide, thioguanine and cytosine. Remission rates of over 80% can be achieved, but these regimens are associated with severe and prolonged myelosuppression, with a significant risk of toxic death. This risk should be carefully considered before curative therapy is attempted. Consolidation therapy is again based on intensive and life-threatening chemotherapy. The risk of CNS relapse is less than with acute lymphoblastic leukaemia. Lumbar puncture with triple intrathecal chemotherapy (methotrexate, hydrocortisone and cytosine) should be given with each course of chemotherapy.*

Prognosis

Less than 50% of these children will be expected to survive long term, with a high risk of toxic death following intensive chemotherapy.

Non-Hodgkin's lymphoma (NHL)

Childhood NHLs are a heterogeneous group of usually diffuse lymphocytic or lymphoblastic neoplasms arising from both B and T cells. Burkitt's lymphoma, a B-lineage NHL, is the most common childhood malignancy reported from tropical Africa, and is also prevalent in South America and in parts of South-East Asia.

Presentation

Lymphomas can arise in any area of lymphoid tissue, and therefore the presenting features are protean. Patients often have marrow involvement and sometimes CNS disease.

- Burkitt's lymphoma is an aggressive tumour, usually affecting the head and neck, but also arising from several abdominal organs. **Progression in size of Burkitt's lymphoma can be rapid, given its 48-hour doubling time.** Head tumours usually present with extensive involvement, with swelling of the jaw and tooth loosening, gum expansion, bleeding, ulceration and exophthalmos.
- The majority of non-Burkitt B-cell lymphomas are disseminated at diagnosis, often with diffuse abdominal disease.
- T-cell NHL presents with thymic and/or nodal involvement, often with signs of airway or superior vena cava obstruction.

Diagnosis

The diagnosis is frequently suggested on clinical examination (e.g. classical features of Burkitt's or T-cell lymphoma). The diagnosis is supported by appropriate imaging (X-ray, ultrasound). Bone-marrow aspiration and lumbar puncture should be performed. Biopsy is necessary if the diagnosis cannot be made on a bone-marrow aspiration.

Treatment

Burkitt's lymphoma

This is an extremely chemosensitive tumour, and a high remission rate can be achieved with a single course of cyclophosphamide. **Repeated courses of cyclophosphamide may be successful in some early-stage patients, but the success of therapy is further improved, particularly for patients with advanced disease, by the use of multi-agent chemotherapy using combinations such as COMP (cyclophosphamide, vincristine, methotrexate and prednisolone), for example, given over a 6-month period. This should be accompanied by administration of intrathecal methotrexate and hydrocortisone.** As with acute lymphoblastic leukaemia, biochemical disturbance as a result of rapid tumour lysis is a major risk, and intravenous fluids, allopurinol and close monitoring of renal function are required.

Non-Burkitt B-cell NHL

Repeated courses of multi-agent chemotherapy with COMP or CHOP (cyclophosphamide, Adriamycin, vincristine and prednisolone) are often successful, especially for early-stage disease. For advanced disease, more intensive regimens such as the French LMB protocols may result in a high success rate, although the toxicity of these regimens is potentially high.

T-cell NHL

In contrast to B-cell NHL, therapy for T-cell disease is usually based on leukaemia-type therapy (with intensification modules and continuing chemotherapy). CNS-directed therapy with cranial irradiation or moderate-dose methotrexate with ongoing intrathecal methotrexate should be used.

Prognosis

Burkitt's lymphoma

The prognosis varies according to the stage of disease, although overall at least 85–90% of patients will be cured with modern therapy in well-resourced countries. Where ability to give chemotherapy is restricted, simpler therapy can yield 50–60% survival rates. However, CNS disease is associated with a poor outcome.

Non-Burkitt B-cell NHL

The prognosis is poorer than with Burkitt's lymphoma, and depends on the stage of disease and the intensity of treatment. In low-stage disease a survival of at least 75% is expected. The prognosis is worse with extensive disease, particularly with bone-marrow or CNS involvement.

T-cell NHL

With modern leukaemia-type therapy, survival rates are around 65–70% or higher.

Hodgkin's lymphoma

Presentation

Unlike NHL, Hodgkin's lymphoma tends to be confined to the lymph nodes or spleen, although spread to other sites, such as the lungs, liver and bone, may occur. Most children present with a primary painless neck mass, although any nodal group may be involved. Patients are staged according to the Ann Arbor system, which incorporates an A and B designation for the absence or presence, respectively, of fever, night sweats and weight loss.

Diagnosis

Diagnosis is generally made by lymph-node biopsy. Essential staging investigations include chest X-ray and abdominal ultrasound. Bone-marrow aspirate and trephine should be performed on patients with evidence of advanced disease.

Treatment

In the past, radiotherapy was widely utilised, often using extensive radiation fields (e.g. the 'mantle' or 'inverted Y' techniques) to cover all known sites of disease. Radiation is still used in localised disease, but generally chemotherapy is preferred for most patients, using regimens such as ChlVPP (chlorambucil, vinblastine, procarbazine and prednisolone) or MVPP (with nitrogen mustard replacing chlorambucil). Six to eight courses are given every month. Such chemotherapy may be given on an outpatient basis, and is relatively non-toxic, although the risk of infertility in boys is high. Some of the toxicity can be avoided by alternating ChlVPP or MVPP with ABVD (doxorubicin, bleomycin, vinblastine and dacarbazine), although this may have the potential to cause cardiotoxicity.

Prognosis

Hodgkin's lymphoma generally carries a good prognosis. For patients with stage I and II tumours, over 80% are expected to be cured. Even with advanced disease, over 50% of patients would be expected to survive.

Brain tumours

These are a heterogeneous collection of several tumours that together represent around 25% of all childhood cancer patients in Europe and North America. The proportion in resource-limited countries is much lower, at least partly due to under-diagnosis as a result of limited availability of neuroimaging (CT and MRI), neurosurgery and neuropathology.

Presentation

About 60% of childhood brain tumours arise in the posterior fossa, and usually present with signs and symptoms of raised intracranial pressure due to obstruction of CSF pathways. A variety of other presenting features may occur, depending on the site and rate of progression of the tumour. These include irritability, behavioural disturbance, cranial nerve palsies, long tract signs (particularly truncal ataxia), endocrine abnormalities, visual disturbance and seizures.

Diagnosis

Modern imaging with **CT scanning, or preferably MRI (if available)** has revolutionised the management of brain tumours, and should be performed if CNS tumours are suspected. Some tumours have characteristic appearances on imaging (e.g. diffuse brainstem glioma and optic nerve glioma), although most tumours require histological confirmation. Imaging of the spine and examination of the spinal fluid is required to assess for CNS spread in high-grade bone tumours (e.g. medulloblastomas, high-grade gliomas).

Treatment

For most tumours, modern neurosurgery (*see* Section 5.16.K) is vital to management. Prompt relief of raised intracranial pressure is often required, and may be

life-saving. This is achieved with dexamethasone, which when used peri-operatively has also been shown to significantly reduce operative mortality.

Surgery may also be required to relieve hydrocephalus (e.g. with ventricular peritoneal shunting). The aim of definitive surgery is to provide a histological diagnosis and usually to shrink the tumour as much as possible. Tumour resection is required for most tumours, including all posterior fossa tumours (except the brainstem), tumours of the cerebral hemispheres and craniopharyngiomas. Some tumour types may be cured with surgery alone (e.g. cerebellar low-grade astrocytoma), although others (e.g. medulloblastoma) require **adjuvant radiotherapy**.

Generally a large dose of radiotherapy is given to the tumour bed, while some tumours (e.g. medulloblastoma) require whole CNS radiotherapy due to the high risk of CSF dissemination. To date chemotherapy has had relatively little impact on the treatment of brain tumours, although it can be used to try to delay radiotherapy in the very young.

Radiotherapy to the whole brain and spine has a very high risk of sequelae, particularly in young children. These include neuropsychological disability, growth failure (growth hormone deficiency and poor spinal growth) and hypothyroidism.

The following is a brief guide to the management and prognosis of individual tumour types.

Medulloblastoma

Prognosis

The prognosis is around 60% for children with non-metastatic disease and 30% for those with disseminated disease. Children with medulloblastoma aged less than 3 years have a much worse prognosis than older children. Radiotherapy may be curative, but most centres do not advocate this, as radiation therapy to the developing brain is associated with a very high incidence of severe handicap. Prolonged chemotherapy can be used to try to delay radiotherapy, but even then survival is only around 20%.

Cerebellar low-grade astrocytoma

Treatment

Surgical resection is performed, and post-operative radiotherapy is not required if the resection has been complete.

Prognosis

The prognosis is at least 80% following total resection.

Supratentorial low-grade astrocytoma

Treatment

Surgical resection is performed for accessible lesions, although many of these tumours (e.g. those involving the hypothalamus and optic pathways) are not fully resectable. In these cases, focal radiotherapy should generally be given, particularly in patients with progressive disease.

Prognosis

The prognosis is variable, mainly depending on the site of the tumour.

High-grade glioma

Treatment

Surgical resection (as complete as possible) is performed, and post-operative focal radiotherapy is required.

Prognosis

Overall, the prognosis is very poor, at around 15%. Patients who undergo complete resection and have Grade 3 (anaplastic astrocytoma) tumours have a much better chance of survival than those who undergo subtotal resection and have Grade 4 tumours (glioblastoma multiforme).

Ependymoma

Treatment

Surgical resection (as complete as possible) is performed, and post-operative focal radiotherapy is required.

Prognosis

The prognosis is around 30–50%, mainly depending on the degree of tumour resection.

Brainstem glioma

Treatment

Focal exophytic tumours are treated with surgery followed by focal radiotherapy.

Prognosis

The prognosis is around 30–50%, mainly depending on the degree of tumour resection.

Diffuse (malignant) brainstem gliomas

Treatment

Palliative radiotherapy may possibly be used.

Prognosis

These tumours are fatal (less than 5% survival).

Craniopharyngioma

Treatment

Surgical resection is performed, although there is a high peri-operative mortality rate. *Radiotherapy is sometimes used for recurrent tumours.*

Prognosis

The prognosis is variable. All patients suffer from panhypopituitarism, which requires hormone replacement therapy.

Neuroblastoma

This biologically unusual tumour can arise from any part of the sympathetic nervous system, although around 60% originate from the adrenal gland. Localised stage I and stage II disease and the unique stage IV S disease of infancy have a good outlook, although for the 80% of patients who present with advanced tumours the prognosis is very poor.

Presentation

A large proportion of patients present with an abdominal (adrenal) or pelvic mass, often extending across the midline. Para-spinal masses that extend into the spinal canal causing cord compression, and thoracic primaries that cause airway obstruction, also occur. Most patients (65%) present with metastatic disease that often causes bone pain and limp, with marrow infiltration mimicking leukaemia, skin infiltration or orbital masses causing proptosis or peri-orbital bruising.

Diagnosis

Ultrasound of the abdomen *(or CT of the abdomen, if*

available), chest X-ray *(or CT of the chest for thoracic tumours, if available)*, abdominal X-ray (calcification is often a feature of primary tumours), **24-hour urine collection or spot urine sample for catecholamine metabolites** (secreted in 85% of cases), bone-marrow aspirate and trephine (bilateral) are all helpful. **MIBG scan and technetium bone scan are performed to investigate metastasis to the bones.** Although the diagnosis can be made without tumour biopsy for patients with classic features of stage IV disease, histological confirmation is required for localised tumours and for advanced disease where the diagnosis is in doubt.

Treatment and prognosis

Patients with stage I and II disease should be treated with surgical excision, which if complete is associated with an 80% or higher survival rate. *For stage III patients, the prognosis is around 40%, with treatment including multi-agent chemotherapy with drugs such as cyclophosphamide, vincristine, Adriamycin, etoposide and platinum, followed by surgical excision of the tumour.* Stage IV disease has a very poor prognosis, and it is essential to provide palliative care to reduce the suffering of these patients.

Retinoblastoma

Although rare in many countries, retinoblastoma is a common paediatric cancer in many areas, including sub-Saharan Africa, Pakistan and India. Two forms are identified, namely an autosomal-dominant heritable form that may affect one or both eyes, and a sporadic (non-heritable) form that is always unilateral.

Presentation

Most children present within the first few years of life with a white mass in the pupil or with a squint. In patients with a family history, routine surveillance may detect an early lesion. Delayed presentation may result in a protruding fungating orbital mass.

Treatment and prognosis

Enucleation of the involved eye is the standard therapy, and is curative in about 75% of patients with localised disease.

Very small tumours may also be effectively treated with a cobalt plaque, local irradiation, light coagulation or cryotherapy. External beam radiotherapy may be curative in early cases, but cataract formation usually results. Extensive spread outside the orbit is usually fatal. Relatively simple chemotherapy (e.g. with carboplatin, vincristine and etoposide) appears to be effective in reducing large tumours, sometimes facilitating preservation of vision and possibly preventing metastatic spread.

Wilms' tumour (nephroblastoma)

This tumour occurs in nearly all parts of the world, and is one of the most curable of all childhood cancers. Approximately three out of four cases occur in children under 5 years of age.

Presentation

Most patients present with a large and generally painless flank mass with or without haematuria and hypertension. The diagnosis may be confused with the abdominal distension associated with malnutrition and with other flank masses, such as neuroblastoma and splenomegaly associated with malaria or haemoglobinopathy.

Diagnosis

The presence of a renal tumour can be confirmed by ultrasonography, which should also assess the presence of inferior vena cava involvement. Alternatively, intravenous urogram (with injection into the feet to perform a cavagram) can be used, as can **CT scan (with contrast) (if available)**. The diagnosis can be made on the basis of clinical presentation and imaging findings. Histopathological confirmation is not mandatory, but is advisable, particularly in those under 6 months of age. A chest X-ray should look for evidence of lung metastases.

Treatment

The SIOP approach of up-front chemotherapy (4 weeks of vincristine and actinomycin D for non-metastatic tumours, and 6 weeks of the two drugs plus Adriamycin for metastatic tumours) followed by surgery is more suited to resource-limited countries. The duration and type of further chemotherapy after surgery depend on the local staging of the tumour and the response to initial treatment. For stage I tumours, further vincristine and actinomycin may be given for 4 weeks or 6 months depending on the histological response. For stage II disease, vincristine and actinomycin should be given for 6 months, a regimen which may also be used for stage III tumours with the possible addition of radiotherapy. *For stage IV tumours and for so-called 'unfavourable (anaplastic)' histology groups, all three drugs should be given for 6–12 months. Radiotherapy to the abdomen should only be given if residual bulky disease is present after surgery. Patients with pulmonary metastases at diagnosis should receive lung irradiation (20 Gy), particularly if the lung metastases persist after pre-nephrectomy chemotherapy.*

Prognosis

For patients with stage I and II tumours (favourable histology), at least 80% should be cured. Stage III and IV tumours have survival rates of around 60–70% and 50–60%, respectively. However, the prognosis is poor for patients with unfavourable histology.

Liver tumours

The two main types of liver tumour are hepatoblastoma and hepatocellular carcinoma (HCC). Although both are rare in Europe and North America, in several parts of the world, such as East Africa and New Guinea, HCC is a relatively frequent childhood malignancy. In children with HCC, as in adults, there is a clear and possibly causative association with hepatitis B infection both in the presence and in the absence of coexisting cirrhosis.

Presentation

Hepatoblastoma generally presents in children under 3 years of age, whereas HCC is seen in older children and adolescents. The presentation in both hepatoblastoma and HCC is similar, with most patients presenting with abdominal distension and a right upper quadrant mass. Additional features, particularly for HCC, include abdominal pain, nausea, weight loss, anorexia and jaundice. Features of underlying chronic liver disease may be present with HCC.

Diagnosis

The liver mass may be seen on ultrasound examination of the abdomen and **CT scan (if available)**. The diagnosis should be confirmed by biopsy. *Alpha-fetoprotein levels are elevated* in nearly all cases of hepatoblastoma and in about 65% of cases of HCC. *In these patients, the alpha-fetoprotein level may be used as a tumour marker to monitor progress.* A chest X-ray should be taken to look for evidence of lung metastases.

Treatment and prognosis

Surgical excision is the definitive treatment for both tumours. *Hepatoblastoma is a chemosensitive tumour, and pre-operative chemotherapy significantly improves the prognosis, facilitating surgical excision and the control of distant metastases. The most active agents are doxorubicin and cisplatin. Cisplatin monotherapy along with surgery is recommended for localised and non-metastatic tumours.* The prognosis for patients with these tumours is around 50%, although the surgery is difficult and carries significant risks.

The overall prognosis for HCC is very poor. This disease is much less responsive to chemotherapy than hepatoblastoma, and unfortunately these tumours are often multi-centric or extensively invasive, making resection possible in less than 30% of patients. Of these cases, only one-third survive long term.

Soft-tissue sarcomas

These tumours arise from undifferentiated embryonic tissue. The most common of these is rhabdomyosarcoma, a tumour of striated muscle. Rhabdomyosarcomas can arise anywhere where there is such striated muscle or embryonic remnants thereof, but the most common sites include the orbit, head and neck (including the nasopharynx), the genito-urinary tract in both boys and girls, and the extremities. Two main histological types are recognised, namely the more common embryonal type, and the less common alveolar type, which generally carries a much poorer prognosis.

Presentation

Most rhabdomyosarcomas present as diffuse masses, but orbital lesions generally present with proptosis and diplopia, and nasopharyngeal lesions often present with nasal obstruction, epistaxis and pain. At least 25% of sarcomas will have metastases at diagnosis, most commonly to the lungs and lymph nodes.

Diagnosis

Histological confirmation is required by biopsy or excision of the primary tumour. Initial radical surgery should not be performed. Primary tumours should be defined by **CT scan (if available)** (this is particularly important for head and neck and orbital tumours), although other techniques such as tomography and ultrasound examination may be useful. For head and neck lesions, lumbar puncture with careful CSF examination is required. Parameningeal tumours are those in which CSF invasion is demonstrated or possible due to the proximity of the tumour to the meninges based on **CT scanning (if available)**. Metastatic surveillance includes chest X-ray, abdominal ultrasound examination **or CT scanning (if available)**, and bilateral bone-marrow aspiration.

Treatment

In view of the high rate of local and distal dissemination, chemotherapy is required for all patients. The VAC regimen (vincristine, actinomycin D and cyclophosphamide, four to nine courses), is most commonly used. In more recently devised regimens, ifosfamide has replaced cyclophosphamide (IVA ifosfamide, actinomycin D and vincristine), although ifosfamide carries a far greater risk of side effects, including haemorrhagic cystitis and nephropathy. Unless the tumour can be completely excised, local therapy should generally be performed after cytoreductive chemotherapy (e.g. after three to six courses). Surgery is the usual local therapy for sites such as the extremities and genito-urinary system. For head and neck tumours, surgical excision of the primary tumour is usually extremely difficult, and **radiotherapy should be considered**.

Radiotherapy is the treatment of choice following chemotherapy for orbital tumours.

For parameningeal tumours, whole CNS radiotherapy and intrathecal methotrexate is advised.

Prognosis

For completely resected tumours, the prognosis is good, with at least 70% survival. For those with regional disease the prognosis is less good, with about 40–50% survival. Survival is particularly poor for patients with metastatic disease (less than 20%) and for parameningeal tumours, so careful consideration is needed before embarking on a curative treatment for these categories. Alveolar histology confers a significantly worse prognosis for all stages and sites.

Kaposi's sarcoma

This tumour has become a major healthcare problem in areas affected by the HIV pandemic. Younger children tend to present with disseminated suppurative lymphadenopathy and conjunctival disease, whereas in older children, skin nodules predominate.

Treatment

Radiotherapy may control locally aggressive tumours. Kaposi's sarcoma may also respond to chemotherapy, including agents such as vincristine, actinomycin D and DTIC.

Bone sarcomas

About 50% of all sarcomas occur in the bone, the predominant types being osteosarcoma and Ewing's sarcoma.

Presentation

A bone sarcoma usually presents as a painful mass which may be hot and tender, mimicking osteomyelitis. Around 95% of osteosarcomas arise in long bones, and about 50% occur in the upper tibia or lower femur. Around 50% of Ewing's sarcomas occur in long bones, usually in the shaft, with the remainder occurring in the pelvis, shoulder, skull and vertebrae. About 20% of patients with Ewing's sarcoma and 10–20% of those with osteosarcoma have metastatic disease at diagnosis.

Diagnosis

The diagnosis is suggested on plain X-ray with osteosarcoma showing bony expansion with osteoblastic and/or lytic activity. Ewing's sarcoma generally appears as an

ill-defined lytic lesion. Diagnosis is confirmed with biopsy, preferably using an open technique under direct vision. Chest X-ray or *CT of the chest (if available)* is used to detect lung metastases, the lung being the most common metastatic site for both tumours.

Treatment and prognosis for Ewing's sarcoma

Chemotherapy using vincristine, actinomycin D, Adriamycin and cyclophosphamide should be given to control both local and metastatic disease. Local therapy with wide surgical excision should be performed. **If this is not possible, high-dose radiotherapy (e.g. 45–50 Gy) should be given**, although for long bone sites amputation may be more appropriate.

The overall prognosis is around 40%, but depends on the site and the adequacy of local tumour control. The prognosis for patients with metastatic disease is very poor.

Treatment and prognosis for osteosarcoma

Amputation of the long bone containing the primary tumour only gives a cure rate of about 20%. *Chemotherapy either before or after local therapy has increased survival to around 50% for non-metastatic patients. Six courses of cisplatinum and doxorubicin (three pre- and three post-surgery) may be feasible in many resource-limited countries. The current American and European protocols use a combination of cisplatinum, doxorubicin and high-dose methotrexate.*

Local control is either with amputation or (if available) with tumour resection and **endoprosthetic bone replacement or rotation plasty**.

Germ-cell tumours (GCTs)

Around 3% of tumours in children are GCTs, which are seen mainly in infants and adolescents. They include benign (mature and immature teratoma) and malignant (e.g. yolk sac tumour, germinoma) subtypes.

Presentation

In infancy, the usual presentation is a pelvic or sacrococcygeal mass often noticed after birth (or sometimes prior to birth on antenatal scans). In adolescents, GCTs present either as an enlarged mass in the gonads (testicular enlargement or a pelvic mass arising from the ovary) or in the mediastinum with signs of airway or superior vena cava obstruction.

Diagnosis

Initial assessment is by X-ray and CT (if available) for mediastinal masses, and ultrasound examination for abdominal and pelvic masses. Assessment of serum alpha-fetoprotein and β-human chorionic gonadotrophin levels can assist in diagnosis and monitoring of the disease.

Treatment and prognosis

For mature and immature teratoma as well as malignant GCTs Stage I, surgery alone can be sufficient, with a survival of more than 90%. For more advanced malignant GCTs, four to six cycles of platinum-compound-based chemotherapy in addition to surgery can achieve a survival of around 70%.

Palliative chemotherapy and radiotherapy

As stated above, if curative treatment is not possible or has failed, the focus must then be on providing palliative care, particularly symptom control, including adequate pain relief (*see* Section 1.15 and Section 1.16). Occasionally, palliative chemotherapy may be appropriate, such as the use of steroids with or without vincristine in relapse or incurable acute lymphoblastic leukaemia and lymphomas. Steroids are also used in the control of symptoms such as headache due to certain brain tumours. Palliative radiotherapy may be useful for treating bone pain caused by tumour infiltration (e.g. in neuroblastoma) and by bone tumours themselves, and may be helpful in controlling symptoms caused by compression of nerves (including the spinal cord) or other vital organs.

Conclusion

Although in many resource-limited countries the curative treatment of children with cancer may not be achievable currently, children will present with often distressing symptoms, which we must strive to alleviate and palliate. As infections in particular become more controllable in resource-limited settings, cancer starts to emerge as a major cause of morbidity and mortality. Some allocation of resources becomes inevitable, and as paediatric oncology requires a multidisciplinary approach, thinking about and acting on the problems faced by children with cancer can lead to improvement of care for all children in hospital.

Organisations working to advance paediatric oncology around the world

World Child Cancer (www.worldchildcancer.org): currently working in Mexico, Colombia, Cameroon, Ghana, Malawi, Mozambique, Bangladesh, the Philippines and the Pacific Islands.

International Confederation of Child Cancer Parent Organisations (ICCCPO) (http://icccpo.org/index.cfm): **an international network of parent support groups and survivor networks that provide psychosocial care for children and their families.**

Maternal Childhealth Advocacy International – Cameroon (www.mcai.org.uk).

St Jude Children's Research Hospital based in the USA (www.stjude.org): a paediatric treatment and research facility. It develops advanced cures for and means of prevention of paediatric cancer through research and treatment. It is involved worldwide in supporting projects through its International Outreach programme, including twinning. It includes the following:

- Cure4kids (www.cure4kids.org): a free online education and collaboration resource dedicated to supporting the care of children with cancer and other catastrophic diseases worldwide.
- Pond4kids (www.pond4kids.org): provides a free database collecting epidemiological data and including a cancer registry.

International Society of Pediatric Oncology (SIOP) (Société Internationale d'Oncologie Pédiatrique) (www.siop-online.org): this organisation has a special focus on paediatric oncology in developing countries (PODC). Some of the relevant working groups include the following:

- twinning, collaboration and support
- graduated-intensity treatment guidelines
- providing advice and support to low-income countries on the most appropriate protocols to use based on the resources available, including financial resources,

training, supportive care, monitoring and investigations, and infection control
- abandonment of treatment
- palliative care
- essential drugs.

International Network for Cancer Treatment and Research (INCTR) (www.inctr.org): this organisation is dedicated to helping to build capacity for cancer research and treatment in developing countries, and it focuses on palliative care, cancer registration, research, training, nursing and pathology services.

Union for International Cancer Control (UICC) World Cancer Congress (www.uicc.org): this organisation focuses on raising awareness, education, and developing a global network of influence.

Franco-African Pediatric Oncology Group (GFAOP) (www.gfaop.org): this runs projects for children with cancer in Africa, including a recent Wilms' tumour protocol trial.

Further reading

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5.15 Eye disorders

BOX 5.15.1 Minimum standards
- Vitamin A.
- Ocular antibiotics.
- Fluorescein.
- Ocular steroids.
- Aciclovir.
- Occlusive pads.
- Glasses and other visual aids.

Introduction

Two of the most important eye disorders in children in resource-limited countries are vitamin A deficiency (xerophthalmia) and trachoma. Both of these can be prevented by appropriate action in the community, which is cheap and very effective for both disorders.

Eye examination and diagnosis: basic equipment

- Vision-testing chart. Show only one letter at a time and get the child to match the letter on a chart (*see* Figure 5.15.1).
- A bright torch light which can give a focused beam of light.
- An ophthalmoscope:
  - The ophthalmoscope is mainly used for examination of the ocular fundus (i.e. the retina, choroid and optic nerve).
  - It can also be used for examination of the ocular media (i.e. the cornea, lens, and aqueous and vitreous humour). Dial a small positive lens (about +2 or +3) in the ophthalmoscope, and hold it about 20 cm from the patient's eye. In the healthy eye with a dilated pupil, there will be a clear red glow of light reflected from the retina, called the red reflex, and any opacity in the cornea, lens or aqueous or vitreous humour will appear as a black shadow against this red reflex.
  - The ophthalmoscope can also be used to act like a magnifying lens to examine in detail the conjunctiva, sclera, iris, etc. To do this a very strong positive lens (about +20) is dialled in the ophthalmoscope, which is then held very close to the patient's eye.

  An ultra-low-cost ophthalmoscope, otoscope and loupe which is solar powered is now available (www.arclightscope.com).
- Mydriatic drops:
  - **Cyclopentolate 1%, or cyclopentolate 0.5%** in children less than 6 months old. **Atropine 0.5%**

FIGURE 5.15.1 Eye testing.

ointment is very long-acting. It can be given to parents to put into the eyes for 2 days prior to a clinic appointment, especially if an initial attempt at refraction and fundus examination has been unsuccessful because of the child becoming distressed when drops were used in the clinic.

- Local anaesthetic drops:
  - **Proxymetacaine 0.5% is ideal for children because it stings less than other topical anaesthetic drops. Tetracaine 0.5% or 1%** is an alternative which is less quickly degraded when not stored in the refrigerator.
- Sterile **fluorescein** paper strips.
- Binocular telescopic magnifying glasses (loupes) are very useful but not essential. Some magnification will be achieved by using a strong pair of reading glasses (+3.00–4.00 DS) perched as far down your nose as possible.
- More sophisticated equipment, such as a tonometer for measuring intra-ocular pressure, a slit lamp and a binocular indirect ophthalmoscope, may only be available in a specialist clinic. However, if available, they greatly add to the diagnosis and treatment that can be offered.

Gaining the confidence and trust of the child is the most important step in a successful eye examination, which should not be painful or unpleasant, except possibly unavoidably when drops are put in the child's eye. If the child finds it hard to cooperate, examine the parents' or older siblings' eyes first to gain the child's confidence. A general anaesthetic may sometimes be required in small children where a serious eye problem (e.g. retinoblastoma) is suspected.

FIGURE 5.15.2 Position in which to examine the eye of a young child.

