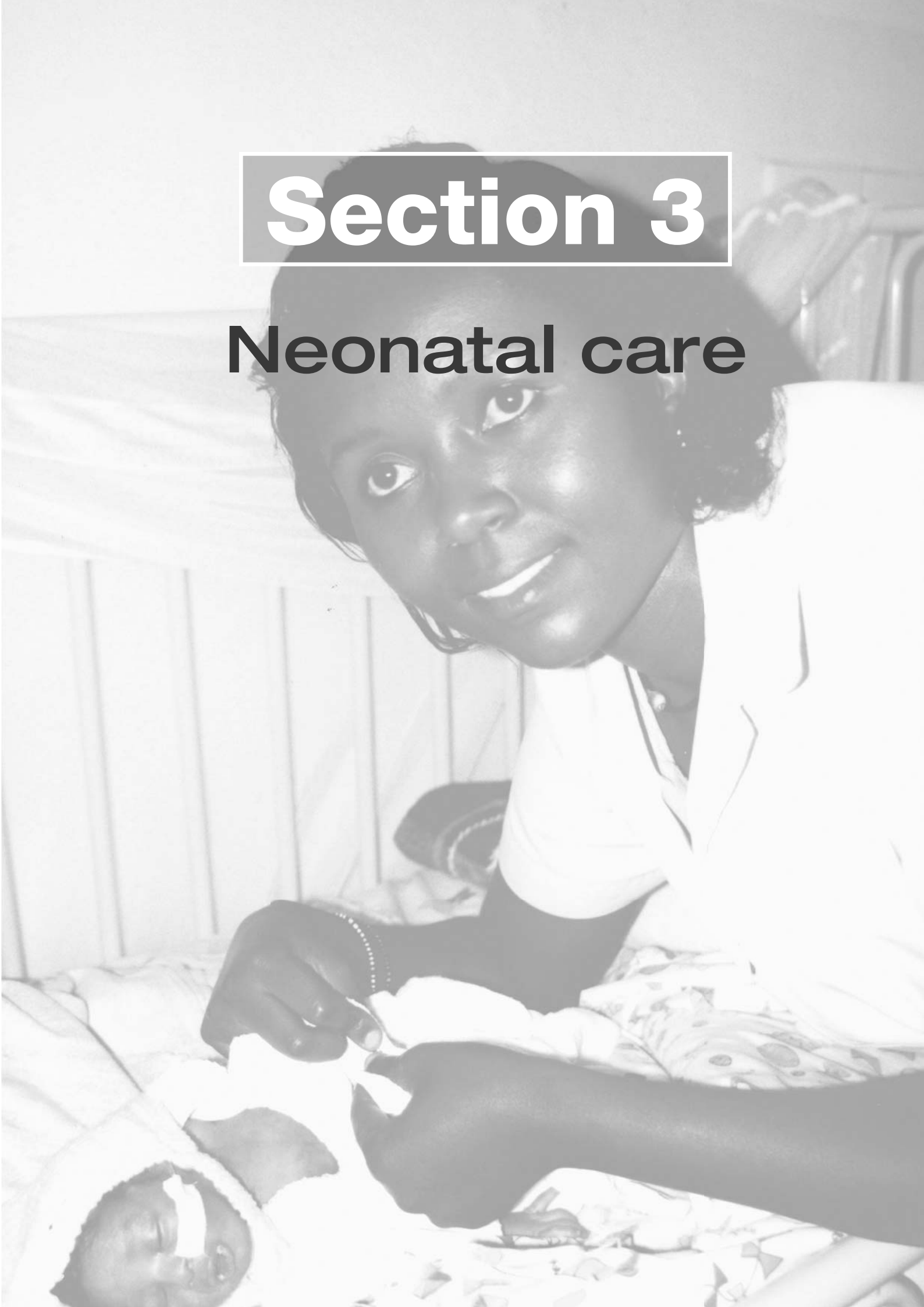

Section 3

Neonatal care

3.1 Preparation for and care of the baby at birth

BOX 3.1.1 Minimum standards
- Two clean dry towels.
- Firm work surface with padding.
- Stethoscope.
- Laryngoscope with straight blades size 0 and 1, spare bulbs and batteries.
- Set of ET tubes 2.5, 3.0, 3.5 and 4.0 with connectors to fit the inflation system.
- Umbilical catheter with fixating system.
- Adrenaline 1:10 000.
- Sodium bicarbonate 8.4%.
- Naloxone.
- Dextrose 10%.
- Ringer-lactate or Hartmann's solution.
- Soft suction device.
- Warming device.
- Food-grade plastic wrapping.

Introduction

Neonatal mortality in resource-limited countries runs at an unacceptably high level. The World Health Organization (WHO) estimates that worldwide there are 9000 neonatal deaths per day. Of these, approximately one-third are a result of neonatal infections, one-third are due to fetal hypoxia and a further one-third are due to prematurity and low birth weight.

If death and long-term or permanent disability are to be avoided, the management of neonatal emergencies must be both coordinated and effective. The care delivered in the first few minutes and hours of life is a major determinant of the outcome. Since in resource-limited countries almost half of the deliveries do not occur in hospitals, it is important that community-based skilled birth attendants (SBAs), traditional birth attendants (TBAs) and community health workers (CHWs) are encouraged to develop skills to recognise the vulnerable baby prior to delivery and provide effective intervention as required after birth.

Basic aspects of newborn care that apply to both community and hospital deliveries

In order to minimise the number of infants dying from birth-related problems (including perinatal asphyxia) or arriving at hospital with major complications which cannot be corrected, it is important for the hospital to work closely with the community.

The following approach has been shown to be helpful.

- All community-based healthcare professionals, including SBAs, TBAs and CHWs, should be able to undertake basic resuscitation of the newborn. Skills-based training involving manikins and the provision of a self-inflatable bag and mask to all these healthcare workers is essential, as delaying newborn resuscitation until the infant reaches the hospital will usually be too late, resulting in death or severe brain damage.
- Clean delivery kits should be available to all such healthcare workers.
- There should be regular clinical audits and educational meetings with participation from all community-based healthcare workers.
- Community-based SBAs, TBAs and CHWs should ensure that mothers with pregnancy-related complications (e.g. preterm birth, breech presentation, twins) are identified and referred to the local hospital where there are good facilities for obstetric and newborn care.
- The local hospital must provide comprehensive emergency obstetric and neonatal care. Good management of labour and delivery is the key to intact neonatal survival.

Mothers who require referral to hospital for delivery include those with:
- **peripartum bleeding**
- **malpresentation (breech, face, shoulder)**
- **preterm labour (< 35 weeks)**
- **twins**
- **abnormal fetal heart rate in labour.**

The baby at risk of developing problems at birth

Preterm birth

Maturity matters more than birth weight. Prematurity is defined as gestation of less than 37 weeks (or less than 259 days from the first day of the mother's last menstrual period). In the absence of special facilities, mortality increases substantially in cases of gestation less than 32 weeks, and survival at less than 28 weeks is unlikely in resource-limited settings. When a preterm delivery is anticipated, realistic expectations should be discussed with the parents, and any limitations on resuscitative efforts should be agreed upon.

Preventative strategies

These may include **minimising the risk of surfactant deficiency** and **stopping premature uterine contractions**.

Minimising the risk of surfactant deficiency: this can be halved if the mother is given a short course of high-dose steroid treatment before delivery:
- dexamethasone, 12 mg IM, two doses 12 hours apart
- *or* dexamethasone, 6 mg IM, four doses 12 hours apart.

Stopping premature uterine contractions:
- Give 20 mg nifedipine orally. Up to three further doses can be given at 30-minute intervals if uterine contractions persist.
- If this stops labour, give 20 mg nifedipine orally three times a day for the next 3 days.

Other problems associated with preterm birth include the following:
- Even very small babies can survive preterm birth

successfully once the early problems associated with surfactant deficiency have been overcome, and as long as they are nursed in a clean environment and not allowed to get cold.
- Preterm babies are at increased risk of infection and hypothermia.

