the infant for a surgical opinion if they are not better by 4 weeks.

**Fractures**
The most common types are skull and clavicular fractures. These usually require no specific treatment. However, significant skull fractures must be evaluated for intracranial bleeding. There should also be consideration of whether the injury is a birth-associated one or a subsequent inflicted injury perpetrated by a caregiver.

**Common external congenital abnormalities**

**Talipes equinovarus**
Talipes equinovarus is a fixed inversion and flexion deformity of the foot at the ankle, in which the foot cannot easily be put in a normal position. It is helpful to note that this form of fixed talipes is usually associated with the presence of a groove on the medial aspect of the foot. Treatment is required. The foot should be splinted and strapped in the position closest to normal, and an orthopaedic surgeon’s advice must be sought (see Section 5.17). Whenever talipes is present, be sure to examine the hips carefully for evidence of developmental dysplasia (also known as “congenital dislocation of the hip”). It is also important to examine the back for a spinal defect and evidence of neurological deficit.

The common variation (positional talipes) where the foot can easily be brought into the normal position does not require treatment.

**Extra digits**
These are very common. It is important to distinguish a simple skin tag from a true extra digit containing bone or cartilage. The latter may be associated with other congenital anomalies, particularly of the heart, spine, kidney or gut. Skin tags are inherited and are of cosmetic significance only. Skin tags are often held by only a thin pedicle of tissue, which can be ligated at the base, usually causing the tag to fall off a few days later.

**Supernumerary nipples and pre-auricular skin tags**
These are often found and are of cosmetic concern only. No intervention is required.

**Further reading**

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**3.4 Neonatal illnesses and emergencies**

**Sepsis in the neonate**

**Recognising and treating neonatal infection**
Bacterial sepsis (septicemia) in the newborn infant may present with any number of subtle non-specific changes in activity or physical findings. A change in feeding pattern, vomiting, irritability, pallor, diminished tone and/or decreased skin perfusion is suggestive of neonatal infection. Other presenting physical findings may include lethargy, apnoea, tachypnoea, cyanosis, petechiae or early jaundice. There may be fever, but this is not common, especially with bacterial infections occurring in the first week. However, temperature instability with hypothermia may be seen. Abnormal glucose homeostasis (hypoglycaemia or hyperglycaemia) and/or metabolic acidosis are commonly associated findings. Infants, especially preterm infants, are very prone to infection and can become ill very rapidly once infection takes hold. Antibiotic treatment is only likely to work if started early, but the recognition of early infection is not easy. A WHO study showed that more than a third of all deaths in the first month of life in most resource-limited countries were caused by infection. It also found that more than 80% of these infants, when first seen, had **one or more of the following eight danger signs associated with infection in the neonate:**

- infant feeding less than well before
- infant lying quiet and making few spontaneous movements
- history of a convulsion
- hypothermia or fever > 38°C
- capillary refill time > 3 seconds
- respiratory rate ≥ 60 breaths/minute
- indrawing of the lower chest wall when breathing, or grunting
- jaundice
- abdominal distension
- skin infections.

All neonates with signs of sepsis need immediate hospital admission if they are not already there, and must be treated with IV antibiotics for at least 10 days after blood and other appropriate cultures have been taken.

Ampicillin (or penicillin) plus gentamicin are the first-line drugs to be used. Consider adding clindamycin or flucloxacillin if there are signs suggesting that *Staphylococcus aureus* is a cause (e.g. skin pustules, abscesses, omphalitis). Blood cultures are ideal although not always possible before starting antibiotics. If the infant does not respond within 48 hours, consider changing the antibiotic. If there is a possibility of meningitis, risk of resistance or Gram-negative organisms, a third-generation cephalosporin such as cefotaxime or ceftriaxone should also be added.
**Causes of early-onset sepsis (first 72 hours)**

Early-onset sepsis usually occurs as a result of bacteria acquired by vertical transmission from mother to infant during late pregnancy, labour and delivery. The most frequently observed organisms vary from one part of the world to another. Gram-negative enterics (especially *Escherichia coli* and *Klebsiella* species) predominate in many regions. Gram-positive cocci are also common, and include group B beta-haemolytic streptococcus, other streptococcal species, *Staphylococcus* and *Enterococcus*. Less commonly, *Listeria monocytogenes* is isolated from newborn infants with sepsis, especially when there are foodborne epidemics.

These infants mostly present with respiratory distress. However, vaginal cultures cannot be used to determine the choice of antibiotics when treating the symptomatic newborn.

**Late-onset sepsis**

Organisms are less likely to reflect those of the maternal genital tract, although the same pathogens may be identified in infants presenting from home. The most common infections are focal infections such as conjunctivitis, omphalitis, skin infections and meningitis. A circumcision wound can also be the site of serious infection.

In the hospital setting, infection is more commonly caused by nosocomial pathogens, including coagulase-negative staphylococci, Gram-negative enteric bacteria (e.g. *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Enterobacter cloacae*), *Staphylococcus aureus*, Pseudomonas species, streptococcal species and *Enterococcus*. Fungal sepsis must also be considered. Investigate as for early-onset sepsis (see below), with the inclusion of a lumbar puncture and suprapubic urine for analysis and culture if indicated, and treat empirically with parenteral broad-spectrum antibiotic therapy directed towards the most commonly encountered pathogens for the particular nursery. Once cultures are positive, therapy must be directed accordingly.

**Laboratory evaluation of the unwell infant**

In the case of an infant who is generally unwell with no clinically obvious infective focus, the following investigations should be performed if laboratory facilities are available:

- **Blood culture (about 1 mL of venous blood):** This should be obtained from a peripheral vein after preparing the skin with an antibacterial wash such as povidone-iodine and/or 70% ethanol or isopropyl alcohol. Blood culture is the gold standard for neonatal sepsis, but it is not 100% sensitive. The sensitivity may be further reduced if intrapartum antibiotics were administered to the mother antenatally.

- **White blood cell count (WBC) with differential cell count:**

- **Chest X-ray:** This may be helpful if there are any respiratory signs, but not if it means taking the infant to another department in the hospital. A portable chest X-ray is ideal (if available).

- **Lumbar puncture if indicated:** cytology, chemistry, Gram stain and culture. Not routinely done on all infants with suspected infection unless there are neurological signs.

- **C-reactive protein (CRP):** This is an inexpensive and useful test which may take 12 hours to become positive if an infection is present. A negative test at 48 hours in a well infant suggests that antibiotics can be stopped.

- **Blood glucose concentration.**

- **Serum bilirubin concentration** if the infant appears jaundiced.

- **Surface cultures** (ear canal, umbilical stump) and gastric aspirate cultures do not correlate with either the likelihood of sepsis or the causative agent in septic infants. **These cultures should not be obtained.**

- **A midstream or suprapubic aspirate of urine for microscopy and culture:** This procedure is of little value in the infant suspected of having sepsis shortly after birth, but it may have a greater yield in infants with new-onset symptoms later in the first week (≥ 3 days). A urinary tract infection should always be considered in neonates with late-onset sepsis, and the same antibiotics should be used as for other serious infections unless cultures dictate otherwise.

In seriously ill infants with suspected sepsis, priority should be given to the structured ABC approach, while simultaneously obtaining a blood culture followed by prompt administration of antibiotics. Other tests, such as a lumbar puncture, can be performed once the infant is stable and antibiotics have been started.

**Specific neonatal infections**

**Meningitis and/or septicaemia**

Meningitis may occur at any time in the neonatal period, and is frequently fatal, with some survivors experiencing long-term sequelae. Survival and later prognosis depend on early diagnosis and rapid treatment. Confirmatory diagnosis from a lumbar puncture may take several hours. Therefore it is urgent and appropriate to start antibiotic treatment empirically as soon as the diagnosis is suspected.

**Presenting features of meningitis:** These include lethargy, reduced or complete lack of willingness to take feeds, irritability, a high-pitched cry, apnoeic episodes, lowered conscious level or even coma, hypotonia, convulsions, generalised signs of accompanying sepsis, and a bulging or tense anterior fontanelle. **Always measure and record the head circumference.**

However, once signs such as the above are present, treatment may be unsuccessful and survivors may be handicapped. Therefore any infant with the following danger signs should be started on antibiotics IV and the relevant investigations undertaken:

- **Infant feeding less well than before**

- **Infant lying quiet and making few spontaneous movements**

- **Hypothermia or fever > 38°C**

- **Capillary refill time > 3 seconds**

- **Respiratory rate ≥ 60 breaths/minute**

- **Indrawing of the lower chest wall when breathing, or grunting**

- **Cyanosis**

- **History of a convulsion.**

**Less common but important signs include the following:**

- **Low respiratory rate (< 20 breaths/minute) or apnoea**

- **Jaundice**

- **Abdominal distension**

- **Skin infections.**
**Treatment of suspected bacterial sepsicaemia with or without early meningitis**

- Ensure that the airway is open and keep it open.
- Ensure that the infant is breathing adequately, and if they are apnoeic, gasping or have a very low respiratory rate, consider ventilation using a bag and mask until they are breathing adequately.
- If the infant is cyanosed, give them oxygen until they are pink or show normal oxygen saturation in air (> 92%).
- Insert an IV cannula, using full sterile precautions. Umbilical vein catheterisation may be the most effective way to gain vascular access quickly in a shocked infant less than 1 week old (see Section 8.4.B). Otherwise it might be necessary to site an intra-osseous line or cannulate a scalp vein.
- Take samples for full blood count, CRP, blood culture, lumbar puncture, blood glucose and other tests (urine microscopy and culture, chest X-ray, biochemical tests) if needed (and available). Failure to stabilise the skin rigorously can render blood culture results uninterpretable. Chlorhexidine, 0.5% aqueous solution, is a very effective antiseptic. Use two different swabs, applying each for 10 seconds, and then leave the skin to dry for 30 seconds. A keyhole drape and no-touch technique will reduce the risk of recontamination, especially when performing lumbar puncture or suprapubic aspiration.
- If possible, check blood glucose levels, but if facilities do not allow this, give 2 ml/kg of 10% glucose IV over 2–3 minutes as an initial bolus, followed by 5 ml/kg of 10% glucose per hour for the next few hours while enteral feeds are established. An infant who becomes alert and active immediately following the initial bolus is suggestive of hypoglycaemia (i.e. a blood glucose concentration of < 2.5 mmol/litre, or < 36 mg/dL), and this may be part of the problem. If an IV line cannot be inserted and hypoglycaemia is suspected, give expressed breast milk or 10% glucose by nasogastric tube or sublingual sucrose.
- Further intermittent monitoring of the blood glucose level should be undertaken and the infusion continued until it is clear that the infant is well enough to be fed orally.
- Give the first dose of ampicillin and gentamicin (or cefotaxime or ceftiraxone) intravenously using the dose regimens outlined at the end of this section. Remember to use the high meningitic dose if meningitis is suspected, and continue it for the duration of therapy if meningitis is confirmed. If IV access is not immediately possible, give the initial antibiotic dose IM. Never wait for the results of cultures before starting antibiotics. Any delay can reduce the infant’s chances of survival as well as leading to permanent damage if meningitis is present.
- Start an IV infusion of 60 ml/kg/24 hours of 10% dextrose (or 1/5 normal saline with 5% dextrose) if at all possible.
- If the infant is shocked, give an IV bolus of 10 ml/kg of Ringer-lactate or Hartmann’s solution. This can be repeated twice (giving a total of 30 ml/kg) if the infant remains shocked. The use of inotropes (dopamine and dobutamine) (if available) can be considered in such situations, although the outlook is bleak if they are needed.
- If the child has any respiratory symptoms, take a portable chest X-ray (if facilities are available). Do not take a sick infant to an X-ray department for this, as the resulting information is not worth the risks of moving them. Look regularly to see whether cyanosis is developing, or use a pulse oximeter (if available) and give supplemental oxygen, preferably using nasal cannulae rather than a head box. Infants who become infected during delivery develop respiratory symptoms with progressive signs of septic shock within a few hours of birth. Do not give anything by mouth to an infant who is breathless, especially if there is additional evidence of oxygen dependency.

**Points to consider**

- Undertake the ABC approach. Oxygen may be needed. If the conscious level is impaired, the airway may be at risk.
- Be alert for the presence of seizures, and treat them as appropriate. Always consider meningitis as a possible cause. If there are any features suggestive of meningitis, perform a lumbar puncture at the same time as blood cultures or within 2 hours of starting antibiotic treatment, because the blood culture is sterile in 15% of infants with early meningitis. Do not delay antibiotic therapy pending the undertaking of a lumbar puncture. Treat seizures with phenobarbitone 20 mg/kg IM or by slow IV injection. If needed, continue with phenobarbitone at a maintenance dose of 3–5 mg/kg/day. Diazepam or midazolam can also sometimes be used to control seizures. However, always have a bag and mask available if diazepam or midazolam are given to stop fitting, as these drugs cause temporary apnoea in some patients, which can easily be managed with bag-and-mask ventilation until the infant is breathing adequately.
- Microscopic examination of the CSF (in meningitis the white cell count is ≥ 25 cells/mm³, low glucose levels and high protein levels with or without Gram stain can provide early confirmation of meningitis. Remember that a differential white blood cell count or a differential count in the CSF do not help with the decision to initiate or continue antibiotic treatment.
- Surface swabs and gastric aspirate cultures have no diagnostic significance. However, urinary tract infection can occasionally be the primary focus of a Gram-negative septicemic illness. Simple microscopy on a clean catch or suprapubic urine specimen may be used to rule out a urinary tract infection. Identification of a urinary tract infection may suggest the need for ultrasound imaging of the renal tract and long-term prophylactic antibiotics.
- Watch for, prevent and correct any sign of hypothermia (skin-to-skin mother care).
- Antibiotics can be stopped after 48 hours if the blood cultures are negative and the infant is clinically well. If available, a normal CRP at 48 hours can help to exclude sepsis. If blood cultures are not available, continue the antibiotics for the full course appropriate for the site of infection (meningitis 14–21 days).
- Think also of herpes infection, congenital TORCH infection (newborn intrauterine-acquired infections, including toxoplasmosis, parvovirus B19, syphilis, HIV, varicella, coxsackie, rubella and cytomegalovirus) or neonatal malaria (rare) in a malaria-endemic region.

**Antibiotic treatment**

- Beta-lactam antibiotics plus aminoglycosides act synergistically in treating some of the most frequently encountered neonatal pathogens. Commonly used
agents are ampicillin and gentamicin, but alternative broad-spectrum coverage may be used. Penicillin may be used if ampicillin is not available, but it has a narrower spectrum, limited to Gram-positive bacteria. Ampicillin may also provide better coverage for certain Gram-positive pathogens, including *Listeria*.