Three ways of examining the eyes of young children

Examining the eyes of babies and young children is often difficult. Patience and encouragement are required to gain the confidence of the child. If it is still difficult to get a good view, the following techniques may be helpful:

1 Let the parent cuddle the child as he or she faces backwards over the parent's shoulder (*see* Figure 5.15.2), especially if the parent's anxiety and sense of obligation to restrain the child is adding to the child's fears. You may then be able to attract the child's interest in participating in the examination from this secure position.
2 In the case of infants, wrap the baby in a sheet or blanket, with their head on the examiner's lap, and their body on their mother's lap (*see* Figure 5.15.3). Gently hold open their lids with the fingers and thumb of one hand. The other hand is then free to instil any eye drops, or hold a torch or condensing lens. This is probably the best way to get a satisfactory view of the eye, but it also provokes the greatest resentment from the baby.
3 If it is difficult to get drops into the child's eye, try lying the child flat on their back, create a puddle of drops at the inner canthus, and wait while the child is held facing upwards (*see* Figure 5.15.4). The child will eventually open their eye, and the medication in the puddle of drops at the inner canthus will then go into the eye.
4 In difficult cases, where a serious eye condition is suspected, it may be necessary to instil a drop of local anaesthetic, and use a speculum to hold open the eyelids. However, this should only be done by an experienced professional in controlled circumstances, and must not be attempted in the face of determined resistance from any but the smallest child.

FIGURE 5.15.3 Supine posture for eye examination.

Presenting symptoms of eye disease

These include the following:

- red, sore, irritable or discharging eyes
- impairment or loss of vision
- squint.

Red, sore, irritable or discharging eyes

- A sticky discharge with no redness, normal cornea and apparently normal vision in a child up to the age of 18 months (and occasionally older) is commonly caused by a blocked tear duct. Teach the mother to express the lacrimal sac with firm pressure to the side of the nose at the inner canthus.
- Bilateral sore red irritable eyes are usually caused by conjunctivitis. If the symptom is **unilateral** the usual cause is an ulcer or injury to the cornea or iritis. Evert the upper eyelid to inspect the upper tarsal conjunctiva. Apply fluorescein stain to the cornea to diagnose an ulcer or identify a foreign body. The green fluorescein dye will stain the ulcer. A foreign body, especially if lodged under the upper lid, may be associated with staining of the cornea.

FIGURE 5.15.4 Seated posture for eye examination.

FIGURE 5.15.5 Expressing the lacrimal duct. © www.medscape.com

Conjunctivitis

- **Acute** bacterial conjunctivitis causes a mucopurulent discharge from the conjunctiva and is usually self-limiting, resolving after a few days. Give topical antibiotics as drops or ointment to speed recovery.
- Acute bacterial conjunctivitis is **dangerous in neonates** when caused by sexually transmitted disease. The cornea in a neonate is at much greater risk, and neonates produce less tears to wash away bacteria. **Treatment is urgent.**
- The WHO-recommended treatment for severe neonatal conjunctivitis is a single IM injection of either **ceftriaxone** 50 mg/kg (maximum 125 mg) or **kanamycin** 25 mg/kg (maximum 75 mg) and hourly **tetracycline ointment** or **chloramphenicol drops or ointment**.
- In presumed gonococcal infection, empirical treatment for possible co-infection with chlamydia – that is, ceftriaxone **and** erythromycin to prevent chlamydial pneumonia in the baby – should be strongly considered.

In addition, we recommend diagnosis and treatment of the mother for uro-genital disease due to gonococcus and/or chlamydia in order to prevent salpingitis.

- **Acute viral conjunctivitis** is a self-limiting disease that usually lasts for a week or so. Tear secretions are watery rather than mucopurulent. There is no specific treatment, but it is customary to give antibiotic drops.
- **Vernal conjunctivitis** is a chronic allergic conjunctivitis which is very common and causes recurrent severe itching of the eyes. Affected children are usually atopic (i.e. suffer from asthma and eczema). In addition to itchy eyes, there may be redness, watering, lid swelling and a mucus discharge. Typically there are papillae of the conjunctiva under the upper lid. In some cases these can be massive in size and may be associated with corneal ulceration in the upper third of the cornea. There may be nodular swelling and opacity at the corneo-scleral junction (i.e. the limbus). Anti-inflammatory drops such as cromoglycate relieve the symptoms, but in severe cases use topical steroids (e.g. hydrocortisone 1%, betamethasone 0.1%, or dexamethasone 0.1% eye drops). However, prolonged use of topical steroids has a high risk of causing steroid-induced glaucoma.

Trachoma

See Section 6.1.M.

Corneal ulcers

- Corneal ulcers are usually **unilateral**. There is usually pain and photophobia. Staining the eye with fluorescein will show the outline of the ulcer.
- **Herpes simplex** ulcers are typically branched and irregular. Treat by applying **aciclovir ointment 3%** every 2 hours until the epithelium has healed.
- **Bacterial corneal ulcers** are more serious and can rapidly progress to destroy the cornea and the eye. They must be treated as an emergency. If possible, first perform a Gram stain and microscopy of tissue scraped with great care from the edge of the ulcer with a scalpel blade. This will often give helpful information about the cause of the ulcer and so make the treatment more specific. Antibiotic drops should be given hourly or 2-hourly for 48 hours and then four times a day. The choice of antibiotic depends on the availability and also the results of the Gram stain. Ofloxacin (0.3%) or ciprofloxacin (0.3%) both have a good spectrum of activity against Gram-positive and Gram-negative bacteria. **In most circumstances one of these is the first choice.** Concentrated locally made antibiotic drops are very helpful if pre-prepared drops are not available. These can be made up by diluting antibiotic powder for injection in 5 mL of sterile water or 0.9% saline. These home-made eye drops should only be used for 48 hours, and should then be discarded. The following are the recommended strengths: gentamicin 15 mg/mL or amikacin 50 mg/mL for Gram-negative organisms; cefuroxime, ceftazidime or cefazolin 50 mg/mL for Gram-positive organisms. If a Gram stain is not possible, two types of drops can be given alternately every hour. Chloramphenicol (0.5%

drops and 1% ointment) is a cheap and readily available alternative if none of the above are available.

- **Fungal corneal ulcers** are very common in hot humid climates. The branching filaments of the fungus can be identified on a Gram stain. The treatment is unfortunately very difficult because topical antifungal drugs are hard to obtain and the response to treatment is slow. Natamycin is sometimes available as an eye ointment. Econazole, clotrimazole and ketoconazole are all available as skin creams, and it may be necessary to use either these or systemic antifungal agents in difficult cases.

Iritis

Iritis is a less common cause of acute red eye. The pupil is constricted and irregular and there are often deposits known as keratic precipitates on the posterior surface of the cornea. Give intensive topical steroids hourly (prednisolone, betamethasone or dexamethasone drops) and keep the pupil dilated with mydriatics (atropine 0.5–1% twice daily).

Vitamin A deficiency (xerophthalmia)

Xerophthalmia usually only affects malnourished children (*see* Section 5.10.A on vitamin A deficiency).

- In the early stages, the conjunctiva appears dry and wrinkled, but this is not easy to detect.
- As the disease progresses, the cornea also appears dry and then shows signs of corneal ulceration. Ulcers may progress very rapidly to destroy the entire cornea. Eventually the whole eye shrinks or the child may be left with a dense corneal scar.
- In communities where vitamin A deficiency is common, older children are frequently found with corneal scars dating from early childhood. In most cases malnutrition is a chronic problem, and the disease is precipitated by an acute infective illness, which is nearly always measles. Xerophthalmia and measles are particularly important because these ulcers are very frequently bilateral, whereas most other causes of corneal ulceration and scarring usually only affect one eye.

There are three other factors which may precipitate corneal destruction in xerophthalmia:

- **Herpes simplex:** severe and often bilateral herpes simplex ulcers may develop.
- **Traditional eye medicines:** application of toxic substances may cause damage and chemical burns to the conjunctiva and cornea.
- **Exposure:** sick and malnourished children may lie with their eyes open and exposed, so the cornea is not protected by the eyelid.

Management

- Apply topical antibiotics and ensure adequate closure of the eyelids. Give **local aciclovir** if **herpes simplex** is suspected. Give **topical steroids** (hydrocortisone 1% or betamethasone 0.1% eye drops or ointment) if a clear history of toxic traditional eye medication is obtained.
- Give vitamin A capsules (200 000 IU/day in children over 1 year of age, 100 000 IU/day for those aged 6–12 months, and 50 000/day for those under 6 months, for 2 days, then another dose in 2 weeks). Systemic antibiotics and rehydration may also be indicated.

The child who cannot see or who cannot see well

If only one eye is affected, the child and their family may not be aware of the problem. However, a child with poor vision in one eye only will often develop a squint in that eye (see below).

Cornea

Bilateral corneal scarring that is severe enough to cause serious visual impairment is most commonly a consequence of xerophthalmia and measles (both of which are preventable, by giving vitamin A and immunisation). Careful refraction may improve the sight. An optical iridectomy or a corneal graft may also help.

Cataract

Cataract is the most common congenital ocular abnormality. It may be present at birth, or may develop in early childhood. It may be complete, presenting as a dense white opacity in the pupil, or be incomplete and less obvious. There will be a normal pupillary light reflex, so that the pupil constricts when a light is shone into the eye. In other causes of a white appearance of the pupil, including retinoblastoma, the reaction of the pupil to a light shone in the affected eye is usually lost.

Congenital cataracts require **early expert surgical treatment**, otherwise the child will develop nystagmus, which will prevent the development of good vision.

Congenital glaucoma

Congenital glaucoma usually presents with photophobia, a hazy cornea and often enlargement of the eye called buphthalmos. Urgent specialist surgery is required to control intra-ocular pressure and save what sight is available, otherwise the child will become irreversibly blind.

Retinal diseases

- **Retinopathy of prematurity** is the commonest cause of acquired retinal disease. It is associated with excessive oxygen given to premature babies (*see* Section 3.4). It is now particularly common in middle-income countries, such as Latin America, Eastern Europe, the Middle East and Asia. In countries with highly developed intensive neonatal care services it is uncommon, and in resource-limited countries most very premature babies do not survive.
- **Retinitis pigmentosa** is the most common congenital disorder of the retina. It affects the peripheral retina and causes night blindness.
- **Vitamin A deficiency** also causes night blindness by affecting rod photoreceptors in the peripheral retina.
- **Retinoblastoma** is important because **it is one of the few eye diseases that can be fatal in a child if not properly treated.** The tumour can present in one eye or in both eyes as a white mass in the pupil, a squint, a painful inflamed eye or a mass in the orbit. If the eye is removed before the tumour has spread, the child's life may be saved.

Optic nerve

Optic nerve hypoplasia or optic atrophy may be congenital. It may also be acquired following meningitis, or rarely following an infection such as typhoid or measles. There is no effective treatment.

Cortical blindness

Cortical blindness occurs following severe brain insults such as meningitis or cerebral malaria. The pupillary light reflex is normal, but the child cannot see. In some cases the vision gradually improves with time.

Management of blindness

- In the majority of cases, management is with rehabilitation and education rather than medical treatment.
- Cataracts and glaucoma in particular must be recognised and diagnosed early to preserve and save as much sight as possible.
- Most blind children have some sight and should have an opportunity to use low-cost visual aids. Simple aids, manufactured locally, may enable children to read and so transform their opportunities for education. These aids may consists of a strongly positive lens worn as spectacles or used as a stand magnifier.

Squint

Squint, or misalignment of the eyes (also known as strabismus), is common in children. When assessing a child for squint, consider the following:

- **Does the child really have a squint?** Look at the corneal light reflexes. If the reflection of light is in the same position in each eye, there is no squint, but if one is asymmetrical then that eye is squinting.
- **Does the squint alternate?** Cover the non-squinting eye. If the squinting eye moves to look at the light or object being held, and if the child can use either eye to fixate, then the squint alternates. This means that the vision is fairly good in each eye, and the treatment of the squint is purely cosmetic.
- **If the squint does not alternate, is there any disease in the squinting eye?** Test the pupillary light reflex and then dilate the pupils with mydriatic eye drops. Look for diseases such as cataract, retinal scar and in particular retinoblastoma. Refer the child for treatment if you find cataract or an abnormality in the retina. Treatment for retinoblastoma is urgent enucleation.
- **Is there a refractive error, such as hypermetropia (long sight) or myopia (short sight)?** This requires refraction tests.
- **Is the squinting eye amblyopic (i.e. is there poor vision in the squinting eye)?** At first, squints cause double vision (diplopia), which the child finds confusing. As time passes, the visual acuity in the squinting eye becomes permanently suppressed. The treatment for amblyopia is to force the child to use the squinting eye by wearing an occlusive patch over the healthy eye for about 1 hour a day for several weeks.

Amblyopia only develops in young children, and it can only be treated in children under 5 years of age. Surgery may be required, but should not be considered until eye disease and refractive errors have been excluded and amblyopia has been treated.

5.16 Neurological disorders

5.16.A Coma

BOX 5.16.1 Minimum standards

- **ABC** and high-dependency care.
- Clinical chemistry.
- Haematology, including blood film for malaria.
- Toxicology, chest X-ray, cultures and lumbar puncture.
- Neuroimaging: CT and MRI (if available).

Introduction

Coma is a state of unresponsiveness, in which the child is unable to be aroused by external stimuli (physical, verbal or sensory) or inner needs. It results from a process either diffusely affecting the cerebral hemispheres or directly impairing the function of the reticular activating system in the brainstem.

It may be caused by:

- systemic disorders (e.g. metabolic encephalopathies)
- intracranial diseases which are either diffuse or focal.

Primary assessment and resuscitation

Coma is a medical emergency that requires immediate assessment and detection of reversible causes. Initial quick resuscitative measures are paramount, before undertaking a full clinical assessment of the child.

History

A detailed history should be taken from the parent or carer, with a focus on the following:

- possible cause of coma
- onset and progression of unconsciousness
- extent of injury
- signs of deterioration or recovery
- past medical history.

Examination

Clinical examination is directed towards identifying signs suggesting the following:

- cause or causes
- extent of injury
- level of consciousness.

A general examination should be undertaken guided by the history and presumptive cause of coma. Identify immediate reversible causes of coma, such as hypoglycaemia, hyperglycaemia, trauma and seizures, and treat them accordingly (*see* Table 5.16.A.1). Look for rashes (e.g. purpura of meningococcaemia), tick bites, signs of trauma, evidence of ingestion of drugs or chemicals, and evidence of organ failure.

TABLE 5.16.A.1 Causes of coma

Trauma	**Head injury** (consider child abuse)
Seizure	Overt **seizures**, status epilepticus, subclinical seizures, post-ictal state
Infections	**Bacterial (meningitis):** *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitidis*, streptococci (group B), *Pseudomonas* species, tuberculosis Consider cerebral abscess
	Viruses: herpes simplex, Japanese B virus (JBV), herpes zoster
	Acute spirochaetaemia: syphilis, Lyme disease, leptospirosis
	Parasitic: malaria, rickettsial
	Fungal: *Cryptococcus neoformans*
Metabolic	**Hypoglycaemia:** Excess insulin or metabolic disorders
	Hyperglycaemia: Diabetic ketoacidosis
	Hypoxaemia
	Electrolyte imbalance: hyponatraemia or hypernatraemia
	Severe dehydration
	Severe malnutrition
	Organ failure: Liver failure, renal failure, Addison's disease, respiratory failure
	Drugs: Opiates, salicylates, organophosphates, benzodiazepines, thiazines, aluminium in patients undergoing dialysis, barbiturates, antidepressants
	Other: Porphyrias, Reye's syndrome
Poisoning	Alcohol, recreational drugs, accidental/deliberate poisoning
Tumours	**Primary:** medulloblastoma, astrocytoma
	Secondary: leukaemias, sarcomas
Vascular	Haemorrhage (subdural/subarachnoid), hypertension, hypotension, thrombosis, aortic stenosis, cardiac asystole, vacuities and collagen vascular syndromes
Shock syndromes	Sepsis, trauma, burns, peritonitis

Causes of coma

The following features found on examination may be indicative of specific causes.

- **Pulse:** bradycardia may indicate raised intracranial pressure (RICP) or reflect the effects of poisons or drug overdose.
- **Blood pressure:** hypertension may indicate hypertensive encephalopathy or signs of RICP; hypotension occurs in shock.
- **Temperature:** this may indicate sepsis.
- **Respiratory pattern:** this may be irregular due to brainstem lesion or RICP, rapid due to acidosis or aspirin ingestion, or slow due to opiate ingestion.
- **Pupil size and reactivity:** pupil may be small due to opiate ingestion, or large due to amphetamine ingestion or RICP; pupils may be unequal and/or unreactive due to RICP.
- **Skin rashes:** these may be due to infections (e.g. meningococcal septicaemia, dengue fever).
- **Breath odour:** this may be caused by diabetic ketoacidosis, alcohol ingestion, or inborn errors of metabolism.
- **Hepatomegaly:** this may indicate Reye's syndrome or other metabolic disorders.
- **Fundi:** Papilloedema may indicate RICP; dilated veins may indicate RICP; retinal haemorrhages may indicate trauma or malaria; and exudates, retinal whitening and orange coloration of vessels may indicate other signs of malaria retinopathy
- **Posture/oculocephalic reflexes** (*see* Figure 5.16.A.2): these are abnormal in RICP.

Neurological examination

The purpose of the neurological examination is not only to identify features of raised intracranial pressure (including herniation syndromes), focal deficits (e.g. space-occupying lesions) and lateralising signs (hemiplegic syndromes), but also to establish a baseline for comparison on subsequent evaluations. Examination may also help to provide prognostic information.

Level of consciousness

Many methods exist for establishing the level of consciousness. Two that are commonly used are the AVPU system, and coma scales.

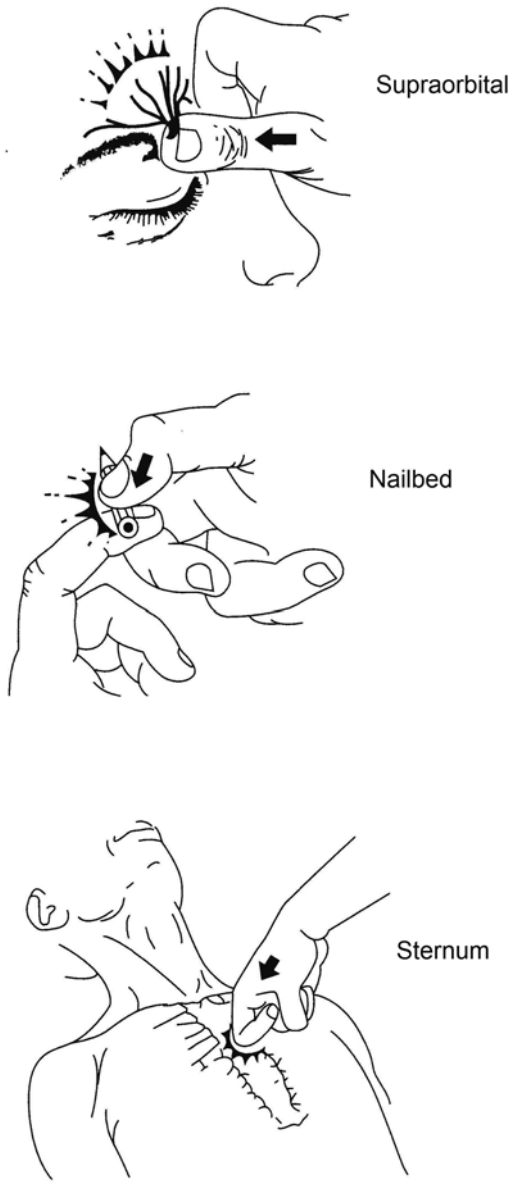

FIGURE 5.16.A.1 Sites for the application of a painful stimulus to elicit a response.

AVPU system

A = Alert
V = Response to Voice command
P = Response to Pain
U = Unresponsive

In this test:

- 'A' means that the patient is awake, alert and interacting with the environment.
- 'V' means that the patient appears to be asleep, but when spoken to opens their eyes.
- 'P' indicates that there is no response to a voice. but a painful stimulus will produce some response (e.g. a withdrawal).
- 'U' indicates that the patient is completely unresponsive to any stimulus.

Figure 5.16.A.1 shows sites for the application of a painful stimulus in order to elicit a response.

TABLE 5.16.A.2 Glasgow Coma Scale

Activity	Best response	Score
Eye opening	Spontaneous	4
	To verbal stimuli	3
	To pain	2
	None	1
Verbal	Orientated	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	None to pain	1
Motor	Follows commands	6
	Localises pain	5
	Withdraws in response to pain	4
	Abnormal flexion in response to pain (decorticate)	3
	Abnormal extension in response to pain (decerebrate)	2
	No response to pain	1

TABLE 5.16.A.3 Adelaide Coma Scale

Activity	Best response	Score
Eye opening	Eyes open spontaneously	4
	To request	3
	To pain	2
	No response to pain	1
Verbal	Orientated, alert	5
	Recognisable and relevant words but less than usual, spontaneous cry	4
	Cries only to pain	3
	Moans only to pain	2
	No response to pain	1
Motor	Obeys commands	6
	Localises painful stimulus	5
	Withdrawal from pain	4
	Abnormal flexion to pain (decorticate)	3
	Abnormal extension to pain (decerebrate)	2
	No response to pain	1

Coma scales

These have been devised to measure the depth of coma and improve agreement between clinicians. Coma scales can also be used to monitor progression or regression of the depth of coma. Although many different versions exist, the most widely used ones are the paediatric modification of the Glasgow Coma Scale (for children between the ages of 4 years and 15 years) and the Adelaide Coma Scale (for children under 4 years of age).

Pupillary reactions

Use a bright torch and from the side shine the light on the cornea of each eye in turn. Observe for pupillary size

(constricted or dilated) and the reaction to light (normal, sluggish or non-reactive). While doing this test consider the effect of drugs used in treatment (e.g. benzodiazepines).

Ocular movements

- Eyelid response.
- Corneal response.

Oculocephalic reflexes (doll's head manoeuvre)

In the normal state while turning the head sharply to one side, the eyes move to the opposite side. In the abnormal state the eyes only partly deviate or remain fixed (*see* Figure 5.16.A.2).

Before performing this test it is important to check that there is no cervical injury.

Oculo-vestibular or caloric response

Tilt the head forward at 30 degrees, and instil ice cold water in the ear. In the normal state the eyes turn to the side of the stimulus (*see* Figure 5.16.A.2). This manoeuvre tests brainstem function.

Before doing this test it is important to ascertain that the tympanic membrane is intact and there is no wax in the external meatus.

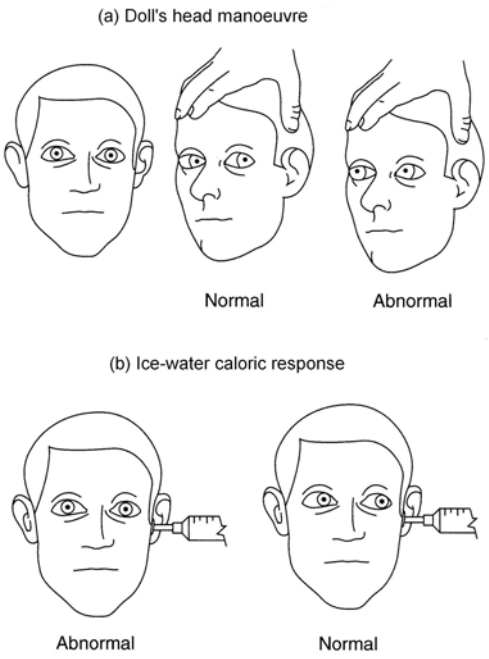

FIGURE 5.16.A.2 Oculocephalic reflex (doll's head manoeuvre) and oculo-vestibular response (ice-water caloric response).

Motor function and activity

Observe for tremors, abnormal movements and tone. The presence of hypertonia or hypotonia indicates a neuro-muscular problem. Exaggerated deep tendon reflexes and clonus may indicate an upper motor neuron type lesion, whereas their absence may indicate a lower motor neuron type problem.

Abnormal postures in an unconscious patient (e.g. decerebrate or decorticate rigidity) may indicate brain damage at cerebral or cortical level (*see* Figure 5.16.A.3).

Respiratory pattern

Abnormal variations in breathing pattern may be difficult to identify in children. The following may be sought for:

- **irregular:** consider seizures
- **Cheyne–Stokes:** raised intracranial pressure, cardiac failure
- **Kussmaul breathing:** acidosis, central neurogenic hyperventilation, midbrain injury, tumour or stroke
- **apneustic (periodic) breathing:** pontine damage, central herniation.

Signs and symptoms of raised intracranial pressure

- Preceding history of headache.
- Recurrent vomiting.
- Sixth (abducens nerve) cranial nerve palsy.
- Sluggish or no pupillary reaction.
- Dilated retinal veins with reduced pulsations.
- Papilloedema.
- Subhyaloid retinal haemorrhages.
- Bradycardia.
- Raised blood pressure.
- Irregular respiration.

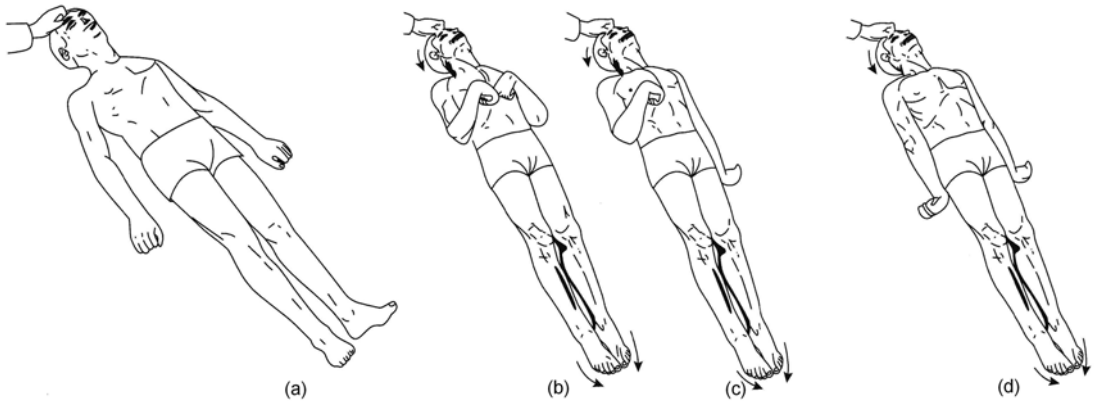

FIGURE 5.16.A.3 Abnormal postures elicited in an unconscious patient by a painful stimulus. (a) No response. (b) Decorticate. (c) Mixed decorticate/decerebrate. (d) Decerebrate.

Investigations

These are guided by the presumptive clinical diagnosis. Essential tests may include the following:

- **Clinical chemistry** for blood glucose, electrolytes, creatinine, urea, blood gases and liver function tests (including clotting profile).
- **Blood film** for malarial parasites.
- **Haematological parameters** such as full blood count and peripheral blood film. Toxicological tests for salicylates, organophosphates, opiates, alcohol and paracetamol.
- **Blood cultures.**
- **Lumbar puncture** if there is a high index of suspicion of central nervous system infection. This should be delayed if there are features suggestive of raised intracranial pressure, the child is too sick, there is infection at the puncture site, there is a bleeding tendency or there is rash of meningococcal septicaemia. The child should be given antibiotics to cover the possibility of bacterial meningitis, and lumbar puncture should be deferred until a later date.
- **Chest X-ray** if there is suspicion of tuberculosis or severe pneumonia.

If facilities are available, consider the following:

- Computerised tomography (CT) scan or preferably magnetic resonance imaging (MRI) scan. These are particularly useful for detecting space-occupying lesions and traumatic injury. Contrast dye should be given if an infection or a tumour is suspected.
- Plasma ammonia level and plasma and CSF lactate levels.
- Urine and plasma for organic and amino acids.

Other investigations (if available)

These will depend on the cause of the coma, and include the following:

- **Hormonal assays:** thyroid hormones, cortisol, ketosteroids (adrenal insufficiency).
- **Electroencephalography (EEG):** this may be helpful in detecting seizures or encephalitis. It may also be useful in establishing the prognosis.
- **Evoked potential responses:** these may help to detect brainstem lesions.
- **Neuroimaging:** magnetic resonance angiography or MRI or CT scan.

Differential diagnosis

A simple way to establish a cause would be to determine whether it is primarily intra- or extracranial. Intracranial conditions may be subdivided into those with or without focal signs. Extracranial causes include encephalopathies arising from metabolic derangements or exogenous toxins. The common causes are listed in Table 5.16.A.1.

Management

The prognosis depends on the aetiology, age of the patient, and level of consciousness at presentation. The presumptive cause of coma guides the treatment and the initial response to appropriate interventions.

See subsequent subsections and disease-specific sections (e.g. meningitis (Section 5.16.B), malaria (Section 6.3.A.d), tuberculosis (Section 6.1.N)). Consider the following interventions for general coma management.