The main challenge is to give these babies enough nutrition for them to start growing again as soon as possible (*see* Section 3.3).
- Here, too, maturity is more important than weight. Babies born before 36 weeks' gestation nearly always need some help with feeding.
- Breast milk is ideal, and everything possible should be done to help the mother sustain her lactation until the baby is ready to feed reliably from the breast. A limited ability to suck and swallow usually appears from 32 weeks' gestation, but it remains unpredictable, unreliable and uncoordinated until 36 weeks' gestation. In the event that breastfeeding cannot be initiated immediately after birth, mothers should be encouraged to start expressing breast milk, to be given by nasogastric tube or cup and spoon.
- Partial breastfeeding can also help the mother to sustain her lactation, but in any event the mother should regularly express milk. Some mothers might find expressing breast milk difficult and may require help with this.

Infection

It is important to identify babies at risk of infection prior to delivery. If identified, the mother should be given antibiotics appropriately. Many of the babies who become infected during delivery develop respiratory signs very soon after birth, but in a few, the features are those of neonatal sepsis. In addition, there are a proportion of babies who are initially asymptomatic, and therefore prophylactic antibiotics should be commenced in the infant if there are risk factors for infection.

When to consider antibiotics for the mother and newborn

- **Symptomatic ascending infection *in utero*** needs urgent treatment. If this is overlooked, both the mother's and the baby's life will be in danger.
- **Asymptomatic infection is, however, a much commoner problem.** This occasionally progresses so rapidly once labour starts that, unless treatment is started at once, the baby will die even if the most appropriate antibiotic is given immediately after birth. Because such infection by definition is silent, it is important that treatment be considered in any mother going into active spontaneous labour before 35 weeks' gestation.
- **Membrane rupture can be both a sign of, and a risk factor for, ascending bacterial infection.** What most people mean by premature rupture of membranes (PROM) is really preterm pre-labour rupture of membranes (PPROM), where the membranes rupture before there is any overt sign of uterine activity or any detectable uterine contractions. When this happens in the preterm baby, it is often a sign of the start of some sort of ascending infectious process. This process has already weakened the amniotic membranes and may stimulate the onset of preterm labour. Antibiotics must be given to the mother.
- **Treatment with antibiotics should also be considered at any gestation if the mother's membranes rupture more than 18 hours before delivery.** If premature rupture of membranes occurs before the onset of premature labour contractions then infection is more likely.
- **Maternal fever (> 38°C) in labour** is a strong indication for initiating antibiotics for the mother. Similarly, foul-smelling or purulent liquor requires IV antibiotic treatment of the newborn from birth without waiting for any signs of infection.

- In mothers with PPROM who show signs of being clinically infected give IV antibiotics.
- In PPROM where there is no evidence of infection and no evidence of labour you can delay delivery by 1 week or more (on average) by giving the mother amoxicillin or, better still, erythromycin.
- In mothers who are in active labour 5 or more weeks before term and who give a clear history that the membranes had ruptured before they were able to detect any uterine contractions, the risk of the baby becoming infected during delivery can be reduced substantially by giving antibiotics IV (ideally probably both penicillin and gentamicin) during labour.

Antibiotic management of perinatal infection

Where facilities allow, a blood count, C-reactive proteins and blood cultures should be taken before starting antibiotics. Because a range of bacteria can be involved, treatment of the baby needs to protect against group B streptococcal, coliform and *Listeria* infection, making a **combination of ampicillin and gentamicin** the best strategy:
- Give ampicillin 50–100 mg/kg IV 12-hourly and gentamicin 5 mg/kg every 24 hours IV if more than 32 weeks' gestation, and 3 mg/kg if less than 32 weeks.

The WHO recommends that a neonate with risk factors for infection (i.e. membranes ruptured > 18 hours before delivery, maternal fever > 38°C before delivery or during labour, or foul-smelling or purulent amniotic discharge) should be treated with prophylactic antibiotics (IM or IV ampicillin and gentamicin) for at least 2 days. After this the neonate should be reassessed and treatment continued only if there are signs of sepsis (or a positive blood culture).

Hypothermia (*see* Section 3.3)

Hypothermia seriously increases the risk of surfactant deficiency and hypoglycaemia, and must be avoided.

Preparation for birth in the home and in hospital

For the majority of deliveries, only a minimum amount of resuscitation equipment is needed.

Equipment for basic resuscitation of the infant at home

The following equipment is needed:
- 2 clean dry towels
- a firm working surface (padded)
- a bulb suction device
- a well-fitting mask (size 0/1)

- a self-inflatable bag
- clean scissors or razor blade
- boiled string (two 6-inch lengths)
- woollen cap or head covering.

Management at delivery of a baby not needing resuscitation

Summary of management of the healthy baby at birth

- Deliver the baby on to the mother's abdomen or a warm surface, dry and cover.
- Clamp cord when pulsation stopped, usually between 2 and 3 minutes after birth and keep the baby between the mother's thighs level or below the placenta.
- Prevent hypothermia by nursing skin to skin with the mother.
- Initiate early breastfeeding.
- Minimise infection by hand washing, cord care and using clean materials.
- Give an injection of vitamin K.

Most babies do not need any resuscitation at birth but only require basic care to prevent infection and hypothermia. Extensive mouth suction, face mask oxygen, and vigorous stimulation in order to provoke a first gasp or cry are unnecessary rituals without clinical justification. As long as the baby becomes pink, and starts to breathe without distress, most babies should stay with their mothers and have a first feed at the breast within minutes of birth.

A simple approach would be to keep newborns without complications in **skin-to-skin contact** *with* their mothers during the first hour after birth to prevent hypothermia and **promote breastfeeding**. Colostrum, the initial milk with a clear, yellowish and thick appearance, is an extremely nutritious and concentrated feed rich in immunoglobulins (it is only present during the first 3 to 4 days). Mothers should be informed of its benefits and that it is ideal for their baby to feed on this as soon after birth as possible and as frequently as possible.

Preventing heat loss after birth

- Once any necessary resuscitation process has finished and as soon as the baby becomes pink, and starts to breathe without distress, they can be given to the mother for skin-to-skin contact and their first feed at the breast. This practice, among other benefits, not only prevents hypothermia but also helps in better uterine contraction following delivery.
- The practice of using water or oil to clean the skin within a few hours of birth before the body temperature has stabilised can make the baby dangerously hypothermic. A simple drying of the skin with a warm towel or sheet is all that is required.
- There is no more effective source of warmth than the mother's own body, so long as the baby is first well dried to minimise evaporative heat loss. A larger sheet or blanket can then be used to protect both mother and baby from the convective heat loss caused by draughts.
- Babies have relatively large heads. Covering the head with a shawl, blanket or woollen cap can significantly reduce heat loss.
- Heat and water loss through the skin can be a particular problem in babies born before 32 weeks' gestation. This can be limited initially by wrapping all but the face in a clean plastic wrapping such as cling film or a food-grade plastic bag with a hole cut in the end of the bag for the baby's head to protrude, for a few hours after birth. **Remember that plastic over the face can cause death from suffocation.** If plastic bags or cling film are not available, the preterm baby must be wrapped well in a clean towel or blanket. However, plastic bags are very good for preventing heat loss, but only in conjunction with an overhead heat source or heated mattress. If the fluid in the bag gets cold it will cool the baby quicker than drying and wrapping.
- Heat supplementation can be provided by locally built and maintained incubators, overhead heating systems, and skin-to-skin (kangaroo) care.
- Ideally, the first bath should be delayed for at least 24 hours.

Managing the placenta, cord and umbilical stump

Babies often become relatively anaemic 4 to 6 months after birth because red cell production does not keep pace with body growth. This problem can be minimised by ensuring that blood intended for the baby is not left in the placenta at birth.

If the baby is held higher than the placenta (i.e. on the mother's abdomen) while the cord is still pulsating, blood will drain out of the baby and into the placenta, so hold the (covered) baby just below the placenta for 2 minutes if the cord is still pulsating. If the cord is clamped before it stops pulsating, this will also reduce the normal 'placental transfusion' at birth, especially if the uterus has not yet contracted.