- **Third-generation cephalosporins** such as cefotaxime and ceftiraxone may be used, but some Gram-positive bacteria may not be covered (e.g. *Enterococcus, Listeria*) if a penicillin derivative is not included. Infants with suspected Gram-negative meningitis and accompanying early-onset sepsis may benefit from inclusion of a third-generation cephalosporin which offers a theoretically greater penetration and killing power for enteric bacteria in the cerebrospinal fluid. These antibiotics may be given intramuscularly if IV access cannot be obtained.

**Frequent use of these drugs may contribute to the development of multi-drug-resistant strains of bacteria in nurseries.** Ceftriaxone has a longer half-life and can be dosed once daily.

- **Cloxacillin** (IV or oral) is preferable if septica mic spots are present, as these are usually caused by coagulase-positive staphylococci.

- **Second-line antibiotics** (e.g. ciprofloxacin, vancomycin, meropenem, piperacillin-tazobactam, linezolid) may be helpful for treating nosocomial infections and resistant organisms. However, their use should be limited to proven multi-drug-resistant organisms. Advice can always be sought on these from nearby referral centres. Inappropriate use of these expensive antibiotics may lead to even more multi-drug-resistant organisms (the so-called ‘superbugs’). It is recommended that these agents should only be used in specified clinical settings.

Empirical antibiotic therapy includes antibiotics used for neonatal sepsis (i.e. a beta-lactam antibiotic plus an aminoglycoside) and a third-generation cephalosporin (e.g. cefotaxime or ceftriaxone) with excellent CSF penetration and bactericidal effect on sensitive Gram-negative bacteria. Therapy can be adjusted once the bacteria have been identified and antibiotic sensitivities determined. The duration of treatment is at least 14 days for uncomplicated Gram-positive bacteria and 21 days for Gram-negative bacteria.

The most frequently used initial combination is ampicillin and gentamicin (see the neonatal formulary at the end of this section). Benzyl penicillin may be preferable for known or suspected group B streptococcal infection. Cefotaxime or ceftriaxone is the drug of choice for most Gram-negative organisms, and ceftazidime is used for *Pseudomonas* infection.

### Investigations for meningitis

- Lumbar puncture is potentially helpful if meningitis is suspected, and should be considered in all newborn infants with neurological signs. It is important to only attempt lumbar puncture once the infant has been stabilised, and ideally within 2 hours of initiating antibiotic treatment. Lumbar puncture is more likely than blood culture to identify the organism responsible, and within a shorter period of time.

- Cerebrospinal fluid (CSF) cell counts, chemistry and Gram stain would often point towards meningitis. An elevated CSF leucocyte count (> 25 white blood cells/mm³) with pleocytosis is characteristic of neonatal meningitis. The CSF protein level in meningitis may be high (> 2.0 g/litre in a term infant), and the CSF glucose level is typically low (< 30% of blood glucose value). Gram staining may reveal bacteria, but antibiotic therapy should not be directed on the basis of this result, as rapidly growing bacilli may be mistaken for cocci, or the state of the organism may result in variable staining.

- Sometimes the CSF picture in preterm infants who have sustained an intraventricular haemorrhage can show a mild reactive pleocytosis in the first few weeks of life, which can be quite misleading. If there is clinical suspicion this should be treated as bacterial meningitis until cultures are known to be negative.

- If a ‘bloody tap’ is obtained it is best to treat the infant as having meningitis, and repeat the lumbar puncture after 24–48 hours. The finding of many white cells or bacteria is significant even if the CSF is bloodstained.

### Diarrhoea in the newborn

#### Special points to remember

- Encourage frequent breastfeeding, as it helps in both preventing and treating diarrhoea in the newborn.

- If the infant is dehydrated, give low-osmolality oral rehydration solution (ORS) in addition to breast milk.

- In the case of sick infants or those infants who are unable to feed orally, consider IV fluids.

- If bloody diarrhoea occurs, it is best to assume that the infant has dysentery, and initiate antibiotic therapy. Avoid the use of co-trimoxazole in the light of much better and more effective antibiotics with better side-effect profiles.

- In the case of the septic and unwell infant, give IV antibiotics as outlined in Table 3.4.1 (p. 358).

Sometimes what is described as diarrhoea by the mother is in fact the normal loose breastfed stools of some infants in the first few days of life. Usually the number of stools passed per day declines quickly, and in some breastfed infants may be as infrequent as once daily.

### Congenital syphilis (see Section 2.8.H)

Congenital syphilis may be acquired from an infected mother via trans-placental transmission of *Treponema pallidum* at any time during pregnancy.

#### Clinical signs in infants

may include any of the following:

- low birth weight with a heavy placenta
- palms and soles showing a red rash, grey patches, blisters or skin peeling
- abdominal distension due to large liver and spleen
- jaundice
- anaemia
- some low-birth-weight infants with syphilis show signs of severe sepsis, with lethargy, respiratory distress, skin petechiae or other signs of bleeding.

#### Investigation

No newborn infant should be discharged from hospital without determination of the mother’s serologic status for syphilis at least once during pregnancy, and also at delivery in communities and populations in which the risk of infection with congenital syphilis is high.

If you suspect syphilis, perform a venereal disease research laboratory (VDRL), rapid plasmin reagent (RPR) or rapid syphilis test.
Treatment
All newborns of mothers with syphilis should be investigated and treated.

Infants should be treated for congenital syphilis if they have proven or probable disease demonstrated by one or more of the following:
1. Physical, laboratory, or radiographic evidence of active disease
2. A reactive result on maternal or infant VDRL testing where the mother has not had 3 weekly doses of benzathine penicillin.

Parenteral penicillin G remains the preferred drug for treatment of an infant with any signs of congenital syphilis. 

Asymptomatic neonates born to VDRL-positive or RPR-positive women should receive 37.5 mg/kg (50,000 units/kg) of benzathine benzyl penicillin as a single IM dose into the anterolateral thigh. Ensure that the needle is not in a vein when this drug is given, by drawing back and ensuring that no blood is in the needle, as it can cause cardiac arrest and severe CNS damage if given IV.

Symptomatic infants require treatment with:
- Procaine penicillin 50,000 units/kg or 50 mg/kg as a single dose by deep IM injection daily for 10 days.

Caution: Accidental intravascular administration may result in cardiac arrest and/or neurological damage
- Or benzyl penicillin (aqueous crystalline penicillin G) 30 mg/kg or 50,000 units/kg IV, 12-hourly for 7 days and then 8-hourly for 3 days.

Treat the mother and partner for syphilis, and check for other sexually transmitted infections.

Infant of a mother with HIV infection
See Section 2.8.C.

Skin, eye and mucous membrane infections
Conjunctivitis
Most conjunctivitis presents as ‘sticky eyes’, but this may not always be of bacterial origin, especially if it occurs in the first few days. However, a bacterial process must be considered in all cases. Infants with a serous discharge without significant conjunctival inflammation may simply have blocked naso-lacrimal tear ducts. This usually responds to gentle pressure/massage applied in a downward motion along the nose immediately adjacent to the eyes. The discharge may be cleaned from the eye with sterile 0.3% saline drops. Show the parent how to clean the infant’s eyes with sterile normal saline or boiled and cooled clean water. The eyes should be wiped from the inside to the outside edge using a clean cotton wool swab for each eye. The hands should always be washed before and after the procedure.

If the condition worsens or if there is conjunctival inflammation or a purulent discharge, use of topical therapy should be considered. Erythromycin, tetracycline, neomycin or chloramphenicol ophthalmic ointments or drops may be considered. Sometimes this condition is due to chlamydia. Apply the ointment 2 to 4 times a day for 5 days after washing away any pus with sterile normal saline as described above. Treat this level of infection as an outpatient, but review every 48 hours.

Gonococcal conjunctivitis
A severe rapidly progressive purulent conjunctivitis occurring within the first few days must always be assumed to be due to Neisseria gonorrhoeae, which must be promptly identified and aggressively treated in hospital with parenteral antibiotics and irrigation. Most strains are now resistant to penicillin. Swab the eye for microscopy (Gram-negative intracellular dipoecocci) and culture (special medium is required, such as Thayer–Martin agar with incubation under increased carbon dioxide). Treatment should be initiated immediately before culture confirmation. Treatment with IV penicillin for 7 days has been used successfully, but because of increased worldwide resistance (penicillinase-producing gonococci), a third-generation cephalosporin is often selected as the first-line therapy:
- Ceftriaxone 125 mg IM, as a single dose
- Or cefotaxime 25 mg/kg (maximum 125 mg) IM, as a single dose
- Or cefixime 20 mg/kg orally, as a single dose.

It is important to repeatedly clean the eye, or irrigate with saline until pus formation stops. It is vital to prevent corneal rupture and subsequent blindness.

In the case of a presumed or diagnosed gonococcal or chlamydial infection, the mother and partner should also be treated.

In countries with a low rate of sexually transmitted diseases, staphylococcal and Gram-negative organisms are more likely to be responsible. Staphylococcal infections can be treated with cloxacillin or flucloxacillin 30 mg/kg orally or IV every 6–8 hours for 5 days.
**Chlamydial conjunctivitis**

*Chlamydia trachomatis* is a common cause of infectious conjunctivitis in the newborn infant. It typically presents between 5 and 14 days. The presentation can vary from mild to moderate conjunctival erythema, and from scant mucoid discharge to copious purulent discharge. Eyelid oedema, chemosis or pseudomembrane formation may also be present. Corneal involvement is unusual initially, although untreated chlamydial conjunctivitis can result in varying degrees of conjunctival scarring and corneal infiltrates.

Chlamydia can be confirmed by culture or rapid antigen detection, but these are highly specialised procedures that may not be readily available. Without a positive laboratory diagnosis, treatment is based on clinical severity. If the condition is mild, clean the eye only. If it is moderate, use a topical antibiotic and consider giving erythromycin 10 mg/kg orally, 6-hourly for 14 days. This effectively treats this infection and may also eradicate upper respiratory tract colonisation. Drug interactions with erythromycin include increased serum levels of digoxin, theophylline and potentially caffeine.

If the condition is severe, beware gonococcal infection, irrigate and use IV or IM cefotaxime or ceftriaxone.

Ensure that the mother is appropriately referred for treatment.

**Skin pustules**

Skin pustules are most commonly caused by *Staphylococcus aureus*. Most often these occur in small clusters in an otherwise healthy asymptomatic infant. Topical therapy with chlorhexidine 0.5% may be all that is needed in most of these cases. Oral therapy with a penicillinase-resistant penicillin (e.g. flucloxacillin 25 mg/kg 6-hourly) or first-generation cephalosporin (e.g. cephalaxin 25 mg/kg 6–12-hourly for 7 days) may also be used if extensive pustules are found. If septicemia is suspected, septic investigations and IV antibiotics after hospitalisation may be needed. Sometimes staphylococcal pustules can be difficult to distinguish from erythematotoxicum (a benign, non-infectious newborn rash).

**Umbilical infection**

A clinically relevant infection of the umbilical stump (omphalitis) presents as redness and oedema of the skin extending from the umbilicus. This should be distinguished from the ooze resulting from an umbilical granuloma, which may develop after a few weeks. If there is skin redness plus oedema extending from the umbilicus, appropriate antibiotics, usually anti-staphylococcal, should be used. Clean the area with soap and warm water and remove or drain pus and crusts. Dry and paint the area with antiseptic such as gentian violet, or use a simple alcohol swab to clean the area at the time of every nappy change. If there is only a ‘sticky cord’, manage it with local treatment only. Pus can be easily removed with a swab, whereas normal cord degeneration cannot be removed.

**Cellulitis**

This is most commonly caused by streptococci, but *Staphylococcus aureus*, Gram-negative enterococcus and anaerobes should also be considered when infection occurs at sites where there have been breaks in the skin. Treatment with parenteral antibiotics (e.g. Flucloxacillin, a penicillinase-resistant penicillin, and gentamicin, an amino-glycoside) should be directed against both Gram-negative and Gram-positive bacteria. Omphalitis may become rapidly progressive and spread to deeper tissues. Infection with *Clostridium* is common in the setting of poor maternal immunity or poor umbilical cord care, and can cause neonatal tetanus.

**Scalded skin syndrome**

This is a rare infection caused by toxin-producing staphylococcal organisms which leads to a toxic reaction producing the effect of both serious infection and burns. Treat it with IV cloxacillin or flucloxacillin.

**Superficial candidiasis (‘thrush’ and ‘monilial’ rash)**

Superficial candidiasis of the oral mucosa ('thrush') commonly manifests as white patches which are not easily scraped with a spatula. The nappy area may also be affected ('monilial' rash). Unlike irritant dermatitis, the erythema extends into skin folds and there may be small raised erythematous lesions. Treat with oral nystatin suspension, 1 mL after feeds (divide it between each cheek with a small syringe). Topical nystatin ointment may be used to treat the skin rash, but only in combination with oral nystatin. Keep the nappy area dry. Apply local treatment to the mother’s nipples if they are also infected.

**Drugs used to treat severe infection in the neonate**

**Ampicillin (or amoxicillin)**

Give 100 mg/kg per dose IM or IV where meningitis is a possibility, and 50 mg/kg per dose in other situations. Give one dose every 12 hours in the first week of life, every 8 hours in an infant aged 1–3 weeks, and every 6 hours in an infant older than this. Oral dosing can sometimes be used to complete a course of treatment.

**Benzyl penicillin**

Give 60 mg/kg (100 000 units/kg) IV if meningitis or tetanus is a possibility. Give 30 mg/kg (50 000 units/kg) per dose in all other situations, including syphilis. Time the interval between each dose as for ampicillin. Oral dosing can sometimes be used to complete a course of treatment.

**Cefotaxime**

Give 50 mg/kg per dose IV or IM. Time the interval between each dose as for ampicillin, except in meningitis, where doses are given 6-hourly.

**Chloramphenicol**

This remains a useful antibiotic, although there is a serious risk of death from liver failure if the dose suggested here is exceeded. **Warning: The problem is not the dose**
but incorrect mixing, as the bottle contains 1000 mg, so it is easy to overdose. Give a 25 mg/kg loading dose IM followed by 12.5 mg/kg once every 12 hours to infants less than 1 week old. Give this dose every 8 hours to infants aged 1–4 weeks, unless there is evidence of liver damage or renal failure. Infants older than this can be given 12.5 mg/kg once every 6 hours from the outset. Oral dosing can be used to complete any course of treatment. (The dose can be doubled in those over 1 month of age with severe infection.) Be very careful if the IV dose has to be diluted to obtain the correct dosage.