Immediate general management: overview – see relevant sections for detail

ABC support of vital functions (*see* Section 1.11)

- **Support respiration** if respiratory effort is not adequate to maintain the desired oxygen saturation and/or carbon dioxide excretion.
- **Support circulation** to maintain adequate cerebral perfusion (aim to keep systolic blood pressure at normal values for age, and avoid hypotension).
- Assess for and treat **hypoglycaemia** (*see* Section 5.8.B)
- **Maintain normoglycaemic state:** be cautious about administering insulin to hyperglycaemic patients, as hyperglycaemia may be stress induced.
- **Assess and maintain electrolyte balance:** avoid hyponatremia: use Ringer-lactate or Hartmann's solution, both with added glucose (50 mL of 50% glucose in 500 mL of crystalloid gives a 5% solution, 100 mL gives a 10% solution). If possible keep serum sodium levels in the normal range (135–145 mmol/litre).
- **Treat seizures** if present and give prophylactic anticonvulsants if the child has repeated seizures (*see* Section 5.16.E and 5.16.D).
- Treat for meningitis if this is an acute illness (*see* Section 5.16.B).
- Treat for cerebral malaria if history and test confirm (*see* Section 6.3.A.d).
- Insert a nasogastric tube to **aspirate the stomach contents**. Perform gastric lavage in circumstances such as drug or chemical ingestion.
- Assess for and treat hypoglycaemia (*see* Section 5.8.B)
- **Regulate the body temperature** (avoid hyperthermia, i.e. temperature > 37.5°C).
- Undertake appropriate **medical management of raised intracranial pressure**.
- **Support ventilation** (maintain a **pCO_2** of 3.5–5.0 kPa).
- **Reduce raised intracranial pressure** by using the following:
  - **Mannitol:** 250–500 mg/kg, i.e. 1.25–2.5 mL/kg of 20% IV over 15 minutes; repeat as required based on response and clinical signs (maximum total dose 2 grams/kg).
  - **Hypertonic saline:** 3 mL/kg of 3% sodium chloride as required, to a maximum increase of plasma sodium level of 10 mmol/litre.
- **Dexamethasone** (for life threatening cerebral oedema surrounding a space-occupying lesion):
  - Child under 35 kg; 20 mg initially then 4 mg 3 hourly for 3 days, then 4 mg every 6 hours for 1 day, then 2 mg every 6 hours for 4 days then decrease by 1 mg daily.
  - Child over 35 kg; 25 mg initially, then 4 mg 2 hourly for 3 days, then 4 mg 4 hourly for 1 day, then 4 mg 6 hourly for 4 days then decrease by 2 mg daily.
- **Catheterisation** for bladder care and urine-output monitoring.
- Plan for continued **regular clinical assessment**, mainly nursing observations of pulse, respiration, blood pressure and level of consciousness.

Intermediate general management

- Prevent the child from falling out of the bed.
- Nutritional support: give enteral nutrients to prevent malnutrition during periods of unconsciousness.
- Skin care: prevent bed sores by turning the patient.
- Use eye padding to avoid xerophthalmia.

- Family counselling, support and consent in the case of invasive procedures.
- Chest physiotherapy is needed to avoid hypostatic pneumonia.
- Restrict fluids to 80% of maintenance if evidence of water retention is seen.
- Prevent deep vein thrombosis by physiotherapy and/or use of anti-embolism stockings.
- Maintain oral and dental hygiene.
- To avoid infection, provide appropriate care for central and peripheral venous or arterial access by maintaining sterility when handling the sites.
- Be alert for hospital-acquired infection.

Long-term management

Provide rehabilitation, family education and support for disabilities that may arise. Seizures need to be looked for and treated.

Cerebral malaria (see Section 6.3.A.d)

In endemic areas, malaria is by far the commonest cause of coma. The majority of children affected are in the second year of life. Onset of coma is dramatic: the child may be well in the morning and comatose by the evening. The fatality rate is high even after prompt administration of antimalarial drugs. Neurological sequelae (i.e. hemiplegia, spasticity, blindness, deafness) may occur.

5.16.B Bacterial meningitis

BOX 5.16.B.1 Minimum standards

- Lumbar puncture.
- Early parenteral antibiotics.
- Antituberculous drugs (if indicated).
- Dexamethasone (if indicated).
- Anticonvulsants.
- Monitoring of vital signs, fluid balance, blood glucose and electrolytes.
- Immunisation and/or prophylaxis for contacts.
- Follow-up for neurological sequelae.

The incidence of bacterial meningitis is about ten times higher in resource-limited than in well-resourced countries, and the outcome is worse. Mortality is reported to be 12–44% in resource-limited countries, and less than 5% in well-resourced countries. In the former, sequelae are under-reported and frequent (20%), including significant neurological impairment and hearing loss.

Pathogens that cause meningitis

- Worldwide, the commonest pathogens are *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria meningitidis*. **Local incidence varies, and in many countries has been altered by vaccine availability.**
- Neonatal meningitis is most commonly caused by group B streptococcus (*Streptococcus agalactiae*) and *E. coli.* Other coliforms and streptococci, as well as *Neisseria meningitidis* and *Listeria monocytogenes*, may also occur. *Listeria monocytogenes* and Group B streptococci cause both early and late neonatal infections, and may have a better prognosis than infections caused by coliforms. Neonatal meningitis has a poorer prognosis than most community-acquired meningitis of later childhood.

Diagnosis of meningitis

Clinical

- **In infants and children:** fever, neck stiffness, bulging fontanelle (in infants), vomiting, headache, altered consciousness and possibly convulsions. In meningococcal meningitis there may be a maculopapular or petechial rash.
- **In neonates:** signs are more subtle and non-specific and include poor feeding, hyper- or hypothermia, convulsions, apnoea, irritability and a bulging fontanelle.

Laboratory

- Contraindications to lumbar puncture include evidence of raised intracranial pressure (especially coma or focal neurological signs), the child being too sick to tolerate a flexed position, infection at the puncture site, bleeding tendency (blood clotting or platelet disorder), or a widespread petechial rash suggesting meningococcal disease. In these situations, antibiotics should be started and lumbar puncture delayed until it is safe to undertake.
- Gram stain of CSF may identify bacteria in about two-thirds of cases, and provides a guide to choice of antibiotic therapy in the absence of culture facilities.
- Other laboratory tests of use include blood culture and polymerase chain reaction (PCR) of CSF, and for general management, full blood count, serum electrolytes and glucose levels, and urine specific gravity. In malarial areas, undertake a blood smear and treat appropriately. Both meningitis and malaria may coexist in a patient and be difficult to distinguish from each other.

Other pathogens

Consider tuberculous meningitis in children who do not respond to the initial antibiotics, particularly if two or more of the following are present: history more than 7 days, HIV known or suspected, patient remains unconscious, CSF has a moderately high white blood cell count (typically > 300–500/mL, mostly lymphocytes), elevated protein levels (0.8–4 grams/litre) and low glucose levels (< 1.5 mmol/litre), Chest X-ray suggests tuberculosis, optic atrophy, focal neurological deficit or extrapyramidal movements (*see* Section 6.1.N).

Children with HIV are more prone to meningitis and septicaemia caused by *Streptococcus pneumoniae* and *Salmonella* species, and relapse is more frequent. Non-typhoidal *Salmonella* (NTS) meningitis is common in post-malarial anaemia and malnutrition, and requires lengthy antibiotic treatment (at least 1 month).

Fungal infections (e.g. *Cryptococcus neoformans*),

TABLE 5.16.B.1 Bacterial meningitis: typical findings in cerebrospinal fluid

Condition	White cell count ($\times 10^9$/L)	Cell differential	Protein (g/litre)	Glucose (mmol/litre)
Normal	0.5 < 22 in full term, < 30 in premature neonates	PMN ≤ 2 but < 15 in neonate	< 0.5	Two-thirds blood glucose
Acute bacterial meningitis*	100 to > 300 000	Mostly PMN. Monocytes in *Listeria* infection	> 1.0	< 2.5
Tuberculous meningitis	50–500 sometimes higher	Lymphocytes early but also PMN	> 1.0	< 2.5, Usually 0
Herpes encephalitis	usually < 500	Mostly lymphocytes PMN early in the disease	> 0.5	Normal
Cerebral abscess	10–200	PMN or lymphocytes	> 1.0	Normal
Traumatic tap	WBC and RBC	RBC/WBC =500/1	Increases by 0.001 g/L per 1000 RBC	

*Bacterial meningitis can occur without a pleocytosis. Partial treatment will alter these findings. PMN, polymorphonuclear granulocytosis; WBC, white blood cell count; RBC, red blood cell count.

mostly in children with HIV, often cause severe headache without neck stiffness. Lumbar puncture may improve symptoms.

Therapy

Antibiotic choices depend upon activity against the infecting organism, CSF penetration, cost and availability of the antibiotic, route of administration, and local patterns of antibiotic resistance (*see* Tables 5.16.B.2, 5.16.B.3 and 5.16.B.4). If national guidelines are available they should be followed. The degree of diagnostic certainty is also important, especially in the case of meningitis with minimal rash, as treatment should be given for all the common causes of bacterial meningitis according to the child's age group.

It is important to know the antimicrobial sensitivities in the local area. Antimicrobial resistance has emerged among the three major bacterial pathogens that cause meningitis outside the neonatal period. In the meningococcus, intermediate penicillin resistance may occur and chloramphenicol resistance is emerging. *Haemophilus influenzae* infections are also frequently beta-lactamase resistant, and chloramphenicol resistance has been described. Third-generation cephalosporins are therefore the drugs of choice for both organisms, although if they are precluded on the basis of cost, chloramphenicol (plus penicillin or ampicillin) is an alternative. Pneumococci resistant to penicillin and to chloramphenicol are widespread in Asia and some parts of Africa, and third-generation cephalosporins are again the drugs of choice. However, pneumococcal resistance to third-generation cephalosporins may occur. Treatment of these strains requires the addition of vancomycin or rifampicin to therapy with third-generation cephalosporins.

Third-generation cephalosporins (ceftriaxone or cefotaxime) may be necessary first-choice antibiotics in some areas. In neonates, ceftazidime, which is also active against *Pseudomonas* infections, may be the most suitable drug.

The antibiotic regimen should be rationalised once culture and sensitivity results for the infecting organism become available.

During confirmed epidemics of meningococcal meningitis and where there are other signs such as petechial rash, lumbar punctures are unnecessary. If resources are very limited, oily chloramphenicol (100 mg/kg IM) as a single dose of up to 3 grams can be curative. If the oily dose is too large for one buttock, divide it into two doses. Alternatively, single-dose IM ceftriaxone, 100 mg/kg up to 4 grams, may be recommended.

Duration of therapy

Neonates require 14–21 days of treatment. In infants and children, a 10-day course is usually adequate for pneumococcal and *Haemophilus* infections, and a 7-day course for meningococcal infections. Seven days of ceftriaxone treatment is usually sufficient. Where antibiotic availability is very limited, some authors have used 5- to 7-day courses of ceftriaxone for uncomplicated meningococcal, pneumococcal or *Haemophilus* meningitis in infants and children.

Corticosteroids

Dexamethasone may reduce the incidence of neurological sequelae and deafness in bacterial meningitis, **although studies in resource-limited countries have been inconclusive. The usually recommended dose of dexamethasone is 0.15 mg/kg four times daily for 4 days (or if this is not available, prednisolone 2 mg/kg per day for 4 days).** The first dose should be given concurrently with, or a maximum of 4 hours after, first antibiotic administration.

There is **no** evidence that corticosteroids are helpful in bacterial meningitis where there is delay in presentation and antibiotics have already been given some hours earlier. Steroids are generally not indicated in meningococcal disease.

Do not use steroids in the newborn or in children younger than 3 months, or in patients with suspected cerebral malaria or viral encephalitis.

Nursing and ongoing care

Monitoring

- Careful observation is essential.
- Raised ICP and shock are the most severe complications. Early recognition and treatment are essential.
- Daily weights and urine specific gravity aid the assessment of fluid requirement.
- Temperature, pulse, blood pressure, capillary refill time (normal value is less than 3 seconds), respiratory rate

and effort, conscious level and pupillary responses should be monitored frequently after admission (4- to 6-hourly), particularly in patients with meningococcal disease (*see* Section 6.1.G). Pulse oximetry is valuable (if available) for monitoring oxygenation and for identifying early evidence of respiratory compromise.

- A critical care pathway is an ideal way of incorporating observations, treatment and laboratory findings on one chart. Doses and treatments can be standardised and incorporated on the chart.
- Ideally, if available, monitor electrolytes (sodium, potassium, calcium and magnesium, urea and/or creatinine) and replacement of fluid deficits (hyponatraemia due to excessive IV administration of hypo-osmolar solutions is common, and can predispose to seizures). Monitoring of full blood count and coagulation screen should be undertaken regularly if these are initially abnormal.

Supportive care

Fluids

Maintenance fluids should be given once any shock or dehydration has been corrected, initially by the IV route but later by nasogastric tube or orally. The degree of dehydration may be underestimated, and deep breathing may be a sign of acidosis. Low serum sodium levels often occur in meningitis. Avoid over-hydration by maintaining careful fluid balance, and in particular avoid IV fluids with low sodium levels such as 5% glucose. Use Hartmann's solution with added glucose (5–10%) or a similar proprietary fluid. If electrolytes are being measured, maintain serum Na^+ in the high normal range and above 135 mmol/litre.

Fluid balance

Urine output should be monitored, particularly in the unconscious child. Weighing nappies can be useful in the infant or young child. Catheterisation, unless undertaken in an aseptic way, can lead to urinary tract infection and is unwise if resources are limited.

Cerebral support

Seizures must be controlled with anticonvulsants, but there are no data to support routine use of prophylactic anticonvulsants (*see* Section 5.16.D and Section 5.16.A on seizures and coma).

If there is a high **fever** (> 39°C), apply temperature reduction methods, including paracetamol.

Blood glucose levels must be monitored every 4 hours, particularly in the infant and young child. Hypoglycaemia must be considered in any child with seizures or altered consciousness and corrected as follows: give 2–5 mL/kg of 10% glucose IV and recheck blood glucose levels 30 minutes later. If they remain low (less than 2.5 mmol/litre), repeat the IV glucose dose (5 mL/kg) and ensure that glucose is included in any infusion.

Gastric and airway protection

A **nasogastric tube** may be helpful in unconscious children or in those who are vomiting, in order to protect the airway. A small amount of milk (1 mL/kg/hour) passed down this nasogastric tube may prevent gastric erosions. Gastric protection may also be provided by using drugs such as ranitidine or omeprazole (if available).

Nutritional support

A **nasogastric tube** should be inserted if the child is unable to feed orally after 24 hours. Continue expressed breast milk if the child is breastfed, or give milk feeds 15 mL/kg every 3 hours.

Bedside care

Turn an unconscious child 2-hourly, keeping them dry, and prevent overheating. Insert a nasogastric tube if there is persistent vomiting.

Include the mother or family members in progress reports, and make them part of the caring team.

Complications

- Convulsions with or without hypoglycaemia (*see* Sections 5.16.D and E for management of convulsions).
- If fever does not settle within 48 hours and if the child's condition deteriorates or is not improving, repeat lumbar puncture and review the CSF findings, and consider drug resistance and tuberculous meningitis.
- If the fontanelle is patent, monitor the head circumference daily to detect hydrocephalus. Consider a head ultrasound scan to look for ventriculitis, ventricular dilatation, subdural effusion or brain abscess. In older children, computed tomography or magnetic resonance imaging may be helpful for assessing the size and position of any intracranial lesion (if available and if intervention is possible).
- Aspiration pneumonia may occur in the unconscious child.
- Hydrocephalus, deafness, visual loss, epilepsy and neurological deficits may develop and be evident either early in disease or at follow-up. Around 20% of cases worldwide will develop serious sequelae.

Follow-up

- Undertake hearing tests in all children, and neurological assessments and head circumference measurements (in infants) on discharge from hospital and at post-discharge visits 1 month and 6 months after recovery. In the absence of effective treatment, a deaf child will require training in lip-reading and sign language, and they and their family will need significant support.
- New sequelae are unlikely to develop after discharge, but may have been missed.
- Physiotherapy may be required if neurological sequelae have resulted in contractures.

Immunisation to prevent meningitis

Highly effective protein-conjugated polysaccharide vaccines are available against *Haemophilus influenzae* and several serogroups of *Streptococcus pneumoniae* and *Neisseria meningitidis*. They are effective in young infants as well as in older children and adults. If they are unavailable, plain polysaccharide vaccines against *Neisseria meningitidis* and *Streptococcus pneumoniae* may be provided. Vaccine availability may be limited in low-income countries.

TABLE 5.16.B.2 Antibiotic choices by age group for immediate treatment and where the infecting organism is not known

Age group	Probable pathogen	Antibiotics of choice	Alternative antibiotics
Neonates	Gram-negative bacteria Group B streptococci *Listeria* *Neisseria meningitidis* *Streptococcus pneumoniae* *Haemophilus influenzae*	Ampicillin **plus** third-generation cephalosporin: cefotaxime/ceftriaxone	Penicillin (but use ampicillin if *Listeria* is suspected) **plus** gentamicin or ceftazidime
1 month to 5 years	*Neisseria meningitidis* *Streptococcus pneumoniae* *Haemophilus influenzae*	Third-generation cephalosporin: cefotaxime/ceftriaxone Add vancomycin or rifampicin if there is *S. pneumoniae* resistance	Chloramphenicol **plus** ampicillin Add vancomycin or rifampicin if there is *S. pneumoniae* resistance
Children over 5 years	*Neisseria meningitidis* *Streptococcus pneumoniae*	Third-generation cephalosporin: cefotaxime/ceftriaxone Add vancomycin or rifampicin if there is *S. pneumoniae* resistance	Chloramphenicol **plus** ampicillin Add vancomycin or rifampicin if there is *S. pneumoniae* resistance

For all age groups, if there is no improvement after the third day, look for evidence of cerebral abscess or subdural effusions, where relevant. These would manifest as continuing fever, localising neurological signs or decreased consciousness. Ultrasound or CT (if available) would be helpful. Seek neurosurgical advice (if available). Repeat the lumbar puncture, looking for evidence of improvement such as a reduced white cell count or increased CSF glucose levels. Add in a third antibiotic. Consider other sites of infection, such as cellulitis, pneumonia with empyema, arthritis or osteomyelitis.

Give all antibiotics parenterally (IV or IM) for at least 3 days. Chloramphenicol can then be given orally if the child is significantly improved.

The IM route may be used if the IV route cannot be accessed. High oral doses of chloramphenicol can be used if there is no alternative, but are not recommended for infants under 3 months of age.

TABLE 5.16.B.3 Antibiotic therapy in bacterial meningitis where the infecting organism is known

Organism	Antibiotics of choice	Alternative antibiotics	Duration
Haemophilus influenzae	Ceftriaxone/cefotaxime	Ampicillin **plus** chloramphenicol*	10–14 days
Streptococcus pneumoniae†	Ceftriaxone/cefotaxime	Ampicillin/benzylpenicillin **plus** chloramphenicol*	10–14 days
Neisseria meningitidis	Ceftriaxone/cefotaxime	Benzylpenicillin **plus** chloramphenicol*	7 days
Gram-negative bacilli (including *E. coli*)	Ceftriaxone/cefotaxime with or without gentamicin	Ampicillin **plus** gentamicin or chloramphenicol*	At least 21 days‡
Salmonella enteritidis	Ceftriaxone/cefotaxime **plus** IV ciprofloxacin (if available)	Meropenem or chloramphenicol* **plus** ampicillin (may be incomplete cover and excess mortality compared with cephalosporins)	At least 21 days‡
Listeria monocytogenes	Ampicillin **plus** gentamicin		10–14 days
Group B streptococcus	Benzylpenicillin **plus** gentamicin or ceftriaxone/cefotaxime		10–14 days
Staphylococcus species	Flucloxacillin **plus** gentamicin	Flucloxacillin **plus** chloramphenicol*	10–14 days

* Chloramphenicol should be used with caution in children under 3 months of age. Monitoring of serum levels is advisable in this group.

† *Streptococcus pneumoniae* infections that are resistant to penicillins and cephalosporins are increasingly prevalent. If resistance is suspected, add either rifampicin or vancomycin (see doses below).

‡ Gram-negative infections are difficult to treat and have a high rate of sequelae. A repeat lumbar pucture to ensure response to antibiotics may be indicated if the clinical picture is not improving.

The choice of antibiotic depends on local antibiotic resistance patterns, national guidelines and drug availability.

Give all antibiotics parenterally for at least 3 days.

Once culture and sensitivity results are available, empirical antibiotics should be changed accordingly.

Do not delay antibiotic therapy if cephalosporins are unavailable; use the next most appropriate antibiotic combination.

Bacterial meningitis: prophylaxis for contacts

Neisseria meningitidis

Give rifampicin to all household contacts for 2 days as follows: adults, 600 mg twice daily; children aged 1 month to 12 years, 10 mg/kg twice daily; neonates, 5 mg/kg twice daily (*see* Section 6.1.G for alternative antibiotics and vaccination regimes).

In many countries, rifampicin is protected from use in any disease other than TB. In this case consider giving ciprofloxacin orally as a single dose as follows: adults, 500 mg; children aged 5–12 years, 250 mg; children aged 1 month to 5 years, 125 mg.

Haemophilus influenzae

Give rifampicin to all non-vaccinated household contacts for 4 days at the doses stated above.

TABLE 5.16.B.4 Bacterial meningitis: antibiotic doses

Antibiotic	Route	Dose
Ampicillin	IV	100 mg/kg/4–6 hourly (max. single dose 2 g every 4 hours)
Benzylpenicillin	IV	50 mg/kg/4 hourly (max. single dose 2.4 g)
Cefotaxime	IV	50 mg/kg/6 hourly (max. daily dose 12 g)
Ceftriaxone	IV or IM	80 mg/kg/24 hours once daily* (max. single dose 4 g) large doses preferably IV
Chloramphenicol	IV	25 mg/kg 6 hourly† (after loading dose of 50 mg/kg)
	Oral	25 mg/kg 6 hourly†
	IM	An oily preparation of chloramphenicol is available and is usually used in a single dose of 50–100 mg/kg with a maximum dose of 3 g. The dose may be repeated after 24 hours. It is recommended only if more suitable alternatives are unavailable
Flucloxacillin or cloxacillin	IV	50 mg/kg 6 hourly (max. dose 8 g/day)
Gentamicin	IV or IM	1 month-12 years 2.5 mg/kg 8 hourly‡ (*see* Section 3.4 for neonatal doses)
Ciprofloxacin	IV	10 mg/kg 8 hourly (10 mg/kg/12 hourly in the neonate)
Meropenem	IV	1 month to 12 years body weight < 50 kg; 40 mg/kg 8 hourly; body weight > 50 kg; 2 g every 8 hours (maximum single dose 2 g) by slow IV injection over 5 minutes 12–18 years 2 g every 8 hours
Vancomycin	IV	15 mg/kg loading dose and then 10 mg/kg 6 hourly‡ (total daily dose should not exceed 2 g)

* Ideally, 80 mg/kg 12-hourly should be given for the first two doses, followed by 80 mg/kg/24 hours.

† Although not recommended in children under 3 months old or in malnourished children, the evidence for this is slight.

‡ Monitoring of drug levels is strongly advised if at all possible, with adjustment of doses.

For doses in the neonatal period, *see* Section 3.4

5.16.C Encephalitis

BOX 5.16.C.1 Minimum standards

- ABCD and intensive care.
- Lumbar puncture, basic clinical chemistry and haematology.
- Temperature control.
- Anticonvulsants.
- Antiviral and antibiotic drugs.

Introduction

Encephalopathy refers to a clinical syndrome of reduced consciousness for which there may be a variety of causes. Encephalitis is an inflammatory process involving primarily the brain parenchyma, but sometimes also the meninges (meningoencephalitis) or spinal cord (encephalomyelitis). Primary encephalitis refers to cases in which the causative agent invades and replicates within the nervous system, whereas in post-infectious encephalitis the clinical manifestations appear to be caused by an immunological response to the agent. In practice it can be difficult to differentiate between the two entities. This subsection focuses on primary infectious encephalitis.

Aetiology

- In many instances no specific aetiological agent can be identified.
- Geographical location and seasonal variation influence the frequency of infection with specific organisms.
- Viruses are the responsible pathogen in the majority of cases (*see* Table 5.16.C.1).
- Arboviruses are an important cause of encephalitis worldwide, but the major contributor within the arbovirus group, the Japanese encephalitis virus (JEV), is limited to Asia and the Pacific Rim.
- Enteroviruses are a common seasonal cause of encephalitis in Europe and the USA. In the last decade there have been periodic large outbreaks of enterovirus 71 infections in Asia, and the overall incidence of enterovirus 71 is increasing in this region.

TABLE 5.16.C.1 Causes of viral encephalitis according to geographical region

America	Europe and the Middle East	Africa	Asia	Australasia
• West Nile Virus • La Crosse • St Louis • Dengue • Rabies	• Tick-borne encephalitis • West Nile virus • Rabies	• West Nile virus • Rift Valley fever virus • Congo-Crimean haemorrhagic fever • Dengue • Rabies	• Enterovirus 71 • Japanese encephalitis • West Nile virus • Dengue • Murray Valley encephalitis • Rabies • Nipah	• Murray Valley Encephalitis • Japanese Encephalitis
• Sporadic causes	• Herpes simplex 1 and 2 • Varicella zoster virus • Epstein–Barr virus • Cytomegalovirus • Human herpes virus 6 and 7 • Coxsackieviruses • Echoviruses • Enteroviruses 70 and 71 • Parechovirus • Poliovirus • Measles • Mumps • Rubella			

TABLE 5.16.C.2 Suggested investigations in children with acute encephalitis, with reference to differential diagnosis

Investigation	Relevance
Blood glucose levels	Hypoglycaemia (common in infants and children with severe infections and poor oral intake/vomiting)
	Hyperglycaemia (diabetes)
	Metabolic encephalopathies, inborn errors of metabolism
Full blood count, blood film	Cerebral malaria (in endemic regions, returning travellers, etc.)
Urea and electrolytes	Hyponatraemia, syndrome of inappropriate secretion of antidiuretic hormone
Liver function tests	Reye's syndrome, metabolic encephalopathies
	Liver failure
Arterial blood gas	Metabolic encephalopathies
	To assess severity, particularly in individuals with brainstem compromise
Ammonia	Reye's syndrome, metabolic encephalopathies
Blood culture and Widal test	Typhoid and other septicaemias may have encephalopathic features
Acute and convalescent serology	To include locally relevant pathogens (e.g. Japanese encephalitis serology in Asia) and those suggested by history and examination (e.g. measles, mumps, varicella, HSV, *Mycoplasma*, *Legionella*)
Toxicology	Heavy metals, pesticides
Erythrocyte sedimentation rate	Collagen vascular disorders
Autoantibodies	Collagen vascular disorders
Cerebrospinal fluid (CSF) • Examination and culture • CSF PCR	Bacterial meningitis Tuberculous meningitis Intracranial haemorrhage HSV Enterovirus 71
Electroencephalography (EEG)	Status epilepticus
Neuroimaging (with contrast enhancement)	Space-occupying lesion (malignancy, brain abscess) Tuberculous meningitis Intracranial haemorrhage

- Herpes simplex type 1 (HSV-1) causes sporadic encephalitis worldwide.
- The common childhood viral infections such as measles, mumps, rubella and chickenpox (varicella zoster virus, VZV) may all involve the nervous system.
- Spirochaetal infections including syphilis, leptospirosis and Lyme disease are a well-recognised cause of meningoencephalitis. Other organisms such as *Brucella* are occasionally implicated. *Mycoplasma pneumoniae* is an important and treatable cause. Neurological

involvement may occur in chlamydial and rickettsial infections, and both fungi (e.g. *Cryptococcus*) and parasites (e.g. *Angiostrongylus cantonensis*) may cause meningoencephalitis.
- Immunocompromised individuals are at particular risk of developing parasitic and fungal infections.
- Encephalitis has been noted to occur following a wide variety of immunisations. Fortunately, improvements in vaccine technology in recent years have meant that such complications are now rare.

Clinical features

Presentation

The following clinical manifestations commonly occur, whatever the aetiological agent:
- An acute systemic illness with fever, headache, nausea and vomiting.
- Generalised seizures, less commonly focal.
- Behavioural or personality changes.
- Deteriorating conscious level, confusion and drowsiness, lapsing into coma.
- Neck stiffness is common but not invariable.
- Signs of involvement of any part of the nervous system may be present (e.g. hemiparesis, ataxia, myelitis, movement disorder, brainstem abnormalities).
- A rash may point to a specific diagnosis (e.g. measles, VZV, enteroviruses).
- Presentation may be subtle and/or subacute in immunocompromised individuals.
- Signs of raised intracranial pressure (ICP) may be present. The possible contribution of raised ICP to the clinical picture should always be considered, as this may be amenable to treatment.

Severity ranges from a mild illness with fever, a single brief seizure and confusion lasting for 2–3 days, to a more prolonged illness with a fluctuating level of consciousness and evolution of neurological signs over several weeks. Occasionally the course may be fulminating, with death occurring within a few days.

Diagnosis

The following investigations (*see* Table 5.16.C.2) should be considered in all cases but may be constrained by lack of resources. Efforts should be directed towards identifying those diseases that are treatable, common locally, or indicated by specific details in the history.

CSF examination and culture provide valuable diagnostic information, but if the child shows evidence of raised ICP, has signs suggestive of a space-occupying lesion or has cardiovascular compromise, lumbar puncture may be contraindicated. Lumbar puncture should be deferred until considered clinically safe, and antimicrobial therapy should be prescribed empirically, directed towards the common pathogens and antibiotic sensitivity patterns in the region.