If, however, blood is artificially 'milked' from the placenta into the baby, it is possible to leave the baby with so many red cells that the blood becomes thick and polycythaemic. Neonatal polycythaemia has many complications, including putting the circulation under strain, making the capillary circulation very sluggish, and increasing the risk of jaundice (see below).

It is recommended after a vaginal delivery to wait for 2 minutes before cutting the cord if it is still pulsating, to maximise the baby's haemoglobin, unless there is a need to start resuscitating the baby.

The cord must be cut cleanly, and the cut stump secured in a manner that minimises the risk of late haemorrhage. Remember that prevention rather than treatment is the key. A supply of fresh disposable razor blades is one widely adopted strategy in some communities where home birth is the norm.

The umbilical stump will shrink as it dries out. Plastic clamps that shut down further as the cord starts to shrink are very effective. They are relatively inexpensive, and they do make it possible to cut the stump about 2–4 cm from the skin. An elastic band, if carefully applied, is a cheap and well-tested alternative. A stump that is left too long provides a reservoir where bacteria can breed and multiply with great speed, and therefore should not be permitted. A length of 2–4 cm is ideal.

A short stump does not need to be covered except to keep it from snagging on clothes and blankets. Recent studies in resource-limited countries have shown that the application of 4% chlorhexidine solution immediately after birth can prevent omphalitis. Other possible antiseptics include surgical spirit or iodine.

Often the cord manifests a little 'stickiness', which may be of no concern. However, a local antiseptic should be applied if a red skin flare suggests early spreading staphylococcal cellulitis. Such babies must also be given an oral anti-staphylococcal antibiotic (cloxacillin or flucloxacillin). If the skin around the stump becomes oedematous with increasing redness, IV cloxacillin or oral flucloxacillin (25 mg/kg three times a day for 7 days) is usually the most logical choice. Babies who are systemically unwell always need urgent broad-spectrum antibiotic treatment, IV or IM, for septicaemia.

The risk of neonatal tetanus can be eliminated by ensuring that all mothers are immunised against tetanus with at least two injections of tetanus toxoid 1 month apart during pregnancy.

The risk of cross-infection during or after birth

Puerperal infection ('child-bed fever') is an illness that killed thousands of recently delivered women for more than two centuries. The fact that this could be eliminated if birth attendants washed their hands thoroughly **every time they moved from one woman to the next** was shown many years before it was ever realised that this lethal illness was caused by group A streptococcal infection. The arrival of antibiotic treatment has reduced the risk of death, but it has not lessened the need for meticulous hand washing before vaginal examination or delivery. Failure to observe this simple but important precaution also puts the baby at risk of cross-infection, especially if the baby is being cared for in a hospital setting.

The WHO estimates that infection is responsible for one-third of all neonatal deaths (over 3000 deaths a day). Kangaroo care has significantly reduced the number of neonatal deaths from infection by colonising babies with the mother's bacteria rather than those of the hospital.

Neonatal examination before discharge of a baby from the hospital

Before discharging the baby it is important that some basic checks are made. These include ensuring that the baby is feeding well, has passed meconium and urine and does not have any gross congenital abnormalities. Always check for jaundice. If there are qualified personnel available, a more detailed check could be undertaken. All examinations should be documented, including abnormalities, even if there is no other action which can be taken. It is also important to check local guidelines, if any.

Pre-Discharge Newborn Checklist

Name **Mother's name**
Date of birth **Gestation**
Mode of delivery **Need for resuscitation**
Birth weight **Head circumference**
Type of feed **Mother's blood group**

	Tick if normal/Describe if abnormal	Common problems to look for
Head		Anencephaly, occipital encephalocele, microcephaly, large fontanelle, abnormal shape of head
Face		Abnormal looking facies
Ears		Low set ears, absent ears, ear tags
Eyes		White-coloured pupil, white cornea
Nose		Blocked nostrils with breathing difficulty
Lips		Cleft lip
Palate		Missing palate
Neck		Swelling on the neck, holding neck to one side
Clavicles		Lumps or bumps on the clavicle
Chest		Shape of chest
Abdomen		Scaphoid (empty) abdomen
Umbilicus		Omphalocoele, gastroschisis, hernia
Genitalia		Abnormal genitalia, undescended testis, hypospadias
Anus		Absent anus, abnormally placed anus
Spine		Spina bifida, meningomyelocele
Upper limbs		Absent limbs, contractures of limbs, not moving arm
Lower limbs		Not moving limbs, unequal limbs
Hands		Missing or extra digits
Feet		Abnormally shaped feet (talipes), missing or extra digits
Hips		Hip dysplasia (Barlow and Ortolani manoeuvres)
Jaundice		
Chest		Air entry (right and left)
CVS		Murmur, femoral pulse, cyanosis
Abdomen		Spleen, liver, kidney, palpable mass
Birth marks		

The following data should be recorded in the notes of every newborn baby.

Baby's name (if given at the time)

Mother's data

- Name, address, date of birth, and any identifying number
- Parity and previous obstetric history
- Blood group
- First day of last menstrual period
- **Results of any antenatal serology (e.g. rubella, syphilis, rhesus titres, HIV status)**
- Illness during the pregnancy
- Drugs taken during the pregnancy
- Family history of any illnesses

Father's data

- Full name, address and date of birth
- Family history of any illnesses

Labour and delivery data

- Time of onset: whether induction of labour or spontaneous
- Time membranes ruptured and any other known risk factors for infection (see below)
- Duration of first and second stage of labour
- Drugs given to the mother in labour
- Presentation and mode of delivery
- Full details of any resuscitation for baby or mother
- Time, dose, route of administration and full generic name of any drugs given to the mother

Baby data

- Temperature shortly after delivery, to document adequate thermoregulation
- Birth weight
- Head circumference (best measured after 24 hours when moulding has subsided)
- Length (ideally)
- Full physical examination, noting any abnormalities or evidence of birth trauma detected
- Details of dose, preparation and route of administration of any drugs given at delivery (e.g. vitamin K)
- **If not already given, ensure that vitamin K 1 mg IM is administered**

Follow-up home visits

Trials in South Asia have shown that three home visits in the first week of life (starting on the day of birth) by trained healthcare workers can reduce neonatal mortality by 30–60%. During their visits, the healthcare workers promote essential newborn care, examine babies for danger signs, and treat or refer when appropriate, counsel the families in how to recognise danger signs and emphasise the importance of prompt referral when they are identified.

The WHO and UNICEF recommend that skilled healthcare workers (nurses or midwives) should undertake these visits, but in many settings this is not possible. Volunteers have also been trained to do this, and recently the effectiveness of this has been shown in Ghana, where a fall in neonatal mortality followed two home visits during pregnancy and three visits in the first week of life.

Further reading

Van-Rheenen P (2011) Delayed cord clamping and improved infant outcomes. *British Medical Journal,* **343**, d7127.

WHO and UNICEF (2009) *WHO/UNICEF Joint Statement. Home visits for the newborn child: a strategy to improve survival*. www.unicef.org/health/files/WHO_FCH_CAH_09.02_eng.pdf

3.2 Resuscitation of the newly born

Introduction

Respiratory changes at birth in a healthy term infant

- During life *in utero*, the infant's lungs are full of lung tissue fluid. The fluid is removed during labour and at birth by the following mechanisms:
  - at the onset of labour, lung fluid production stops
  - as labour progresses, re-absorption of lung fluid occurs
  - about 35 mL of fluid are expelled from the lungs as a result of thoracic compression during vaginal delivery
  - the first breaths generate relatively high pressures to inflate the lungs, which has the effect of pushing this fluid into the circulation. These first breaths establish the infant's functional residual capacity.
- Surfactant is produced in the alveoli to prevent them collapsing completely during expiration.
  - Production starts slowly at 20 weeks' gestation, and increases rapidly from 30–34 weeks and thereafter.
  - Surfactant production is reduced by hypothermia, hypoxia and acidosis.