Cloxacillin (or flucloxacillin)
Give 100 mg/kg per dose IM or IV if serious infection is present, and 50 mg/kg per dose in other situations. Time the interval between each dose for ampicillin. Oral treatment can often be given to complete a course of treatment (25 mg/kg standard, 50 mg/kg severe, 100 mg/kg in infections such as osteomyelitis).

Erythromycin
Give 12.5 mg/kg per dose orally once every 6 hours. There is no satisfactory IM preparation.

Eye drops (and ointments)
Prophylactic chloramphenicol 0.5% eye drops or 1% eye ointment can be used to minimise the risk of gonococcal infection (IM/IV ceftriaxone is being used for overt infection). Tetracycline ointment 1% should be used (with oral erythromycin) to treat chlamydia conjunctivitis (this condition is not prevented by silver nitrate use). Pseudomonas infection requires treatment with systemic antibiotics and topical gentamicin 0.3% eye drops.

Gentamicin
Give 5 mg/kg IM or IV once every 24 hours. If the infant weighs less than 2 kg, give 4 mg/kg per dose. Leave 36–48 hours between each dose if there is renal failure.
- If the infant is less than 32 weeks’ gestation, give 4–5 mg/kg 36-hourly.
- If the infant is more than 32 weeks’ gestation, give 4–5 mg/kg 24-hourly.

Hepatitis B vaccine
Give 0.5 mL IM into the thigh as soon as possible after or within 12 hours of birth. Remind the mother that the infant will require booster injections at 6 weeks and 14 weeks after birth. Infants born to mothers infected during pregnancy or who are known high-risk carriers with a positive hepatitis B e-antigen should also be given 200 units of hepatitis B immunoglobulin (HBIG) IM into the other thigh within 24 hours of birth. Breastfeeding can safely continue.

Isoniazid
See Section 6.1.N for the latest advice on the treatment of children with TB or suspected TB.

Metronidazole
Give a 15 mg/kg loading dose and 7.5 mg/kg per dose once every 12 hours in infants less than 4 weeks old, and every 8 hours in children older than this. Treatment can be given IV or orally, but solubility makes IM use unsatisfactory. If the IV route is used, start the maintenance dose 24 hours after loading. If the oral route is used, give the first dose 12 hours after loading.

Miconazole
This controls infection with candida (‘thrush’) more effectively than topical nystatin. Use the oral gel at least four times a day and the skin cream twice a day for at least 7 days. Topical treatment with 0.5% aqueous gentian violet for not more than 4 days may be equally effective. Oral nystatin drops (1 mL four times a day) can be used to reduce heavy intestinal tract carriage.

Nevirapine
See Section 2.8.C and national protocols for the latest advice on the use of Nevirapine in the prevention of mother-to-child transmission of HIV infection.

Procaine and benzathine penicillin
Give asymptomatic infants born to mothers with evidence of untreated syphilis a single 37.5 mg (50 000 units/kg) dose of benzathine penicillin IM injection. Never give this drug IV. Infants thought to be infected at birth are often given procaine penicillin 50 mg/kg (50 000 units/kg) IM once a day for 10 days, but repeated IM injections can cause a sterile abscess with subsequent muscle fibrosis and atrophy. IV benzylpenicillin for 10 days (as specified above) is just as effective. Infants born to mothers who have been fully treated for syphilis (1.8 grams, or 2.4 mega-units, of benzathine benzylpenicillin) at least 4 weeks before birth need no further treatment after birth.

Zidovudine
See Section 2.8.C and national protocols for the latest advice on the use of Zidovudine in the prevention of mother-to-child transmission of HIV infection.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Single dose</th>
<th>Frequency</th>
<th>Postnatal age</th>
<th>Gestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>IV, IM</td>
<td>50–100 mg/kg</td>
<td>12 hourly</td>
<td>&lt; 7 days</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td>50–100 mg/kg</td>
<td>8 hourly</td>
<td>7–21 days</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td></td>
<td>50–100 mg/kg</td>
<td>6 hourly</td>
<td>&gt; 21 days</td>
<td>Any</td>
<td></td>
</tr>
</tbody>
</table>

Reduce dose frequency in severe renal impairment and birth asphyxia
Use higher doses in case of suspected Group B strep infection or meningitis
### Section 3.4

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Single dose</th>
<th>Frequency</th>
<th>Postnatal age</th>
<th>Gestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzyl Penicillin</td>
<td>IV, IM</td>
<td>25–50 mg/kg</td>
<td>12 hourly</td>
<td>&lt; 7 days</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25–50 mg/kg</td>
<td>8 hourly</td>
<td>7–21 days</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25–50 mg/kg</td>
<td>6 hourly</td>
<td>&gt; 21 days</td>
<td>Any</td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Reduce dose frequency in severe renal impairment and birth asphyxia</td>
<td></td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>IV, IM</td>
<td>50 mg/kg</td>
<td>12 hourly</td>
<td>&lt; 7 days</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 mg/kg</td>
<td>8 hourly</td>
<td>&gt; 7 days</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Reduce dose by 50% in severe renal impairment</td>
<td></td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>IV, IM</td>
<td>50 mg/kg</td>
<td>12 hourly</td>
<td>&lt; 7 days</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 mg/kg</td>
<td>8 hourly</td>
<td>&gt; 7 days</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Reduce dose interval to 24 hours in severe renal impairment</td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>IV, IM</td>
<td>50 mg/kg</td>
<td>12 hourly</td>
<td>&lt; 7 days</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 mg/kg</td>
<td>8 hourly</td>
<td>&gt; 7 days</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Avoid in infants &lt; 36 weeks' gestation or if jaundiced. Follow special IM preparation instructions</td>
<td></td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>IV, IM</td>
<td>12.5 mg/kg</td>
<td>12 hourly</td>
<td>&lt; 7 days</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12.5 mg/kg</td>
<td>8 hourly</td>
<td>&gt; 7 days</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>There is a serious risk of death from liver failure if the dose suggested is exceeded</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Oral dosing can be used to complete any course of treatment</td>
<td></td>
</tr>
<tr>
<td>Clonazepam</td>
<td>IV infusion</td>
<td>100 micrograms/kg</td>
<td>(loading dose)</td>
<td>Not for &gt; 3 days</td>
<td>Not for &gt; 3 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10–30 micrograms/kg/ hour</td>
<td>Not for &gt; 3 days</td>
<td>Not for &gt; 3 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Up to 200 micrograms/kg/24 hours may be required in first 48 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Use slow IV over 20 minutes</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Caution: respiratory depression and increased pulmonary secretions particularly if accumulation occurs</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>If not ventilated use lower doses because of respiratory depression</td>
<td></td>
</tr>
<tr>
<td>Clomoxacin</td>
<td>IV, IM</td>
<td>50 mg/kg</td>
<td>12 hourly</td>
<td>&lt; 7 days</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 mg/kg</td>
<td>8 hourly</td>
<td>&gt; 7 days</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Double the dose in severe infection and if CNS is involved</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Increase dose interval to 24 hours in severe renal impairment</td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>PO</td>
<td>12.5 mg/kg</td>
<td>6 hourly</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>There is no satisfactory IM preparation</td>
<td></td>
</tr>
<tr>
<td>Gentamicin</td>
<td>IV</td>
<td>5 mg/kg</td>
<td>48 hourly</td>
<td>&lt; 7 days</td>
<td>&lt; 29 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 mg/kg</td>
<td>36 hourly</td>
<td>&gt; 7 days</td>
<td>&lt; 29 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 mg/kg</td>
<td>36 hourly</td>
<td>&lt; 7 days</td>
<td>30–33 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 mg/kg</td>
<td>24 hourly</td>
<td>&gt; 7 days</td>
<td>30–33 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 mg/kg</td>
<td>24 hourly</td>
<td>&lt; 7 days</td>
<td>&gt; 34 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Trough and peak levels are not needed</td>
<td></td>
</tr>
<tr>
<td>Isoniazid</td>
<td></td>
<td></td>
<td></td>
<td>See Section 6.1.N for details on its use.</td>
<td></td>
</tr>
<tr>
<td>Metronidazole</td>
<td>IV, PO</td>
<td>5 mg/kg</td>
<td>(loading dose)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.5 mg/kg</td>
<td>12 hourly</td>
<td>&lt; 28 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.5 mg/kg</td>
<td>8 hourly</td>
<td>&gt; 28 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Infuse over 30 minutes</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Injection solutions can be given rectally</td>
<td></td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Single dose</th>
<th>Frequency</th>
<th>Postnatal age</th>
<th>Gestation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Miconazole</strong></td>
<td>Oral gel</td>
<td></td>
<td>6 hourly</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Skin ointment</td>
<td></td>
<td>6 hourly</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>0.5% Aqueous</strong></td>
<td><strong>Gentian violet</strong></td>
<td>Apply</td>
<td></td>
<td>Once daily for</td>
<td>4 days</td>
</tr>
<tr>
<td><strong>Oral nystatin</strong></td>
<td><strong>drops</strong></td>
<td>PO</td>
<td>1 mL</td>
<td>6 hourly</td>
<td></td>
</tr>
<tr>
<td><strong>Nevirapine</strong></td>
<td><strong>See Section 2.8.C</strong></td>
<td>for details on its use.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Paraldehyde</strong></td>
<td>Rectal</td>
<td>0.2 to 4 mL/kg (loading dose)</td>
<td></td>
<td>Can repeat once 4–5 hours later</td>
<td></td>
</tr>
<tr>
<td><strong>Phenobarbitone</strong></td>
<td>IV, IM, PO</td>
<td>20 mg/kg (loading dose)</td>
<td></td>
<td>followed by maintenance 12–24 hours later</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Slow IV over 5 minutes. Loading dose may be repeated by at 10 mg/kg if clinically indicated</td>
<td></td>
<td>3–5 mg/kg/24 hours</td>
<td>Once daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monitor plasma levels</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Phenytoin</strong></td>
<td>IV, PO</td>
<td>15–20 mg/kg (loading dose)</td>
<td></td>
<td>Give IV infusion over 20–30 minutes diluted in 10 mL of normal saline</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Slow IV over 20–30 minutes</td>
<td></td>
<td>1.5–3 mg/kg/12 hourly</td>
<td></td>
</tr>
<tr>
<td><strong>Procaine</strong></td>
<td>penicillin</td>
<td>IM</td>
<td>10 mg/kg</td>
<td>Single dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Give to asymptomatic babies born to mothers with evidence of untreated syphilis</td>
<td></td>
<td>100 mg/kg</td>
<td>Once daily</td>
</tr>
<tr>
<td><strong>Zidovudine</strong></td>
<td>See Section 2.8.C</td>
<td>for details on its use.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Polycythæmia**

This potentially harmful condition occurs in up to 4% of births and risk factors are: being both small or large for gestational age or wasted, born to mothers with diabetes and being one of a multiple birth. Milking of the umbilical cord at birth, by increasing the amount of blood transferred into the baby, can also produce this condition.

Polycythæmia is defined as a venous haematocrit > 65% or Hb > 22 g/dL. Capillary samples can have higher haematocrit and if > 65% should be confirmed by venous sample.

Screen high risk babies at 2, 12 and 24 hours by capillary blood measurement of PCV and then if > 65% confirm by venous sample.
Above a PVC of 65%, the viscosity of blood increases exponentially and can produce dangerously reduced capillary perfusion in many organs which, when most severe, can produce cerebral, renal or mesenteric vein thrombosis.

Clinical presentation
The baby can be hypotonic, drowsy, have poor sucking, be irritable, jittery and, when severe, have convulsions. These are important danger signs.

There may also be jaundice, hypoglycaemia, and hypocalcaemia. With a high PCV the blood glucose reading may be falsely low with a normal serum glucose.

Management
First exclude dehydration and if present treat by supervised feeding and if necessary increased enteral or even IV fluids. The best way to check for dehydration is to weigh the baby and compare weight with that at birth. Normally babies lose 5–7% of their body weight in the first 3–4 days and regain their birth weight level by 10–14 days. If the baby’s weight at 24 hours of age has dropped by 5% or more from the birth weight then dehydration is present.

Check blood glucose and bilirubin levels and treat appropriately (see below).

If venous PCV is 65–70% and no signs, bilirubin is below phototherapy levels, and no hypoglycaemia is present treat conservatively by regular examination for the signs described above, ensure adequate fluid intake by direct observation of feeding and regular accurate weighing before and after feeds.

If venous PCV is 70–75% and there are no danger signs, treat polycythaemia by giving additional fluid of 20 mL/kg per day enterally or IV. Also treat jaundice with phototherapy and hypoglycaemia with glucose, if necessary IV.

If PCV is > 75% or there are any danger signs as described above then partial exchange transfusion (PET) should be undertaken urgently.

PET involves the exchange of 20 mL/kg by repeatedly taking off aliquots of blood of up to 5 mL at a time and replacing IV with equal volumes of Ringer-Lactate or 0.9% saline. Ideally blood will be taken from a peripheral vein but, if this is not possible, either use an umbilical venous catheter placed aseptically or a peripheral arterial cannula. At the end of the procedure, re-check the PCV, Hb, bilirubin and blood glucose levels (ideally also blood calcium value).

Continue to monitor the clinical state of the baby and the PCV until it is shown to fall below 60%. Re-check blood glucose and bilirubin levels as appropriate.

Respiratory disorders
Features of respiratory distress in the newborn
These include the following:
- tachypnoea (respiratory rate > 60 breaths/minute)
- recession of the chest wall and sternum
- expiratory grunting
- nasal flaring
- prolonged apnoea (lasting for more than 20 seconds) or intermittent shorter apnoea with cyanosis or severe falls in oxygen concentration (< 90%)
- gasping
- tachycardia
- $\text{SaO}_2 < 92\%$ in air
- cyanosis is a relatively late presentation of a respiratory or cardiac cause.

These signs are relatively non-specific, arising from conditions that affect the respiratory system, as well as from cardiac, neurological and metabolic abnormalities.

Cardinal signs that characterise distress due to respiratory disorders
- Central cyanosis in room air.
- Tachypnoea: respiratory rate > 60 breaths/minute (always measure over at least 1 minute, as the infant’s breathing may be irregular).
- Retractions (recessions): tugging of the soft tissues between the ribs or at the edges of the rib cage.
- Grunting: a prolonged expiratory effort, usually with an audible noise.

Two of these signs are sufficient to make the diagnosis. Cyanosis may not be present, especially if the infant is receiving oxygen.