Typical findings in the CSF in viral encephalitis are documented in Table 5.16.C.3, together with characteristic features on EEG and neuroimaging. In general it is possible to differentiate between viral and bacterial CNS infections on the basis of the CSF picture. If there is doubt, however, empirical antibiotic therapy should be given pending CSF culture results (*see* Section 5.16.B). Alternatively, if the child is stable, the lumbar puncture should be repeated after 24–48 hours while observing the clinical condition closely.

TABLE 5.16.C.3 Typical findings in viral encephalitis

Investigation	Findings
CSF microscopy and biochemistry	• Rarely may be normal • Usually lymphocyte-predominant pleocytosis (from a few to several thousand white blood cells/mm^3) • In early disease, polymorphonuclear cells may predominate • Mildly elevated or normal protein levels • Normal CSF/plasma glucose ratio • Absence of microorganisms on Gram stain • Eosinophilia suggests parasitic infection • India-ink stain: cryptococcus • Normal CSF opening pressure (< 25 cmH_2O)
Electroencephalography (EEG)	• Virtually always abnormal • Diffuse slow waves; occasionally unilateral patterns may suggest particular causative agents, such as HSV (see below) or subacute sclerosing panencephalitis
Neuroimaging: CT or MRI	• May be normal • Cerebral oedema is common • Features may suggest particular causative agents (e.g. HSV, Japanese encephalitis virus)

Management

In the majority of cases no specific treatment is available, and management is primarily supportive.
- Provide bed rest, and analgesia for headaches. Care is needed with sedation, as a deterioration in conscious level may be obscured and/or respiratory depression may occur.
- Antipyretics may be used to alleviate distress, but are no longer recommended solely to reduce the temperature.
- Ensure adequate oxygenation (SaO_2 > 94%).
- Regularly monitor electrolytes and review fluid balance. **Fluid restriction may not be appropriate if the cardiac output is low.** Aim to keep the serum sodium level (and other electrolytes) within the normal range. Consider the possible causes of hyponatraemia (e.g. vomiting/gastrointestinal losses, excessive hypotonic intravenous fluids, over-hydration, syndrome of inappropriate secretion of antidiuretic hormone) and act accordingly.
- Critically ill children, particularly those with evidence of brainstem involvement or raised ICP, should be managed in an intensive-care unit if possible. Assisted ventilation and cardiovascular support should be

instituted early if there is evidence of compromise. Children should be nursed with the head in the midline and tilted 20 degrees up. If they are ventilated, normocapnia should be maintained.
- Control of seizures (*see* Section 5.16.D and E). Caution is required when using anticonvulsant drugs with the potential to cause respiratory depression. EEG monitoring may reveal subclinical seizure activity.
- Intermittent use of mannitol (250–500 mg/kg per dose, which may be repeated after 1 hour) or hypertonic saline may be helpful if there is evidence of raised intracranial pressure (ICP), but remember that electrolyte and fluid balance monitoring are critical (hypernatraemia is as dangerous as hyponatraemia). ICP monitoring should only be undertaken in centres that are experienced in this technique.
- If there are pointers in the history, examination and/or preliminary investigations that suggest a specific diagnosis such as HSV, *Mycoplasma* or Lyme disease, the relevant treatment should be given (see below).
- If bacterial or tuberculous meningitis cannot be excluded, and the child is severely ill, consider providing cover with appropriate drugs until these diagnoses can be definitively ruled out (*see* Section 5.16.B and Section 6.1.N). A second lumbar puncture performed 24–48 hours after admission may aid this decision (provided that raised ICP is not present).

Long-term prognosis

The illness may be prolonged, and survivors may be left with significant neurological sequelae. Physiotherapy and rehabilitation should be commenced once the acute stage of the illness is over and the child is stable. Some children remain in hospital for many months, and relatives require considerable support to cope with the often devastating effects on the family. A number of children without overt neurological sequelae are left with subtle problems, including visual and hearing impairments, learning difficulties and behavioural problems. Long-term follow-up is needed to detect and manage these problems.

Features of specific viral infections that cause encephalitis

Enterovirus 71

- There have been recurrent outbreaks in Asia since the 1990s, and a rising prevalence in the region.
- Children under 5 years of age are most commonly affected.
- These infections can be associated with hand, foot and mouth disease (HFMD) (with vesicular lesions on the hands, feet or mouth) or herpangina (mouth ulcers)
- Neurological involvement includes aseptic meningitis, acute flaccid paralysis, Guillain–Barré-type illness and brainstem encephalitis (cranial nerve involvement, myoclonic jerks and autonomic disturbance). The onset of neurological problems is commonly within the first 3 days of illness.
- Diagnosis is primarily clinical, but viral culture on throat, rectal or vesicle swabs provides supportive evidence. If available, PCR is advisable to identify the specific serotype of enterovirus.
- Children affected with brainstem encephalitis are at risk of cardiopulmonary complications such as shock, pulmonary oedema and/or haemorrhage. They should be managed in a paediatric intensive care unit if possible.
- Polyclonal IgG (2 grams/kg in 24 hours) may be given when there is neurological involvement, although there is no direct evidence to support this therapy at present. There are potential adverse effects, such as anaphylaxis, and IVIG should only be administered with cardiac monitoring facilities.
- High-level supportive care is necessary for patients with cardiopulmonary compromise, but there is a high case fatality and morbidity in this group.

Japanese encephalitis virus

- This is the most common cause of encephalitis worldwide. There are an estimated 50 000 cases and 15 000 deaths each year.
- It is currently limited to Asia and the Pacific Rim, but there is evidence that previously non-endemic regions such as Tibet have cases.
- The virus is transmitted by *Culex* mosquitoes, with an enzootic cycle involving pigs and birds.
- Most infections are asymptomatic (200–300 asymptomatic cases for every case of encephalitis).
- Extrapyramidal and brainstem involvement is common in patients with encephalitis. Patients may have Parkinsonian features acutely, with some later developing choreoathetoid movement disorders. Gradual improvement over several months is usual in survivors.
- Myelitis may occur, usually accompanied by some encephalitic features. The prognosis for recovery from myelitis is poor.
- Diagnosis rests on IgM/IgG capture ELISA in serum and CSF. Viral isolation is difficult, as the viraemia is short-lived.
- Thalamic, basal ganglia and brainstem lesions are often apparent on CT or MRI imaging (if available).
- There are no specific features on EEG.
- Treatment is supportive only, but effective vaccines are available.
- The prognosis is poor. Up to 30% of patients with encephalitis die in the acute stage. Neurological sequelae are common in survivors, but do tend to improve with time.

Herpes simplex virus

- This causes sporadic encephalitis worldwide.
- Encephalitis is more frequently a manifestation of recurrent than primary infection. There is no correlation between the presence of herpetic skin lesions and the diagnosis of HSV encephalitis.
- Seizures (both focal and generalised) are a prominent feature.
- Personality changes, temporal lobe phenomena, and dysphasia are also common.
- CSF findings:
  - Lymphocytic pleocytosis: < 50 to 2000/mm^3.
  - Red blood cells are present in CSF in more than 80% of cases, reflecting haemorrhagic necrosis.
  - Protein levels are usually moderately elevated, but may reach very high levels as the disease progresses (3–5 grams/litre).
  - Up to 25% of cases may have a relatively low CSF glucose concentration.

  - Occasionally the CSF is entirely normal in early disease.
- Diagnosis is by polymerase chain reaction (PCR) or serology on CSF. Viral isolation is difficult.
- If the initial CSF PCR is negative but there are ongoing clinical features suggestive of HSV infection (e.g. deteriorating level of consciousness, focal seizures), a repeat lumbar puncture more than 72 hours after the onset of neurology is advisable. Early CSF for PCR may be falsely negative.
- EEG may show a typical pattern of multifocal periodic lateralising episodic discharges (PLEDs) on a slow background, often with a temporal lobe focus.
- CT and MRI (if available) may show lesions (often haemorrhagic) in the temporal lobes. In early disease, scans may be normal.
- **Treatment is with high-dose IV aciclovir for 21 days as an infusion over one hour** (neonate to 3 months 20 mg/kg; 3 months–12 years 500 mg/m^2 (*see* Section 9 for chart on surface area); 12–18 years 10 mg/kg. All doses given 8 hourly: in older child use ideal weight for height if obese).
- Treatment may be stopped if the patient is diagnosed with a clear alternative cause of the encephalitis.
- In those with a definitive diagnosis, it is advisable to have a negative CSF PCR at the end of the treatment course.
- Early diagnosis and treatment improve the outcome significantly. HSV is a possibility in all patients with encephalitis, although in areas of the world where other pathologies such as enterovirus 71 encephalitis are endemic, HSV is responsible for only a very small minority of the total number of cases. **If resources permit, start aciclovir (at the dosage stated above) in all cases without a definitive diagnosis and continue until HSV has been excluded, or an alternative diagnosis has been reached.**
- Mortality can still be up to 20%, with around 15% of cases left with severe sequelae. Relapses occur occasionally, but these are less likely to occur if treatment is continued for 21 days.

Varicella zoster virus (VZV)

- VZV infection usually only results in mild encephalitis, with acute cerebellar ataxia as the main feature. Seizures and coma are rare, and the prognosis is good.

Measles (*see* Section 6.2.E)

- Acute encephalitis may occur 6–8 days after the onset of the rash, and may be severe, with up to 10% mortality and frequent sequelae.
- Delayed chronic encephalitis may also occur in the form of subacute sclerosing panencephalitis (SSPE), presenting with cognitive deterioration and myoclonic jerks. In such cases the EEG shows stereotypic polyphasic complexes on a background of excess slow activity.

Rabies (*see* Section 6.2.H)

- Saliva (plus virus) from an infected mammal enters via a bite, skin abrasion, or rarely through intact skin or mucous membranes.
- The incubation period varies from a few days to many months. A history of animal bite may not be elicited at the time of presentation.
- There is an initial prodrome of fever and malaise lasting a few days, followed by a second phase of excitement, hyperacusis, hydrophobia and pharyngeal spasms.
- Lastly, a paralytic phase occurs (rarely this may be the only manifestation).
- Death is inevitable once neurological signs are apparent.
- Effective prevention is available with the human diploid cell vaccine, and should be combined with passive immunisation if exposure has occurred.

Other organisms

Mycoplasma

- Neurological involvement occurs in up to 7% of infections.
- Both direct invasion of CNS and immune-mediated disease occur.
- Aseptic meningitis, transverse myelitis and Guillain–Barré syndrome are the most common manifestations.
- Diagnosis is by complement fixation titres (if available).
- If the diagnosis is suspected, treat intravenously or enterally if tolerated, with erythromycin, 12.5 mg/kg/dose 6-hourly for 10 days. However, this is not effective for the immune-mediated disease.

Cryptococcus

- This can cause acute fulminant meningoencephalitis in immunocompromised children.
- It may present more subtly in an immunocompetent child.
- Consider when there is prolonged headache, fever, vomiting and focal neurology.
- It it important to have a baseline CSF opening pressure (provided that there are no contraindications).
- There may be normal CSF biochemistry and cell count.
- Diagnosis is based on India ink smear or CSF culture or rapid antigen assay in CSF or serum.
- Start with a 2-week induction treatment phase of an IV infusion over 4–6 hours of amphotericin 250 micrograms/kg once daily increasing as tolerated to 1.5 mg/kg once daily (after a test dose of 100 micrograms/kg to be included in the first calculated dose) plus flucytosine 25 mg/kg/every 6 hours, or fluconazole 6–12 mg/kg/day up to a maximum of 800 mg/day.
- Children with HIV may require higher doses of amphotericin (up to 5 mg/kg/day)
- Amphotericin therapy requires pre-hydration and close supervision for toxicity, including hepatic and renal function tests, electrolyte monitoring and regular full blood counts.
- In settings where amphotericin is not available, fluconazole 12 mg/kg/day up to 1200 mg/day with or without flucytosine 100 mg/kg/day **or** fluconazole 12 mg/kg/day up to 1200 mg/day alone may be used.
- Initial treatment should be followed by an 8-week consolidation phase using fluconazole 6–12 mg/kg/day, up to a maximum of 400–800 mg/day.
- For the maintenance treatment phase, fluconazole 6 mg/kg/day up to a maximum of 200 mg/day is used.
- Raised intracranial pressure may develop during treatment, and prompt recognition is important. If identified, repeated therapeutic lumbar punctures can be helpful in controlling headache and limiting the development of ventricular dilatation, blindness and cranial nerve palsies.
- In HIV-infected individuals, consider antiretroviral therapy

once antifungal treatment is established, but there is a risk of immune reconstitution syndrome.

Human angiostrongylus

- This is predominantly found in the Pacific Islands and Asia, where it is the most common cause of eosinophilic meningoencephalitis.
- The main mode of infection is via consumption of raw snails or other molluscs, freshwater prawns, frogs and contaminated vegetables.
- The hands may become contaminated with larvae that are then directly carried to the mouth by small children.
- Presentation is commonly with acute severe headache, low-grade fever, cranial nerve involvement, visual disturbances, paraesthesia or hyperaesthesia, and raised intracranial pressure.
- Peripheral blood eosinophilia may be very marked.
- Eosinophils are also seen in the CSF. Organisms may invade both the meninges and the brain parenchyma, especially involving the posterior fossa.
- Diagnosis is primarily clinical, relying on a history of likely ingestion of contaminated food, with typical clinical findings and an eosinophilic CSF picture. Serological tests are available, but may be normal in the early stages, and are also difficult to interpret because there is great cross-reactivity with other parasites.
- MRI (if available) may show multiple micronodular enhancing lesions.
- In many cases the symptoms spontaneously resolve within several weeks (mean period of 20 days).
- It is rarely fatal, and sequelae are usually minimal. A minority of patients have persistent paraesthesia and weakness associated with chronic infection.
- Provide analgesia for headache: consider giving a 2-week course of albendazole and prednisolone orally, but the evidence for treatment regimes in children is lacking, and most cases resolve with time.

5.16.D Epilepsy

BOX 5.16.D.1 Minimum standards

- Anticonvulsants: phenobarbitone, phenytoin, sodium valproate, carbamazepine, ethosuximide.
- Temperature control.
- Prednisolone.
- EEG and neuroimaging with CT and MRI (if available).

Introduction

Epilepsy is a symptom caused by a central nervous system (CNS) disorder, and is usually defined as the occurrence of two unprovoked seizures. In over 70% of cases a cause cannot be identified (idiopathic epilepsy), although genetic causes may be important, as there is often a family history. Most children with epilepsy live in disadvantaged communities where the incidence rates are estimated to be twice those in western countries, and where more than 70% of affected individuals are untreated.

The impact of epilepsy on children and families is wide-ranging. To reduce disability, management is best shared with other healthcare workers who can visit the family closer to home, such as community doctors, and healthcare or disability workers.

Confirming the diagnosis of epilepsy

There is no justification for a trial of anti-epileptic drugs if the diagnosis is unclear. The diagnosis of epilepsy is purely a clinical one, and is usually based on a good history or eyewitness account or ideally a video (often taken with a mobile phone) of an event.

Important features of the seizures include the following:

- timing and duration
- provocation factors
- the early phase of the attack; look for localising features
- movements
- sensory symptoms
- level of responsiveness
- nature of offset.

In early childhood, breath-holding attacks, reflex anoxic seizures and febrile syncope may be commonly mistaken for epileptic seizures. Syncope, hypoglycaemia and non-epileptic attacks such as extensor spasms also enter the differential diagnosis.

Role of investigations

The history and sometimes the examination will usually indicate the cause. Children can be managed without the need for an electroencephalogram (EEG) or neuroimaging. EEG and neuroimaging (preferably an MRI scan, but sometimes a CT scan may be informative) should be reserved for intractable cases or those with neurological signs suggesting a space-occupying lesion. Such problems, and the imaging needed to identify them, will usually require the support of a specialised neurosurgical centre, at least one of which should exist in every country.

Prognostic features of epilepsy

When a syndrome cannot be identified precisely, the features in Table 5.16.D.2 can serve as a guide to the prognosis.

Once the diagnosis and prognosis have been assessed, draw up a problem list as follows:

- What effect does the epilepsy have on the development of the child?
- Are learning or motor problems present?
- Is the child attending school and getting opportunities to play with other children?
- Are there any behavioural problems?

Selecting appropriate anti-epilepsy drugs

Phenobarbitone, phenytoin, carbamazepine and sodium valproate should be available.

Convulsive status epilepticus (*see* Section 5.16.E).

TABLE 5.16.D.1 Clinical classification: most common syndromes of epilepsy in children

Syndrome	Features	Treatment
Generalised		
Tonic or tonic–clonic (grand mal)	Loss of consciousness Stiffening, convulsive movements Incontinence Post-ictal drowsiness, headache	Phenobarbitone Phenytoin Sodium valproate Carbamazepine
Absences	Vacant stare, with decrease in awareness, responsiveness and memory Precipitated by hyperventilation	Ethosuximide (may not be affordable) Sodium valproate **Avoid** carbamazepine and phenytoin
Myoclonic	Head nodding or jerks of limbs	Ethosuximide (may not be affordable) Sodium valproate **Avoid** carbamazepine and phenytoin
Infantile spasms	Sudden flexion of head, trunk and limbs; sometimes extensor spasms Associated with hypsarrhythmia on the EEG and developmental delay	Steroids (these require careful monitoring; **avoid** using them if this is not feasible) Sodium valproate
Lennox–Gastaut syndrome	Multiple seizure types: tonic (especially night), atonic, absences, generalised tonic–clonic. Associated with slow spike and wave on EEG and developmental delay	Sodium valproate Carbamazepine Phenytoin Combinations of the above
Secondary generalised seizures	Seizures starting as partial, and developing (sometimes rapidly) into generalised tonic–clonic seizures	Carbamazepine Sodium valproate Phenytoin Phenobarbitone
Partial		
Simple	Convulsive movements involving the eyes, face and parts of limbs. May have sensory symptoms	Carbamazepine Sodium valproate
Complex	Aura of abdominal discomfort, vacant stare, loss of contact with surroundings, lip smacking, chewing, swallowing, facial flush, hallucinations Post-ictal tiredness and headaches May produce apnoea	Carbamazepine Sodium valproate Phenobarbitone
Benign epilepsy of childhood with Rolandic spikes	Most common, usually starts at 3–10 years of age Predominantly simple partial seizures involving oropharyngeal muscles (gurgling), face or limbs, mostly during sleep Characteristic EEG, normal intelligence	Often do not need treatment Carbamazepine Sodium valproate Phenobarbitone

TABLE 5.16.D.2 Prognosis in epilepsy

Good outcome	Adverse outcome
Single seizure type	Multiple seizure types
No additional impairment	Additional neurological impairment (especially cognitive)
Late age of onset (for the syndrome)	Early age of onset (for the syndrome)
Provoked by illness, stress, flashing lights	Unprovoked
Short seizures	Status epilepticus
Low frequency of seizures	High frequency of seizures
Good initial response to anti-epileptic drugs	Poor initial response to anti-epileptic drugs, requiring polytherapy

How to start treatment

- Monotherapy is the aim, to reduce the side effects and interactions.
- Try to avoid using drugs that impair development (e.g. phenobarbitone, except in infancy).
- If possible, always prescribe the same brand, as there may be pharmacodynamic differences.
- Always start in low doses to minimise side effects and increase the likelihood of compliance.
- Remember to warn the child and their family about any likely side effects, especially if they are temporary, such as drowsiness.
- Increase the drug dose gradually (every 2–4 weeks) until the seizures stop or are significantly reduced, or side effects become significant (*see* Table 5.16.D.3).

How to monitor treatment

- Case notes should record the diagnosis, problem list, dates and types of seizures, indication for treatment,

past treatment with response and side effects of treatment, and information that has been given to the child and their parents or carers.
- Hand out medical cards to be kept as a seizure diary, reminder of prescription and clinic dates. Graphic symbols can be used for the illiterate.
- Regularly review the child to check on their progress. Review them more often if seizure control has not been achieved, or if are side effects or drug changes.

When to change treatment
- Consider changing treatment if side effects are troublesome.
- Introduce the second anti-epileptic drug in the normal way, first checking for possible drug interactions. Once established, begin to withdraw the first anti-epileptic gradually. If seizure control is not achieved with monotherapy, seek a specialist referral.

When and how to stop treatment
In children with a good prognosis, 12–24 months of freedom from seizures is associated with a 70% risk of continuing seizure remission. Withdrawal must be a gradual and closely monitored process. If seizures recur after a decrease in drug dose, they usually remit once the last decrease has been reversed. The withdrawal period depends on the drug (e.g. phenobarbitone over 4–6 months, carbamazepine over 2–3 months).

Whom to refer
This depends upon local facilities. One-third of patients will be intractable to treatment with first-line anti-epileptic drugs. Some of them may not have epilepsy, and others may have syndromes with a poor prognosis. They will require specialist assessment and treatment advice. Epilepsy may also be a part of complex developmental disorders involving the CNS, and these children may also benefit from specialist input.

TABLE 5.16.D.3 Doses of common anti-epileptic drugs

Drug	Usual dose	Side effects and toxicity
Carbamazepine	1 month–12 years initially 5 mg/kg at night or 2.5 mg/kg twice daily increasing to 5 mg/kg three times a day Maximum dose 20 mg/kg per day 12–18 years Initially 100–200 mg 1–2 times daily increasing to 200–400 mg two or three times daily. Maximum up to 1.8 g daily	Ataxia, diplopia, aplastic anaemia (bruising, mouth ulcers)
Phenobarbitone	One month to 12 years initial dose 1.5 mg/kg twice daily increasing to 2.5–4 mg/kg/day once or twice daily 12–18 years 60–180 mg once daily	Drowsiness, agitation, rashes, developmental impairment
Phenytoin	1 month–12 years initial dose 1.5–2.5 mg/kg twice daily then increasing to 2.5–5 mg/kg twice daily 12–18 years initial dose 75–150 mg twice daily increasing to 150–200 mg twice daily (maximum 300 mg twice daily)	Gum hypertrophy, hirsutism, acne, ataxia, diplopia, nystagmus, neuropathy, choreoathetosis, encephalopathy, lymphoma, megaloblastic anaemia
Sodium valproate	1 month–12 years initial dose 5–7.5 mg/kg twice daily increasing to 12.5–15 mg/kg twice daily 12–18 years initial dose 300 mg twice daily increasing to 0.5–1 g twice daily	Nausea, epigastric pain, alopecia, weight gain, tremor, hepatitis, pancreatitis, encephalopathy

Social issues

Promoting social integration
Children need to participate as fully as possible in the normal activities of their peers, at school, at play, in the home and preparing for employment. Community workers should be involved in the wider management, and parents' fears and anxieties discussed.

Supporting parents
Parents often tend to overprotect their children who have epilepsy, and may lack confidence in dealing with seizures. In many societies epilepsy carries a stigma. Opportunities to discuss first aid, behaviour and other concerns are vital, and can be provided by healthcare workers or parent groups.

First-aid advice
The general theme to be emphasised is that children with epilepsy should be encouraged to live as full and normal a life as possible. There are very few absolute restrictions, but these include climbing trees or riding bikes or motorcycles. Children should be accompanied when swimming or when near to hazards such as stoves and fires. During a convulsion, place the child in the recovery position, protect them from hard or sharp objects in the vicinity, and cushion their head. Do not put anything in their mouth or try to restrain their limbs. Let them recover by themselves. They may need to rest or sleep, but keep them under observation because they may start convulsing again. As a rough guide, a convulsion that does not stop spontaneously within about 10 minutes is likely to continue for longer, and may need intervention with anti-epileptic drugs given IV, rectally or bucally. The use of rectal diazepam at home by parents and carers is described later in this subsection.

Febrile seizures

A febrile seizure is a seizure that occurs in children aged between 6 months and 7 years with febrile illness not caused by an intracranial disease. The commonest age of onset is 14–18 months. Febrile seizures are common, occur in 2–5% of all these children, and account for about one-third of all childhood seizures.

Clinical presentation

Febrile seizures are usually brief, generalised, clonic or tonic–clonic convulsions lasting less than 10 minutes with minimal post-ictal confusion or weakness. About 20% of febrile seizures are complex (i.e. focal), or last longer than 15 minutes, or occur more often than once in 24 hours. Complex febrile seizures may suggest an underlying central nervous system cause and are associated with a poorer outcome (cognitive impairment or epilepsy).

Febrile seizures occur while the child has a recognisable infection, most commonly an upper airway infection or a viral illness such as gastroenteritis. Other causes include pneumonia, urinary tract infections and after vaccinations. Shigellosis, roseola infantum and malaria have an unusually high incidence of seizures. Most children have a core temperature of 38–41°C, but it may occur at the onset of the febrile illness, and the child may have a normal temperature at the time of seizure.

An increased frequency of febrile seizures occurs in the children of parents and siblings who have had febrile seizures, and siblings with epilepsy.

Identify the cause

Check blood glucose levels (by finger-prick test if available), take a careful history and examine the patient thoroughly, especially with regard to alertness and ability to play, looking for common and serious sites of infection. Where relevant, look at rapid test or film for malaria parasites, and full blood count. Consider urinalysis, lumbar puncture, cultures of blood, urine, pharyngeal swab and cerebrospinal fluid, and relevant X-rays in children whose history and examination offer clues to serious infection. A lumbar puncture is mandatory if meningitis is thought to be a possibility (unless there is evidence of raised intracranial pressure, when IV antibiotics should be given until meningitis can be excluded; *see* Section 5.16.A and Section 5.16.B).

Differential diagnosis

Exclude the following:

- meningitis
- encephalitis
- acute encephalopathies of metabolic or toxic origin
- cerebral malaria
- electrolyte disorders
- hypoglycaemia
- anoxia
- trauma
- haemorrhage
- tumour.

Other entities that can be confused with febrile seizures include the following:

- febrile delirium (in which the patient is speaking but not making sense)
- febrile rigors (in which the patient is shaking with a fine tremor).

Treatment

No treatment is necessary in simple self-limiting febrile seizures provoked by a minor febrile illness. Advice to parents should consist of the following:

- Reassurance that the condition is almost always benign and that the large majority of children stop having seizures after 5 or 6 years of age, while many have only one seizure.
- Practical demonstration of the recovery position for use if a further seizure occurs (*see* Section 5.16.E).
- Advice to seek medical help if a further seizure occurs, both in case it is prolonged (less than 5% of cases, but see below) and, importantly, so that the source of the provoking infection can be identified.

Sequelae

- About one-third of children with febrile seizures will have another febrile seizure.
- Around 3% will have at least one afebrile seizure.
- Around 2% may develop epilepsy (recurrent afebrile seizures).
- Approximately 65% of children with simple febrile seizures will have had no further seizures by 7 years of age.
- Recurrent seizures tend to re-occur, particularly in children aged less than 1 year at the onset of the febrile convulsions or those with a positive family history.

Risk of later epilepsy

The risk factors for the development of epilepsy are as follows:

- complex febrile seizures
- previous abnormal neurological function
- multiple febrile seizures
- family history of epilepsy
- age less than 1 year at the first seizure.

Long-term care: home treatment

- Rectal diazepam for parents to administer if there are prolonged seizures (2.5 mg for children under 1 year, 5 mg for those aged 1–3 years, 10 mg for those aged over 3 years). **The parents must also be taught what to do if their child stops breathing (i.e. they should be equipped with a bag and mask and shown how to use it).**
- Oral or rectal paracetamol to prevent or treat febrile seizures.
- Advice to parents as described above.

5.16.E Convulsive status epilepticus

BOX 5.16.E Minimum standards
- **ABC** and high-dependency care.
- Anticonvulsants:
  - lorazepam
  - phenobarbitone
  - phenytoin
  - paraldehyde
  - diazepam
  - midazolam
  - thiopentone.
- Temperature control.
- Mannitol.
- Dexamethasone.

Introduction

Convulsive status epilepticus (CSE) is a life-threatening condition in which the brain is in a state of prolonged electrical discharge. It is defined as a generalised convulsion lasting for more than 30 minutes, or recurrent convulsions which occur very frequently over a 30-minute period, where the patient does not regain consciousness between seizures.

The duration of the convulsion is highly relevant, as the longer the duration of the episode, the more difficult it becomes to control it. Convulsions that persist for longer than 10 minutes are much less likely to stop spontaneously. Therefore it is usual practice to institute anticonvulsive treatment when the episode has lasted for 5 minutes or more.

Common causes of convulsions in children

These include the following:
- fever with a predisposition to febrile convulsions (usually between the ages of 6 months and 6 years)
- meningitis
- epilepsy
- hypoxia
- metabolic abnormalities
- abrupt withdrawal of anti-seizure medication, especially phenobarbitone
- an acute cerebral event or injury (e.g. haemorrhage, trauma)
- ingestion of medication.

Tonic–clonic status occurs in approximately 5% of patients with epilepsy. Up to 5% of children with febrile seizures will present with status epilepticus. The mortality rate of status epilepticus can be high (up to 20% in adults), especially if treatment is not initiated quickly. However, with optimal management and adherence to a structured and standardised management plan, the mortality in children is much lower and patients can survive with minimal or no brain damage.