Caesarean section is associated with delayed clearance of pulmonary fluid, and reduces the initial functional residual capacity

Most infants breathe well and do not need active 'resuscitation' at birth. Simply drying the infant with a warm dry sheet/towel will in most cases stimulate a cry from the infant thus expanding the lungs (*see* Section 3.1). Attempts to clear the airway, to stimulate breathing, or to give facial oxygen are unnecessary. Therefore routine airway suctioning is not needed. Most infants make all the circulatory adjustments required at birth without external intervention as the lungs expand. All that the birth attendant has to do

is to optimise the conditions needed for these changes to occur smoothly

Around 5% of infants do not breathe spontaneously after delivery. However, breathing can be started in almost all these infants by correctly applying bag-and-mask ventilation. With lung inflation there is an immediate and easily detectable rise in heart rate. It may be difficult to identify the infant's pulse rate by palpation at any site, so the best way to determine the heart rate is to listen over the chest with a stethoscope.

Far less commonly, infants are born cyanosed, shocked, limp and hypotonic. Around 1% do not respond to bag-and-mask ventilation, and need further help with advanced resuscitation.

Resuscitation at birth

Equipment needed for resuscitation

The following equipment is needed:

- Two clean dry towels.
- A firm working surface.
- Heat and light source.
- Sterile gloves.
- Sterile scissors.
- Sterile cord clamps.
- Food-grade plastic wrapping (cling film).
- Clock.
- Soft well-fitting face masks (size 0/1 and 00).
- A self-inflatable bag.
- A source of oxygen.
- A pressure-limiting device at 30 cmH_20 if T-piece is used.
- A stethoscope.
- A laryngoscope, with straight blades size 0 and 1, and spare bulbs.
- A set of endotracheal tubes (2.5, 3.0, 3.5 and 4.0 mm) with adaptors to fit the inflation system.
- An endotracheal stylet.
- An umbilical venous catheter (or use a sterile feeding tube).
- A pulse oximeter (if available).
- A roll of zinc oxide tape for name-band.
- Syringes: 1 mL, 5 mL and 10 mL.
- Emergency drugs: 1 in 1000 adrenaline plus sterile water for dilution to make 1 in 10 000.
- Ringer-lactate or Hartmann's solution.
- Glucose 10%.
- Nalorphine (naloxone) if opiates are used during labour.

Immediate preparation

Two clean dry towels are needed, one to dry the infant and one to keep them warm, a firm working surface in a warm well-lit area, a self-inflating bag with good soft well-fitting face mask (see below), and a suction device and a source of oxygen if possible is all that most infants who have not started breathing spontaneously need.

Self-inflating bag, valve and masks

A soft close-fitting face mask is essential. Access to a range of sizes of mask makes it possible to manage infants weighing as little as 500 g or as much as 5000 g at birth. It provides a near-airtight seal between mask and face in a way that mimics the effectiveness and efficiency of an endotracheal tube. Hence it is possible to use a mask as effectively as an endotracheal tube along with a self-inflating bag to administer slow inflating pressures up to a maximum inspiratory pressure of 30 cmH_2O to the fluid-filled lung of an infant who is not breathing or who is making poor respiratory efforts at birth. The bag-valve-mask inflates the lungs, enabling the infant's respiratory centre to be oxygenated and initiate spontaneous respiration.

Suction devices

A range of simple suction devices, with a soft wide-bore tube (10 or 12) either mechanically or electrically operated, are available. Suction is rarely needed and should not be performed routinely. Mouth-to-mouth suction can be effective, but places the operator at risk of infections such as HIV or hepatitis. A double mucus trap may be used to help to prevent infected material being accidentally drawn into the mouth, but even this may be insufficient for user protection.

Circulatory access and drugs

An umbilical vein catheter may be used to administer drugs, but it is important to note that infants who require drugs during resuscitation have poorer outcomes and are at increased risk of death and long-term neurological sequelae. Ringer-lactate or Hartmann's solution, plasma expander or blood in the case of hypovolaemia due to fetal bleeding (see below) may occasionally be required and would use the umbilical vein route. The intra-osseous route is also now being used, either using a purpose-made needle and drill set or by using an venepuncture needle and the medial side of the tibial bone, below the growth plate (*see* Section 8.N). For a discussion of drugs, see below.

Timing

A clock will help you to document the duration of resuscitation and the timing of interventions.

Additional equipment

A heat and light source is needed plus food-grade plastic wrapping for infants under 32 weeks' gestation.

An oxygen source is helpful but not essential for infants who need advanced resuscitation.

A pulse oximeter can be of help in monitoring the improvement in oxygenation and detecting the occasional infant with sub-clinical cyanosis requiring further intervention or evaluation for cardiac or pulmonary disease. It is also useful to prevent hyperoxia when oxygen is used in resuscitation, especially in the preterm infant.

A roll of zinc oxide tape half an inch wide can be used to make a simple name band for infants not delivered in their own homes. Take six inches of this tape, write the date and the mother's name at one end, turn the last two inches of the other end back on itself (so the tape does not stick to the skin), and then turn this into a simple bracelet round the child's wrist. Ensure that the bracelet is loosely fitting to avoid a tourniquet effect.

Guidelines from the 2010 International Liaison Committee on Resuscitation (ILCOR)

The main changes that have been made to the Neonatal Life Support (NLS) guidelines relevant to resource-limited countries are as follows:

- The use of food-grade plastic wrapping (cling film) is recommended to maintain body temperature in very small preterm infants.
- Ventilatory resuscitation may be started with air. However,

where possible, additional oxygen should be available if there is no rapid improvement in the infant's condition.
- Adrenaline should be given by the IV route, as standard doses are likely to be ineffective if given via a tracheal tube.
- If there are no signs of life after 20 minutes of continuous and adequate resuscitation efforts, discontinuation of resuscitation may be justified.

Sequence of actions during resuscitation of the newborn

There are agreed guidelines from the 2010 International Liaison Committee on Resuscitation (ILCOR). The sequence below and that of 'Helping Infants Breathe' are both practical applications of these principles.

First call for help

Start the clock or note the time. Keep the infant dry and warm and assess their breathing and heart rate.

- Infants are born small and wet. They get cold very easily, especially if they remain wet and in a draught. Whatever the problem, **dry the infant well, including the head**. Remove the wet towel, and **wrap the infant in a dry towel**. It is helpful if the towels are warm.
- There is good evidence that for very preterm infants (30 weeks' gestation or earlier), placing the infant under a radiant heater after drying, and immediately covering the head and body, apart from the face, with clean plastic wrapping, is the most effective way of keeping these very small infants warm during resuscitation.
- **Drying the infant** immediately after delivery will provide significant stimulation during which **colour, tone, breathing and heart rate can continue to be observed**.
- It is important to **monitor the infant's breathing. Observing the colour, heart rate and tone helps to document the infant's condition and assess their response to resuscitation**.
- **Reassess** these observations regularly (particularly the heart rate), every 30 seconds or so, throughout the resuscitation process. The first sign of any improvement in the bradycardic infant will be an increase in heart rate.
- A healthy infant may be born blue but will have good tone, will cry within a few seconds of delivery, will have a good heart rate (the heart rate of a healthy newborn infant is about 120–150 beats/minute) and will rapidly become pink during the first 90 seconds or so. An ill infant will be born pale and floppy, not breathing, and with a slow or very slow heart rate.
- The heart rate of an infant is best judged by listening to the chest with a stethoscope. It can also sometimes be felt by palpating the base of the umbilical cord, but a slow rate at the cord is not always indicative of a truly slow heart rate, and, if the infant is not breathing, must not delay the immediate application of lung inflations. In addition, if the infant is not breathing, feeling for peripheral pulses is potentially harmful as it delays the onset of life-saving lung inflations. If a stethoscope is not available, you can listen to the heart by placing your ear on the infant's chest or using a Pinard's stethoscope.

Airway: Keep the airway open

- Before the infant can breathe effectively the airway must be open.
- The best way to achieve this in an infant who is not breathing well is to place the infant on their back with the head in the **neutral position** (i.e. with the neck neither flexed nor extended). Most newborn infants will have a relatively prominent occiput, which will tend to flex the neck if the infant is placed on their back on a flat surface. This can be avoided by placing some support using a folded nappy or cloth under the shoulders of the infant, but be careful not to overextend the neck.
- If the infant is floppy it may also be necessary to apply chin lift or jaw thrust.