If pulse oximetry is available, the $\text{SaO}_2$, in infants with respiratory impairment will usually be less than 92% in air (often less than 90% in more severe cases).

Causes of early respiratory distress
‘Early’ respiratory distress (presenting in the first 12 hours of life) may result from a number of causes, including the following:
- ‘transient tachypnoea of the newborn’ associated with a delay in clearing of fetal lung fluid
- congenital pneumonia or sepsis (e.g. group B streptococcus sepsis)
- surfactant deficiency (hyaline membrane disease or respiratory distress syndrome)
- pneumothorax
- meconium aspiration
- congenital abnormalities of the lung or airways (including diaphragmatic hernia)
- hypothermia.

Maternal fever during labour and prolonged rupture of the membranes (more than 18 hours) particularly point to pneumonia or sepsis. Pneumonia may also be due to congenital syphilis. Pneumothorax should be considered if the infant has been resuscitated using positive-pressure ventilation (although it has also been described as occurring spontaneously in about 1% of normal term infants).

Transient tachypnoea is more common among infants delivered by elective Caesarean section (in the absence of spontaneous labour). Surfactant deficiency and infection are the most likely causes in preterm infants.

Congenital heart disease does not usually cause early respiratory distress. Cyanosis/severe hypoxaemia is the more likely presentation (see Section 5.4.A).

Respiratory distress associated with heart failure normally occurs after the first week of life, in association with tachycardia, pallor, sweating, hepatomegaly and excessive weight gain.
Causes of respiratory distress in the newborn

Common causes
- Lack of surfactant causing respiratory distress syndrome in the preterm infant.
- Infection acquired before or during delivery.
- Transient tachypnoea of the newborn (wet lung).

Less common causes
- Meconium aspiration.
- Persistent pulmonary hypertension of the newborn.
- Pneumothorax.

Rare causes
- Pulmonary hypoplasia.
- Congenital abnormalities (e.g. diaphragmatic hernia, choanal atresia, tracheo-oesophageal fistula).
- Pulmonary haemorrhage.
- Metabolic causes (inborn error of metabolism).

Non-respiratory causes
- Congenital heart disease.
- Hypothermia.
- Severe anaemia.

Principles of treatment of respiratory diseases of the newborn
- Ensure that the infant is breathing. If the infant is apnoeic, gasping or has a very slow respiratory rate, use chest inflations with a bag valve mask to re-establish breathing.
- The infant should be offered enough supplemental oxygen to treat any degree of central cyanosis and ideally to keep SaO₂ in the normal range (86–92% in preterm and 92–96% in term infants). It should never be in the hyperoxic range (above 96%), especially in a preterm infant who is receiving additional inspired oxygen.
- Oxygen should be given either with an oxygen concentrator or from cylinders. An oxygen supply must be available at all times in areas where newborn infants are treated.
- Pulse oximetry should be employed (if available) to assess initial disease severity, to monitor subsequent progress, and to ensure that such supplies of oxygen are available and optimally used. Wind-up versions of pulse oximeters are available (www.PET.org.za).
- Tents and incubators are not an efficient way of giving oxygen. Giving oxygen into a clear plastic hood (head box) placed over the head stops the oxygen supply from dropping every time a tent or incubator door is opened. Oxygen is an expensive resource and must not be wasted by giving it into incubators.
- Nasogastric tubes can contribute to upper airway resistance, so an orogastric tube is preferred in infants with respiratory distress, although it is more difficult to keep in place, so compromise may sometimes be necessary.
- Infants less than 2 days old should be started on an IV infusion of 10% dextrose at 60–90 mL/kg/24 hours. For infants more than 3 days old sodium chloride should be added to 10% dextrose to provide 2–3 mmol/kg/day and used at the age-appropriate giving rates (see fluid management section on p. 347). It is recommended that in neonates it is best to use a paediatric burette (chamber) where 1 mL = 60 micro-drops (1 drop/minute = 1 mL/hour). Caution: A standard infusion set gives 20 drops/mL and can lead to dangerous fluid overload if it is not carefully controlled.
- Give antibiotics IV or IM (the IV route is preferable) at least for the first 48 hours in all infants with respiratory distress, as bacterial infection is a likely reason for the infant’s respiratory problems. Take blood for culture first wherever possible. Antibiotics can be stopped if the blood culture results are negative and the infant is well after 72 hours.
- In order to gain further insight into the probable cause of the problem, a portable chest X-ray machine (if available) can be useful.
- Take stringent steps to prevent nosocomial cross-infection within the unit. This can be a particular problem not only with some bacterial infections (e.g. E. coli, Klebsiella), but also with some troublesome viral infections (e.g. respiratory syncytial virus, RSV) that are more commonly seen later in the first month of life.
Management issues in specific respiratory conditions

Primary surfactant deficiency (respiratory distress syndrome (RDS), or hyaline membrane disease)

The principles of treating IRDS are as follows:
1. Minimal handling of the infant.
2. Supplementary oxygen.
3. IV fluids.
4. No oral feeding.
5. Continuous positive airways pressure (CPAP).
6. Avoidance of hypothermia.

Surfactant deficiency is by far the commonest cause of respiratory distress in a preterm infant in the first 3 days of life. It is a self-limiting condition, because birth always triggers a gradual increase in surfactant production. The challenge therefore is to support the infant for the first 2–3 days (72 hours) of life without doing further damage to the lung, until such time as the deficiency resolves itself.

The key features of RDS (cyanosis, an expiratory ‘grunt’, tachypnoea, and intercostal and/or subcostal recession) become clinically obvious within 4 hours of birth. Supplemental oxygen, minimal handling and IV fluid, keeping the infant ‘nil by mouth’, have been the standard ingredients of care for the last 50 years. Elective surfactant administration (which is expensive) and ventilation (which is complex) have become the standard approach to management in the last 20 years. However, it is now becoming clear that the very small infant can pay a high price for chronic tracheal intubation, which by interrupting ciliary flow can interfere with the way that necrotic material is normally cleared from the lung.

Most infants will manage well for themselves as long as they are offered help in preventing the lung from closing down and becoming airless for the 72-hour period it takes for the surfactant production to ‘switch on’. The expiratory grunt that is a characteristic feature of this condition is the infant’s own method of sustaining positive end-expiratory pressure (PEEP) and holding the alveoli open. Making the infant breathe against a constant positive airway pressure gradient achieves the same result. By applying this pressure at the nose (nasal CPAP), the complications associated with tracheal intubation can often be avoided.

To be maximally effective, we now know that CPAP should be applied as soon as there is any evidence of respiratory distress in a preterm infant. CPAP given via paired short cannulae or a specially made nasal mask is probably best, as it minimises airway resistance.

Transient tachypnoea of the newborn

This is almost indistinguishable from RDS. However, unlike RDS, the signs do not progress with time in the hours after birth. Most of these infants are born at or near term. All are tachypnoeic, and a few are obviously cyanosed for 6–12 hours after birth. The condition seems to be caused by a delay in clearing lung fluid after birth. All of these infants will recover on their own so long as handling is kept to a minimum and they are not fed until their respiratory signs improve.
have subsided. Some need supplemental oxygen, but few need it for more than 72 hours. The condition appears to be more common after Caesarean section.

**Aspiration pneumonia**

Aspiration of particulate matter can occasionally almost completely block the trachea. More commonly it can also cause a chemical pneumonitis. Meconium can be particularly irritant in this regard, making the term infant very oxygen dependent for the best part of a week. Aspiration of particulate matter may also trigger persistent fetal circulation (see below).

Contrary to the findings of some studies originating from well-resourced centres in the developed world, suctioning meconium-stained infants during deliveries as soon as the head is on the perineum has made a dramatic difference to the risk of meconium aspiration syndrome in India and South Africa.

Nevertheless, with minimal handling, IV fluid and supplemental oxygen, most of these infants can be expected to make a complete recovery provided that there has been no associated hypoxic cerebral damage. Providing unnecessary respiratory support may actually make matters worse by increasing the risk of pneumothorax. Antibiotics should probably be given until it is clear that there is no associated bacterial infection.

Aspiration after birth can cause a similar picture. Milk can block the trachea, but it seldom causes much of an inflammatory reaction. However, gastric acid can be much more damaging. Recurrent minor unrecognised reflux and aspiration is probably more common than a single massive episode of aspiration, and it can certainly over time render the infant quite oxygen dependent. Infants who are hypotonic and have a poor cough reflex or repeated apnoea are probably at particular risk in this regard. Aspiration is common after an apnoeic event.

**Bacterial pneumonia**

This should be managed as outlined in the section on suspected infection, remembering that there may be septicaemia as well as pneumonia.

**Persistent fetal circulation**

- This is relatively common in resource-limited countries, and is a potentially life-threatening condition leading to poor lung perfusion after birth. It may complicate fetal hypoxia, meconium aspiration, early bacterial pneumonia, diaphragmatic hernia, respiratory distress syndrome or (very occasionally) be a primary disorder.
- After birth the pressure in the pulmonary vessels remains high, so that the normal fall in pressure in the right atrium, right ventricle and pulmonary arteries does not occur. As a result of this, the blood flows via the fetal circulation (i.e. the foramen ovale and ductus arteriosus) from the right side of the heart to the left. This blood has not been oxygenated, so the infant soon becomes cyanosed. It is difficult to differentiate this from a congenital cardiac malformation. Serious cyanosis in an infant with a well-aerated lung on chest X-ray and progressive acidosis can cause rapid self-perpetuating cyclical deterioration.
- The treatment in the first instance is oxygenation, minimal handling, IV fluids and avoidance of oral feeds. Metabolic acidosis should be vigorously and rapidly corrected or even over-corrected. Drugs that cause pulmonary vasodilatation, such as sildenafil or magnesium sulphate, have been used to some effect. However, they can lead to serious hypotension and should be used very selectively in a controlled environment in specialised centres.
- Survival is more likely in a unit that is capable of providing sustained respiratory support, and early transfer should be considered when possible.

**Pneumothorax**

This is present more frequently than expected, and may occur spontaneously in up to 1–2% of infants. It is often asymptomatic, and may be associated with meconium aspiration, too high inflation pressures used during mechanical ventilation or resuscitation, and respiratory distress syndrome. It does not automatically need to be treated, unless there is progressive respiratory distress. Confirmation by chest X-ray (if available) is often too time-consuming, especially in the case of a rapidly developing tension pneumothorax. It may be possible to diagnose a pneumothorax clinically by simple observations. The abdomen is often distended by downward displacement of the liver and spleen. The breath sounds may be reduced on the affected side. A hyper-resonant chest with mediastinal shift (trachea deviated away from the side of the suspected pneumothorax) and rapidly deteriorating clinical condition with severe hypoxaemia and/or cardiovascular compromise (bradycardia, hypotension) strongly suggests a tension pneumothorax. This requires an immediate needle thoracocentesis followed (if this results in an immediate improvement in respiratory and cardiovascular function) by the insertion of a chest drain into the fourth or fifth intercostal space in the mid to anterior axillary line (see Section 8.3). In an emergency situation with a rapidly deteriorating cardiac and respiratory function, this must be done without prior X-ray confirmation. Transillumination can be useful if a "cold light" (fibre-optic light source) is available (the affected side may glow brightly).

A pneumothorax that does not result in severe respiratory distress, and is not under tension, may spontaneously resolve without mechanical removal of the pleural air, but oxygen and careful monitoring are required.

**Lung hypoplasia due to oligohydramnios**

Chronic loss of liquor for many days before birth can occasionally impede lung growth enough to threaten survival, but what looks like a serious problem at delivery can occasionally resolve quite rapidly after 1–2 days. However, where the oligohydramnios is due to bilateral renal agenesis or dysplasia, the prognosis for survival is very poor. The stiffness of the small malformed lungs in these cases causes marked intercostal and subcostal recession with unrecoverable cyanosis. Chest X-ray will often reveal an untreatable pre-terminal pneumothorax. The infant's face may appear flattened and there may be limited extension of the elbows and knees due to oligohydramnios.

**Congenital malformations**

The most common congenital defect causing respiratory distress soon after birth is diaphragmatic hernia. This occurs in 1 in 4000 births, and more commonly affects the left side. Clinical examination reveals respiratory distress, and reduced air entry on the affected side with a displaced
apex beat and scaphoid abdomen. The chest X-ray is diagnostic. It used to be thought that early surgery improved the likelihood of survival, but it is now known that this is not the case. Therefore immediate transfer does not have to be considered until the child’s initial respiratory problems have stabilised. During the interim period, an IV line and open nasogastric tube should be in place to keep the gut empty of gas, and feeding should be withheld. Restricted lung growth means that only about 50% of these infants have any chance of survival. Use a headbox rather than nasal cannula oxygen, and place an open nasogastric tube to prevent bowel distension, which makes the condition worse.

Management of diaphragmatic hernia

This includes the following:

- oxygen supplements
- minimal handling
- IV fluids and withholding of oral feeds
- a nasogastric tube to keep the stomach empty
- stabilisation of respiration with mechanical ventilation following intubation or continuous negative extra-thoracic pressure (CNEP) can be helpful if available
- transfer to surgical care if the infant responds to treatment.

A number of rare generalised skeletal abnormalities that affect rib growth also cause severe untreatable lung hypoplasia.

Congenital heart disease can occasionally cause overt cyanosis from birth, but there are seldom any associated signs of respiratory distress (see Section 5.4.A).

Apnoeic/hypoxaemic episodes

Apnoea is the cessation of respiration or a hypoxaemic event associated with signs of cardiorespiratory decompensation (bradycardia, cyanosis and pallor). Apnoeic episodes are common in preterm infants under 32 weeks’ gestation (“apnoea of prematurity”). In term infants, apnoea usually signifies an underlying pathological condition.

Apnoea of prematurity

This is often characterised by a brief cessation of respiration that responds to gentle tactile stimulation, and may vary significantly in duration and severity, especially in very-low-birth-weight infants. Sometimes, isolated bradycardia with brief oxygen desaturation events is identified without a clinically apparent apnoea. The aetiology of apnoea of prematurity is often a mixture of impaired central nervous system respiratory control (‘central apnoea’), intrapulmonary shunting and upper airway obstruction. Sometimes recurrent apnoea is associated with gastro-oesophageal reflux, particularly in neurologically compromised infants with poor airway-protective reflexes. Oral theophylline or caffeine, by its effect on the respiratory centre, may reduce or even eliminate the severity and frequency of apnoeic events. Caffeine has become the preferred methylxanthine by some neonatologists, because it has a long half-life (allowing once daily dosing), fewer side effects and serum levels do not have to be monitored. Continuous positive airway pressure (CPAP) or rarely mechanical ventilation may become necessary to control recurrent apnoea.