Evaluation and immediate management of status epilepticus

During a seizure:
- Turn the child on their side.
- **Adopt an ABC approach. It is vital to ensure satisfactory respiration and circulation and to exclude or treat hypoglycaemia before giving anti-epileptic drugs.**
- Ensure that the airway is patent and that there is adequate respiratory effort and circulatory volume. Institute corrective measures immediately if these are required.
- If available, administer oxygen via a mask.
- Check glucose levels and treat if they are low (< 2.5 mmol/litre or 45 mg/dL). If in doubt or unable to check the levels, it is safer to treat as if hypoglycaemia is present and give 10% dextrose IV 2–5 mL/kg as an initial bolus and, if safe to do so, follow this with an infusion containing a glucose-containing fluid to avoid the risk of rebound hypoglycaemia.
- If the seizure has lasted more than 5 minutes (or if the duration is not known), prepare for anticonvulsant treatment. Short recurrent seizures lasting less than 5 minutes should also be treated (*see* Figure 5.16.E.1).
- **A self-inflating bag with non-return valve (e.g. Ambubag) and a suitably sized face mask must be available in case excessive respiratory depression is caused by benzodiazepines** (*see* Section 1.12).
- Treat the fever (if present) with exposure, tepid sponging and rectal paracetamol (40 mg/kg loading dose, 20 mg/kg if less than 3 months of age).

Drugs

Lorazepam (intravenous or intra-osseous route)

Lorazepam is a benzodiazepine with a fast onset of action and a longer duration of effect (12ldren zures lasting with diazepam (which is less than 1 hour). It produces less respiratory depression than other benzodiazepines, and is less likely to require additional anticonvulsants to stop the seizure. However, absorption from the rectal route is poor. Lorazepam is not available in every country, but is no more expensive than diazepam.

Dose: 50–100 micrograms/kg/dose by IV or intra-osseous route (the dose can be repeated after 10 minutes if necessary).

Midazolam (buccal application)

Midazolam is an effective fast-acting anticonvulsant that has an onset of action within minutes but has a shorter lasting effect (15–20 minutes). Most children do not convulse again once the seizure has been terminated.

Buccal midazolam is twice as effective as rectal diazepam, but both drugs produce the same degree of respiratory depression. This occurs only in about 5% of patients, is short-lived, and is usually easily managed with bag-valve-mask ventilatory support.

Midazolam can be given by the buccal or IV route. However, the ready-made buccal midazolam may not be available in some countries. In such situations the standard IV preparation can be used instead via the buccal route. Simply draw the required dose in a syringe using a needle so as to filter off any glass fragments, and after removing the needle apply the drug on the buccal mucosa between the lower lip and the gum.

Dose:

- 500 micrograms/kg/dose (maximum 10 mg) with buccal application (the dose may be repeated).

Diazepam

Diazepam is an effective, commonly used, readily available and fast-acting anticonvulsant with similar characteristics to midazolam. It is widely used, but may now be superseded by the more effective lorazepam or buccal midazolam where the latter is available. The rectal dose is well absorbed.

Dose:

- 500 micrograms/kg/dose rectally
- 200–300 micrograms/kg/dose by the IV or intra-osseous route (the dose may be repeated).

Lorazepam (intranasal route)

This has been found to be safer than IM paraldehyde, and is also less expensive and easier to access. It is directly instilled into one nostril, with the patient in a supine position, drop by drop over 30–60 seconds.

Dose: 50–100 micrograms/kg/dose intranasally.

Paraldehyde

Paraldehyde is an effective and cheap anticonvulsant with a sustained level of effect and a good safety profile. However, it may be difficult to find in some countries. Paraldehyde takes 10–15 minutes to start to take effect, and its action is sustained for 2–4 hours.

It is generally given by the rectal route after mixing the required dose with an equal amount of any edible oil (e.g. olive oil). This mixture is then quickly pushed up the rectum using a simple feeding tube attached to a syringe. **Do not leave paraldehyde standing in a plastic syringe for longer than a few minutes, as the drug dissolves plastic.** The IM route can also be used, but is very painful and can lead to abscess formation, so is better avoided. Paraldehyde causes little respiratory depression, but should not be used in patients with liver disease.

Dose: 0.4 mL/kg rectally (0.4 grams/kg).

Phenytoin

Phenytoin is a readily available anticonvulsant that can give very good results with little effect on respiration. It has a peak action within 1 hour, and a long half-life. Its action is therefore more sustained than that of diazepam.

It is administered as an IV infusion mixed with 0.9% sodium chloride solution made up to a concentration of 10 mg/mL, given over a 20-minute period. Phenytoin can cause dysrhythmias and hypotension (especially if given rapidly), so it is important to monitor the electrocardiogram (ECG) and blood pressure if these are available. In addition, local irritation, phlebitis and dizziness may accompany IV administration.

If the child is known to be on oral phenytoin it is better to either avoid using phenytoin (use phenobarbitone instead) or use a lower loading dose (i.e. 10 mg/kg).

Dose: 20 mg/kg IV infusion given over 20 minutes (only use normal (0.9%) saline for dilution).

Phenobarbitone

Phenobarbitone is a time-tested anticonvulsant and readily available in many countries; the parenteral preparation is on the WHO essential drug list. It can be used to good effect in all age groups, and causes little respiratory depression. It is given by the IV route as a slow injection over 5–15 minutes, and can also be given by the IM route, although the absorption is variable. It has a sustained effect that lasts over 12–24 hours.

There is now evidence to suggest that phenytoin and phenobarbitone may have some synergistic effect when used sequentially. It is thought that one primes the brain in readiness for the other, thus producing a beneficial effect. However, there is controversy about which drug should be used first.

Dose: 20 mg/kg IV infusion over 5–10 minutes.

Thiopental

Thiopental (thiopentone) sodium is a drug better used by experienced staff who are familiar with it (usually anaesthetists: *see* Section 1.24) and who are capable of intubating difficult cases. It is a general anaesthetic agent with no analgesic properties but with marked cardiorespiratory effects. It is usually given after paralysis and intubation in induction of anaesthesia. Other anti-epileptic medication must be continued. The child should not remain paralysed, as continued seizure activity cannot otherwise be monitored. A paediatric neurologist should continue to give clinical advice and support.

General measures once seizures are controlled

- **Maintain a normoglycaemic state** using 5% glucose-containing solutions (10% in young infants). Often children may show a hyperglycaemic pattern following seizures as a stress-induced response. This does not require correction with insulin.
- **Normal maintenance fluid volume** can be given to avoid hypoglycaemia and to maintain electrolyte balance. However, evidence of raised intracranial pressure or increased antidiuretic hormone secretion should necessitate fluid restriction.
- **Assess and maintain electrolyte balance**, maintaining serum sodium levels within the normal range (135–145 mmol/litre). Avoid hyponatraemia by using Ringer-lactate or Hartmann's solution.
- **Aspirate the stomach contents** by inserting a gastric tube, and perform gastric lavage or give charcoal (1 gram per year of the child's age) if appropriate for specific drug ingestion.
- **Regulate the temperature**, ensuring that temperatures above 37.5°C are avoided.
- **Treat raised intracranial pressure**, if clinically present (*see* Section 5.16.K), as follows:
  - Support ventilation (maintain a pCO_2 of 4.5–5.5 kPa).
  - Maintain a 20-degree head-up position.
  - Give 20% mannitol, 250–500 mg/kg (1.25–2.5 mL/kg) IV over 15 minutes. This may be repeated on a 2-hourly basis as required.
  - Alternatively, hypertonic saline can be used (2.7% or 3% at a dose of 3 mL/kg). This may not be associated with a 'rebound' rise in pressure or induce a diuresis like mannitol but rather augments plasma volume.
  - Give dexamethasone, 500 micrograms/kg twice daily (for oedema surrounding a space-occupying lesion).
- **Catheterise the bladder**, as distension may aggravate raised intracranial pressure.
- **Frequent reassessment of ABC** is mandatory, as

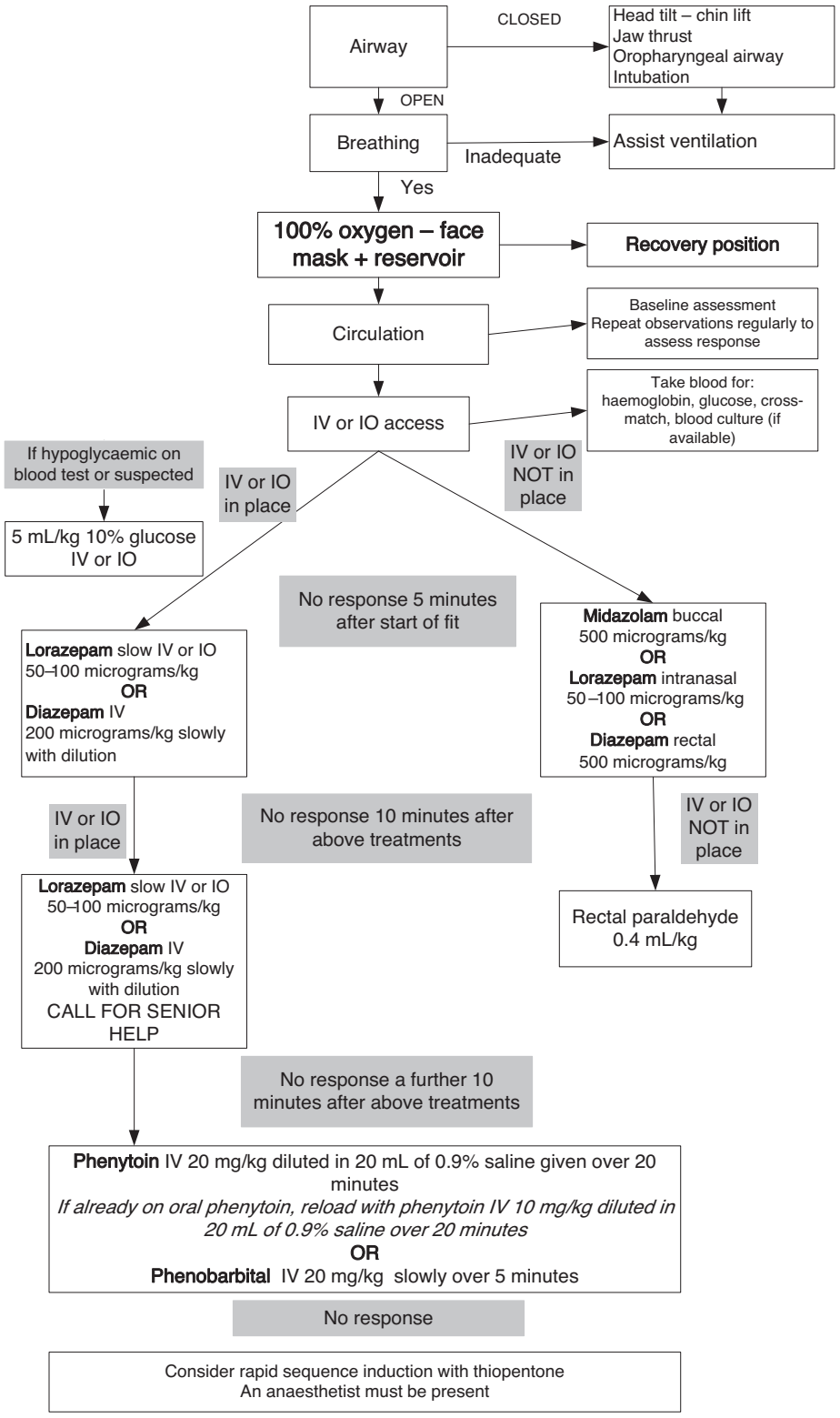

FIGURE 5.16.E.1 Algorithm for the treatment of status epilepticus in children.

therapy may cause depression of ventilation or hypotension, especially if benzodiazepines or barbiturates have been used.

- If available, a standard EEG can be done to establish cessation of electrical seizure activity.
- **Identify and treat the underlying cause** of the convulsion.
- Following seizure control there are several regimes for continued drug control of the convulsions, but they are beyond the scope of this text.

5.16.F Neuropathies

BOX 5.16.F Minimum standards
- Muscle biopsy.
- Prevention of scoliosis.
- Prevention of muscle contractures.

Introduction

Neuropathies are diseases that affect the anterior horn cells and/or the peripheral nerves.

Anterior horn cell disease

The most common neuropathies are:
- poliomyelitis (*see* Section 6.2.G)
  - spinal muscular atrophy.

Spinal muscular atrophy

This is a motor neuron disease of the spinal cord and brainstem, inherited as an autosomal-recessive disorder and associated with deletions of the survival motor neuron (SMN) and neuronal apoptosis inhibitory protein (NAIP) genes. It is the second commonest autosomal-recessive disorder after cystic fibrosis.

Clinical features

These children have delayed motor development but normal social, language and intellectual development. They are floppy and weak. The weakness is proximal more than distal, and affects the lower limbs more than the upper ones. The children are areflexic, and fasciculation of the tongue is diagnostic (observed with the tongue at rest in the mouth). There are three clinical subtypes based on severity.
- **Severe infantile type:** These infants never sit, crawl or walk. The onset is before or soon after birth. They have severe intercostal and bulbar weakness but the diaphragm is spared. Most die from respiratory failure before their second birthday.
- **Intermediate type:** These infants can sit but are unable to walk. They may or may not have respiratory and bulbar weakness, and this factor determines their prognosis. If it is absent, these children can survive into adulthood.
- **Mild type** (also known as Kugelberg–Welander type). The onset is later and these children can walk, but they do so late and with difficulty. Respiratory and bulbar weakness is not usually present. A coarse tremor of the hands is frequently seen in this and the intermediate form. This is a useful sign for distinguishing this type from muscular dystrophy, with which it is often confused (*see* Table 5.16.F.1).

Diagnosis

Since the discovery of the gene defect, muscle biopsy is rarely needed. Deletion of the *SMN* gene is found in almost all cases of spinal muscular atrophy of all three types. It can be detected rapidly by the polymerase chain reaction (PCR). Blood (2–5 mL in an EDTA tube), or DNA extracted from it, can be sent by post to a laboratory that will perform the test and confirm the diagnosis within a few days.

TABLE 5.16.F.1 Comparison of spinal muscular atrophy (mild type) and Duchenne muscular dystrophy

Feature	Spinal muscular atrophy	Duchenne muscular dystrophy
Motor milestones	Delayed	Normal or delayed
Hypotonia	+++	+/–
Pseudohypertrophy	+/–	+++
Hand tremor	+++	–
Tongue fasciculation	+	–
IQ	Normal	Normal or low
ECG	Baseline tremor	R- and Q-wave changes
Creatine kinase	Normal or slightly raised (× 2)	Very high (× 100)
EMG	Chronic denervation	Myopathic
Muscle biopsy	Denervation	Dystrophic

Management

Management is supportive. The most important complication in the intermediate form is the development of scoliosis. This can be delayed by getting the child to stand with support of lightweight callipers for as long as possible. If the child is confined to a wheelchair, a brace may be needed to control the scoliosis. Surgery (fusion of the spine) may be necessary. Children with symptoms of nocturnal hypoventilation (disturbed sleep, headaches, daytime drowsiness and poor concentration) may benefit from assisted non-invasive night-time ventilation with a nasal mask (*see* Section 8.2).

Peripheral neuropathy

The two commonest causes of peripheral neuropathy in children are Guillain–Barré syndrome (*see* Section 5.16.G) and hereditary motor and sensory neuropathy.

Hereditary motor and sensory neuropathy

This is the commonest chronic peripheral neuropathy in children. It is progressive, and there are several types, but the commonest is type I (peroneal muscular atrophy). It is dominantly inherited, and most children are asymptomatic until late childhood, when unsteady clumsy gait with frequent falls develops. There is weakness and wasting of the muscles of the anterior compartment of the leg. The parents

are often asymptomatic. The diagnosis is confirmed by the finding of very low motor conduction velocities in both the child and one of the parents, indicating demyelination. Type II is similar, but rare, and shows axonal rather than demyelinating changes in nerve conduction studies. There are no treatments for these diseases other than special boots and ankle orthoses to stabilise the ankle.

Other peripheral neuropathies

These include leukodystrophies (where peripheral nerve demyelination occurs as part of CNS demyelination), toxic neuropathy (due to glue or benzene sniffing, lead, or drugs) and diphtheria (*see* Section 6.1.C).

5.16.G Guillain–Barré syndrome

BOX 5.16.G Minimum standards
- ABC resuscitation and emergency care.
- Lumbar puncture.

Introduction

This is the commonest peripheral neuropathy seen in childhood. It is a demyelinating neuropathy induced by an autoimmune process that is precipitated by a preceding viral or other infection. It has a peak incidence at around 8 to 9 years of age in well-resourced countries and 3 to 4 years of age in resource-limited ones, possibly due to overcrowding. Rarely, an acute axonal form occurs, especially in some countries, such as China.

Clinical features

The onset is usually acute. There is often a history of a preceding upper respiratory or gastrointestinal tract infection and insidious sensory symptoms (e.g. muscle tenderness, occasionally an unsteady gait, and frequent falls). The weakness starts in the lower limbs and ascends to affect the trunk, upper limbs, and the respiratory (intercostal and diaphragm), bulbar and facial muscles. It is usually symmetrical and affects both proximal and distal muscles, and may take 10–30 days to reach its maximum. Cranial nerve involvement often precedes respiratory difficulties. Reflexes are frequently absent. Sensory loss is minimal and of the 'glove-and-stocking' distribution. Ophthalmoplegia, papilloedema and bladder involvement rarely occur. Autonomic dysfunction occurs in many children, resulting in hypertension, hypotension and cardiac arrhythmias. In some patients the paralysis occurs rapidly with quadriplegia and respiratory paralysis within 2–5 days.

Chronic inflammatory demyelinating polyradiculoneuropathy

The disease may evolve into chronic inflammatory demyelinating polyradiculoneuropathy. This disease is similar to Guillain–Barré syndrome, consists of progressive or relapsing motor and sensory dysfunction, and lasts at least 2 months, with hyporeflexia of all four limbs. The importance of identifying this condition is that it responds to steroids (prednisolone 2 mg/kg/day).

Diagnosis

The diagnosis is confirmed by an abnormal nerve conduction stimulation, but a high CSF protein level and almost normal cell count are very suggestive. These findings are usually present after the first week of onset. Other causes of acute flaccid paralysis such as poliomyelitis in endemic countries need to be considered (*see* Table 5.16.G.1).

Management

Supportive care is the cornerstone of successful management of the acute patient. Of greatest concern is respiratory failure due to paralysis of the diaphragm (the muscle that is most important for breathing). **Intubation** may be needed if there is evidence of impending respiratory failure. The following steps in management should be taken:

- Admit the child to hospital to monitor for impending respiratory and bulbar paralysis and autonomic dysfunction.
- Measure the respiratory rate, heart rate and blood pressure, perform pulse oximetry and if possible measure vital capacity (or peak flow), and check airway protection frequently. Blood gas analysis may be helpful.
- If the vital capacity is less than 50% of normal for age **and/or there is significant respiratory failure with hypoxaemia and hypercapnia**, ventilate the child if possible.
- If bulbar and respiratory paralysis occurs, airway protection, tube feeding and ventilatory support will be necessary. Airway protection can be achieved by intubation or tracheostomy.
- Plasma exchange (also called plasmapheresis) and high-dose immunoglobulin therapy may lessen the severity of the illness and accelerate recovery in some patients, but are not widely available. These two treatments are equally effective, and a combination of the two is not significantly better than either alone. However, immunoglobulin is easier to administer.
- Children who require ventilation can be given high-dose human immune globulin if available (0.4 grams/kg IV over 6 hours daily for 5 days). This can be repeated if there is no response, if deterioration occurs or if there is a relapse.

Prognosis

Recovery is usually complete within 4–6 months in most children, but may take up to 2 years. About 5% of children will have minor motor sequelae, and around 2–3% will die from respiratory failure or autonomic dysfunction. Poor prognostic factors include onset of weakness within 8 days of preceding infection, rapid progression, cranial nerve involvement and a CSF protein level of > 800 mg/litre in the first week of the disease. The prognosis is generally better in children than in adults.

TABLE 5.16.G.1 Other causes and features of acute flaccid paralysis

Cause	Features
Spinal cord	
Poliomyelitis	Preceding fever, headache and meningeal irritation, asymmetrical weakness, CSF pleocytosis
Enterovirus: Japanese B encephalitis	Similar to poliomyelitis
Trauma	History and evidence of trauma
Myelitis	Paraplegia, segmental sensory loss Bladder and bowel sphincter disturbance
Epidural abscess	Fever, vertebral tenderness
Neuropathies	
Guillain–Barré syndrome	Symmetrical, areflexia, ascending weakness
Diphtheria	Preceding history of diphtheric pharyngitis, cardiac involvement, deep sensation impaired
Botulism	Bulbar symptoms before onset of weakness, ophthalmoplegia
Tick paralysis	Rapid progressive paralysis, no sensory loss, normal CSF protein levels Resolves quickly once tick has been removed
Metabolic	
Acute intermittent porphyria Hereditary tyrosinaemia	Family history, other symptoms
Muscle	
Myasthenia gravis (rare but treatable)	Fluctuating weakness that is worsened by activity and better after rest Tensilon test is positive
Acute viral myositis	Tender muscles, limp, fever, elevated muscle enzymes (creatine phosphokinase or aldolase)
Other causes	
Organophosphate poisoning	History of exposure, excessive salivation, twitching of muscles, meiosis, tachycardia

5.16.H Muscular dystrophy

BOX 5.16.H.1 Minimum standards
- Creatine kinase measurement.
- Prevention of scoliosis and contractures.
- Prednisolone.

Introduction

The muscular dystrophies are a group of inherited disorders that cause progressive muscle weakness and share a common pathological process of muscle fibre degeneration and fibrosis.

Duchenne muscular dystrophy

This is the most common muscular dystrophy, caused by deficiency of dystrophin, a structural protein found on the inner side of the sarcolemmal membrane. The deficiency is caused by deletions or point mutations of the dystrophin gene, which is located on the short arm of chromosome Xp21.

Clinical features

Duchenne muscular dystrophy is X-linked; it affects boys and is transmitted by females. Affected infants are normal in the first 2 years but will have very high serum creatine kinase levels. They usually present between 2 and 5 years of age with delayed walking, frequent falls, and difficulty in climbing stairs and in getting up from the floor. The weakness affects proximal more than distal muscles, and the pelvic girdle more than the shoulder girdle. The facial muscles are unaffected. Prominent calves and thighs are characteristic. With time, these children walk on their toes with marked lumbar lordosis and a waddling gait. The arm reflexes are lost early but ankle jerks are preserved. Once confined to a wheelchair, they rapidly develop contractures of the knees, hips and ankles and scoliosis. Intellectual impairment may occur or develop in some patients, often related to the onset of respiratory failure. The ECG shows dominant R waves in right-sided leads, deep Q waves in left-sided leads, and inverted T waves in most patients.

Diagnosis

The serum creatine kinase activity is very high (100 times normal). The electromyogram (EMG) is myopathic, and muscle biopsy shows dystrophic changes and absent

dystrophin. Deletions in the dystrophin gene can be identified by the polymerase chain reaction (PCR) in DNA extracted from blood in 60–80% of patients.

Management

There is no effective drug treatment. A course of oral prednisolone (0.75 mg/kg/day) for 3–6 months can produce a small but significant improvement in muscle strength, but has many side effects, and these must be weighed against the slight benefit. Night splints to keep the ankles at 90 degrees may delay shortening of the tendo-achilles. When walking is becoming difficult, the fitting of lightweight callipers and intensive physiotherapy may keep the child ambulant for a few more years. Once the child is wheelchair-bound, a rigid seat and adequate postural support of the spine may prevent scoliosis.

Prognosis

The weakness is progressive, and by 10–12 years of age a wheelchair will be needed. Later, as respiratory muscle weakness develops, nocturnal hypoventilation may cause disturbed sleep and morning headaches (due to hypoventilation and carbon dioxide retention). Assisted non-invasive ventilation (using a nasal mask) at night will improve the child's quality of life (*see* Section 8.2). Death occurs in the twenties from respiratory or cardiac failure.

Genetic counselling

An elevated creatine kinase activity (on three separate occasions) in female relatives indicates carrier status. Some will also have an abnormal muscle biopsy, with some fibres showing normal and others absent dystrophin. Normal creatine kinase and muscle biopsy does not exclude the carrier state. Prenatal diagnosis is possible in some but not all families, but requires specialised molecular genetic techniques.

Becker muscular dystrophy

This is a milder variant of Duchenne muscular dystrophy, and is rare. Onset is between 5 and 10 years of age, and ambulation is maintained beyond 15 years and often into adulthood. This disorder is caused by partial deficiency of dystrophin.

Limb girdle muscular dystrophies

These are rare and vary in severity. A severe form is prevalent in North Africa. It has a clinical picture similar to Duchenne muscular dystrophy, but affects boys and girls and has more prominent involvement of the shoulder girdle muscles, with winging of the scapulae. It is associated with deficiency of one of the sarcoglycans, a group of sarcolemmal proteins intimately linked to dystrophin. This can be demonstrated in muscle biopsy specimens. The intelligence remains normal and the heart is unaffected. Genetic tests for diagnosis are available in specialised laboratories.

Congenital muscular dystrophy

Infants with congenital muscular dystrophy are born floppy and weak and have contractures. They have delayed motor milestones, and most are unable to walk. They develop a characteristic long thin expressionless face with an open mouth. There is no ophthalmoplegia. There are several subgroups, some with eye or brain abnormalities and demyelination. Merosin is deficient in one subgroup. Inheritance is autosomal recessive and the gene defect is known for most of them. The creatine kinase may be elevated or normal, and the diagnosis is made by muscle biopsy or genetic testing. Management is supportive. Congenital muscular dystrophy must be distinguished from other causes of hypotonia (i.e. other congenital myopathies, infantile spinal muscular atrophy and organic acidaemias).

5.16.I Breath-holding episodes

BOX 5.16.I.1 Minimum standards
- Haemoglobin measurement.
- Oxygenation measurement.

Introduction

Breath-holding episodes occur in about 4% of children under the age of 5 years. They typically start between the ages of 6–18 months, and usually cease before the age of 5 years. They are infrequent, usually occurring less than once a month, but occasionally occur more often. There are two types of episodes, which are differentiated by the presence of **cyanosis** or **pallor**. The underlying mechanism of the two types is different.

Type of episodes

Cyanotic breath-holding episodes

These are provoked by anger, frustration, fright or pain. The infant cries vigorously, holds their breath in expiration, goes blue, loses consciousness and becomes limp. Rarely this is followed by a brief stiffening of the body. The infant then starts breathing again and the attack ends. These attacks may be due to cerebral ischaemia from a sudden rise in intrathoracic pressure that impedes venous return. Intrapulmonary right–left shunting also plays a part.

Pallid asystolic spells

These are less common than the cyanotic type (about 20% of all cases), and may occur in the context of a minor illness. The attack is provoked by pain, usually from a mild injury on the head. The child cries, loses consciousness, develops marked pallor and goes stiff. Occasionally the child loses consciousness immediately after the injury without crying. A few clonic jerks (reflex anoxic seizures) may occur. These pallid spells are caused by vagal asystole, and can be induced by pressure on the eyeballs (oculo-cardiac reflex), although it is not necessary to elicit this reflex, and if thought to be important, this should only be done under controlled conditions with EEG and ECG monitoring. **There is also a risk of damaging the eyeballs when pressing on them.**

Diagnosis

The diagnosis is based on a careful history of the sequence of events. These attacks are frequently confused with epilepsy. In epilepsy, the cyanosis occurs after the tonic–clonic phase of the seizure. In breath-holding spells cyanosis occurs before but, more importantly, the diagnosis rests on the fact that the attacks are always precipitated by an appropriate stimulus. An EEG is not necessary except when the diagnosis is in doubt and epilepsy is suspected. **An ECG must be done in pallid asystolic spells to exclude long QT interval syndromes. Always exclude anaemia, which is a well-documented cause of breath-holding episodes. Also exclude chronic hypoxaemia, which is also a cause from unrecognised cardiac or respiratory disease.**

Prognosis

These attacks are frightening for the parents, but are harmless. They eventually cease with time, and if there is no underlying pathology they do not have any long-term effects. There is no risk of subsequent epilepsy. Some infants with the pallid type go on to develop faints in later childhood.

Management

The parents need to be given an explanation of these attacks and reassured about their harmless nature. There is no effective drug and no need for drug treatment. Treat anaemia and hypoxaemia if these are present.

5.16.J Migraine

BOX 5.16.J.1 Minimum standards

- Paracetamol and ibuprofen.
- Anti-emetics.
- Propranolol, clonidine and pizotifen.

Introduction

Migraine is a common cause of recurrent headaches in children. Its prevalence increases with age. It may be preceded by a history of recurrent abdominal pain and vomiting at a younger age (abdominal migraine, cyclical vomiting). The headache is typically throbbing in nature, temporal or frontal in location, more often bilateral than unilateral (in contrast to adult migraine), and commonly associated with nausea, vomiting, pallor and sometimes photophobia. It usually lasts for 1–3 hours, but sometimes persists for 24 hours, and it is relieved by sleep. Migraine is precipitated by stress (e.g. school examinations, family pressure, unrealistic expectations) and sometimes by hunger, fatigue, lack of sleep, exposure to sun, and some foods (e.g. chocolates, Coca-Cola, caffeinated drinks, nuts, cheese). A positive family history of migraine, especially on the maternal side, is found in over 90% of patients, and the diagnosis of migraine must be questioned in the absence of such a history. Between the attacks the child is well.