The best way to stabilise an infant's condition at birth is to ensure that the upper airway remains unobstructed. The child will then have little difficulty in drawing air into its lungs for itself when it takes its first spontaneous gasp or cry. Unfortunately, books often talk of the need to keep the airway 'clear', giving the false impression that the infant is going to find it difficult to breathe unless all the fluid and mucus is first sucked out of the way. There is no evidence that this is ever necessary unless the infant is meconium stained or does not breathe well. **Moreover, blind deep suction of the nose or mouth can stimulate the vagus nerve, leading to bradycardia, apnoea and laryngospasm.**

However, the upper airway of any infant who is born limp and hypotonic certainly needs to be opened and maintained in just the same way as the airway of any other unconscious patient. In an unconscious patient, pharyngeal tone decreases even more than it does during sleep, causing the upper airway to narrow or close. When such a patient is laid on their back the tongue also falls back, further obstructing the airway. There are three key ways to counter this:

1 Hold the head in the neutral position *and*
2 Support the chin *or*
3 Push the jaw forward.

Because of moulding, most infants have quite a prominent occiput at birth. Lying supine (on their back) on a flat surface, the neck becomes flexed, and the airway becomes obstructed. Exactly the same thing can happen if the neck is over-extended. The aim is to ensure that the head is in a 'neutral' position – a posture most easily achieved by placing a small (2 cm high) pad under the infant's shoulders.

It is important that all healthcare workers who conduct deliveries are taught how to open the airway correctly.

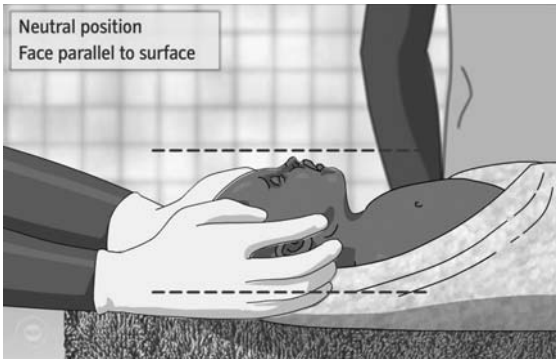

FIGURE 3.2.1 Neutral position of the head and neck in a newborn. Reproduced with the permission of Medical Aid Films, www.medicalaidfilms.org

FIGURE 3.2.2 Chin lift in a newborn.

FIGURE 3.2.3 Jaw thrust in a newborn. Note that the operator's thumbs are in a position to hold a mask in place.

If tone is poor it may also be necessary to support the chin. It is important to support the bony part of the chin. Pressure anywhere else may merely push the base of the tongue backwards, making matters worse.

If tone is **very** poor it may be necessary to use one or two fingers under each side of the lower jaw, at its angle, in order to push the jaw forwards and outwards ('jaw thrust'), but this will require a second person to give the inflation and ventilation breaths with the bag-valve-mask.

Although it is rare for debris to completely block the trachea, this should be suspected if an infant tries to breathe but remains cyanosed and bradycardic, with laboured breathing and marked inter-costal and/or sternal recession. This is one of the few situations where tracheal intubation can be life-saving at birth.

Meconium

It is estimated that around 15% of infants have meconium-stained liquor at birth. Meconium aspiration syndrome (MAS) can occur in about 1 in 10 such infants. The development of MAS is not entirely dependent on suctioning at birth. It is possible for infants to aspirate meconium into the large airways *in utero* if there is hypoxia and gasping. However, some infants may aspirate meconium during delivery, and these are the ones in whom the risk of MAS can be reduced by suctioning when the infant's head is on the perineum.

Studies based on experience from Africa and India have shown that suctioning the mouth of infants with meconium-stained liquor during birth when the head is at the perineum has dramatically reduced the incidence of meconium aspiration syndrome (MAS) and death. There is subsequently no need for further suctioning after birth if the infant breathes well.

What to do if the trachea appears to be blocked

If the infant is born through meconium and is unresponsive (or 'not vigorous') at birth, the oropharynx should be inspected and cleared of meconium. If intubation skills are available, the larynx and trachea should also be cleared under direct vision. If meconium has entered the trachea, resuscitation here is only possible if the accumulated debris can be immediately removed. The easiest way to do this is to pass an endotracheal tube and then remove the debris by direct suction to the endotracheal tube. Sometimes the meconium debris is so large that it cannot be sucked through the tube. The tube can then be removed and replaced with a clean tube to clear the remaining obstructive material. Suction may also make it easier to see the larynx during intubation. Giving mask ventilation for the infant who is not breathing before the meconium has been cleared (as above) may force the meconium deeper into the lungs.

Breathing

- If the infant is not breathing adequately **give five inflation breaths as soon as possible** (unless the baby is very preterm, in which case such breaths may injure immature lungs: give ordinary ventilation breaths in this situation). Until now the infant's lungs will have been filled with fluid. Aeration of the lungs in these circumstances is best with slow inflations at pressures of about 30 cmH_2O with the bag and mask; these are called 'inflation breaths'. These initial ventilation breaths should last 2–3 seconds each. The aim is to mimic the initial breaths taken by a normal infant to open the airways, remove lung fluid and achieve its functional residual capacity.
- If the heart rate was below 100 beats/minute initially then it should rapidly increase as oxygenated blood reaches the heart. If the heart rate does increase then you can assume that you have successfully aerated the lungs and there is adequate tissue oxygenation. If the heart rate increases but the infant does not start breathing, then continue to provide regular ventilation breaths at a rate of about 30–40 breaths/minute until the infant starts to breathe.
- The chest may not move during the first one or two breaths as fluid is displaced. Adequate ventilation is usually indicated by either a rapidly increasing heart rate or a heart rate that is maintained at more than 100 beats/minute. Therefore reassess the heart rate after delivery of the first five breaths. It is safe to assume that the chest has been inflated successfully if the heart rate improves. Once the chest has been seen to move and the heart rate has increased, ventilation should be continued at a rate of 30–40 breaths/minute. Continue ventilatory support until regular breathing is established.
- If the heart rate does not increase following inflation breaths, then either you have not aerated the lungs or the infant needs more than lung aeration alone. By far the most likely possibility is that you have failed to aerate the lungs effectively. If the heart rate does not increase, and the chest does not passively move with each inflation breath, then you have not aerated the lungs.

Under these circumstances consider the following:

- Are the infant's head and neck in the neutral position?
- Do you need jaw thrust?
- Do you need a second person's help with the airway or to squeeze the bag? A relative or ward orderly can be shown immediately how to effectively squeeze the self-inflating bag while you ensure that the mask is held firmly and in the best position on the face over the mouth and nose with the airway open.
- Is there an obstruction in the oropharynx (laryngoscope and suction under direct vision)?

Bag-and-mask inflation of the lung

Having positioned the infant correctly it is then usually quite easy to use a self-inflating bag and mask to provide inflations.

Remember that the infant cannot breathe through the bag-valve-mask system, so do not leave the mask sealed to the face and expect the infant to breathe from the bag. The valve between the bag and the mask prevents this. When the infant is breathing, remove the mask and watch closely to ensure that adequate breathing continues.

Most infants will respond to bag-and-mask ventilation by gasping and then starting to breathe on their own without further support. If this does not happen, it is still easy to confirm that lung aeration has been achieved, because the heart rate will rise reliably and consistently above 100 beats/minute. If lung aeration has been achieved and the infant still has a slow heart rate, proceed to support the circulation (C). If oxygen is available, applying this through the bag and mask may also help.

It is essential that the skills of correct bag-and-mask ventilation are taught to all healthcare workers who conduct deliveries. This is best done on a mannequin. Correct bag-and-mask ventilation is the single most important skill needed to provide active resuscitation.

There is good evidence that most infants can be resuscitated using mask resuscitation without any need for tracheal intubation. However, in certain situations (e.g. infants less than 1000 g not responding to inflation, prolonged bag-and-mask ventilation with no spontaneous breathing, etc.) infants require early intubation, so the equipment and the skill to intubate should be available.