The diagnosis of ‘apnoea of prematurity’ is one of exclusion, as various other processes may cause or exacerbate apnoea. In the case of a preterm infant, these include the following:

- respiratory distress (surfactant deficiency, pneumonia, pulmonary oedema due to a persistent ductus arteriosus)
- intraventricular haemorrhage
- hypoglycaemia
- over-heating or hypothermia
- sepsis
- severe anaemia may also contribute to apnoea.

Pulmonary parenchymal disease

Any condition that causes decreased lung compliance or impaired gas exchange can contribute to apnoea. Appropriate pulmonary support should be provided for adequate gas exchange, and the underlying pulmonary condition should be treated.

Airway obstruction

This may result from simple malpositioning of the head (e.g. hyper-flexion or hyper-extension of the neck), especially in preterm infants. Congenital airway anomalies such as tracheo-oesophageal fistula or an aberrant thoracic blood vessel compressing the trachea (vascular sling) may also present as apnoea. Maintaining proper head positioning or surgical correction of the underlying anomaly should be provided.

Infection

Infection must always be excluded and antibiotics administered until infection has been ruled out by subsequent clinical findings and laboratory results (complete blood counts, chest X-ray, blood cultures, etc.).

Convulsions (see below)

Convulsions may present primarily as apnoea. This possibility should be considered especially in term or near-term infants with no other identifiable cause of apnoea. In such cases there may be a poor response to positive pressure ventilation. Convulsions in the first 1 to 3 postnatal days are usually due to intrapartum hypoxia. If there is a history of an operative vaginal delivery (e.g. forceps) or other birth trauma, this may indicate the possibility of an intracranial haemorrhage.

Maternal medication

A common cause of apnoea in the newborn can be intrapartum morphine or pethidine administration for maternal pain or sedation during the last 4 hours before delivery. The effects can be reversed by administering naloxone hydrochloride (100 micrograms/kg, usually given IM). Naloxone should not be given if there is a history of drug abuse with narcotics in pregnancy, as acute neonatal narcotic withdrawal may be precipitated (see Section 3.3).

Exposure to high levels of magnesium sulphate has also been associated with apnoea in the immediate postnatal period. This is usually a self-limiting process that very rarely requires mechanical ventilation.

Continuous monitoring, preferably with a pulse oximeter, is needed especially if the infant becomes bradycardic or cyanosed with the apnoea.
Treatment

- Gentle stimulation is usually all that is required to start the infant breathing again.
- Bag-and-mask resuscitation may occasionally be called for, and there should always be equipment immediately available and ready to use (not locked away in a cupboard) should this be necessary.
- If available, oral caffeine may reduce the number of episodes in a preterm infant. Caffeine seldom causes the tachycardia and other side effects associated with theophylline. It is advisable to continue caffeine for 4–5 days after cessation of apnoea. Recurrent apnoea that does not respond to caffeine occasionally requires a period of nasal CPAP or mechanical ventilation.
- If an apnoea monitor is available it can be used, but a pulse oximeter with the alarm turned on for hypoxaemia is much safer, as apnoea (absent ventilation) can occur despite continued breathing movements. This will also identify any baseline low oxygen saturation which, when treated, may help to prevent apnoea.

### Haemorrhage in the neonate

#### Causes of haemorrhage

An infant’s blood volume approximates 80 mL/kg of body weight. Peripartum haemorrhage of relatively small amounts of blood can therefore result in hypovolaemic shock in the newborn. Common causes may include a slipped ligature on the umbilical cord, intrauterine feto–maternal haemorrhage (diagnosed by the Kleihauer–Betke test), or subgaleal haemorrhage. Vasa praevia or an accidental incision of the placenta during Caesarean section are other causes.

The Kleihauer–Betke test is a blood test used to measure the amount of fetal haemoglobin transferred from the fetus to the mother’s bloodstream. It is usually performed on Rhesus-negative mothers to determine the dose of Rho(D) immune globulin needed to inhibit the formation of Rh antibodies in the mother and prevent Rh disease in future Rh-positive children. It is also the standard method of quantitatively determining feto–maternal haemorrhage.

The test exploits the differential resistance of fetal haemoglobin to acid. A standard blood smear prepared from the mother’s blood is exposed to an acid bath. This removes adult haemoglobin, but not fetal haemoglobin, from the red blood cells. Subsequent staining makes fetal cells (containing fetal haemoglobin) appear rose-pink in colour, whereas adult red blood cells are only seen as ‘ghosts’. The percentage of fetal to maternal cells is calculated under a microscope.

Bleeding in the first week of life is uncommon, but may signify haemorrhagic disease of the newborn or clotting factor deficiency.

### Presenting features

The infant will appear pale with weak peripheral pulses, tachypnoea and a tachycardia that may exceed 200 beats/minute. Blood pressure may be low or undetectable even in a term infant but is very difficult to measure in neonates.

The haematocrit and haemoglobin concentration may be normal in an infant with acute hypovolaemic shock, whereas adult red blood cells are only seen as ‘ghosts’. The percentage of fetal to maternal cells is calculated under a microscope.

Blood lost in the first few hours after the bleed. Obvious blood loss rarely results in hypovolaemic shock. Common sites of blood loss include the umbilical stump and the gastrointestinal tract. In the latter case, there may be doubt as to whether blood is of maternal origin (blood swallowed at delivery or from a bleeding nipple) or infant origin. In some cases this can be resolved by the Apt test.

#### Apt test

Mix 1 part of the blood-containing fluid (vomitus, gastric aspirate or liquid stool) with 5 parts of distilled water. Centrifuge it, and then mix 1 mL of the supernatant with 0.25 mL of 0.25% sodium hydroxide (NaOH). A yellow-brown colour signifies maternal blood, whereas fetal haemoglobin remains pink. The solution must be pink to start with.

#### Treatment

- In an emergency in a shocked infant take a blood sample for blood grouping and cross-matching. Give O Rh-negative or cross-matched blood (20 mL/kg) at a rate depending on the degree of shock (usually the first 10 mL/kg can be safely given over 5 minutes), monitoring the response and reducing the rate of infusion as improvement occurs. Sometimes a further 10–20 mL/kg of cross-matched blood may be necessary.
- If O-negative or cross-matched blood is not available, use 10–20 mL/kg of 4.5% albumin or Ringer-lactate or Hartmann’s solution.
- If there is overt bleeding, take a blood sample for blood grouping and cross-matching, haemoglobin, platelet count, film and clotting studies. Then give 1 mg of vitamin K (phytonadione or phytonadione) IV. If bleeding continues, give 20 mL/kg of fresh-frozen plasma (if available). Administer platelets if the count is < 60,000/mm³. Bleeding due to haemorrhagic disease of the newborn usually stops within 30 minutes of vitamin K administration.

The neonate with jaundice

Many infants become jaundiced for a few days after birth. This is because bilirubin released from the breakdown of red blood cells has to be excreted by the infant after birth. In utero, bilirubin would cross the placenta to reach the maternal liver, from where it would be processed and eliminated. The neonatal liver takes time to develop normal....
functioning. The serum bilirubin level usually rises after the first 24 hours of life and peaks at 100–300 µmol/litre by 3 to 5 days after birth.

Causes of physiological jaundice in the neonatal period include the following:
- increased breakdown of red blood cells in the first few days of life
- reduced lifespan of red blood cells (70 days, compared with 120 days in the adult)
- less efficient metabolism of bilirubin by the immature liver enterohepatic circulation of bilirubin.

‘Physiological jaundice’ is common, affecting at least one-third of normal term infants. Jaundice can be considered physiological and does not require treatment or investigation if the following criteria are met:
- Jaundice is not present in the first 24 hours of life.
- The infant is well, and free from signs of infection, without enlargement of the liver or spleen.
- The bilirubin concentration does not exceed 300 µmol/litre (approximately 17 mg/dL) at any stage (term infants only). A much lower acceptable level is set for preterm infants.
- The bilirubin concentration reaches a peak on the fourth or fifth day of life.
- The jaundice has fully resolved by the end of the second week of life.

The risk of jaundice can be reduced by encouraging early unrestricted demand breastfeeding.

There is no evidence whatsoever to support the widely held belief that giving extra water for the infant to drink either reduces the risk of jaundice or is helpful in treatment. In fact the opposite has been shown. Giving water is likely to reduce the frequency of breastfeeds and increase the risk of jaundice. Dehydration should be avoided by encouraging frequent breast feeds.

Assessing the degree of jaundice

Various means of estimating the degree of jaundice make it easier to determine which infants really need any intervention. Healthcare professionals can sometimes make a rough estimate of the degree of jaundice by looking at the skin colour (this is best undertaken in natural daylight), but it can only be divided into simple categories such as ‘slight’, ‘moderate’ or ‘severe’. The face is often the first part of the body to show signs of jaundice. The trunk usually only becomes yellow as jaundice deepens. Finally, the palms of the hands and soles of the feet become jaundiced. These observations are just estimates, and sometimes have to be confirmed by other means. Jaundice in the newborn infant can be missed in infants with dark skin, but can be more easily judged once the skin is blanched free of blood by finger pressure.

Bilirubin encephalopathy (kernicterus) in the absence of overt haemolysis is excessively uncommon in the term infant, unless the serum bilirubin level exceeds 425 µmol/litre.

Note:
- µmol/litre divided by 17.1 = mg/dL
- mg/dL multiplied by 17.1 = µmol/litre.

Several electronic devices have been developed for assessing skin colour, but none have yet been shown to work significantly better than the simple ‘icterometer’ devised in 1960 and still in use. Jaundice is assessed by pressing the clear plastic of this simple device against the tip of the nose (or against the gums or tongue in a dark-skinned infant, where it has been shown to be accurate in a South African study), and then matching the colour of the skin against the icterometer’s colour scale. Levels in excess of 350 µmol/litre are unlikely to be missed if a blood sample is taken once the icterometer reads ≥ 3.5. This too little known device, which costs only US$39, is still made by Cascade Health Care Products of Salem, Oregon, in the USA. Measuring the degree of jaundice by this method is of no value once phototherapy has been started.

The bilirubin concentration can be most simply and accurately measured by simple spectrophotometry of serum obtained by centrifuging blood in a capillary tube. Several easily operated machines are available. Ward-based devices for assessing the bilirubin content of a spun micro-haematocrit tube optically are accurate until the level exceeds 350 µmol/litre, and are adequate for most clinical purposes. If these devices are used, staff should be trained in this technique, and the machine should be calibrated daily and checked with control specimens of known bilirubin content. Using dirty tubes (or cuvettes), haemolysed or lipaemic samples can produce significant errors. Use plastic tubes, not glass ones, to avoid HIV infection if the tubes break.

The accurate measurement of values in excess of 350 µmol/litre is only possible in a biochemistry laboratory. A laboratory spectrophotometer reading is needed before initiating an exchange transfusion.

Direct or conjugated bilirubin presents no threat to the brain. It only accounts for a small fraction of the total serum bilirubin level in the first week of life. Decisions about treatment should therefore be based on the total serum bilirubin level, remembering that even laboratory estimates have limited precision.

Collecting blood

- Only a small amount of blood is needed to check the bilirubin level. Although described as a heel prick, sticking a needle into the heel runs a high risk of entering the underlying bone, and can lead to osteomyelitis, so should be avoided.
- It is safe to take blood from any part of the back third of the foot.

Try to use a disposable 2.4-mm blood lance, but never use the same lance for more than one infant, because of the risk of transmitting hepatitis or HIV infection. It is not necessary or appropriate to try to stabilise the skin first, so long as it is clean. A spring-loaded lance does seem to render the procedure less painful. The infant will also show fewer signs of distress if held or given something to suck during the procedure.

Grip the foot firmly enough to make it go red but not white. Stab the back of the foot just once and then squeeze gently and intermittently to stimulate blood flow. The use of a standard lance should optimise blood collection because it helps to ensure that the skin is punctured to a standard depth. A shallower prick is unlikely to reduce the pain inflicted because it will almost certainly prolong the procedure. A double puncture may help if a lot of blood is needed. Slight finger pressure exerted through a cotton ball on the site for about a minute is usually enough to stop any further
bleeding after the procedure is over. The healthcare worker should be careful not to prick their own finger.

![This is the preferred site for infrequent heel sampling](image)

**FIGURE 3.4.3** Unsuitable (top) and suitable (bottom) positions from which to obtain capillary blood from the foot of a neonate.

**Biliary atresia**

In prolonged jaundice (jaundice persisting beyond 14 days of age), it is important to determine not only the total bilirubin concentration but also the proportion of conjugated bilirubin. Conjugated bilirubin is not neurotoxic, but its presence signifies the presence of biliary obstruction attributable to potentially serious conditions such as neonatal hepatitis or biliary atresia.

The history can be informative if laboratory investigations are not available. The presence of pale unpigmented stools or dark urine would be suggestive of biliary obstruction. Urine can also be tested with a reagent strip for bilirubin (if positive for bilirubin, the diagnosis of biliary obstruction is supported, provided that the infant is not receiving phototherapy when unconjugated bilirubin appears in the urine).

It is important to identify biliary atresia promptly, as operative intervention is more likely to be successful if undertaken within 8 weeks of birth. Even mild jaundice merits review if the stool becomes grey or putty coloured rather than yellow or green. Similarly, in the absence of a neonatal screening programme (a situation that is prevalent in the majority of resource-limited countries), it is important that congenital hypothyroidism and glucose-6-phosphate dehydrogenase (G6PD) deficiency are identified. This can be done by tests including $T_{4}$, TSH, G6PD assay, bilirubin (total and direct), complete blood picture and reticulocyte count.

**Breast milk jaundice**

Around 10% of breastfed infants are still slightly jaundiced 1 month after birth. Laboratory investigations seldom reveal anything that needs treatment, and the infant is otherwise well. This scenario may be suggestive of breast milk jaundice. However, it is important that other common causes, including congenital biliary atresia, hypothyroidism and G6PD deficiency, are ruled out. Remember that breast milk jaundice is a diagnosis of exclusion.

Ill infants with continuing jaundice should be given a prophylactic 1 mg IM injection of vitamin K if it is not clear that they received such an injection at birth, to minimise the risk of potentially fatal late vitamin K deficiency bleeding.