Classification of migraine

Migraine is classified into three types.

- **Common migraine:** There is no aura in this type. It is the commonest form in children, accounting for over 80% of children with migraine.
- **Classical migraine:** An aura precedes the headache, which is rare in children (about 10%). Visual aura include hemianopia (loss of half of the visual field), scotoma (small areas of visual loss), fortification spectra (brilliant white zigzag lines), blurred vision and flashes of lights. Occasionally sensory auras occur, consisting of paraesthesia round the mouth and numbness of the hands and feet.
- **Complicated migraine:** Rarely neurological signs occur during the headache and persist for varying periods after it. Ophthalmoplegic migraine (third cranial nerve palsy) is rare, and must be distinguished from a berry aneurysm or other space-occupying lesion compressing the third cranial nerve.
  - **Hemiplegic migraine** is the occurrence of hemisyndrome (weakness or numbness down one side of the body) with the headache. Recurrent attacks of hemiplegic migraine are rare in children, but occasionally, starting in infancy, a child may have alternating hemiplegia as a manifestation of migraine.
  - **Basilar migraine** results from vasoconstriction of the basilar and posterior cerebral arteries. Symptoms include vertigo, tinnitus, diplopia, blurred vision, ataxia and occipital headaches. There is complete recovery after the attack. Minor head trauma may precipitate basilar migraine.

Management

A careful history and examination is essential to confirm the diagnosis of migraine. Investigations are rarely needed. Explanation of the attacks and the relatively benign nature and good prognosis will reassure the parents and the child, and by itself will lead to a reduction in frequency and severity of the headaches in over 50% of these children. Where possible, precipitating factors need to be identified and eliminated or reduced. In particular, dietary factors such as chocolate, Coca-Cola, caffeinated drinks and cheese should be avoided.

Acute attack

Rest and sleep in a quiet darkened room is usually preferred by patients. A simple analgesic alone or in combination with a non-steroidal anti-inflammatory agent is often all that is required, and if given at the onset will abort or reduce the severity of the headaches. Paracetamol (20 mg/kg per dose, repeated every 6 hours as necessary) and ibuprofen (5 mg/kg per dose) are useful agents.

If nausea and vomiting are troublesome, an anti-emetic may be prescribed, such as metoclopramide. Aged 5–9 years 2.5 mg and 9–18 years 5 mg three times daily orally or 100–150 microgram/kg slowly (over 2 minutes) by IV injection (maximum 1 mg). Children weighing over 60 kg can have metoclopramide orally 10 mg three times daily

Prochlorperazine is also useful, 200 micrograms/

kg (maximum 12.5 mg) orally IM or IV immediately, then 100 micrograms/kg per dose 6- to 8-hourly, orally or rectally. Prochlorperazine is not licensed for use in children who weigh less than 10 kg. Extrapyramidal side effects may occur.

The triptans (sumatriptan, zolmitriptan and rizatriptan) are serotonin-receptor agonists and are highly effective for the acute attack, but their use in children under 12 years of age awaits further evaluation. The dose of sumatriptan for adults is 50–100 mg orally as soon as possible after onset. It must not be used for basilar or hemiplegic migraine.

Prophylactic treatment

If the headaches are frequent (at least three to five per month) and troublesome, continuous prophylaxis is required, usually for a period of 1 year. If the headaches recur, the course of treatment is repeated. The drug of choice for children is propranolol, but pizotifen and clonidine have both been tried in children, with varying degrees of success.

- Propranolol is a beta-blocker, and can be given to children over 2 years of age (the dose for children aged 2–12 years is 200–500micrograms/kg three times daily orally; for children over 12 years it is 20–40 mg two to three times daily). **Propranolol must not be given to children with asthma or diabetes, and it may cause depression.**
- Clonidine can be given at a dose of 2 micrograms/kg every 8 hours (maximum dose 200 micrograms/day).
- Pizotifen is given for children aged 5–10 years at an initial dose of 500 micrograms, increasing to 1 mg at night or 500 micrograms 8-hourly. For children aged 10–12 years give 1 mg at night or 500 micrograms 8-hourly. For children aged 12–18 years give 1.5 mg at night, increasing to 1.5 mg 8-hourly. It may cause weight gain.

Prognosis of migraine

The prognosis is generally good. About 50% of children with migraine will undergo spontaneous prolonged remission after the age of 10 years. In most children the headaches are infrequent and rarely interfere with schooling or daily activities. In some the headaches are frequent and troublesome, and these will require prophylactic treatment.

5.16.K Neurosurgical disorders

BOX 5.16.K.1 Minimum standards

- Maternal folic acid before and during pregnancy.
- Dexamethasone and mannitol.
- High-dependency care.
- Antibiotics.
- Anticonvulsants.
- Shunts.
- Regional/national centre (with CT and MRI scanning facility).

Introduction

Every country needs at least one hospital equipped to manage children with neurosurgical problems. The central and essential component of accurate assessment of the most frequently encountered intracranial neurosurgical emergencies is the prompt identification of the presence of raised intracranial pressure (ICP). Once this is recognised and controlled, the precise diagnosis of the site and cause can await sophisticated neuroimaging by ultrasound examination, computed tomography (CT) or magnetic resonance imaging (MRI).

Raised intracranial pressure

The signs and symptoms are different for pre-speech and younger infants compared with older children.

Babies and children under 2 years

The signs and symptoms are as follows:

- abnormally rapid head growth
- separation of cranial sutures
- bulging of the anterior fontanelle (note that the anterior fontanelle usually closes by 18 months of age)
- dilatation of scalp veins
- irritability
- vomiting
- loss of truncal tone
- fluctuating level of responsiveness
- irregular rate and rhythm of breathing, usually with slowing of the respiratory rate
- irregular heart rate, usually with bradycardia, but occasionally with tachycardia
- decerebrate attacks.

It is important to note that features may be non-specific (as in irritability and vomiting), that there may be marked fluctuations in the younger child's condition from minute to minute and from hour to hour, and that frank unconsciousness occurs relatively late, often being preceded by apnoea. Decerebrate attacks can be mistaken for epileptic seizures; in the former, the child extends all four limbs and trunk, whereas in the latter, flexion of the upper limbs is more usual and there are clear tonic–clonic phases.

Older children

The signs and symptoms are as follows:

- headaches
- vomiting
- loss of postural control of the trunk
- **failing vision**
- diplopia
- **neck pain and extension**
- **decerebrate attacks**
- irregular rate and rhythm of breathing, usually with **slowing of the respiratory rate**
- irregular heart rate, usually with bradycardia, but occasionally with tachycardia, and mounting hypertension with widening pulse pressure
- **diminishing level of consciousness**.

The most urgent features are failing vision, neck pain and extension, decerebrate attacks, diminishing level of consciousness and cardiorespiratory failure, as they all indicate incipient terminal events. Failing visual acuity is also urgent, as it indicates severe papilloedema and a danger of permanent visual loss. The absence of papilloedema does not exclude raised intracranial pressure; its presence does indicate that there is a risk of permanent visual loss.

Accurate cerebral localisation on a clinical basis is difficult in children and virtually impossible in babies and young children, but the following can be fairly dependable features of a supra-tentorial mass lesion:

- dysphasia
- visual field defects
- epileptic seizures.

Unilateral pupillary dilatation indicates a mass ipsilateral to the dilated pupil, or on the side of the pupil that dilated first in the case of bilateral pupillary dilatation.

Management

Although the definitive solution is removal of the causative lesion, this will often have to await the availability of imaging by computed tomography and transfer to a neurosurgical facility. The emergency relief of raised intracranial pressure can be achieved by one or more of the following medical measures:

- dexamethasone by slow IV injection (500 micrograms/kg immediately and then 100 micrograms/kg every 6 hours)
- 20% mannitol by IV infusion (250–500 mg/kg and repeated as required based on response and clinical signs; maximum total dose 2 grams/kg infusion over 20 minutes).
- alternatively, hypertonic saline can be used (2.7% or 3% at a dose of 3 mL/kg). This may not be associated with a rebound rise in pressure as may occur with mannitol and does not induce a diuresis like mannitol but rather augments plasma volume.
- intubation and artificial ventilation to $PaCO_2$ of about 4 kPa (if available).

In an extreme emergency, and faced with a rapidly deteriorating child with no immediate prospects of evacuation for neuroimaging and specialist neurosurgical care, the following measures can be employed if there is no history of head injury.

Babies

Trans-fontanelle needle tapping of the subdural space is undertaken, and if there is no subdural effusion, the needle is then advanced into the cerebral ventricle in the hope of finding and relieving hydrocephalus.

Infants and children

Right frontal burr-hole and ventricular drainage is undertaken (see below).

If there is a history of head injury, the procedure for 'blind' burr-holes is followed (see below).

Head injuries (*see* Section 7.3.C).

Intracranial abscesses

Spontaneous extradural, subdural or intracerebral abscesses most commonly arise in children as a complication of an acute, or very occasionally chronic, episode of infection in the paranasal sinuses or middle ear. The cardinal clinical features are as follows:

- raised intracranial pressure
- signs of focal neurological disturbance, including epileptic seizures
  - systemic signs of sepsis; these may be absent.

The diagnosis can be confirmed by CT scan with IV contrast enhancement (if available).

- Evacuation of pus is important both to relieve raised intracranial pressure and mass effect, and to provide material for accurate microbiological diagnosis. Intracerebral abscesses can often be drained satisfactorily by burr-hole aspiration, which may have to be repeated. Extradural and subdural collections will usually require a major craniotomy.
- Raised intracranial pressure will usually be very severe, and may require the use of mannitol.
- Pending microbiological diagnosis, or in the absence of such support, the most useful antibiotics are a combination of cefuroxime (IV 60 mg/kg 6-hourly for 3 days, then 25 mg/kg 6-hourly) and metronidazole (7.5 mg/kg by IV infusion over 20 minutes every 8 hours) for a minimum of 3 weeks. A further 6 weeks of an appropriate oral antibiotic, such as amoxicillin, is usually necessary.
- Amoxicillin route: oral:
  - Dose: 1 month to 18 years of age, 40 mg/kg daily in 3 divided doses maximum dose 1.5 g daily in 3 divided doses.
- An ENT surgeon may need to drain fronto-ethmoid sinuses or mastoids to prevent recurrence.

Hydrocephalus

Hydrocephalus can be diagnosed by trans-fontanelle ultrasound in infants with an open anterior fontanelle, and by CT (if available) in older infants and children. CT will also demonstrate the likely cause.

- The emergency relief of hydrocephalus, or suspected hydrocephalus, is by trans-fontanelle needle drainage in babies, or by burr-hole drainage and insertion of an external ventricular drain in older children.
- The best site for burr-hole drainage is on the right coronal suture in the mid-orbital line. The landmarks for trans-fontanelle puncture are the same as for subdural puncture (see above), but the needle is angled more steeply. Most babies will tolerate venting of up to 50 mL of CSF. Following withdrawal of the needle, the skin puncture is closed with a suture to prevent external leakage of CSF.
- It is important to have the CSF examined by a microbiology laboratory, remembering that sub-acute, partially treated, 'neglected' pyogenic meningitis and tuberculous meningitis can present with hydrocephalus.
- Definitive treatment may involve removal of the obstructing lesion in the case of a tumour or other mass, or establishment of a permanent CSF diversion by inserting an implanted ventriculo-peritoneal shunt.
- Shunt blockage is common and must be diagnosed quickly. The symptoms of shunt blockage are essentially those of raised intracranial pressure, and require urgent attention if death or disability is to be avoided. **The most reliable eye sign is loss of upward gaze.** Blockages

usually affect the ventricular end of the catheter rather than the peritoneal end. Many children develop abdominal distension after shunting. This is due to the unusual load of CSF. In the absence of vomiting and constipation, it should be treated conservatively.

- Shunt infections can present acutely with features of cerebral irritation, fever and seizures if there is major ventriculitis occurring within a few days of insertion; however, this is relatively rare. **The only method that is guaranteed to eliminate shunt infection is removal of all components, including any loose or retained fragments from earlier procedures, interval external drainage, appropriate antibiotics and shunt reinsertion through fresh incisions. As with all serious infections, success is dependent upon accurate microbiological diagnosis.** The most frequently encountered organisms are *Staphylococcus epidermidis* and *Staphylococcus aureus.* The most useful antibiotic is vancomycin by IV injection children 1 month to 18 years 15 mg/kg every 8 hours to a maximum daily dose of 2 grams. The duration of treatment depends on how rapidly the CSF becomes sterile, but a minimum of 7 days is recommended.

Myelomeningocoele

Myelomeningocoele is the commonest major congenital malformation compatible with survival. Its incidence has been progressively falling for 20 years. Although there are regional variations, the overall frequency is 0.7–0.8 per 1000 live births. The objective of management in the immediate postnatal period is the prevention of infection of the central nervous system. This is achieved by early closure of the lesion.

- The level of the open lesion is noted and an assessment made of the sensorimotor level, the state of the sphincters, any orthopaedic deformity, and the presence of major hydrocephalus, as evidenced by signs of raised intracranial pressure (see above).
- **The ideal is to achieve closure within 24 hours of birth. The majority of lesions have adequate skin in the wall of the sac, as long as this is not unnecessarily sacrificed by a wide incision. The technique employed involves mobilisation of the neural placode, watertight dural repair and closure of the skin.** While awaiting closure, the lesion should be protected with a dressing of moist sterile 0.9% saline, which must be replaced every few hours to prevent desiccation.
- Most babies will require surgical treatment for hydrocephalus in the first few weeks of postnatal life.

In children who are paralysed and without urinary or bowel control, the commitment is a lifelong one, and this is a challenge to families and healthcare systems. Before offering treatment to these children, it is important that their future prognosis and quality of life is discussed with the parents.

The aim should be to prevent as many as possible of these anomalies by adequate maternal nutrition prior to conception and during pregnancy.

Folic acid taken prior to conception and for the first trimester of pregnancy abolishes 75% of cases of myelomeningocoele and anencephaly.

See Section 5.10.A.

5.17 Orthopaedic problems

BOX 5.17.1 Minimum standards

- Antibiotics.
- X-rays.
- Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).
- Antituberculous drugs.
- Orthopaedic procedures.

Introduction

Injuries are by no means the only paediatric orthopaedic problems in resource-limited countries. There is a great burden of orthopaedic infective conditions which, if treated suboptimally, can lead to considerable handicap. Furthermore, there is the same spectrum of non-infective conditions as is seen in well-resourced countries which, due to the limited resources available in under-resourced healthcare systems, represents a considerable diagnostic and therapeutic challenge.

Infections

Paediatric musculoskeletal infections are a common presentation in resource-limited countries. Morbidity and mortality can be prevented by prompt diagnosis, antibiotics and surgery where indicated. Infection should be suspected in any child presenting with pain or swelling in the limbs, spine or pelvis.

Pyomyositis

- Pus is present within skeletal muscle, most commonly in the thigh and gluteal regions.
- It is caused by bacterial infection of muscle, in nearly 70% of cases due to *Staphylococcus aureus.*
- It is common in the tropics, but exceedingly rare in the developed world.
- There may be a history of previous injection or trauma to the site.
- Signs include general malaise, swinging fever, decreased range of motion, fluctuant swelling in the later stages, and tenderness.

Treatment

If diagnosed early (which is unusual), pyomyositis may respond to antibiotic therapy (flucloxacillin), but most cases will require incision and drainage of the abscess under general anaesthesia.

At operation

- Incise along the long axis of the tender/swollen area.
- **Mark this area prior to giving anaesthesia.**
- Drain all pus.
- Irrigate thoroughly.
- Insert a wick to maintain drainage and prevent recurrence of the abscess.

Post-operative care

- Give analgesia.
- Give a 5-day course of antibiotics.
- Change the dressings daily.
- Evaluate for signs of recurrence and other foci of infection.

Osteomyelitis

This is infection within bone. It is common in resource-limited countries, and has a number of different manifestations:

- acute haematogenous osteomyelitis
- neonatal osteomyelitis
- subacute haematogenous osteomyelitis
- chronic osteomyelitis.

Acute haematogenous osteomyelitis

Pathogenesis

- The causes are unknown.
- Infection starts in metaphyseal venous sinusoids.
- There is thrombosis of the vessels.
- Pus develops in the medullary cavity, leading to a build-up of pressure.
- If untreated, pus bursts through the cortex and spreads under the periosteum, rendering bone ischaemic (see **chronic** osteomyelitis below).
- In infants and children the pathogen is almost always *Staphylococcus aureus* (for neonates, see below). The exception is in sickle-cell disease, where *Salmonella paratyphi* is common. In this situation, use cefotaxime or ciprofloxacin.

Diagnosis

- Any child with fever and unexplained bone pain.
  - High index of suspicion.
  - Around 50% of cases will have a history of recent infection.
  - The child refuses to move the affected limb.

Investigations

- In resource-limited countries, **clinical examination is the mainstay of diagnosis**.
- White blood cell count is unreliable.
- Erythrocyte sedimentation rate is raised in 90% of cases.
- Blood culture is positive in 40–50% of cases.
- Plain X-rays: bony changes take 7–14 days.
- Aspiration and Gram stain; look for acid-fast bacilli.
- Bone scan (if available).

Treatment

- Prior to the formation of pus in the medullary cavity, antibiotics alone may suffice.
- Due to the predominance of *Staphylococcus aureus* as the causative organism, the initial antibiotic should be flucloxacillin while culture results are awaited (50 mg/kg IV or orally (maximum individual dose 2 grams) 6-hourly for 3 weeks).
- Once an abscess has formed this should be drained surgically.

Operative treatment

- Undertake incision, drilling and drainage of the osteomyelitic abscess.
- Mark the area of maximal swelling and tenderness prior to anaesthesia.
- Make a longitudinal incision.
- Dissect on to and incise the periosteum.
- Drill the cortex of the bone. If there is no pus at one site, drill further holes proximally and/or distally until pus is obtained.
- Copious irrigation is needed.
- Leave the wound open, and apply a dry or antiseptic dressing.
- Monitor post-operatively for recurrence and other foci of infection, and leave the wound to granulate.

Neonatal osteomyelitis

There are several features unique to neonatal osteomyelitis.

- In the neonate, metaphyseal vessels communicate with epiphyseal ones, thus permitting the spread of infection into the epiphysis and ultimately into the joint. Therefore acute haematogenous osteomyelitis and septic arthritis may occur together. This can lead to complete lysis of areas such as the femoral head and neck and the proximal humerus, or premature physeal arrest.
- As the immune system of the neonate is immature, there may be a less marked inflammatory response to infection, with an absence of fever, raised white blood cell count or erythrocyte sedimentation rate.
- Multiple foci of infection are more common.
- A wider spectrum of infecting organisms is found (not only *Staphylococcus aureus* but also group B streptococci and Gram-negative coliforms).
- Antibiotic treatment consists of gentamicin plus flucloxacillin.

Subacute haematogenous osteomyelitis

This differs in presentation from acute haematogenous osteomyelitis in the following ways:

- It often has an insidious onset.
- The clinical signs are less marked.
- Investigations may be inconclusive or equivocal.
- The location is usually metaphyseal, with plain X-rays showing a solitary lytic lesion (abscess) with a sclerotic margin.
- The differential diagnosis includes a neoplasm.

The usual **causative organism** is, as for acute haematogenous osteomyelitis, *Staphylococcus aureus.*

Treatment consists of surgical curettage of the lesion followed by antibiotic therapy.

Chronic osteomyelitis

If acute osteomyelitis goes untreated, the pressure due to the intramedullary pus eventually increases until it bursts through the cortical bone into the subperiosteal space. If still undecompressed, the pus spreads proximally and distally, stripping the periosteum and thus rendering this cortical bone ischaemic (having been deprived of both intramedullary and periosteal blood supply).

The avascular cortical bone therefore dies and becomes a focus of chronic infection called a 'sequestrum'. Simultaneously, a periosteal reaction occurs under the stripped periosteum, resulting in the laying down of new bone or 'involucrum'.

The appearance on plain X-ray is characteristic, with sclerotic sequestrum separated (by the abscess cavity) from an irregular and enveloping involucrum.

Chronic osteomyelitis is difficult to treat even with optimal resources. Some guidelines on its management are as follows:

- If an osteomyelitic abscess is beginning to point, or there are signs of an underlying abscess, this should be incised and drained.
- In weight-bearing bones there should be no attempt at removal of sequestrum until the overlying involucrum is mature. This maintains the potential for weight bearing and ambulation.
- Periods of immobilisation should be minimised in order to retain ranges of motion and function of nearby joints.
- Sequestrum that begins to point through the skin can be removed or excised.
- In many cases the clinical picture that results is one of intermittent flare-ups of infection which can be treated by incision and drainage of abscesses, excision of sequestrate, and antibiotic (flucloxacillin) suppression of infection as required.
- Curative treatment is often elusive even in specialised centres, and a degree of morbidity is unfortunately inevitable.

Septic arthritis

Septic arthritis is infection of a synovial joint.

Features

- It is more common in males than in females.
- The peak incidence is at around 2 years of age.
- The first symptom may be a reluctance to use the limb.
- There is a swollen tender warm joint with a restricted range of motion.
- There is commonly fever (38–40°C).
- The patient is usually **systemically unwell**.

Diagnosis

- The mainstay of diagnosis is **clinical examination**.
- The white blood cell count is raised in 30–60% of cases.
- Elevation of the erythrocyte sedimentation rate is more sensitive (except in the neonate).

Plain X-rays are often normal until there is evidence of bone destruction at 7–14 days. Common pathogens include *Staphylococcus aureus*, *Haemophilus influenzae*, group A and B streptococci, pneumococci and Gram-negative coliforms (in neonates).

Aspiration of the joint is the definitive test.

Treatment

- Antibiotic therapy should not begin until after joint aspiration and blood cultures have been taken.
- Start with flucloxacillin (infants and children) or flucloxacillin and gentamicin (neonates).
- Some studies have shown that a combination of **aspiration** and antibiotic therapy is sufficient treatment, but this must be followed by close monitoring to ensure improvement.
- If the child fails to improve, surgical washout and drainage is required either via open arthrotomy or by arthroscopic means (but only if a skilled operator and equipment are available).

Post-operative care

- Continue antibiotic therapy, and monitor for recurrence.
- Early mobilisation of the affected joint is needed to prevent stiffness.
- If treated early, the prognosis for functional recovery is good. However, if presenting late there may already have been destruction of the articular surface.
- Be alert for coexisting osteomyelitis, which is present in around 15% of cases of septic arthritis.

Tuberculosis

Tuberculosis as an entity is covered in detail in Section 6.1.N, but it is important to remember the potential orthopaedic manifestations.

- It can cause both osteomyelitis and septic arthritis.
- In both cases the signs are less marked than in their non-mycobacterial forms, and the history is usually more chronic.
- It may be associated with systemic manifestations of tuberculous disease (respiratory and renal).
- Spinal tuberculosis (Pott's disease) can be the cause of both paraplegia and scoliotic deformity.
- Treatment consists of surgical drainage and curettage of abscess cavities combined with antituberculous chemotherapy. For chronic disease and joint destruction, spinal stabilisation and joint arthrodeses may be indicated.

Non-infective conditions

The non-infective paediatric orthopaedic conditions described below can be extremely difficult to treat in resource-limited settings. First, without any form of population screening procedure in place or comprehensive primary healthcare provision, many cases will present late. Secondly, the advanced diagnostic modalities (ultrasound and arthrography) that are needed to direct treatment may not be available. Finally, where surgery is indicated, the operative techniques often need highly specialist training and/or specialised resources such as internal fixation and perioperative fluoroscopy, which are unlikely to be available in most resource-limited countries.

Fortunately, the conditions described are rare, typically occurring at a rate of less than 0.1%. They thus present far less commonly than the orthopaedic paediatric infections, and cause a lesser burden of handicap overall.

Developmental dysplasia of the hip

Formerly known as 'congenital dislocation of the hip', this complex condition has now been renamed 'developmental dysplasia' in recognition of its variable characteristics, such

as the fact that it is not always present at birth, nor does it always feature hip dislocation.

- Reported initial (neonatal) rates range from 3 to 17 per 1000 live births, but the rate of established dislocation is much lower, at around 1 per 1000.
- The aetiology is multifactorial; increased rates are seen in female children, firstborns, breech position and oligohydramnios, and there is undoubtedly a genetic influence (increased rates are associated with a positive family history and affected siblings).
- Early detection depends upon neonatal screening, which is often not available in resource-limited countries.
- If screening is to be carried out, it should involve Barlow and Ortolani tests for newborns followed by subsequent re-examination and ultrasonography of suspected cases at 1 month of age.
- Plain X-rays are of limited use before 6 months of age.

Treatment

As mentioned above, treatment of this condition in resource-limited settings is extremely difficult.

- Up to 6 months of age, gentle closed reduction can be undertaken, and then maintained in a Pavlik harness.
- If a Pavlik harness is unavailable, a plaster spica, maintaining the hips in flexion and abduction, will achieve the same objective.
- In children over 6 months of age, closed reduction can still be attempted, but is increasingly less likely to be successful due to the interposed joint capsule preventing stable concentric reduction.
- If closed reduction fails, open reduction can be attempted if surgical skills allow and infection is avoided.
- Later presentation with proximal femoral and acetabular abnormalities may require complex secondary reconstructive procedures, but these can only be undertaken in specialist hospitals by a specialist surgeon.

The reality of developmental dysplasia of the hip in resource-limited countries is that cases will often not present until after the age of 18 months, when the child has failed to walk or has an obviously abnormal gait. By this time bony changes may have occurred, the only treatment then being complex secondary procedures, the skills and resources for which are usually unavailable in a resource-limited setting.

Congenital talipes equinovarus

More than two-thirds of cases of talipes equinovarus occur in developing countries. Most children receive either no treatment or substandard care. This results in physical disability that is entirely preventable.

There are three classes of talipes equinovarus (clubfoot):

- **Postural:** this arises from intrauterine positioning, and resolves fully with passive stretching within a few weeks of birth. Parents can be trained to do this.
- **Congenital:** this arises in an otherwise normal child, and has varying degrees of severity. It occurs in 1 in 1000 live births, and is bilateral in 30–40% of cases.
- **Syndromic:** this is associated with other syndromes, such as arthrogryposis, is often severe and is refractive to treatment.

Treatment

- The goal of talipes treatment is to obtain a functional plantigrade stable foot by the time the child begins to walk (i.e. before 1 year of age).
- If it is recognised in the neonatal period, gentle daily parental manipulation may be successful, or alternatively manipulation and taping by qualified healthcare professionals (e.g. a physiotherapist). Ponseti management has gained popularity as it does not require surgery and is easily learned (www.global-help.org/publications/books/help_cfponseti.pdf).
- For cases that fail to resolve in the first 6–12 weeks, serial manipulation and plaster casting is indicated, with cast changes every 2–4 weeks.
- If the deformity still fails to resolve, there may be a place for limited percutaneous soft tissue releases (Achilles tendon or plantar fascia) at the age of 3–9 months. These techniques are relatively easily learned, have low morbidity, and are user-friendly in resource-limited settings. They should be combined with manipulation and casting.
- For the case that still fails to resolve, more extensive surgery, such as a postero-medial release, is required. The timing of this surgery is usually between 6 months and 1 year of age. Although specialist training is required to learn this operation, it can be relatively easily assimilated by the non-orthopaedic surgeon and, being only a soft tissue release, does not require any 'high-tech' surgical resources.
- Unfortunately, as with developmental dysplasia of the hip, children with this condition in resource-limited countries commonly present late (over 18 months of age), when the deformity is fixed and secondary bony changes have occurred. Correction at this stage requires a combination of bony and soft tissue surgery which can really only be undertaken by an orthopaedic specialist surgeon.
- In the adolescent child with fixed chronic deformity, the procedure of choice may be an arthrodesis (fusion) combined with correction of deformity performed at skeletal maturity.

Perthes disease (Legg–Calve–Perthes disease)

Perthes disease is a disease of uncertain aetiology involving a process of fragmentation and repair of the femoral head, possibly due to underlying idiopathic osteonecrosis.

- It usually occurs in susceptible children between 4 and 8 years of age, but can occur in children as young as 2 years or as old as 12 years.
- It is five times more common in boys, 10% of cases are bilateral, and it is associated with hyperactivity.
- It presents with a limping or waddling gait with groin, thigh or knee pain.
- X-rays show varying degrees and stages of fragmentation and repair of the femoral head.
- The prognosis depends on the degree of fragmentation and the potential for repair and remodelling prior to epiphyseal closure. A good prognosis is therefore associated with early onset and male gender (as the epiphyses close later).

Treatment

- In the majority of cases no specific treatment is indicated. The femoral head will repair and remodel satisfactorily, and the eventual outcome will be good. Bed rest, activity

restriction and abduction braces have no proven impact on the natural history of the disease.
- In the small proportion of cases that may benefit from surgery, the issue is **containment**. A very deformed femoral head may not sit or move properly in the acetabulum, and thus leads to secondary arthrosis. A proportion of these cases may benefit from varus osteotomies of the proximal femur or pelvic osteotomies. Assessment for these procedures requires arthrography at the very least, and the procedures themselves are very much the preserve of the orthopaedic specialist surgeon in a specialist hospital.