Deciding whether to use air or 100% oxygen for resuscitation of the newborn

Concern about the possible injurious effects of excess oxygen, particularly in preterm infants, and the apparent effectiveness of air in a number of randomised controlled human studies of resuscitation at birth, have resulted in a change in guidelines.

There is evidence to suggest that air is safer for initial resuscitation. However, where possible, it is recommended that additional oxygen should be available for use if there is not a rapid improvement in the infant's condition. Equally, hyperoxia should be avoided, especially in the preterm infant. If a pulse oximeter is available this can be done. Try to keep the SaO_2 between 88% and 95%.

When to cut and clamp the cord in an infant who needs resuscitation at birth

There are advantages to delaying clamping of the cord for 2 minutes after birth to allow placental transfer of blood to the infant (see above). However, it is important to ensure that by doing this there is no harm to the mother (e.g. if she needs resuscitation) or to the infant (e.g. if they require resuscitation). Usually the umbilical cord is clamped and cut immediately if the infant needs to be moved for active resuscitation.

Mouth-to-mouth resuscitation

Most current guidelines on neonatal care steer clear of discussing the role of mouth-to-mouth resuscitation. The risk of HIV infection or hepatitis has further fuelled that reluctance. However, there is no doubt that this can be a very effective way of reviving an apparently lifeless infant in the absence of equipment. Remember the following:

- Keep the upper airway open by optimising the position of the head and jaw as described above.
- Cover the infant's nose and mouth with your mouth (or cover the mouth of a big infant and just pinch the nose).
- Use the pressure you can generate with your cheeks, and try to aerate the lung by slow inflations for 2–3 seconds.
- Only use as much air for each breath as you can keep in your cheeks (i.e. do not 'blow' air into the infant, but just small puffs).
- Watch for chest movement, and allow time for lung recoil.
- Once the chest starts to move, sustain what has been achieved with 20–25 artificial breaths/minute.

Checking progress before moving on

- If the heart rate has **not** risen to over 100 beats/minute after the five initial breaths or within 30 seconds of adequate ventilation, something is wrong. The most likely problem is that you have not successfully ventilated the infant. **Never** move on to deal with the issues covered under letter C of the resuscitation alphabet until you are quite sure you have achieved objectives A and B. To do so is quite futile. Chest compression will never restore the circulation until the blood being massaged from the lung to the heart contains oxygen.
- Look to see whether the chest moves each time you apply mask pressure. Movement should not be difficult to see once the first few breaths have aerated the lungs. It is usually easier to judge success with your eyes than with a stethoscope. In a newborn, breath sounds can be heard when only the airway is being aerated, so are not a good way to judge ventilatory success.
- Check that the infant's head is well positioned. Check chin support and jaw thrust, and that the mask is correctly applied with no air leaks. Ask a second person to help you position the infant optimally and provide inflations by squeezing the bag while you hold the airway open and the mask in place.
- Few infants need support with their breathing once their lungs have been aerated. Most will gasp, cry or breathe just as soon as an attempt is made to get air into the lungs, and then continue breathing adequately.
  - However, a few may benefit from further support if they do not start to breathe regularly, or only gasp occasionally. Some may have suffered severe hypoxia *in utero*, and a few may be drowsy because of drugs given to the mother during labour. Check that the heart rate remains normal (above 100 beats/minute) and that there is no central cyanosis (best judged by looking at the colour of the tongue).
  - Try to assess whether there is hypoxemia (cyanosis

or SaO_2 less than 90% with a pulse oximeter), if the infant's breathing remains laboured and irregular or if the child's colour remains blue. Give oxygen then if it is available, preferably with SaO_2 monitoring. Hyaline membrane disease, meconium aspiration syndrome, pneumonia or transient tachypnoea of the newborn are most likely.

Other possibilities include:
- intra-partum pneumonia (common)
- diaphragmatic hernia
- pneumothorax
- pulmonary hypoplasia (possibly associated with a skeletal or renal abnormality)
- cyanotic congenital heart disease (although this usually takes a little time to appear)
- persistent fetal circulation.

- If breathing requires continuous support it is important to try and reduce mask inflation pressures to little more than half of what was needed to aerate the lung in the first place. It is easy to over-ventilate an infant with healthy lungs and to wash out so much of the carbon dioxide that normally provides the main stimulus to breathing that all such activity stops for a while. There is also increasing evidence that sustained over-ventilation can seriously reduce cerebral blood flow.

Endotracheal intubation

As discussed earlier, most infants who need resuscitation can be managed with bag-valve-mask intubation. However, occasionally endotracheal intubation is required, but this must be done by someone skilled and practised in the technique. It is most likely to be required for prolonged resuscitation, in meconium aspiration, and in preterm infants with surfactant deficiency. A straight-bladed laryngoscope is preferred, and tube sizes are around 3.5 mm for a term infant and 2.5 mm for a preterm infant. Sizes larger and smaller than these should be available.

Preterm infants

- Infants with surfactant deficiency may have difficulty in expanding their lungs, and in developing a normal functional residual capacity at birth.
- However, the preterm lung is quite a delicate structure with relatively little elastic support, and any use of undue pressure or excessive ventilation during resuscitation can damage the lungs.

While an inspiratory pressure of 30 cmH_2O may well be necessary to begin aerating the lungs at birth, the pressure should be reduced as rapidly as possible to a level that ensures that the chest is moving adequately. The key aim must be to conserve such surfactant as already exists by sustaining the lung's functional residual capacity (an objective best achieved by providing at least 5 cmH_2O of positive end-expiratory pressure (PEEP). Aim to achieve this consistently throughout transfer to the nursery. This can be achieved using nasal prongs (nasal PEEP), thus avoiding tracheal intubation altogether (*see* Section 8.2).

Circulation: chest compressions

- Most infants needing help at birth will respond to successful lung inflation with an increase in heart rate followed quickly by normal breathing. Chest compression should be started only when you are sure that the lungs are being aerated successfully.
- If the heart rate remains very slow (less than 60 beats/minute) or absent following 60 seconds of ventilation with good chest movements, start chest compressions.
- In infants, the most efficient method of delivering chest compressions is to grip the chest in both hands in such a way that the two thumbs can press on the lower third of the sternum, just below an imaginary line joining the nipples, with the fingers over the spine at the back. This can only be done if there is a second operator ventilating the lungs (*see* Figure 3.2.4).
- If you are alone, the two-thumb method is not possible, as ventilations also need to be provided. In this situation, use the first two fingers of one hand to depress the lower sternum, while the other hand holds the mask in place. Then move the hand from the sternum to squeeze the bag.
- Compress the chest quickly and firmly, reducing the antero-posterior diameter of the chest by about one-third.
- Because oxygenation is such an important part of neonatal resuscitation, **the recommended ratio of compressions to inflations in newborn resuscitation is 3:1**.
- Chest compressions move oxygenated blood from the lungs back to the heart and out into the ascending aorta. From there the two coronary arteries will then quickly deliver oxygen to the failing anoxic heart muscle. It is important to allow enough time during the relaxation phase of each compression cycle for the heart to refill with blood, at the same time ensuring that the chest is inflating with each breath.

FIGURE 3.2.4 Two-thumb compression of the chest, with a second operator ventilating the lungs, here using a T-piece as an alternative to bag and mask.

- The rate of chest compressions is around 120/minute. However, with pauses for ventilation, the actual number of compressions is less than 120/minute.

Drugs

Rarely inflation of the lungs and effective chest compression will not be sufficient to produce adequate circulation and perfusion in infants. In these circumstances, drugs may be helpful. However, drugs are needed only if there is no significant cardiac output despite effective lung inflation and chest compression.

Very few drugs have proved to be of benefit in such circumstances. The drugs used are adrenaline (1:10 000) and dextrose (10%). Drugs are best delivered via an umbilical venous catheter. In those where IV access is not possible, the intra-osseous route may be used. Each injection of a

drug should be followed with a bolus of 2–3 mL of Ringer-lactate or Hartmann's solution. Unfortunately, most of the infants in whom cardiac output only returns after such treatment require specialist neonatal care (often with mechanical ventilation) and do not survive to discharge. Most of those who do survive later develop profound disabling spastic quadriplegia.