**Pathological jaundice**

There is an increasing risk that high levels of unconjugated serum bilirubin will breach the blood-brain barrier, causing critical damage to many cells in the brain. This becomes more likely if, in the presence of haemolysis, the unconjugated serum bilirubin level is allowed to rise above 350 µmol/litre. Indeed, in a small preterm infant who is also ill, the safe limit may be nearer to 250 µmol/litre, or sometimes even less.

Once this happens there is nothing that can usefully be done to reverse the resultant brain damage. Infants may manifest this by seizures, or by becoming stiff with arching of the back and neck signifying a severe encephalopathy. Many of these infants will die after becoming severely ill. The survivors will almost all become severely deaf, and the majority may develop athetoid cerebral palsy.

**Causes of abnormally raised bilirubin levels**

These include the following:

- **haemolytic disease**
- **neonatal sepsis**
- **polycythaemia**
- **severe malnutrition**
- **hypothyroidism**
- **congenital infection (usually obstructive jaundice):**
  - syphilis
  - toxoplasmosis
  - cytomegalovirus
  - rubella
  - hepatitis.

In the first week of life, the following factors may lead to jaundice that is sufficiently severe to require treatment:

- **Preterm delivery:** Even moderate prematurity significantly increases the risk of early or severe jaundice and associated sequelae. Consequently, the bilirubin treatment charts give lower treatment thresholds for infants born at 31–34 weeks’ gestation. At less than 31 weeks, treatment is started at even lower bilirubin levels.
- **Haemolytic disease:** This may be isoimmune (e.g. Rh or ABO incompatibility) or due to red blood cell disorders (e.g. hereditary spherocytosis, G6PD deficiency).
- **Infection:** Haemolysis and impaired elimination of bilirubin may be associated with septicaemia. Congenital infection (e.g. syphilis) may also be associated with jaundice, but other features such as rash, hepatosplenomegaly and thrombocytopenia will be present, and there is usually a significant conjugated bilirubin level.
- **Polycythaemia.**
- **Rarer causes:** These include inborn errors of metabolism (e.g. galactosaemia), congenital hypothyroidism, other intrauterine infections and neonatal malaria.
- **Obstructive jaundice:** This rarely presents in the first week of life, but is important in the differential diagnosis of prolonged jaundice.

**Haemolysis**

Clinically noticeable jaundice within 24 hours of birth, especially if the mother is blood group O and the infant is blood group A or group B, or the mother is Rhesus negative and the infant is Rhesus positive, should suggest the possibility of a haemolytic disease.

Term infants with physiological jaundice seldom need treatment with phototherapy unless there is an unusually
high rate of red cell breakdown. However, phototherapy should be started as soon as jaundice becomes apparent if there is evidence of haemolytic disease. The trend in the bilirubin level should then be checked twice a day (the level cannot be assessed from skin colour once phototherapy has commenced).

Investigation
A good principle to remember is to measure bilirubin levels and investigate if:
- jaundice appears on day 1 in any infant
- jaundice appears on day 2 in any preterm infant
- the palms of the hands or soles of the feet are yellow in any sick neonate and in any infant of any age.

Jaundice should never last for more than 3 weeks.

In an infant who develops jaundice in the first 24 hours, the most likely causes are infections, haemolytic disease and polycythaemia. The history and examination may be helpful. It is important to determine whether the mother has

Phototherapy
This uses light in the blue-green region of the spectrum (not ultraviolet) to convert bilirubin to its water-soluble isomer "luminrubin", which can be excreted in urine and stools.

In infants who are very yellow, it is best to use light from a bank of at least six 60-cm 20-watt fluorescent strip lights suspended not more than 30 cm above the unclothed infant (lights placed 60 cm from the infant are only about half as effective). Placing a white sheet under and round the infant will increase the effectiveness of any treatment. While under phototherapy, it is important to monitor body temperature and to protect the infant from draughts. It is also standard practice to mask the eyes to protect them from the bright light. The infant should be nursed naked in an incubator, under a radiant heater or in a cot, allowing maximum skin exposure. Feeding, especially breastfeeding, should continue without interruption, as more frequent breastfeeding is helpful not only in eliminating meconium from the bowel but also in enhancing bilirubin clearance via the stools and urine. During phototherapy, the infant can be removed for breastfeeding as necessary (intermittent treatment has been shown to be as effective as continuous treatment). Fluid...
other than breast milk (e.g. breast milk substitute, water, sugar water) should not be given. However, the total daily fluid intake may need to be increased by about 10%, especially in preterm infants, in order to minimise additional water losses from evaporation and convection.

Troublesome side effects of phototherapy include rashes and profuse watery stools, but these are rare and do not require treatment. Phototherapy can be stopped when the serum bilirubin level is 50 mmol/litre (3 mg/dL) below the phototherapy threshold.

**Exchange transfusion**

Bilirubin levels that rare above certain threshold values place the infant at risk of developing bilirubin encephalopathy (kernicterus). In such cases, the bilirubin level needs to be immediately lowered with a double-volume exchange transfusion. A volume of the infant’s blood equal to the body weight in kg × 2 × 80 mL is exchanged in small aliquots with O Rhesus-negative blood, or blood cross-matched against maternal antibodies.

Double-volume exchange transfusion is recommended in term infants if:
- they are haemolysing or are ill and have a bilirubin level higher than 300 µmol/litre
- they are well and not haemolysing but their bilirubin level is higher than 425 µmol/litre.

The functions of exchange transfusion include the following:
- removal of maternal antibodies
- removal of antibody-coated red blood cells before they haemolysse
- correction of anaemia
- lowering of total bilirubin levels, if there is sufficient time for equilibration between intravascular and extravascular levels.

Exchange transfusion is generally only undertaken if the rate of red blood cell breakdown is likely to exceed the ability of phototherapy to control bilirubin levels. This is very likely to occur in infants with a positive Coombs’ test who are already anaemic (because of fetal haemolysis) at birth. A cord blood haemoglobin level of less than 140 grams/litre already anaemic (because of fetal haemolysis) at birth. A cord blood haemoglobin level of less than 140 grams/litre

**Exchange transfusion**

1 Calculate the infant’s circulating volume (= 80 mL/kg). Twice this amount of blood will be required. Do not exceed this (usually 1 bag of whole blood = 450 mL).
2 Check that the blood has either the same ABO group with each draw and infusion. This is roughly as follows:
   - baby weighing < 1500 grams: 5 mL
   - baby weighing 1500–2500 grams: 5–0 mL
   - baby weighing 2500 grams: 10–15 mL.

Although the potassium concentration of the blood is often 8–10 mmol/litre, this does not usually cause significant hyperkalaemia. Exchange transfusion should only be undertaken once all of the attendant risks have been considered. Even in experienced hands, 1% of infants may suffer a sudden cardiac arrest during or shortly after the procedure. This should respond to prompt intervention using the approach adopted when dealing with cardiac arrest at birth, but the infant needs to be monitored closely, and staff need to be prepared for such a possibility if this is not to prove fatal.

Air embolism can kill within minutes, and faulty technique can cause sudden hypoxia or hypervolaemia, or introduce later sepsis. The use of donor blood more than 5 days old can cause serious hyperkalaemia and an arrhythmia. Blood used straight from the fridge at 4ºC can impose a major cold stress. Cytomegalovirus (CMV) infection may occur if the baby weighs less than 1500 grams, but a position below the liver is also acceptable if the line will sample and flush easily. A line positioned in the liver should not be used.

Ideally, use a blood warmer (especially for low-birth-weight infants). Otherwise warm the blood bag by placing it under the mother’s clothing next to the skin.

Set up a closed circuit with either a four-way tap, or two three-way taps. The four links are:

- the infant
- the syringe for removing and replacing blood
- the blood to be transfused
- the route for discarding the infant’s blood.

Make sure that the total blood in and out is recorded. Plan to spend 1.5–2 hours on the procedure.

If you use small aliquots, remember to add an allowance for the ‘dead space’ in the tubing between the syringe and the baby. You should draw out each aliquot over 2–3 minutes to avoid abrupt changes in blood pressure, and replace over 3–4 minutes with the observer keeping a running total.

Send the first aliquot for measurement of bilirubin, electrolyte and calcium concentrations.

Halfway through the procedure check the blood glucose, calcium and potassium concentrations.

Measure them again, together with the bilirubin concentration, at the end of the procedure.

Sometimes it is necessary to exchange more than once in quick succession. Symptomatic hypocalcaemia may occur as the citrate in donor blood binds calcium. This responds best to halting the procedure for 15 minutes. Giving calcium gluconate is of little benefit and may be hazardous, so is best avoided.

Human immunoglobulin 500 mg/kg, given as an IV infusion over 2 hours, reduces the number of infants who require an exchange (especially if due to Coombs’ positive Rhesus or ABO incompatibility). It also decreases the number who require a ‘top-up’ transfusion for late neonatal anaemia.

**Exchange transfusion**

1 Calculate the infant’s circulating volume (= 80 mL/kg).
2 Check that the blood has either the same ABO group with each draw and infusion. This is roughly as follows:
   - baby weighing < 1500 grams: 5 mL
   - baby weighing 1500–2500 grams: 5–0 mL
   - baby weighing 2500 grams: 10–15 mL.

Although the potassium concentration of the blood is often 8–10 mmol/litre, this does not usually cause significant hyperkalaemia. Exchange transfusion should only be undertaken once all of the attendant risks have been considered. Even in experienced hands, 1% of infants may suffer a sudden cardiac arrest during or shortly after the procedure. This should respond to prompt intervention using the approach adopted when dealing with cardiac arrest at birth, but the infant needs to be monitored closely, and staff need to be prepared for such a possibility if this is not to prove fatal.

Air embolism can kill within minutes, and faulty technique can cause sudden hypoxia or hypervolaemia, or introduce later sepsis. The use of donor blood more than 5 days old can cause serious hyperkalaemia and an arrhythmia. Blood used straight from the fridge at 4ºC can impose a major cold stress. Cytomegalovirus (CMV) infection may occur if the blood does not come from a CMV-negative donor. It is also critical to avoid causing HIV or hepatitis B or C infection. In addition, there is a definite but poorly understood risk that the procedure will trigger serious necrotising enterocolitis. If possible it is best to avoid the use of heparinised blood.
The neonate with anaemia

Causes of anaemia
These include the following:
- haemorrhage
- twin-to-twin transfusion
- feto–maternal transfusion
- placental abruption
- haemolysis due to
  - Rh disease
  - ABO incompatibility
- ABO incompatibility.

Treatment of anaemia
Haemolysis may continue for several weeks after birth even if it is not severe enough to require intervention in the first week of life. An attempt should therefore be made to check all infants with a positive Coombs’ test for late anaemia when they are about 6 weeks old. Infants with a capillary haemoglobin level of less than 80 grams/litre or a haematocrit (PCV) of less than 25% should then receive a ‘top-up’ transfusion of 20 mL/kg of cross-matched or group O Rh negative blood given over 2 hours. Red cell concentrate or packed cells are preferable. Daily folic acid (1 mg/day) for at least 1 week can help to reduce anaemia.

The neonate with seizures, spasms or reduced conscious level
Seizures (also called fits or convulsions) have been reported to affect about 0.1% of term infants and 10% of those weighing less than 1500 grams at birth.

Presenting features
Seizures may be subtle (apnoea, staring, lip smacking/grimacing, deviation of the eyes, cycling movements of the limbs) or more obvious (tonic extensor posturing or clonic jerks) or benign myoclonic movements. Involvement of a limb or one side of the body does not necessarily imply a focal cause in the neonate. A bulging anterior fontanelle may suggest intracranial haemorrhage or infection. It is important to always measure and note the head circumference. Sometimes involuntary movements (e.g. extreme jitteriness) or benign myoclonic jerks can be difficult to distinguish from seizures. The presence of associated autonomic instability and/or lateral eye deviations may signal seizure activity, whereas the absence of these findings or elimination of these movements when the limbs are restrained indicate a non-seizure event.

Causes of seizures
These include the following:
- hypoxia
- hypoglycaemia
- meningitis
- drug-related seizures
- sepsis
- polycythaemia
- tetanus
- hypocalcaemia
- hyper- or hyponatraemia
- metabolic abnormalities
- hypoxic ischaemic encephalopathy: this is the most common cause of seizures in a term infant. Onset is usually within the first 24 hours, and it almost never starts after the third day
- intracranial haemorrhage, subarachnoid haemorrhage or cerebral infarctions: these are also common causes of neonatal seizures. With subarachnoid haemorrhage, seizures may or may not be focal. However, unilateral tonic–clonic seizures are often observed with cerebral infarction. Although intraventricular haemorrhage occurs most frequently in low-birth-weight infants or at gestational ages under 32 weeks, very rarely it may manifest in term or near-term infants with neonatal seizures. Always give 1 mg IV vitamin K.
- infection: although meningitis is not the commonest cause of neonatal convulsion, it must always be excluded by lumbar puncture and antibiotics commenced urgently pending the results of culture
- metabolic causes of seizures may include:
  - hypoglycaemia: always check blood glucose levels
  - hypocalcaemia: check plasma calcium and magnesium levels
  - hyponatraemia and hypernatraemia: seizures are uncommon unless the plasma sodium level is < 120 mmol/litre or > 160 mmol/litre. Seizures in infants with hypernatraemia may result from associated cavernous sinus thrombosis. A rapid fall or rise in serum sodium level, as may occur with too rapid therapeutic correction, may be more injurious than the absolute value of serum sodium level. A slow correction is desirable in such situations
  - bilirubin encephalopathy (see above section on jaundice)
- rare inborn errors of metabolism (e.g. urea cycle defects, non-ketotic hyperglycaemia) require measurement of serum amino acids, urine fatty acids, serum lactate, serum pyruvate and blood ammonia levels. Measuring the anion gap can also be quite helpful. A high value may be suggestive of an inborn error of metabolism.

Note: anion gap = (Na + K) – (Cl + HCO3). Normal anion gap = 5–17 mEq/litre in neonates
- maternal substance abuse, particularly opiate withdrawal
- tetanus remains a problem in many low-resource countries.

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Because of all these risks, if at all possible exchange transfusion should only be undertaken in a neonatal unit where the staff are experienced in the use of this procedure.

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<table>
<thead>
<tr>
<th>TABLE 3.4.4 Differentiating between seizures and jitteriness</th>
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<tbody>
<tr>
<td><strong>Well but jittery infant</strong></td>
</tr>
<tr>
<td>No abnormal eye movements</td>
</tr>
<tr>
<td>No apnoea</td>
</tr>
<tr>
<td>No colour changes</td>
</tr>
<tr>
<td>No heart rate changes</td>
</tr>
<tr>
<td>Easily triggered by handling and stopped by gentle passive flexion of the affected limb</td>
</tr>
<tr>
<td>Rhythmtical movements</td>
</tr>
</tbody>
</table>
When managing neonatal seizures it is best to focus on the limited number of conditions where immediate treatment can have a major impact on long-term outcome. There are many situations where seizures are simply the outward sign of damage that cannot be reversed, even though it may be possible to stop continuing seizure activity from making matters worse.