Slipped upper femoral epiphysis

Slipped upper femoral epiphysis (SUFE) (also known as slipped capital femoral epiphysis, SCFE) is a disease in which the epiphysis becomes posteriorly displaced on the femoral neck.
- The prevalence is 1–10 per 100 000, and is higher in black populations.
- It is twice as common in boys as in girls, the at-risk age group being 10–17 years for boys, and 8–15 years for girls. Most affected children are obese, and in 40% of cases there is bilateral hip involvement.
- The aetiology is unknown, but is possibly endocrine related.
- The onset may be abrupt or gradual. Sudden slips present with severe pain and inability to walk; chronic slips present with pain often referred to the knees, a slight limp, and limited internal rotation of the hip.
- Plain antero-posterior and lateral X-rays are the most important diagnostic investigations. Severity can be classified according to the degree of epiphyseal displacement. Greater than 30% displacement can result in premature osteoarthrosis.

Treatment

- The goal of treatment for SUFE is to stabilise the slippage and to promote premature fusion of the epiphysis if possible.
- Ideal treatment is fixation *in situ* with a single cannulated screw. Given the posterior position of slippage, the point of entry of the screw needs to be anterior on the femoral neck. This procedure needs to be done under fluoroscopic or X-ray control in a specialist hospital.
- Where internal fixation or peri-operative imaging is not available, an alternative would be spica cast immobilisation. However, this is often logistically difficult, and the physis may still be open even after cast removal.
- For the most severe degrees of slippage, in the hands of a specialist surgeon, reduction and fixation of the slip or femoral neck realignment osteotomies may be indicated.
- The commonest complications of operative treatment for SUFE are chondrolysis and osteonecrosis of the femoral head due to vascular compromise.

Genu varum and genu valgum

Varying degrees of bowed knees and knock-knee are common in the paediatric population. Most of these are merely variants of the normal physiological knee-angle development appropriate to the child's age. Very few will require any form of intervention.
- Normal development: Babies are born with a varus knee angle that reduces with growth to become neutral at 18 months to 2 years of age. Thereafter the knee becomes increasingly valgus, reaching a peak at 5–7 years, after which the angle gradually declines to the 5–9 degrees of valgus seen in most adults.
- **Blount's disease** is a developmental condition that affects the proximal tibial physis and results in progressive varus deformity.
- Treatment of degrees of genu valgum and genu varum depends upon the age of the child and the severity of the condition. Bracing is of no proven benefit. Various corrective osteotomies are possible, but these should be restricted to those cases with functional handicap, and are certainly not indicated merely on cosmetic grounds.

Scoliosis

Scoliosis is deformity of the spine characterised by lateral curvature and rotation.
- The commonest cause of paediatric scoliosis in resource-limited countries is probably tuberculosis (Pott's disease). X-ray appearances can be strongly suggestive of this diagnosis, and then antituberculous chemotherapy is commenced.
- The scoliotic deformity is described as idiopathic where there is no known aetiology. Contrary to popular belief, most idiopathic scoliosis is only of cosmetic significance; only the most severe cases will have any degree of cardiorespiratory compromise.
- Scoliotic bracing is expensive, has compliance problems and is unlikely to be available in resource-limited countries. If available it may have a role in slowing the progression of curves which are between 20 and 40 degrees.
- Curves that are under 40 degrees at the time of skeletal maturity are unlikely to progress further.
- Surgical correction requires a specialised hospital and a skilled fully trained surgeon and support staff.

5.18 Skin disorders

BOX 5.18.1 Minimum standards
- Anti-scabies treatment.
- Antibacterial treatment.
- Antifungal treatment.
- Topical steroids.
- Emollients.
- Antiviral treatment.

Introduction

In resource-limited countries, skin disease is dominated by bacterial infections such as impetigo and parasitic conditions such as scabies and pediculosis. It is often poorly managed, and may incur a significant economic cost to families through use of ineffective remedies. It is important to recognise whether cases reflect individual or community problems; treatment of single cases of scabies will have little impact if there is widespread infection in the community.

Scabies

Scabies is a parasitic infection caused by the mite, *Sarcoptes scabiei*, which spreads from person to person, usually by direct contact. The adult female burrows a tunnel into the stratum corneum or outer skin layer, producing eggs which hatch into larvae within 3–4 days.

'Outbreaks' in communities may follow a cyclical pattern, with peaks of incidence occurring every 4–7 years. Infection in adults usually reflects overcrowding in households and transmission through contact with infected individuals, including infants.

TABLE 5.18.1 Topical treatment of scabies

Anti-scabies preparation	Treatment	Side effects
Sulphur	Given as a 5–10% application in white soft paraffin or as soap. Treat for 1–2 weeks	Local irritation
25% Benzyl benzoate emulsion	Initial application, followed by a second one 2–3 days later	Local itching, eczema
5% Permethrin cream	One application (another is often necessary)	Minimal itching
0.5% Malathion lotion	One or two applications	Itching
1% Gamma-benzene hexachloride lotion	One to four applications	Use with caution in children; seizures have been recorded
1% Crotamiton cream	1–2 weeks of treatment	Not very effective, although it can reduce itching

Clinical presentation

The main sites of infection include fingers, wrists, elbows, ankles, genitals and buttocks; the face and head may be affected in babies, but these sites are seldom involved in older children. Important clues include the following:
- itching in several members of the same household
- lesions in characteristic sites, particularly the lateral borders of the fingers
- papules, pustules and sinuous tracks or burrows (5–10 mm).

In onchocerciasis (*see* Section 6.3.C.g), itching is also common but lesions are seldom found on the fingers.

Diagnosis

Remove mites from their burrows with a sterile needle and examine them under low power of the microscope.

Complications

Secondary bacterial (streptococcal) infection is common (see below). In severely immunocompromised individuals (e.g. those with AIDS) a crusted form of scabies, without severe itching but with large numbers of mites, may occur.

Treatment

The cheapest treatment options are sulphur based. However, they are slow to take effect, and require daily applications for 7–14 days. Permethrin is the most rapidly active but also the most expensive option.

All potentially affected areas are treated, including the soles of the feet and, in babies, the scalp.

Failure of anti-scabetic agents often occurs because there is no place where individuals can apply these treatments in privacy. Treat all members of the household, including those without itching.

Clothes should be cleaned or changed after the first treatment. Resistance to gamma-benzene hexachloride occurs. Ivermectin (oral) is highly effective for crusted scabies, but is not suitable for children under 5 years (single dose of 150 micrograms/kg). No food should be taken for 2 hours before or after the dose.

Community-based treatments, although ideal, are seldom practised as they are difficult and, although individually cheap, comparatively costly to apply to large numbers.

Impetigo

The term **pyoderma** is used to describe a range of superficial bacterial infections that include impetigo, folliculitis, abscesses (furunculosis) or secondary bacterial infection (e.g. of scabies). Impetigo is a form of pyogenic infection that involves the epidermis and is caused by Group A

streptococci or *Staphylococcus aureus*. It is not possible to separate the two infections clinically.

Ecthyma occurs when impetigo penetrates deeper, to affect the dermis and cause ulceration.

Clinical presentation

Impetigo presents with oozing and yellowish crusted plaques, often on exposed sites such as the face. These plaques may be multiple, and form blisters, in which case *Staphylococcus aureus* is the usual cause. This may be transmitted to other parts of the body and to other children. Secondary infection of scabies may occur; papules become pustular and there may be surrounding impetiginised crusts on scabetic burrows.

Boils (furuncles) are also common, and are always caused by *Staphylococcus aureus*. Lesions are large tender fluctuant masses with surrounding inflammation. They may occur in other members of the same household.

Complications

A serious complication of streptococcal impetigo or pyoderma is glomerulonephritis, which follows infection by nephritogenic strains. In tropical environments, post-streptococcal glomerulonephritis more often follows skin infection rather than throat infection.

Management

Impetigo is transmissible, and treatment should include other contacts with lesions. Cover both *Staphylococcus aureus* and streptococci, unless laboratory facilities for culture are available. A topical agent may be used, but for widespread lesions oral treatment is usual (*see* Table 5.18.2). The choice of medication is influenced by cost, extent of disease and type of lesions.

Most *Staphylococcus aureus* strains, even in remote communities, are resistant to both penicillin and tetracycline. Most topical azole antifungal agents (e.g. clotrimazole, miconazole), apart from ketoconazole, have activity against Gram-positive bacteria. Boils are best managed by incision and drainage.

TABLE 5.18.2 Treatment of impetigo

Agent	Route	Use	Cost
Cloxacillin, flucloxacillin	Oral: 12.5–25 mg/kg four times a day	For widespread and severe impetigo. Rapid effect, with clearance in 3–5 days	Expensive
Mupirocin	Topical	For localised infections. Rapid effect, with clearance in 3–7 days	Moderate
Fucidin	Topical	As for mupirocin	Moderate
Clioquinol	Topical	Slow to take effect (7–14 days). May stain skin; irritant	Cheap
Potassium permanganate (alternatives are chlorhexidine and povidone iodine)	Topical	Simple to use, stains skin. Slow to take effect (7–14 days)	Cheap

Tropical ulcer (tropical phagedenic ulcer)

Tropical ulcer mainly occurs in children and teenagers, but is seldom seen in developed countries. It is patchily distributed in endemic foci throughout Africa, India and the West Pacific. It is associated with humid regions or areas subject to local flooding.

Tropical ulcer is considered to result from synergistic bacterial infection, of which one anaerobic organism is usually *Fusobacterium ulcerans*. Other bacteria present in lesions include spiral bacteria and Gram-negative bacteria. *F. ulcerans* has also been isolated from mud and stagnant water in the vicinity of cases.

The initial lesion is a soft papule with surrounding hyper-pigmentation overlying an area of skin necrosis. This develops over at least 1 week, and when the overlying skin sloughs a regular and deep ulcer, 3–10 cm in diameter, is revealed.

Complications

With proper care and regular irrigation or cleansing of lesions the area will heal. About 5–10% of lesions may progress to chronic ulceration, and in some cases secondary squamous carcinoma or more serious infection (e.g. underlying osteomyelitis) may develop.

Management

The objective of treatment is to allow rapid healing without secondary infection.

Regimen

- Dilute antiseptic (e.g. potassium permanganate solution), or 0.9% saline for cleansing the ulcer and surrounding skin.
- Daily dressings.
- A single IM dose of benzyl penicillin (50 mg/kg) or oral metronidazole (7.5 mg/kg every 8 hours for 5 days). The former is particularly important in areas where yaws is also endemic, as it will cover both conditions.
- If healing is delayed, local pinch grafting may be necessary.

Cutaneous leishmaniasis (*see* Section 6.3.A.c).

Superficial fungal infections

Common childhood fungal infections are scalp ringworm or tinea capitis and oropharyngeal candidiasis.

Tinea infections are caused by dermatophyte fungi, which are adapted to survive on the outer layer of the skin, the stratum corneum, or structures such as hair or nails derived from it. Dermatophyte infections are caused by one of three genera of fungi, *Trichophyton*, *Microsporum*

and *Epidermophyton*, which are acquired by spread from soil, animal or human sources (geophilic, zoophilic or anthropophilic infections, respectively). By convention they are referred to by the term tinea followed by the appropriate Latin word for the site affected – for example, tinea pedis (feet), tinea corporis (body) or tinea capitis (scalp).

Tinea capitis is often endemic in rural or urban areas of resource-limited countries and inner-city areas of industrialised countries. Prevalence rates may reach over 20% in some communities.

The main signs of infection are as follows:

- scaling
- hair loss: this may be diffuse or in localised patches; scalp hairs in affected areas may break at scalp level or a few millimetres above the skin
- itching: this is variable.

The key to the diagnosis is the presence of broken hairs. Confirmation is by culture of scrapings taken from the scalp surface with a sterilised scalpel or sterile scalp brushes. The presence of infection can also be verified by microscopy of hair samples.

Complications

- Kerion is a severe pustular reaction on the scalp, which accompanies a strong immune response to ringworm infection.
- Favus is a widespread crusting form.
- Secondary infection with bacteria may occur, usually where there are crusts overlying the surface of inflamed lesions.

Management

Culture of fungus can distinguish whether infection is from a human or animal source, i.e. zoophilic species (*Microsporum canis*, from cats and dogs; *Trichophyton verrucosum*, from cattle) or anthropophilic species (*Trichophyton violaceum*, *T. tonsurans*, *T. soudanense* or *Microsporum audouinii*).

The presence of infections in close contacts (e.g. schoolmates or family) may signal child-to-child spread and alert schools to other infected children. In resource-limited countries, mass treatments have a low priority because of health resources and because cases usually self-heal.

Children with severe symptoms (e.g. kerions, favus or widespread hair loss) should be treated.

- Whitfield's ointment or imidazole antifungal agents (e.g. clotrimazole) are generally ineffective in scalp ringworm.
- The treatment of choice is griseofulvin, which is available in oral tablet or solution form, 10 mg/kg once daily (after food) and up to 20 mg/kg in refractory infections. Single-dose treatments with a 1-gram immediate dose, sometimes repeated after 1 month, have been successful for mass treatment of infected classes in school.
- Terbinafine child 10–20 kg 62.5 mg; child 20–40 kg 125 mg; child > 40 kg 250 mg all once daily for 4 weeks in tinea capitis is an alternative.
- If possible, a topical treatment such as an imidazole cream (clotrimazole) two or three times daily, ketoconazole shampoo or selenium sulphide shampoo should be given to prevent spread to others. Occasionally, kerions may require topical or oral steroids, but these are not part of their initial treatment.

Eczema (atopic dermatitis)

Eczema is a specific inflammatory disease involving the epidermis and dermis. In childhood the commonest form of eczema is atopic dermatitis. The latter is uncommon in rural areas of resource-limited countries, and appears to be associated with urban environments and increased affluence.

Clinical presentation

Severe itching and a scaling rash affect the skin flexures (e.g. the elbows, behind the knees, the neck). Scratching may be very severe, and sufficient to disturb sleep.

Management principles

- **Moisturise the skin with emollients.** Thicker more greasy preparations such as white soft paraffin or a 50:50 mixture of white soft paraffin and liquid paraffin are preferred to creams, as they provide longer-lasting effects.
- **Treat inflammatory lesions with topical corticosteroids** (once or twice daily). Weaker-strength preparations (1% hydrocortisone) are best, although it may be necessary to use medium to strong topical steroids in some cases (never use the latter on the face). Use corticosteroids only intermittently, relying on emollients for long-term management.
- **Treat complications.** These are secondary bacterial infections, usually *Staphylococcus aureus* and acute herpes simplex (eczema herpeticum): apply aciclovir cream five times a day for 5–10 days (until healed) or aciclovir orally if severe, 20 mg/kg four times a day for 5–7 days, and contact dermatitis which may include allergy to topical medicaments such as lanolin and corticosteroids. An oral antibiotic (e.g. cloxacillin or flucloxacillin 12.5–25 mg/kg four times a day) in acute flare-up of eczema may produce a good response.

Atopic eczema ranges from a mild skin rash to a severe condition that can dominate family life and may cause major family stress. Food allergy is a rare cause, and skin testing for precipitating factors is usually not helpful. In industrialised countries there are patient organisations (e.g. the National Eczema Society in the UK) which provide support and advice to patients and their families.

Hypopigmentation and hyperpigmentation disorders

These are often secondary to other inflammatory processes which should be treated. There are no effective, cheap or easily administered treatments for the pigmentary changes themselves. The common fungal disease, pityriasis versicolor, may present with hypopigmented patches on the trunk which coalesce; however, these are scaly. Treatment with topical antifungal azole creams (e.g. clotrimazole, miconazole) is effective.

Further reading

Regular updates on the management of skin disease in resource-limited environments are available in the *Community Dermatology Journal*, which can be accessed without charge on www.ifd.org

WHO (1997) *Drugs used in skin diseases.* http://apps.who.int/medicinedocs/en/d/Jh2918e

5.19 Surgical disorders

BOX 5.19.1 Minimum standards
- Surgeon experienced in working with children's disorders.
- Anaesthetist experienced in children's anaesthesia.
- Equipped theatre with appropriately sized instruments where relevant.
- Pain relief.
- Fluid management.
- Ultrasound.
- Radiography.
- Blood transfusion
- Cytology.
- Chest drain insertion.

Introduction

Children's surgery is a specialist subject. There are some emergency operations that may have to be performed by a competent general surgeon, such as appendectomy and surgery for a strangulated inguinal hernia, but most of the operations that are needed on very young children and infants require specialist knowledge and experience. Children's surgery is therefore likely to be a tertiary-level referral service.

Indirect inguinal hernia

This is the protrusion of the abdominal viscus into a peritoneal sac (the processus vaginalis) in the inguinal canal. The contents of the sac are usually intestines, but may be omentum, Meckel's diverticulum, or ovary and Fallopian tube in females.

- Around 50% of cases are seen in the first year of life, mostly before 6 months of age.
- Patent processus vaginalis (not a hernia) is present in 80% of boys at birth, in 40% at 2 years, and in 20% of adult men.
- A bulge in the groin, which sometimes extends to the scrotum, and which appears when the child cries or strains but disappears when he relaxes, is certainly a hernia. Hernias are seldom symptomatic except when they are very large or are incarcerated or strangulated. On physical examination, cough or crying impulse is the most important sign. A soft bulge that is reducible on digital pressure is also a diagnostic feature. Hernia in neonates may be transilluminant, so it is not a very reliable test to differentiate with hydrocoele.

Needle aspiration is contraindicated in any inguinal swelling because of the risk of perforating the intestines.

Differential diagnosis

This should include the following:

- **Lymphadenopathy:** firm, immobile, non-reducible, and no cough impulse.
- **Hydrocoele:** can reach the upper pole of the swelling, transilluminant, no cough impulse is present.
- **Hydrocoele of the cord:** separate from testes, non-reducible, no cough impulse, upper limit is reachable, moves on pulling on the same-sided testis.
- **Undescended testis:** scrotum empty and hypoplastic, cough impulse, may be reducible.
- **Femoral and direct inguinal hernias:** rare, but should be kept in mind.

Treatment

All inguinal hernias should be promptly repaired unless there is another medical condition that makes the anaesthetic risks prohibitive. Premature infants with hernia should not be discharged without a repair of the hernia, as the risk of incarceration is high. An anaesthetist with paediatric anaesthesia experience is required, as anaesthesia-related risks are higher in children. Post-operative apnoea may occur in premature babies and at times may require ventilatory support. If these facilities are not available, the baby should be referred to higher centres or the surgery deferred until the risks associated with anaesthesia are low.

There are reasons for avoiding delay, especially in infants.

- Spontaneous disappearance of inguinal hernia does not occur.
- The risk of incarceration is greater in infants.
- Operation is technically more difficult and the risk of injury to the vas and testicular vessels is greater in long-standing and incarcerated hernia.
- Increasing age does not affect the risk of anaesthesia so long as an experienced anaesthetist is available.

A herniotomy is performed through an incision in the lowermost transverse inguinal skin crease. The sac is identified and transfixed. Herniorrhaphy is not required, as the cause is a patent processus vaginalis. Bilateral exploration and repair are indicated in patients with bilateral hernias, but routine contralateral prophylactic exploration is no longer recommended.

Incarcerated hernia

This occurs when the intestine becomes stuck at the internal inguinal ring. If it is prolonged, the blood supply may also become compromised, causing strangulation. There is a sudden increase in the size of the hernia with severe pain and symptoms of bowel obstruction (vomiting and abdominal distension). On examination a hard tender fixed mass in the groin is palpable, with increased bowel sounds on auscultation. It may be confused with the torsion of testis, acute inguinal lymphadenitis and tense infected hydrocoele.

Treatment

This includes the following:

- adequate sedation and administration of analgesics to calm the baby
- cold fomentation (to reduce the oedema)
- the application of gentle pressure to reduce the hernial contents (however, signs of peritonitis are a contraindication).

After reduction of the hernia, the child should be admitted to the hospital and checked hourly to ensure that there is no damage to the intestine or testis, and to reduce a recurrent incarceration promptly if it occurs.

Herniotomy is performed after 48 hours to allow tissue oedema to subside.

Hydrocoele

This is accumulation of fluid in the scrotum; there is communication via a patent processus vaginalis (PPV) with the peritoneal cavity. Rarely hydrocoele is secondary to epididymo-orchitis, tumour and torsion of the testis.

- It is usually asymptomatic.
- The testis is not palpable separately, and the upper pole of the swelling is reachable, reduces on lying down and is transilluminant (hernia in a neonate may also be transilluminant).
- No cough impulse is present.

Differential diagnosis

Hydrocoele should be differentiated from **inguinal hernia**, and underlying pathology such as **tumours** and **torsion of testis** should not be missed. In older children, **spermatocoele** and **varicocoele** are non-transilluminant, have a worm-like feeling on palpation, and are separate from the testes.

Surgical treatment

This is rarely indicated. More than 90% of hydrocoeles will spontaneously disappear. **Surgery is indicated if it has not disappeared by the age of 2 years**, and for hydrocoeles that are larger and symptomatic. Herniotomy or PPV ligation, as performed for inguinal hernia, is the procedure of choice.

Undescended testis (cryptoorchidism)

An undescended testis is one that cannot be made to reach the bottom of the scrotum. It is the second most common problem in paediatric surgery after indirect inguinal hernia, and should be distinguished from the more common **retractile testis**.

The incidence of undescended testis is 2.7–3% at birth in full-term infants, decreasing to 1.5% after 1 year of age, and thereafter the incidence remains the same. It is more common in premature infants, approaching 100% at a gestational age of 32 weeks or less.

- An **ectopic testis** is one that has strayed from the inguinal canal, usually to the thigh, perineum, base of the penis, or femoral or abdominal region.
- An **ascending testis** is one that is in the scrotum at birth, but the spermatic cord fails to elongate at the same rate as body growth, so the testis becomes progressively higher in the inguinal canal during childhood.

An **impalpable testis** is quite uncommon (less than 10%), and **agenesis** is rare (20% of all impalpable testes). A fully descended but grossly hypoplastic testis may be impalpable and only identified by exploration. Normal descent of testes occurs around the seventh month of fetal life when the gubernaculum swells and shortens, drawing the testis through the inguinal canal into the scrotum. Failure of descent may occur because of hormonal failure (inadequate gonadotrophins and testosterone), a dysgenetic testis, or an anatomical abnormality such as an abnormal or malplaced gubernaculum, obstruction of the inguinal canal or scrotum, or a short vas or vessels.

Sequelae of non-descent

- The higher temperature of the extrascrotal testis causes testicular dysplasia with interstitial fibrosis and poor development of seminiferous tubules, thus hampering spermatogenesis. Testosterone production is unaffected by position. Thus a male with bilateral undescended testes will develop secondary sexual characteristics, but will be sterile.
- Due to dysplasia, there is an increased risk of malignancy (10- to 20-fold higher). The risk of malignant degeneration is not altered greatly by orchidopexy, but a position where it is palpable helps early diagnosis and gives a better prognosis. Malignancy usually develops in the second or third decade of life.
- A testis in the inguinal region is more prone to direct trauma and torsion.

Examination

An unhurried examination with warm hands and environment greatly helps in picking up a testis in an abnormal position. A hypoplastic scrotum may suggest that it has never housed a testis. In older children, squatting may coax the testis into the normal position, thus differentiating a retractile testis. Always look for an associated hernia. The position and size of the testis should be noted. If it is impalpable, ectopic locations of the testis should be examined. For a testis that cannot be felt at all, an ultrasound examination may be helpful. Bilateral non-palpable testes may require laparoscopic examination and hormonal profiles in a higher centre.

Treatment

The histological changes in the testes occur as early as 6 months of postnatal life, and therefore a child who has an undescended testis should be operated at the earliest time possible to prevent such changes.

The best time for orchidopexy is about 1 year of age, and preferably before the child's second birthday.

- The hernial sac should be dissected from the cord structures and a high ligation done.
- The testis is placed in an extra-dartos pouch in the scrotum after an adequate dissection and mobilisation of the vas and vessels. Retroperitoneal dissection and careful snipping off of lateral peritoneal bands will give an adequate length to the cord.
- In about 50% of cases of impalpable testis a useful testis can be brought down, and in the remaining 50% there is either no testis present (testicular agenesis or intrauterine torsion-vanishing testis), or there is a useless and potentially neoplastic testis, which is removed.
- For an abdominal testis, laparoscopy is useful for identifying and confirming the position of the testis and

simultaneously permitting the ligation of spermatic vessels (Fowler–Stephen's stage I operation). Later the testis can be brought into the scrotum after dividing the artery, the testicular blood supply being supported by the artery to the vas.
- For psychological reasons, if orchidectomy has been undertaken, prosthetic replacement should be performed later on.
- In bilateral undescended testes, especially with hypospadias, an intersex disorder should be suspected and the child should be further investigated.

Prognosis
There is a 2% recurrence rate, 2–5% incidence of atrophy, 70–80% fertility after unilateral orchidopexy, and 40% fertility after bilateral orchidopexy.

Phimosis
Phimosis is defined as excessive tightness of the foreskin, preventing retraction behind the glans. It occurs in 1–2% of males. The foreskin normally cannot be retracted in infants, and non-retractability of the foreskin is not pathological until the age of 3 years. Forced retraction may cause phimosis by producing tears in the foreskin, which heals with scarring and contraction. If there is pooling of urine and repeated attacks of balanoposthitis, simple dilatation of the foreskin can be done and the mother given advice about local hygiene.

After the age of 3 years, the foreskin becomes naturally retractile. Explain to the mother that daily retraction and cleansing of the glans will prevent recurrence of the phimosis. At the same time it is of utmost importance to emphasise the importance of reducing the prepuce over the glans to avoid paraphimosis, which is an inability to bring the foreskin into its natural position because it is trapped in the sulcus at the base of the glans.

Circumcision for phimosis is only indicated where the prepucial skin is scarred and fibrotic due to balanitis xerotica obliterans.

Hypospadias
This is a condition where the urethra opens on the ventral aspect of the penis at a point proximal to the normal site. When it opens on the dorsal aspect (termed 'epispadias') there is usually associated exstrophy of the bladder.
- Hypospadias is one of the commonest congenital anomalies of the male genitals, occurring in 1 in 300 male births. There are various degrees of severity depending on how far back the urethral meatus lies. It may be associated with undescended testes, and in severe cases there is a possibility of an intersex problem.
- Ventral curvature of the shaft of the penis is called a 'chordee'. It is due to fibrosis of the urethral plate, shortened skin, or fibrosis of the corpora cavernosa. The prepuce is deficient ventrally, and an unsightly dorsal hood of redundant skin is present.
- Congenital short urethra is a deformity where there is ventral curvature of the shaft of the penis without hypospadias.

The disabilities of hypospadias are cosmesis of the penis, a stream that is deflected downwards or splashes, and in severe hypospadias, boys have to void in a sitting position (like females). Uncorrected chordee interferes with intercourse, and there is infertility in severe hypospadias (penoscrotal and perineal), as semen is not directed into the vagina.

Treatment
Hypospadias should be corrected before school age so that the child does not feel ostracised in society. In severe cases of hypospadias, intersex disorders and associated urological abnormalities such as pelvic-ureteric junction obstruction or renal agenesis should be ruled out.

Principles of surgery
These are as follows:
- correction of chordee to straighten the penis (orthoplasty)
- movement of the urinary meatus to its normal position on the tip of the penis (urethroplasty)
- correction of the deformity of the glans to give it a conical shape (glansplasty).

No infant with hypospadias should be circumcised, as the prepuce is essential for the repair. Repair can be undertaken as a one-time or staged procedure. It depends on the degree of chordee and the severity of the hypospadias.

Bladder stones
In resource-limited countries, bladder stones are quite common due to the prevalence of malnutrition. The stones are composed of ammonium acid urate and oxalate, and are seen in lower socio-economic groups. Such stones are usually related to a high dietary intake of rice or wheat and low intake of milk and animal protein (*see* Section 5.10.B).

Children present with increased frequency of urine and strangury or haematuria (the child usually holds the penis and rubs it with the finger and cries during micturition). Children may present with an episode of retention of urine if the bladder stone becomes impacted at the bladder neck or in the urethra.

During rectal examination, a stone may be palpable on bimanual palpation. A plain abdominal X-ray may reveal calcified stones. Abdominal ultrasonography will detect non-calcified stones.

Treatment
Open stone surgery is the modality of choice. Endoscopic removal can be performed in some children if the necessary equipment and expertise are available.

If there is no infection, two-layered closure of the bladder is sufficient, requiring no catheter or suprapubic drainage. Once the stones have been removed, recurrence is rare.

Cervical swellings
The neck is one of the commonest sites of cystic and solid swellings during childhood. Lesions are either developmental anomalies arising from the remnants of branchial arches, thyroglossal tract, jugular lymphatics or the skin, or acquired as in diseases of the salivary gland, lymph nodes or thyroid gland.
- Lymphangiomas (cystic hygroma).
- Branchial cysts/fistulae.
- Thyroglossal cyst.

- Ectopic thyroid/thyroid swellings.
- Epidermal cyst.
- Swelling of salivary glands.
- Haemangiomas.
- Lymph-node swellings.