Where the cause of the child's terminal apnoea is a sudden and much more abrupt hypoxic event (such as shoulder dystocia or an occasional case of late cord prolapse) these reservations may be less valid. Here there is at least anecdotal evidence that the outlook is much less bleak if the circulation can be restarted.

Acidosis not serious enough to precipitate circulatory standstill (asystole) will nearly always correct itself spontaneously within 90 minutes once the circulation has been restored and the infant starts to breathe for him- or herself. It does not therefore call for sodium bicarbonate, the use of which is controversial. Indeed, giving bicarbonate may increase carbon dioxide levels, worsening intracellular acidosis, and increases the amount of sodium that the potentially compromised kidney will need to excrete over the next few days.

- **Adrenaline:** The recommended dose of adrenaline is 10 micrograms/kg body weight (0.1 mL/kg body weight of 1:10 000 solution). If this is not effective, a dose of up to 30 micrograms/kg (0.3 mL/kg body weight of 1:10 000 solution) may be tried. Ideally, have ready-made and well-labelled 1:10 000 adrenaline solutions available on all emergency trolleys. In situations where this is not available in a ready-made state it could be prepared by adding 1 mL of 1:1000 solution to 9 mL of normal saline or Ringer-lactate or Hartmann's solution. **It is potentially dangerous to leave inadequately labelled and made up doses of adrenaline around, as giving the same volume of 1:10 000 as 1:1000 solution could cause cardiac arrest.** Do not use a higher dose by these routes (IV) as it is harmful.
- **Glucose:** The recommended dose of glucose is 200 mg/kg (2 mL/kg of 10% dextrose). Higher concentrations or larger doses can induce hyperglycaemia, which is associated with cerebral oedema and cerebral haemorrhage, and may lead to rebound hypoglycaemia. It is known that severe hypoglycaemia is rare immediately after birth, but tends to present after 1–2 hours. However, hypoglycaemia (**less than 2.5 mmol/litre (45 mg/dL)**) is a potential problem for stressed or hypoxic neonates, so 10% dextrose should be considered in cardiac arrest, as the heart will not recover in the presence of hypoglycaemia. This should be followed by an infusion of 5 mL/kg/hour of 10% glucose if there is confirmation of hypoglycaemia by a blood test. This should be continued until feeding is well established. **Never give any drug into the umbilical artery.**
- **Naloxone (nalorphine)** can be used to reverse profound opiate-induced respiratory depression, but has no real role in neonatal resuscitation. If it does prove necessary, it is best to give it intramuscularly and give a full 200-microgram 'depot' dose irrespective of body weight. If naloxone is given as a single dose IV it will be eliminated from the body faster than the opioid drug, causing a return of the respiratory depression, and therefore the infant will stop breathing again without a naloxone infusion. Naloxone does not reverse the respiratory depressing effects of non-opiate drugs.

Acute blood loss as a cause of circulatory arrest (circulatory volume support)

- Sudden acute blood loss is a rare, but often unrecognised, cause of acute circulatory collapse. Bleeding from an aberrant placental blood vessel (vasa praevia) or snapped umbilical cord can rapidly lead to hypovolaemic death. The response to a rapid generous infusion of any IV fluid can be equally dramatic. Speed is of the essence. Circulatory collapse probably does not occur until the infant has lost 30–40 mL/kg of blood, but 20 mL/kg of Ringer-lactate or Hartmann's solution will usually reverse the immediate critical hypovolaemia rapidly. The initial intravenous fluid bolus should be **10 mL/kg** of Ringer-lactate or Hartmann's solution **or blood group O Rh-negative blood (if immediately available). This can be repeated *once* if there is no or only minimal response**. A similar response can be achieved with plasma, albumin or some artificial plasma-expanding agent (e.g. gelatin). A packed red cell transfusion using group-specific or group O Rh-negative duly cross-matched blood can be given later to correct the associated anaemia.
- Other less well-recognised causes of hypovolaemic collapse include acute feto–maternal blood loss, sudden twin-to-twin transfusion, and accidental incision of the placenta during Caesarean delivery and cord ligature that has come off and not been detected.

Apart from these specific indications, fluid should not be used during neonatal resuscitation. There is no evidence to suggest benefit from routine use, which only compounds the problem of fluid balance that can develop over the next 2 to 3 days if severe intrapartum stress causes secondary renal failure.

Environment

This is always at risk of being overlooked, but it should be the first issue to receive attention in all infants, before and at birth.

- A **clean**, **warm** and **well-lit** environment for resuscitation is the objective in all cases. It only takes a few seconds to dry the infant and provide a clean dry blanket for warmth. The room in which delivery takes place should also be clean, warm and free of draughts.
- Small infants in particular rapidly become cold, especially if left wet, which can be lethal. Enclosing the trunk and the limbs in a clear plastic drape or bag (plus a woollen cap if available) can greatly reduce evaporative heat loss. Indeed, infants born more than 10 weeks early have skin that is so thin that it is not really 'waterproof'. This will cause excessive evaporative heat loss to persist for several days after birth.

Family

- The mother's needs come first if you are on your own. Most infants are quite good at looking after themselves, once they are breathing and wrapped. If possible keep the infant with the mother.
- If you are not on your own, things become much easier. The 'ABC' summary really only comments on the care that should be given to the infant. Remember that

parents need to be told what is happening. They will fear the worst, more so if the infant was only taken away from them even for a few minutes at birth for stabilisation or resuscitation.

- If you tell the parents that their infant needed 'resuscitation' at delivery, they may well start to think that their child was in the process of dying. That might make you feel that you have done something useful, and it may make the parents very grateful. However, it will also make them feel that something must have gone 'wrong' during delivery, and it may lead them to worry that their child could be 'brain-damaged' as a result. The words that we use matter. Parents can easily read meanings into them that we never intended.
- Write down what you see and do, distinguishing fact from opinion and making no assumption as to the causation. Use adjectives with great care and do not make judgemental comments on the actions of others. Document everything.

Poor response to resuscitation

If the infant either fails to respond or shows a poor response to resuscitation, the most likely problem is inadequate oxygenation. The following steps should be considered:

- Check the airway and ventilation.
- Check for technical faults if using equipment.
  - Is the oxygen attached?
  - Is the airway blocked?
  - Is the endotracheal tube in the correct place?
- Re-examine the chest to see if a pneumothorax has developed. This is not common, but may cause a problem. Drain a tension pneumothorax with a small cannula over needle (21 gauge) in the second intercostal space in the mid-clavicular line. This should be followed by the insertion of a chest drain (*see* Section 8.3).
- Consider the possibility of a congenital heart lesion if the infant remains cyanosed despite breathing and having a good heart rate.
- Consider the possibility of maternal opiates or sedation, such as diazepam or phenobarbitone, if the infant is pink, well perfused, but requires assisted ventilation.
- Shock, caused by acute blood loss, should respond to a rapid bolus of 10–20 mL/kg of O-negative blood.
- Consider the possibility of hypoglycaemia.

Stopping resuscitation

Even with the most effective resuscitation, not all infants will survive.