**Focal seizures** can sometimes be the sign of what was otherwise a silent haemorrhagic infarction of part of the brain. While investigation would explain what was going on, it would not alter management.

If the infant is alert and well between episodes of seizure activity, appears normal on examination, and is feeding normally, sometimes it may be perfectly appropriate to do nothing.

**Investigations**

These should include the following:

- Lumbar puncture and blood culture
- Full blood count, PCV, CRP
- Blood glucose, calcium, urea and electrolytes, and blood ammonia (if available)
- Arterial blood gas analysis to help further assess acid-base status
- Cranial ultrasound (if available)
- Intracranial imaging (head computed tomography if available)
- Baseline and follow-up electroencephalograms (if available)
- Save urine, plasma and CSF for metabolic studies (if available) if seizures are protracted.

**Treatment**

Management of a neonate with seizures is as follows:

- **Airway.**
- **Breathing.**
- **Circulatory access.**
- **Give glucose, IV or intra-osseous (2 mL/kg of 10% glucose).**
- **Give antibiotics, IV or IM, as there is a strong possibility of meningitis or sepsis.**
- **Stop the seizures with an anticonvulsant:**
  - Phenytoin is dangerous in infants with hypoxic ischaemic encephalopathy who may also have ischaemic hypoxic heart injury.
  - Phenobarbital is the second-line drug for neonatal seizures. Initial seizure control with this drug requires the presence of a saline-filled IV line (because the drug crystallises out in dextrose solutions). The same problem also renders the IM route unavailable. Give a 20 mg/kg loading dose (diluted in 10–15 mL of normal saline) IV slowly over 10–20 minutes (monitor for hypotension and cardiac arrhythmia, making sure that the drug does not leak into the tissues), and then 2 mg/kg IV or by mouth once every 8 hours. Infants more than 2 to 3 weeks old may need a considerably larger maintenance dose. Oral absorption of phenytoin may be quite unpredictable, so this would need to be monitored.
  - Phenytoin is dangerous in infants with hypoxic ischaemic encephalopathy who may also have ischaemic hypoxic heart injury.
- **Paraldehyde** is the third-line drug for neonatal seizures. Give a single 0.4 mL/kg dose mixed with an equal volume of mineral oil by the rectal route. This route offers excellent bioavailability of the drug. The same dose can be repeated once if seizures persist. Give within 10 minutes after preparation when using a plastic syringe (because paraldehyde interacts with many plastics). Paraldehyde can also be given by the IM route. However, problems with muscle necrosis make this a less desirable route.
- **Diazepam** is an alternative to phenobarbital as first line treatment for neonatal seizures. However, it is vital that hypoglycaemia has been excluded and treated before giving this drug. A working bag-valve-mask of suitable size must be ready next to the infant before this drug is given. It can be given IV at a dose of 300 microgram/kg IV slowly or 500 microgram/kg rectally.
- **Treat hypoglycaemia if present.**
- **Monitor the heart rate and respiratory rate, and oxygenation (ideally with pulse oximetry).** Treat low SaO2 or cyanosis with oxygen.
- **Consider anticonvulsant therapy:** the earlier the fits appear, the more frequent they are (more than two or three per hour) and the longer they last (more than 3 minutes), the more likely it is that anticonvulsants will be needed. Fits that interfere with respiration need to be treated and may require respiratory support.

**Anticonvulsant treatment**

Phenobarbital is the first-line drug for neonatal seizures. Give a 20 mg/kg IV loading dose slowly followed by 3–5 mg/kg once every 24 hours. Seizure control may be achieved more quickly if the first dose is given IV, but this loading dose must be given slowly, over at least 5 minutes, to minimise the risk of shock, hypotension or laryngospasm. Some texts recommend the use of a higher dose if the standard dose fails, but this can cause respiratory depression. **Always have a bag-valve-mask available to support ventilation.** With hypoxic encephalopathy usually only a loading dose is needed. Seizures have been reported to respond to this dose 40% of the time. An additional 10 mg/kg may be required if seizures persist or recur (70% response rate).

Phenytoin is the second-line drug for neonatal seizures. Initial seizure control with this drug requires the presence of a saline-filled IV line (because the drug crystallises out in dextrose solutions). The same problem also renders the IM route unavailable. Give a 20 mg/kg loading dose (diluted in 10–15 mL of normal saline) IV slowly over 10–20 minutes (monitor for hypotension and cardiac arrhythmia, making sure that the drug does not leak into the tissues), and then 2 mg/kg IV or by mouth once every 8 hours. Infants more than 2 to 3 weeks old may need a considerably larger maintenance dose. Oral absorption of phenytoin may be quite unpredictable, so this would need to be monitored.

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Clonazepam: The loading dose is given as 100 micrograms/kg by slow IV infusion. It should not be administered for more than 3 days.

Midazolam: This has an immediate effect but a short duration of action. It can be given into the buccal cavity or IV. Like diazepam it can cause respiratory depression, so a bag and mask must be available when it is used, and the infant must be monitored closely.

Anticonvulsants may precipitate a need for respiratory support. Therefore always have a bag-valve-mask available.

Once seizures are controlled, maintenance therapy (which is rarely needed) with a single agent (usually phenobarbinate) is often possible. Discontinuation of treatment depends on the underlying aetiology, but aim to withdraw anticonvulsants as soon as possible.

It is essential to consider the four main treatable causes of fitting, namely hypoglycaemia, hypocalcaemia,
meningitis and tetanus, as any delay in diagnosis could have serious consequences.

Hypoglycaemia (glucose < 2.5 mmol/litre or < 45 mg/dL)
Hypoglycaemia is a common problem in the nursery; it can occur in infants who appear well, as well as in those who are sick. It is important to identify any infant at risk and implement preventative and curative measures as early as possible. Untreated symptomatic hypoglycaemia can result in brain damage.

Infants at risk of developing hypoglycaemia include the following:
- infant of diabetic mother
- preterm infant
- small-for-gestational-age or wasted infant
- large-for-gestational-age infant
- post-term infant
- sick infant with infections and respiratory failure
- infant who is not receiving adequate breast milk.

The definition of hypoglycaemia is controversial, and no studies have determined an absolute value at which organ dysfunction will occur. However, it is known that a prolonged low level of symptomatic hypoglycaemia is associated with brain injury. At the time of writing, most neonatologists prefer to maintain blood glucose levels above 2.5 mmol/litre (45 mg/dL).

Causes of neonatal hypoglycaemia
Increased utilisation of glucose (hyperinsulinism)
- Infants of diabetic mothers.
- Respiratory distress.
- Abrupt interruption of high glucose infusion.
- Polycythaemia.
- Hypothermia.

Rare causes of hyperinsulinism include:
- erythroblastosis fetalis
- islet-cell hyperplasia
- Beckwith–Wiedemann syndrome
- insulin-producing tumours
- maternal beta-agonist tocolytic therapy
- rarely malpositioned umbilical arterial catheter infusing a high concentration of glucose into coeliac and mesenteric arteries (T11–T12), stimulating insulin release.
Decreased production/stores of carbohydrate
- Prematurity.
- Small-for-gestational-age or wasted infant.
- Inadequate caloric intake.

Mixed increased utilisation and/or decreased production from other causes
- Perinatal stress (e.g. due to hypoxia, sepsis, shock, hypothermia).

Rare causes
- Defects in carbohydrate metabolism (galactosaemia, fructose intolerance, glycogen storage disease).
- Endocrine deficiency (adrenal insufficiency, hypothalamic insufficiency, glucagon deficiency).
- Defects in amino acid metabolism (maple syrup urine disease, propionic acidemia, methylmalonic acidemia, tyrosinaemia).

Diagnosis of hypoglycaemia
- There are few data on normal blood glucose levels in the first week of life, particularly for healthy breastfed term infants. Moreover, there is little evidence that a transient low blood glucose concentration in term infants who show no physical signs is harmful. However, asymptomatic hypoglycaemia may rapidly progress to symptomatic hypoglycaemia. Fits due to hypoglycaemia typically start in a previously well infant on or after the second day of life.
- Indications for measuring the blood glucose concentration of a term infant include lethargy, poor feeding, temperature instability, respiratory distress, new-onset apnoea/bradycardia, jitteriness, pronounced hypotonia, diminished consciousness and seizures. The association between such signs and low blood glucose levels is described as ‘symptomatic hypoglycaemia’.
- Beware of blaming ‘hypoglycaemia’ alone for these signs. Remember that an infant who seems drowsy may be infected, and low blood glucose concentration may merely be an associated finding. It is important to try to establish the underlying cause of the problem.
  - Although laboratory estimates of blood glucose concentration are ideal for diagnosing and managing this condition, reagent strips can be helpful.
  - The blood glucose concentration in the first 6 hours of life is very often low (1.5–2.0 mmol/litre). There is no evidence that this is harmful for otherwise healthy term infants, who adapt by mobilising other fuels. Consequently, early testing (under 6 hours of age) is pointless, unless neurological signs are present or there are other conditions that necessitate testing.
  - In newborn infants the serum glucose concentration is about 0.5 mmol/litre lower than that of whole blood.

When to test
- Symptomatic infants (lethargy, poor feeding, temperature instability, respiratory distress, new-onset apnoea/bradycardia, jitteriness and seizures) should be tested immediately.
- Infants at risk should be tested within 1 hour after birth (as such infants rapidly become hypoglycaemic after delivery) and then 3-hourly until blood glucose levels are stable at 2.5 mmol/litre (45 mg/dL) or higher. Continue to monitor until feeds are well established.
- In infants with hypoglycaemia, check the blood glucose concentration every 20–30 minutes from the beginning of treatment, then hourly until it is stable at 2.5 mmol/litre (45 mg/dL) or higher. Continue to monitor frequently (every 4–8 hours) during treatment, and while decreasing supplemental IV glucose infusions.

Laboratory diagnosis
- Reagent strips are useful and rapid, but in general are less reliable than laboratory plasma glucose measurements. Reagent strips may show a glucose level as much as 15% lower than plasma glucose levels. Whenever possible, it is preferable to use a calibrated glucometer.
- Laboratory plasma glucose determinations (if available) are useful for confirming hypoglycaemia detected by reagent strips, but blood samples must be processed promptly for accurate values, as glycolysis occurs in standing whole blood samples. Do not wait for laboratory confirmation before initiating therapy.

Management of hypoglycaemia

Infants at risk of hypoglycaemia but appearing to be well
- Initiate early feeding within 1 hour after birth with breast milk or formula (only if breast milk is not available) and repeat every 2–3 hours.
- Feeding with 5% glucose is not recommended in infants, because milk provides more energy.
- Infants of diabetic mothers are unlikely to develop hypoglycaemia on the second day of life if tests in the first 24 hours are satisfactory.

Infants with symptomatic hypoglycaemia who are unable to feed or who failed correction of glucose levels with enteral feeding
- Establish an IV line using sterile precautions, and take a sample for blood culture and other biochemical tests (if available).
  - Give an IV glucose bolus 200 mg/kg over 5 minutes (2 mL/kg of 10% glucose in water). If the infant almost immediately becomes more alert and active ‘on the end of your needle’ you have made the diagnosis, even before the laboratory report comes back.
  - In such situations it is then important to keep the blood glucose level stable by starting a sustained infusion of 10% dextrose at 5 mL/kg/hour (or 5–8 mg/kg/minute) for the next 2 to 4 days while gradually building up oral feeds.
- If further episodes of symptomatic hypoglycaemia occur, the bolus should be repeated and the infusion rate increased by 10–15%.
- An infant who seems drowsy may be infected, and a low blood glucose concentration may be an associated finding rather than the main cause of the problem. It is important to exclude infection and initiate antibiotics if indicated.
- When administering boluses, never use higher concentrations of glucose (> 10%) because of the risk of intra-ventricular haemorrhage and/or cerebral oedema.
- The concentration of glucose in the maintenance fluids
can be adjusted in accordance with the total daily fluid requirements.

- If using concentrations higher than 12.5%, a central venous line or umbilical venous catheter needs to be inserted because of the risk of tissue damage in the event of fluid extravasation.

- Most infants will correct hypoglycaemia with infusion of 5–8 mg/kg/minute; not infrequently, however, infants with severe intratracheal growth restriction or wasting and those with hyperinsulinism may require infusion rates of up to 12–15 mg/kg/minute.

- When normal blood glucose levels have been stable for 12–24 hours and the infant is tolerating enteral feeding, decrease the IV glucose infusion by 10–20% each time levels are higher than 2.5 mmol/litre (45 mg/dL).

- Always decrease the IV infusion gradually because of the risk of precipitating hypoglycaemia.

- If you are unable to gain IV access, a feed of breast milk should be started if the infant is conscious. Hyposmotic Gel, an oral glucose mixture containing 500 micrograms of glucose/mL, can be helpful (if available). Apply 1–2 mL to the oral mucosa.

- If hypoglycaemia persists beyond the first 48 hours of life and requires large infusions of glucose (greater than 8 mg/kg/minute), evaluation for endocrine or metabolic disorders should be considered.

**Meningitis**

See p. 353.

**Tetanus**

Do not forget tetanus. Neonatal tetanus has to be considered if a previously well and still conscious infant starts to develop increasingly frequent muscle spasms 3–14 days after birth. This becomes more relevant if there is any doubt about the way the umbilical cord was managed at birth, or if there is no proof that the mother was ever immunised with tetanus toxoid vaccine. Involuntary muscle contractions are typically triggered by quite light touch or sound, and the hands and jaw are often held firmly clenched.

- **Airway and breathing** are frequently compromised. Secure and maintain the airway, and ensure adequacy of ventilation. Oxygen may help if the spasms are causing cyanosis, but in severe cases survival may be dependent on the availability of respiratory support, sometimes with tracheostomy to protect the airway. Intubation may trigger very dangerous spasms of the airway and must be undertaken by a skilled professional.

- Insert an IV line for drug and antibiotic administration.

- Give high-dose benzyl penicillin 60 mg/kg IV one dose every 12 hours in the first week of life, every 8 hours in an infant aged 1–3 weeks, and every 6 hours in an infant over 3 weeks of age. Oral dosing (with phenoxymethylpenicillin) can sometimes be used to complete a course of treatment.