Lymphadenopathy

Enlargement of the lymph nodes may result from acute or chronic infection and from primary or secondary neoplasia.

- Infection is the commonest cause of lymph node enlargement in childhood, secondary to scalp and skin infections, including lice.
- Tuberculosis is the most important pathogen in resource-limited countries.
- In many cases the lymph nodes are reacting to an upper respiratory tract infection or an ear infection. This is known as **non-specific reactive hyperplasia**, and is much more common. Thus not every enlarged lymph node needs a surgical biopsy.
- Primary tumours of the lymph nodes include lymphoma and leukaemia.

Enlargement of a lymph node by more than 1 cm is significant, and a persistent node more than 3 cm in diameter requires fine-needle aspiration cytology or surgical biopsy.

A careful history with regard to repeated upper respiratory tract infections, boils on the scalp or drainage area, and ear discharge, should be taken. A positive family history of tuberculosis is an important feature of tubercular lymphadenitis. A history of the pattern of fever, loss of weight and appetite, and the presence of night sweats are important features when making a differential diagnosis.

On careful physical examination, all sites of lymph nodes (cervical, axillary, inguinal and abdominal) should be examined. The size, number, consistency, tenderness, and presence or absence of fluctuations should be noted. On abdominal examination, liver, spleen and mesenteric lymph nodes should be palpated. The drainage area of the lymph nodes should be examined for boils, furuncles, injury or neoplastic swelling. The tonsils should be inspected for enlargement and suppuration.

- In **acute lymphadenitis**, the affected nodes are enlarged, painful and tender, restricting movement of local areas of the body. Fever and leukocytosis are common. Untreated infections may resolve spontaneously, progress to suppuration and abscess formation, or become chronic.
- In **tubercular lymphadenitis**, lymph nodes are enlarged and painless, and become matted together and fixed to adjacent structures. Caseation leads to the formation of 'cold' abscesses, which lack the local and systemic signs of acute inflammation (fever, tenderness and erythema). When a cold abscess ruptures through the deep fascia (a 'collar-stud abscess') the skin becomes red and thin, takes on a blue tinge and then gives way to establish an indolent tubercular sinus. On aspiration, straw-coloured fluid is present, in contrast to the thick pus that is usually present in an acute abscess. Confirmation depends on culture of the organisms or visualisation of acid-fast bacilli on microscopy.
- In **primary neoplasia (e.g. leukaemia)** the nodes are painless, rubbery in consistency and discrete. Liver and spleen enlargement may or may not be present. Systemic features of low-grade fever, night sweats, or loss of weight and appetite point towards the diagnosis.
- **Secondary enlargement of the lymph nodes** due to neoplasia is rare in childhood.
- **Primary cancers** are soft-tissue sarcomas and very rare. The nodes are large, firm to hard in consistency, and fixed to underlying structures.

Investigations

- Full blood count.
- The erythrocyte sedimentation rate is usually raised in chronic infection and neoplasms. Leukocytosis is seen in acute lymphadenitis and abscess formation. Leukaemia will usually be diagnosed by the appearance of leukaemic cells in peripheral blood.
- Mantoux test. To diagnose tuberculosis, start with 1 in 10 000 and then 1 in 1000. A strongly positive test is a pointer towards the diagnosis; if the test is negative, it does not rule out the disease (especially in the presence of HIV infection).
- X-ray of the chest.
- To identify there is the pulmonary lesion of primary complex or the hilar lymphadenopathy seen in cases of tuberculosis. Mediastinal widening is seen in patients with lymphomas.
- Fine-needle aspiration cytology (FNAC) is helpful if there are persistent lymph nodes that do not decrease in size after a 1-week course of antibiotics and another week of observation. Lymphomas cannot be definitely diagnosed on FNAC, and a surgical biopsy is mandatory.

Treatment

Acute lymphadenitis

- Antibiotics are prescribed. Penicillin is usually appropriate, as most infections occur outside the hospital setting. Oral or IV preparations may be used. If improvement has not occurred within 48 hours, a broad-spectrum antibiotic such as an oral or IV cephalosporin may be started.
- Anti-inflammatory medication (to relieve the pain and reduce the swelling).
- Hot fomentation (to relieve the pain and reduce the swelling).

Fluctuation, or other local signs of abscess formation, indicate the need for **incision and drainage of pus**, which is best performed under general anaesthesia. All of the loculi are broken and necrotic material is curetted out. **Always visualise and remember the important structures nearby.** A sample should be sent for microscopy (including Ziehl–Neelsen staining), culture and sensitivity, and appropriate antibiotics prescribed. The precipitating cause of acute lymphadenitis should also be treated.

Tubercular lymphadenitis

Antitubercular treatment leads to resolution (a full course of 9 months should be undertaken, with four drugs for 2 months and two drugs for the next 7 months; *see* Section 6.1.N).

Cold abscesses require drainage, and repeated aspirations may be preferable to avoid sinus formation, pending diagnosis and initiation of treatment.

Lymphomas and leukaemias

After diagnosis, further investigations will be required to stage the disease and its treatment (*see* Section 5.14).

Cystic hygroma

This is a hamartoma of the jugular lymph sac which presents in infancy and is more common in boys than in girls. It produces a major neck swelling and is diagnosed by inspection. The swelling is usually found as a unilateral, fluctuant, transilluminant swelling centred on the carotid triangle. The cysts are of varying sizes and contain clear fluid. A haemangiomatous element may be present in the swelling, giving it a reddish tinge instead of a light blue colour. Cysts may enlarge suddenly due to viral or bacterial infection or haemorrhage. If the cyst compresses airways and vessels, it may cause stridor, respiratory distress and superior vena caval syndrome. Initially these lesions can be treated by aspiration and intralesional injection of bleomycin (a less expensive anti-cancer drug), at a dose of 300–600 micrograms/kg; these procedures can be repeated every 2–6 weeks, producing excellent results in the majority of cases. Surgical excision is difficult, and removal should be attempted without sacrificing important structures, in some cases in conjunction with sclerotherapy.

Branchial cysts, sinuses and fistulae

Sinuses and fistulae most commonly arise from the second branchial cleft, and occasionally from the first or third one. They present as a small discharging sinus on the skin overlying the lower third of the sternomastoid muscle. Parents often notice a drop of clear fluid coming from a very small opening. Sinuses and fistulae usually present in early childhood, and may sometimes be complicated by infection and abscess formation. Treatment consists of surgical excision of the whole tract up to the pyriform fossa to prevent recurrence. Methylene blue is injected or a nylon thread guided in the fistula to delineate it during surgical dissection for appropriate excision.

Thyroglossal cyst

The descent of the thyroid gland from the floor of the fetal mouth leaves a tract from the foramen caecum of the tongue to the thyroid isthmus. A cyst lined by respiratory epithelium may arise anywhere along the tract, but is usually subhyoid (75%). The swelling is in the midline and moves with swallowing and also with protrusion of the tongue. An infected cyst may be mistaken for acute bacterial lymphadenitis, or an ectopic thyroid may cause a similar swelling.

The thyroglossal cyst and the entire tract along with the central portion of hyoid bone should be excised to minimise the risk of recurrence (Sistrunk's operation).

Epidermoid cyst

Inclusion dermoid cysts arise from ectodermal cells that become detached during fetal growth. They are often in the midline or along lines of embryonic fusion. They contain sebaceous cheesy material surrounded by squamous epithelium. They enlarge slowly and should be removed completely; the capsule should not be breached to prevent recurrence.

Haemangiomas

These are the most common tumours of infancy and the most common congenital anomalies. They are present in around 1–3% of all newborn infants. This figure increases to 10% by 1 year of age. Haemangiomas can be capillary or cavernous, although both types may be present.

The natural history of capillary haemangiomas is as follows:

- They initially present shortly after birth as a pale pink or bright red spot or patch on the skin.
- There is subsequently rapid growth in infancy for 3–6 months, followed by a static phase.
- At 18–24 months the lesion starts to involute. Around 50% will involute by 5 years and 90% by 7 years. Rarely the lesion persists and requires excision.

A cavernous haemangioma has a deeper component in subcutaneous tissues or muscles, and is less likely to regress completely.

Management

Management of these lesions consists of an accurate diagnosis and careful observation. Parents need reassurance when the lesion is growing rapidly. Problems of ulceration, bleeding and (rarely) infection occur secondary to minor trauma. These are best treated non-operatively.

- Surgical excision is indicated when there is functional or gross cosmetic disability (e.g. a haemangioma on the eyelid), or a vital organ is threatened.
- Steroids may be used to induce involution in large haemangiomas (prednisolone 1–2 mg/kg/day for 2–4 weeks; the dose is tapered off before stopping the therapy). These can be repeated in cycles, with a gap of 4–6 weeks. Intra-lesional steroids can be used to induce regression in the size of haemangiomas in and around the eye.

Obstructive jaundice in infancy

This is most commonly caused by extrahepatic biliary atresia, choledochal cyst or inspissated bile syndrome.

- The most difficult differential diagnosis is neonatal hepatitis.
- If jaundice in the newborn persists, the stools are never yellow or green, and the urine is brown, a conjugated bilirubin level should be measured and urobilinogen and bilirubin looked for in the urine.
- Ultrasound may help in diagnosis. Strongly suspected cases need referral for radioactive scan and further management.

Empyema thoracis (*see* Section 5.3.B)

This is defined as an accumulation of pus in the pleural space. In most children this results from an infected pleural effusion associated with ongoing uncontrolled pulmonary sepsis or pneumonia. An infection of the pleural space is unlikely when there is a healthy underlying lung that is completely expanded. Empyemas and effusions may be diffuse and involve the entire pleural space, or they may be intralobar, diaphragmatic or paramediastinal.

Before the advent of antibiotic therapy, *Pneumococcus* and *Streptococcus* species were the organisms most frequently associated with empyema. Currently

Staphylococcus aureus is the most common organism. In resource-limited countries, *Mycobacterium tuberculosis* is an important cause.

Other reasons for empyema include extension of lung abscess, trauma and extension of subphrenic abscess.

An empyema usually presents with pleuritic chest pain and a heavy sensation on the involved side. The child is febrile, tachypnoeic, tachycardic and may have a cough that is productive (purulent sputum).

Examination

On examination there is reduced respiratory excursion, pain and dullness on percussion. A friction rub or distant to absent breath sounds may be heard on auscultation of the involved side.

- Chest X-rays in the antero-posterior and lateral views are necessary for the accurate localisation of the empyema. The underlying lung may show consolidation or evidence of infection by tubercular organisms. There may be evidence of a mediastinal shift to the opposite side. The presence of pneumatocoeles indicates staphylococcal infection.
- An ultrasound scan may help to distinguish fluid from consolidation in a patient with complete opacification. It is also helpful for localising a loculated empyema that may be drained. It is essential for evaluating the condition of the underlying lung in order to decide whether to proceed with decortication or pneumonectomy.

Management

Treatment depends on the cause, whether the condition is acute or chronic, the state of the underlying lung, the presence of a bronchopleural fistula, the ability to obliterate the space, and the patient's clinical condition and nutritional status.

- Fluid from the effusion should be aspirated (by thoracocentesis) under ultrasound control after giving local anaesthesia (*see* Section 5.3.B).
- If the fluid is serosanguinous, thoracocentesis and appropriate antibiotics (benzylpenicillin and flucloxacillin) given by the IV route until the temperature settles (change the antibiotics according to sensitivity), and then orally, for a total period of 6 weeks, can be a definitive treatment.
- If the fluid is thick and purulent, a tube thoracostomy is indicated. An intercostal tube should be placed in a dependent position to encourage the pleural space to drain completely. Simultaneously, physiotherapy should be instituted to expand the lung and obliterate the space (*see* Section 8.3 for placement of chest drains).
- If loculated and undrained pockets are present and the lung is not expanding on tube thoracostomy, an open surgical procedure (decortication) will be required, but adequate time should be given to non-operative treatment. If the underlying lung is badly damaged, and will not expand on vigorous physiotherapy, pneumonectomy is indicated.
- In tubercular empyema, a 6- to 8-week course of antitubercular treatment (*see* Section 6.1.N) is essential for optimum results. Surgical therapy should be withheld, except for emergency drainage, until the tubercular disease in the lung has regressed or stabilised, as shown on the serial chest X-rays.

Urinary tract infection (UTI) due to surgical causes

Recurrent UTI requires investigation to exclude the following structural and functional abnormalities:

- vesico-ureteric reflux (*see* Section 5.6.B)
- posterior urethral valves
- neurogenic bladder (*see* Section 4.2.D)
- urethral strictures
- bladder stones (see above)
- diverticulum of the bladder and urethra
- voiding dysfunction.

Umbilical pathology

Umbilical hernia

- This is a defect in the umbilical ring, which generally closes at birth, leading to protrusion of a loop of bowel or omentum through it. Some degree of herniation is seen in 20% of newborn babies, and still more in premature babies or when there is any increase in intra-abdominal pressure (e.g. due to ascites or VP shunt).
- Swelling appears on crying and straining, and decreases when the child is calm.
- It can be reduced with an audible gurgle.

Most umbilical hernias close spontaneously in the first 12 months of life, but they may take up to 3 years. Strangulation and incarceration are virtually unknown; therefore it is safe to wait. **Strapping with coin application is contraindicated**, as it leads to maceration of skin and infection, without any real advantage of inducing closure.

Surgical indications are a large hernia that has not closed by 3 years of age or an incarceration.

Umbilical discharge

- **Purulent discharge** is seen in umbilical sepsis. **Neonatal tetanus** is a serious condition in which mortality is very high (*see* Section 3.4) (cow dung application, as practised in rural India, is one cause). Portal thrombosis may occur secondary to it and manifest later as portal hypertension. Appropriate antibiotics (benzylpenicillin) should be instituted at the earliest possible stage, and local hygiene maintained.
- **Mucus/serous discharge** is seen in umbilical polyps and **granulomas**. Silver nitrate application will enable these to epithelialise. If these persist, excision will be required. Umbilical fistula may be present and require exploration and excision.
- **Urinary discharge** is seen with a patent urachus in association with a lower urinary tract obstruction. It is quite rare. Surgical treatment involves excision of the urachal remnant after investigation and relief of any underlying outlet obstruction.
- **Faecal discharge** is seen with a patent vitello-intestinal duct. This is a persistence of the connection between the yolk sac and the midgut, which normally disappears at about the sixth week of gestation. All remnants need to be excised, which may necessitate a laparotomy to search for any discontinuous segments of the tract.

Appendicitis

Appendicitis is the most common abdominal surgical emergency. Although diagnosis and treatment have improved,

appendicitis continues to cause significant morbidity, and is still (although rarely) a cause of death. However, abdominal pain unrelated to appendicitis is also common, and in many cases a few hours of active observation are recommended before proceeding to surgery.

Appendicitis results from luminal obstruction following infection or impaction by a faecolith. Inflammation of the appendix does not inevitably lead to perforation, as spontaneous resolution may occur.

Clinical presentation

- Presentation is very variable.
- Pain is invariably present and nearly always the first symptom. Early visceral pain is non-specific in the epigastric or umbilical region, and **only later does pain become localised over the appendix**, most typically at McBurney's point. Pain with a pelvic appendix is often delayed in onset because the inflamed appendix does not contact the peritoneum until rupture occurs and infection spreads. Pain of a retrocaecal appendix may be in the flank or back.
- Anorexia, nausea and vomiting typically follow the onset of pain within a few hours.
- Diarrhoea occurs more frequently in children than in adults, and can result in misdiagnosis. It may indicate a pelvic abscess.
- The child with acute appendicitis lies in bed with minimal movement. There may be fever and tachycardia.
- The patient may be asymptomatic before perforation occurs, and symptoms may be present for longer than 48 hours without perforation. In general, however, the longer the duration of symptoms, the greater the risk of perforation.

Examination

Examination of the chest to rule out a lower respiratory tract infection is essential.

The single most important aspect of evaluation is serial examination undertaken by the same person. This decreases the number of unnecessary operations. Analgesia should not be withheld as was previously advised.

Investigation

There may be an increase in the white blood cell count, but this is unreliable.

Ultrasonography is an effective diagnostic aid, with a sensitivity of about 85% and a specificity of about 90%. Demonstration of a non-compressible appendix that is 7 mm or larger in antero-posterior diameter is the primary criterion.

Management

- The initial management involves IV fluids and adequate analgesia.
- In a patient who presents with peritonitis, adequate fluid resuscitation (*see* Section 5.5.B) must be performed before surgery is undertaken.
- For early non-ruptured appendicitis, peri-operative antibiotics (cefuroxime and metronidazole) should be given.
- For perforated appendicitis after appendicectomy, saline irrigation of the peritoneal cavity with the patient in the head-high position is advisable in an attempt to remove as much infected material as possible. Intravenous antibiotics should be given for at least 5 days:
  - Cefuroxime (50 mg/kg 8- to 12-hourly) plus metronidazole (7.5 mg/kg 8-hourly IV over 20 minutes)

  OR
  - Ampicillin IV (25–50 mg/kg 8-hourly; maximum 4 grams/day) plus gentamicin (7 mg/kg once daily) plus metronidazole (7.5 mg/kg 8-hourly).
- If the initial presentation is with an appendicular mass, conservative treatment with IV antibiotics is given until the symptoms subside, with a plan for an interval appendicectomy.

Complications

Complications following appendicectomy include wound infection, abscess formation (local, subphrenic or pelvic) and paralytic ileus. A late complication may be an adhesive bowel obstruction.

Pyloric stenosis

This is a classical cause of gastric outlet obstruction in infants. It has a prevalence rate of about 1.5 to 4 in 1000 live births among white populations, but is less common in Africans and Asians. It is more common in males than in females, with a ratio of between 2:1 and 5:1. There appears to be an increased risk to firstborn infants with a positive family history.

Cause

No definite cause has been established. Pathologically there is marked muscle hypertrophy, primarily involving the circular layer, which produces partial or complete luminal obstruction.

Presentation

Pyloric stenosis typically presents at 2–8 weeks of age, with a peak occurrence at 3–5 weeks. The **vomiting is projectile and non-bilious**. Occasionally there is coffee-ground vomiting due to gastritis or oesophagitis. The child remains hungry after vomiting, and is otherwise not ill looking or febrile. Around 2–5% of infants have jaundice associated with indirect hyperbilirubinaemia. Non-bilious projectile vomiting, visible gastric peristalsis in the left upper abdomen, and in those presenting late a hypochloraemic hypokalaemic metabolic alkalosis are the cardinal features of pyloric stenosis.

Diagnosis

A definite diagnosis can be made in 75% of infants with pyloric stenosis by careful physical examination of the upper abdomen. **An absolute prerequisite for this is a calm and cooperative child, a warm environment, good light and patience.** With the patient in the supine position, in the mother's left arm and sucking on the left breast, and the surgeon sitting on the left side of the patient, the left hand is used to feel the classically described 'olive' to the right of the rectus muscle, often palpated against the spinal column. Visible gastric peristalsis is often noticed.

Investigations

- Ultrasonography is the most commonly used imaging technique for diagnosis. A positive finding is a pyloric canal length of 16 mm or more and a pyloric muscle thickness of 4 mm or more. A diameter of more than 14 mm is also considered abnormal.

- Blood investigations in an advanced situation may show the typical hypochloraemic hypokalaemic metabolic alkalosis.

Management

- It is most important to prepare the patient appropriately and adequately for anaesthesia and surgery.
- Intravenous fluid resuscitation with 5% glucose in 0.9% saline with 20–40 mEq/litre of potassium chloride is the optimal fluid.
- Urine output and serum electrolytes should be monitored.
- The stomach should be aspirated before the operation.
- Ramstedt's pyloromyotomy performed through a right upper quadrant or supraumbilical incision is curative, and is associated with a low morbidity.
- The majority of these patients can be started on feeds about 6 hours after surgery.
- Those who present with haematemesis from gastritis may benefit from delay of feeding for an additional 6–12 hours after surgery.
- Vomiting in the early post-operative period is thought to be secondary to discordant gastric peristalsis or atony.

Intussusception

This is the telescoping of a portion of the intestine into the lumen of an immediately adjoining part. Typically it occurs in a well-nourished child aged 4–12 months. The male:female ratio is 3:2, and it is more common in Caucasians.

The pathogenesis of intussusception is unclear. It usually originates in the ileum close to the ileocaecal junction and proceeds into the ascending colon. In 2–8% of cases there is a specific lead point such as a Meckel's diverticulum, polyp or duplication cyst. Adenoviral infection resulting in lymphoid hyperplasia may act as a lead point.

Clinical presentation

- The infant is suddenly disturbed by what appears to be violent abdominal pain. The pain is colicky, intermittent and severe. With spasms the infant draws up the knees to the abdomen, screams, becomes pale and may sweat, and vomiting occurs soon afterwards. The infant may pass a normal stool, appears to recover immediately, and may resume normal eating habits, until stricken by another bout of colicky abdominal pain. The vomiting is initially reflex, but with a delayed diagnosis becomes secondary to intestinal obstruction and is often bile-stained.
- Classically, the infant passes stool that resembles redcurrant jelly. Many parents describe this as the presenting symptom, and consequently it is often treated as bacillary dysentery initially.
- **The triad of pain, vomiting and blood per rectum is present in only one-third of patients.** One in 10 infants with intussusception will have diarrhoea before signs and symptoms attributable to intussusception become obvious. This is often a cause for delay in diagnosis.
- Pallor, persistent apathy and dehydration are common signs.
- Abdominal examination reveals emptiness in the right lower quadrant and a **sausage-shaped mass in the right hypochondrium**, extending along the line of the transverse colon. **The mass is not always easy to palpate, and its absence does not rule out an intussusception.**
- Fever and leukocytosis are common, and tachycardia results from episodes of colic and hypovolaemia from dehydration.

Investigations

- Abdominal X-ray may show a soft tissue mass across the central abdomen with dilated loops of bowel.
- **Ultrasonography has become the standard non-invasive diagnostic test, and is very reliable. Doughnut (target or concentric ring) and pseudo-kidney sign suggest a diagnosis of intussusception.**

Management

The most important aspect of treatment is adequate resuscitation prior to intervention. This involves establishing reliable IV access, collecting blood for baseline investigations and for cross-matching, passing a nasogastric tube for decompression, and giving IV fluids and analgesia. Some patients may require one or more boluses of 10–20 mL/kg of albumin or Ringer-lactate solution when first seen.

Broad-spectrum IV antibiotics such as a combination of cefuroxime (25–50 mg/kg 8-hourly, depending on the degree of infection) and metronidazole (7.5 mg/kg 8-hourly IV over 20 minutes) are started, and the urine output is monitored.

Management is initially non-surgical (i.e. with the use of air or barium enema). Sedation should be used for the procedure.

- **A surgeon and theatre should be ready when the radiologist attempts reduction. If perforation occurs, surgery should be performed immediately.**
- **An absolute contraindication to rectal reduction is evidence of peritonitis, indicating the presence of a gangrenous intestine.**

If hydrostatic reduction fails and if the patient is stable, a repeat reduction may be attempted. Once the intussusception reduces, the child should be observed overnight with careful monitoring of fluid and electrolytes.

If reduction fails, the child is taken for surgery, where by gentle manipulation (pushing and not pulling) the intussusception can be reduced. The appendix may be removed, recorded and the parents informed. If a pathological lead point is found, a resection anastomosis is performed. If the bowel is not viable, it is resected and a primary anastomosis is performed. Feeds are started the day after the operation and increased gradually.

Intravenous antibiotics should be given for at least 48 hours, and longer (for 7 days) if peritonitis is present.

The interval between the onset of symptoms and institution of treatment is of paramount importance, and mortality can be reduced if the condition is recognised and treated early.

Intestinal obstruction

This is the most common condition requiring emergency surgery in infants and children. Most causes result from complications of congenital anomalies or from inflammatory conditions that affect the bowel.

Causes

- **Extrinsic causes:** incarcerated hernia and vascular bands, intussusception, anomalies of rotation (volvulus and Ladd's bands, paraduodenal and paracaecal hernias), post-operative adhesions.
- **Intrinsic causes:** inspissation of bowel contents (meconium ileus, distal intestinal obstruction syndrome in patients with cystic fibrosis), roundworm obstruction.
- **Peristaltic dysfunction:** Hirschsprung's disease.
- **Inflammatory lesions:** tuberculosis, Crohn's disease.

Symptoms and signs

Patients present with cramping abdominal pain with anorexia, nausea and vomiting, which progresses to become bile-stained. Abdominal distension occurs, with the degree being directly related to the site of obstruction in the gastrointestinal tract, such that the distension is greater the more distal the obstruction.

On examination, the patient may have tachycardia and signs of dehydration. Tenderness and hyperactive bowel sounds are present on abdominal examination.

Chest and abdominal films are taken to confirm the diagnosis of obstruction and rule out the presence of free air.

Treatment

- The goal of treatment is to relieve obstruction before ischaemic bowel injury occurs.
- Intravenous access is established and blood collected for baseline investigations, including a full blood count, urea, creatinine and electrolytes, and cross-matching.
  - Intravenous fluids (Ringer-lactate or Hartmann's solution with 10% glucose) are started according to the guidelines of 4 mL/kg/hour for the first 10 kg, 2 mL/kg/hour for the next 10 kg, and 1 mL/kg/hour for the next 10 kg.
  - For example, a child weighing 22 kg would need 40 + 20 + 2 = 62 mL/hour.
- Some patients may need one or more IV boluses (10–20 mL/kg) with Ringer-lactate or Hartmann's solution or albumin at the start of resuscitation.
- A nasogastric tube is passed for decompression.
- Give broad-spectrum IV antibiotics such as:
  - cefuroxime 50 mg/kg 8-hourly or 12-hourly in the neonate, and metronidazole 7.5 mg/kg 8-hourly IV **or**
  - benzylpenicillin 50 mg/kg 6-hourly plus gentamicin 7 mg/kg once daily plus metronidazole 7.5 mg/kg 8-hourly.
- Once the patient is adequately resuscitated and fluid and electrolyte imbalances have been corrected, laparotomy is performed and the cause treated. Transfer to a facility where paediatric surgical and anaesthetic skills are available should be undertaken if the patient's condition will tolerate this. Otherwise, or in the absence of such a facility in the country, surgery should be performed.
- At all times adequate analgesia should be given (*see* Section 1.15).

Hirschsprung's disease

This is characterised by an absence of ganglion cells in the affected intestine. The incidence is about 1 in 4400–7000 live births; the male:female ratio is about 4:1, and in long segment disease it approaches 1:1. The longer the segment of aganglionosis, the higher is the familial incidence.

Associated conditions

These include Down's syndrome (4–16%), Waardenburg syndrome, multiple endocrine neoplasia 2A and Von Recklinghausen's disease. A higher incidence of enterocolitis has been noted in patients with Hirschsprung's disease and Down's syndrome.

Presentation

The usual presentation is with delay of passage of meconium beyond 48 hours after birth. (Around 95% of full-term infants pass meconium within 24 hours after birth, and the remainder pass it within 48 hours.) The child then has episodes of constipation, abdominal distension, vomiting and poor feeding, and fails to thrive. They may also present with a history of constipation with explosive diarrhoea, the latter indicating the development of enterocolitis.

Differential diagnosis

Hirschsprung's disease should be considered in the differential diagnosis of any child who has constipation dating back to the newborn period. However, childhood constipation related to dietary and habitual problems needs to be carefully ruled out in order to avoid unnecessary X-rays and biopsies.

Examination

On examination the child has a distended abdomen, and after a rectal examination there is often explosive passage of flatus and faeces.

- A plain X-ray of the abdomen may show dilated bowel loops with paucity of air in the location of the rectum. Barium enema may show the characteristic coning, although a simple colonic dilatation can occur in any chronic constipation.
- Rectal biopsy remains the gold standard for diagnosis. It should be performed at least 2 cm above the anal valves, as the normal anus has a paucity or absence of ganglion cells at the level of the internal sphincter. Although suction rectal biopsy with acetylcholinesterase staining has become the accepted standard for diagnosis in most centres, a full-thickness rectal biopsy under general anaesthesia is equally useful if such facilities are not available.

Treatment

Enterocolitis remains the major cause of morbidity, and has a mortality rate of around 6–30%. It manifests clinically as explosive diarrhoea, abdominal distension and fever. The pathophysiology is not fully understood. The diagnosis is made on clinical grounds, and treatment is conservative, consisting of IV fluids and rectal washouts to decompress the colon.

Surgery

The surgical treatment of Hirschsprung's disease has evolved from a three-stage procedure (initial colostomy with multiple seromuscular biopsies, pull-through of the ganglionic colon as the second stage, and closure of colostomy as the third stage) through a two-stage procedure (colostomy at the transition zone initially, and pull-through as a second stage) to a one-stage procedure without a colostomy. The essential prerequisite for a primary pull-through is adequate preparation with colonic washouts.

Perforative peritonitis

The causes of perforation include amoebiasis, typhoid, tuberculosis, roundworm perforation and Hirschsprung's disease (*see* Section 6).

Management starts with an adequate history and clinical examination, followed by chest and abdominal X-rays. Adequate resuscitation should be carried out as outlined in the section on intestinal obstruction. After this a laparotomy is performed and the cause treated. Treatment includes fluid resuscitation if necessary, and antibiotics (either a third-generation cephalosporin or an aminoglycoside plus metronidazole).

Further reading

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