- Give an 150 unit/kg dose of IM human tetanus immunoglobulin. Other IM injections must be avoided altogether, as they will provoke spasms.

- If the infant/child is in acute spasm, this should be terminated by giving diazepam by bolus IV infusion over 15 minutes (dose 200 micrograms/kg) or rectally (400 micrograms/kg). Ensure that for IV infusion, diazepam is diluted to 100 micrograms/mL, and that extravasation (very irritating) does not occur. Slow and incomplete absorption means that IM diazepam is not effective. Always ensure that a bag and mask are immediately available when giving diazepam, in case apnoea occurs.

- Also give an IV loading dose of 25–40 mg/kg of magnesium sulphate over 20–30 minutes.

- Subsequently give 10–20 mg/kg of magnesium sulphate IV 2- to 4-hourly to control spasms. If this is not available or does not control spasms, give IV diazepam 200 micrograms/kg every 4–6 hours.

- Stop diazepam if magnesium sulphate alone controls the spasms.

- Reduce the dose of diazepam if apnoeic episodes occur.

- Always have a bag and mask available in case the patient stops breathing as a result of the diazepam plus magnesium.

- When stable, a nasogastric tube, ideally passed by an anaesthetist, will allow fluids, food and drugs to be given with minimal disturbance. Feeds need to be given frequently (ideally hourly) and in small amounts due to reduced gut motility. Regular breast milk feeds via a nasogastric tube are essential.

- Excision of the umbilical stump is not indicated.

- The disease itself does not induce immunity, so after recovery tetanus vaccine must be given for future prevention.

- Treat any obvious umbilical infection with an additional broad-spectrum antibiotic.

- Minimise handling, provide care in a quiet dark room and give frequent small tube feeds.

- Immunising the mother (give two 0.5-mL doses 1 month apart) will prevent a similar tragedy in any future pregnancy.

- Severe cases may need muscle paralysis and ventilation in a specialist unit (if available).

**Treatment of neonatal tetanus**

- Airway and Breathing: Oxygen as needed and tracheostomy may be required.

- Benzyl penicillin.

- Human tetanus immunoglobulin.

- Consider giving diazepam IV or by the rectal route to control spasms (with bag and mask available).

- Magnesium sulphate has been recently shown to help prevent spasms in tetanus.

- Minimise handling.

- Give frequent small tube feeds of breast milk.

**Other causes of neonatal seizures**

Rule out any other cause, including biochemical causes other than hypoglycaemia.

Remember that biochemical disturbance may not be the main underlying problem. In many infants, the evidence of hypoglycaemia or any other biochemical disturbance is only a sign of another more serious underlying illness. Of these, by far the most important treatable condition is meningitis. Unless the infant is otherwise entirely well it is important not to miss this possibility.

Other important diagnostic possibilities include hypocalcaemia, hyponatraemia and hypernatraemia. Often a history and clinical features will aid the recognition of these biochemical abnormalities, and a serum level will clinch the diagnosis. Any existing problem will be made worse if hypernatraemia is corrected too rapidly.
• Fits due to hypocalcaemia (a serum total calcium level of < 1.7 mmol/litre), with or without hypomagnesaemia, are generally benign and occur unexpectedly in an otherwise well but hyper-reflexic child more than 2 to 3 days old. As with hypoglycaemia, signs may settle “on the end of the needle” if the infant is given 1–2 mL/kg of 10% calcium gluconate in equal dilution as a slow IV infusion. Such seizures usually respond extremely well to oral supplementation. It is appropriate to investigate the mother for an unrecognised endocrine abnormality (if facilities allow this). Do not allow IV calcium to go outside the vein as it will cause severe tissue damage.

• Toxic substances provided by a traditional healer create important causes of seizures and reduced conscious level in neonates in some countries.

Bilirubin encephalopathy
Infants with brain damage due to jaundice are stiff and semi-conscious, but seldom have fits. Signs usually appear quite abruptly 3 to 6 days after birth, but by the time they appear it is too late to initiate treatment.

Inborn errors of metabolism
Other more complex biochemical disturbances are usually associated with metabolic acidosis and progressively deepening coma in a child who was initially well for 1 to 2 days after birth. They are generally too complex to treat without substantial biochemical support, but it may be appropriate to take specimens for later diagnostic evaluation, because many of these conditions are familial and genetically determined. Pyridoxine deficiency is one of the few rare treatable conditions.

Hypoxic-ischaemic encephalopathy
This is an abnormal neurological state of infants who have suffered significant lack of oxygen and/or circulation to vital organs before, during or immediately after birth. It is characterised by the following:

- signs of fetal distress in labour, cord blood pH < 7.0, and low Apgar score (≤ 3 at 5 minutes) despite appropriate resuscitation measures
- neonatal neurological abnormalities soon after delivery
- evidence of multi-organ dysfunction such as oliguria (signifying acute tubular necrosis), increased transaminase levels (hepatic necrosis), necrotising enterocolitis or myocardial dysfunction.

Hypoxic-ischaemic encephalopathy-related problems in the days after birth
• Reduced consciousness and/or convulsions: treat with phenobarbital and check glucose levels to rule out hypoglycaemia.
• Apnoea: this is common after severe perinatal asphyxia, and is sometimes associated with convulsions. Manage with oxygen administered by nasal cannulae and resuscitation with bag and mask.
• Inability to suck: feed with expressed breast milk via a nasogastric tube. Beware of delayed emptying of the stomach, which may lead to regurgitation of feeds.
• Poor motor tone: the infant may be floppy or have limb stiffening (spasticity).

Sarnat’s clinical grading system (see Table 3.4.5) may be used to help to guide treatment and give some indication of the prognosis.

Treatment
• Treatment is generally supportive, with close attention to monitoring of good respiratory function, glucose levels and fluid balance. Avoid hypoglycaemia, which may result from inappropriate antidiuretic hormone secretion and excessive IV hypotonic solutions. Acute renal failure is often present; if so, restrict fluids to measured urine output and gut losses plus 15 mL/kg/24 hours for full term and 24 mL/kg/24 hours for preterm infants (to reflect insensible losses), and avoid giving potassium supplements.
• Seizures are treated as described above. Note, however, that increasing doses of anticonvulsants may precipitate a need for mechanical ventilation and confound the clinical staging criteria below, which apply only to non-sedated infants.
• Keep the axillary temperature at 35.5–36.0°C. Avoid overheating.

Cooling infants for 72 hours under carefully controlled conditions has shown improved neurological outcomes. This should only be undertaken by experienced teams.

Prognosis
The prognosis is good in stage 1, guarded in stage 2 and very poor in stage 3.

About 50% of stage 2 infants will recover without sequelae. Infants in stage 3 will either die or be left severely disabled. A decision must therefore be made with the family about the implementation or continuation of intensive care in such cases.

<table>
<thead>
<tr>
<th>TABLE 3.4.5</th>
<th>Sarnat’s grading of hypoxemic-ischaemic encephalopathy</th>
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<tbody>
<tr>
<td></td>
<td>Mild (stage 1)</td>
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<tr>
<td>Conscious</td>
<td>Hyper-alert</td>
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<tr>
<td>level</td>
<td></td>
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<tr>
<td>Muscle tone</td>
<td>Normal</td>
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<td>Seizures</td>
<td>Rare</td>
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<tr>
<td>Feeding</td>
<td>Sucks weakly</td>
</tr>
<tr>
<td>Respiration</td>
<td>Spontaneous</td>
</tr>
</tbody>
</table>

Management
Once bacterial meningitis has been excluded, intrapartum hypoxia or birth trauma will turn out to be the underlying problem in most infants presenting with fits in the first 2 to 3 days of life. Most of these infants already look stressed and unwell within a few hours of birth. The onset may be a little more sudden and abrupt in the preterm infant who suffers a sudden intra-ventricular haemorrhage. These infants usually become progressively more stuporous and unresponsive over time, and there is relatively little that can be done to improve the long-term outlook. An attempt should be made to minimise hypoxia, and anticonvulsant treatment is sometimes initiated in the hope that it will reduce the number of apnoeic episodes. Many of these infants are too ill to accept even tube feeds, and, where this is the case, it...
may be appropriate to minimise the risk of hypoglycaemia by giving IV glucose. Unfortunately, an infusion of more than 3 mL/kg of 10% dextrose per hour may result in water retention if there is accompanying renal failure. The outlook is fairly bleak for infants who have not recovered and started to feed normally within 1 week of birth.

**Other less common causes**

**Drug-related seizures:** Accidental infiltration of the fetal scalp during the injection of lidocaine into the maternal perineum prior to episiotomy can cause fits simulating intrapartum hypoxia. With supportive treatment there is every prospect of complete recovery.

Some infants born to **drug-dependent mothers** show signs of drug withdrawal, starting 1 to 2 days after delivery. A small minority may have seizures. Minimal handling in a quiet dark room with small frequent feeds and a more gradual withdrawal from the drug to which they have been exposed is the only treatment usually necessary.

**Congenital brain abnormalities:** It is said that up to 10% of otherwise unexplained neonatal seizures are associated with the existence of some underlying cerebral problem (often cortical dysgenesis). Some of these infants will benefit from continuing anticonvulsant treatment.

**Other miscellaneous neonatal problems**

**Gastrointestinal problems**

- **Oesophageal atresia** should always be considered in the infant with a history of polyhydramnios or excessive frothy salivation following delivery. Surgery is much more likely to be successful if it can be performed before aspiration pneumonia develops. Pass a large-bore catheter as far down the oesophagus as possible and aspirate frequently. If an X-ray shows that the tube has stopped at the level of the heart and has not entered the stomach, the diagnosis is made. Such an infant needs urgent referral for surgery, with steps taken to suck the blind upper oesophageal pouch clear of all accumulating secretions at least every 15 minutes before and during transfer. Site an IV line and ensure that the infant does not become hypoglycaemic.

- **Severe vomiting,** often associated with abdominal distension, in the first few days of life suggests the existence of a problem that requires referral for surgical review. This is particularly true if the vomit is green ( bile stained), as this is suggestive of **duodenal atresia** or bowel obstruction requiring urgent surgical intervention. If severe vomiting develops in a infant who has passed changing stool, the diagnosis of **volvulus, pyloric stenosis** or **intussusception** must be considered. Duodenal atresia is more common in infants with Down’s syndrome. A paediatric surgical opinion should be sought if available.

**Necrotising enterocolitis (NEC)**

This is a very serious condition with a mortality of approximately 20–40%. Preterm or small-for-dates infants are at increased risk of developing this condition. Prevalence is inversely related to birth weight and gestation. NEC is more common in ill infants. Although it is more common in infants who have received feeds, about 15–20% of affected infants may never have been fed. It is much less common in infants fed exclusively on human milk. NEC may occur in epidemics due to cross-infection in the nursery.

**Presenting features**

The condition should be suspected in an infant who had started to accept oral feeds and then develops an ileus or becomes lethargic and starts passing a bloody stool. The problem is caused by the sudden focal invasion of bacteria into an area of ischaemic gut, and an abdominal X-ray will often show gas accumulating within the gut wall.

Common signs of NEC include the following:

- abdominal distension or tenderness
- intolerance of feeding
- bile-stained vomit or bile-stained fluid up the nasogastic tube
- blood in the stools.

Features of multisystem failure, such as coagulopathy, petechial haemorrhage, oliguria and haematuria, may be associated with NEC.

**Investigations**

A plain abdominal X-ray may show an abnormal gas pattern in the form of:

- **free intra-peritoneal air,** best seen with a left side down (lateral decubitus) X-ray, where free air may be easily seen overlying the dense hepatic tissue
- **intramural gas (pneumatosis intestinalis)** or gas in the portal tracts of the liver.

A complete blood count with differential cell count, blood culture and serum electrolytes should be obtained. Regular weighing, frequent blood pressure measurements, and continuous heart and respiratory rate monitoring are required.

**Treatment**

- Stop all enteral feeds for at least 5 days and provide IV fluids, typically 120 mL/kg/day of 10% glucose with added electrolytes. Adjust fluids as indicated based on weight change, urine output and serum electrolyte values.

- If available, place an orogastric tube on low-pressure continuous suction or leave the tube open with intermittent gastric aspiration (every 4 hours). The goal here is to keep the intestines decompressed. The volume of gastric fluid aspirated is usually relatively small, so replacement fluid is seldom required.

- Start parenteral broad-spectrum antibiotics (usually ampicillin and gentamicin). Because of the probable association of Gram-negative anaerobes, also give metronidazole, especially if there is pneumatosis, perforation or evidence of peritonitis. Broader-spectrum antibiotics may be considered in the presence of extensive disease or poor response, or based on culture results.

- Treat any accompanying shock with Ringer-lactate or Hartmann’s solution or colloid, such as 4.5% albumin, 10 mL/kg over 15 minutes. Repeat if necessary.

- Measure the haemoglobin concentration daily and transfuse if it falls below 10 g/dL. If the infant is bleeding, give 1 mg vitamin K IV and fresh-frozen plasma 10 mL/kg (if available).

- The principal goal of therapy is to rest the bowel and treat any contributing or evolving bacterial infection with antibiotics. The duration of this therapy is usually...
10–21 days, depending on the severity of the process. Serial abdominal X-ray studies (if available) are indicated early in this disease to monitor for pneumatosis intestinalis or perforation. Ideally, parenteral nutrition should be given at this time in place of simple 10% glucose and electrolytes. Enteral feeds (breast milk) are reintroduced slowly at the end of antibiotic therapy (initially 20–30 mL/kg/day), with careful monitoring for abdominal distension or other signs of obstruction.

In seriously ill infants or infants who do not improve after 48 hours a surgical opinion should be sought.

Even in hospitals with good surgical support, perforation of the bowel is not necessarily an indication for a laparotomy. The conventional surgical approach has been laparotomy with resection of the perforated and adjacent necrotic bowel. A stoma and mucus fistula may be created with later anastomosis. An alternative surgical approach is to place a peritoneal drain, with laparotomy reserved for later complications, if they develop (e.g. bowel obstruction from adhesions or bowel wall strictures). Although there is some controversy about which approach is best, studies suggest that the overall mortality may be similar with either approach.

Immediate mortality is quite high, but many cases resolve without surgical intervention (although a stricture may occasionally develop about a month later in the affected area of gut), where it is usually possible to reintroduce feeds after about 5 days. An infant who is sucking and showing interest in feeding is usually ready for feeding. Intestinal perforation is generally the main indication for surgical intervention, but the prognosis really depends on whether there is generalised peritonitis and whether some part of the gut has become totally dead and gangrenous.