If the infant has been without a cardiac output after 20 minutes of resuscitation and does not respond despite

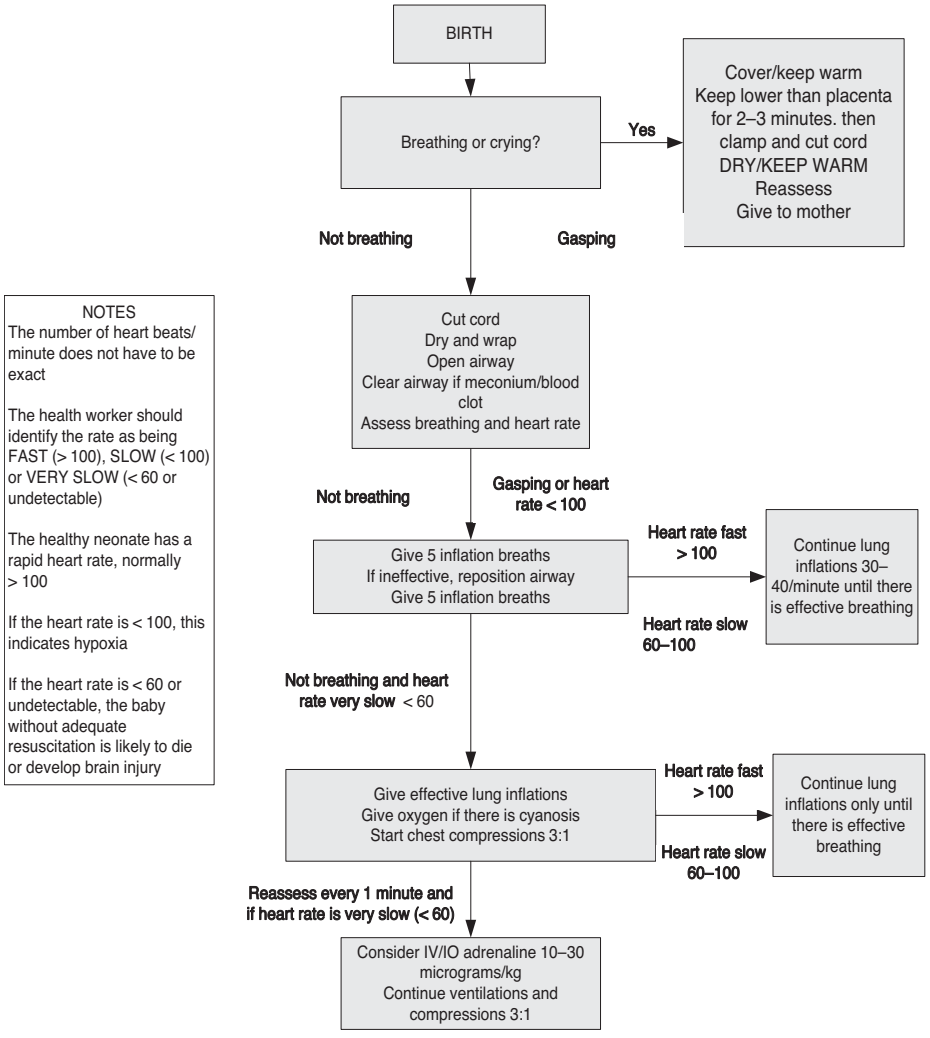

FIGURE 3.2.5 Algorithm for resuscitation of the baby at birth.

effective ventilations and chest compressions, the outcome is unlikely to be altered by the use of drugs, although these should be considered. The decision to stop resuscitation should be taken by the most senior healthcare worker present, and the reason for the decision should be clearly documented.

Explain sensitively to the parents that the infant has died. The infant should then be handled in accordance with cultural preference and practice.

Documentation

It is important to keep accurate records of the steps taken during resuscitation. The reason for any decision must be clearly documented, including the decision to start and end resuscitation. This is important irrespective of the immediate outcome of the resuscitation effort. As with any documentation, keep to the facts and make a complete record of all the steps taken, their timing, and the impact that they had on the infant's progress.

Remember to sign and date the record.

Vitamin K prophylaxis against haemorrhagic disease of the newborn

Following resuscitation/stabilisation, all newborn infants should receive vitamin K 1 mg IM. Vitamin K is given to prevent haemorrhagic disease of the newborn (HDN), which may cause significant bleeding and even death. The IM route is preferred as it provides a depot over many weeks.

Similarly, neonates requiring surgery, those with birth trauma, preterm infants and those exposed *in utero* to maternal medication that is known to interfere with vitamin K are at especially high risk of bleeding and must be given vitamin K 1 mg IM. This is often forgotten in the rush to get the infant to the nursery.

Resuscitation guidelines algorithm

As discussed earlier, all resuscitation guidelines are based on the international evidence-based science agreed in 2010 at the International Liaison Committee on Resuscitation. The algorithm shown in Figure 3.2.5 summarises the recommendations in the text.

Suggested reading

World Health Organization, London School of Hygiene and Tropical Medicine, Save the Children *et al.* (2011) Neonatal mortality levels for 193 countries in 2009 with trends since 1990: a systematic analysis of progress, projections and priorities. *PLoS Medicine*, **8**, e1001080.

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Aschner JL *et al*. (2008) Sodium bicarbonate: basically useless therapy. *Pediatrics*, **122**, 831.

3.3 Clinical care of the infant in the early months of life

Prematurity and low birth weight

- A **low-birth-weight infant** is one weighing less than 2.5 kg at birth. Low birth weight may be attributable to preterm delivery or intrauterine growth restriction.
- A **preterm infant** is one born before 37 completed weeks have elapsed since the first day of the last menstrual period (259 days). Most preterm infants are born after 32 weeks' gestation.
- A **small-for-gestational age (SGA) infant** is one whose birth weight falls below the 10th percentile on a birth weight centile chart.

  Probably at least 25% of SGA infants are just constitutionally small by virtue of maternal weight, and not secondary to poor placental perfusion. The mean birth weight of infants born to mothers 4 feet 10 inches (147 cm) tall is about 500 grams less than that of infants born to mothers 6 foot 0 inches (183 cm) tall. This discrepancy increases to about 1 kg if extremes of mid-pregnancy weight are also taken into account.
- **Intrauterine growth restriction (IUGR)** refers to a slowing of fetal growth velocity. Most but not all IUGR infants are SGA at birth. Some IUGR infants are just wasted.
- A **large-for-gestational age (LGA) infant** is one whose birth weight is greater than the 90th percentile on a birth weight centile chart.

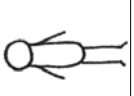
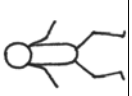
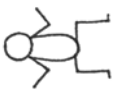
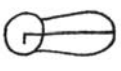
For most clinical purposes it is sufficient to classify infants as 'low birth weight', 'preterm' or 'small-for-gestational age'.

Assessing gestational age

Sometimes a mother cannot recall the date of her last menstrual period. The infant's gestational age can then be assessed to within ± 2 weeks based on a combined physical and neurological score (*see* Table 3.3.1). Wasted infants underscore on physical criteria.

TABLE 3.3.1 Ballard's scoring system for gestational assessment

Sign	Physical criteria score							Sign score
	–1	0	1	2	3	4	5	
Skin	Sticky, friable, transparent	Gelatinous, red, translucent	Smooth, pink, visible veins	Superficial peeling and/or rash, few veins	Cracking, pale areas, rare veins	Parchment, deep cracking, no vessels	Leathery, cracked, wrinkled	
Lanugo	None	Sparse	Abundant	Thinning	Bald areas	Mostly bald		
Plantar surface	Heel–toe 40–50 mm: –1 < 40 mm: –2	> 50 mm no crease	Faint red marks	Anterior transverse crease only	Creases anterior two-thirds	Creases over entire sole		
Breast	Imperceptible	Barely perceptible	Flat areola, no bud	Stippled areola, 1–2 mm bud	Raised areola, 3–4 mm bud	Full areola, 5–10 mm bud		
Eye/ear	Lids fused loosely: –1 tightly: –2	Lids open, pinna flat, stays folded	Slightly curved pinna; soft; slow recoil	Well-curved pinna; soft but ready recoil	Formed and firm; instant recoil	Thick cartilage, ear stiff		
Genitals (male)	Scrotum flat, smooth	Scrotum empty, faint rugae	Testes in upper canal, rare rugae	Testes descending, few rugae	Testes down, good rugae	Testes pendulous, deep rugae		
Genitals (female)	Clitoris prominent and labia flat	Prominent clitoris and small labia minora	Prominent clitoris and enlarging labia minora	Labia majora and minora equally prominent	Labia majora large, labia minora small	Labia majora cover clitoris and labia minora		
Total physical maturity score								

Sign	Neurological criteria score							Sign score
	–1	0	1	2	3	4	5	
Posture								
Square window								
Arm recoil								
Popliteal angle								
Scarf sign								
Heel to ear								
Total neuromuscular score								

Notes on calculating the scores:

Posture: With the infant supine and quiet, score as follows:

- Arms and legs extended = 0
- Slight or moderate flexion of hips and knees = 1
- Moderate to strong flexion of hips and knees = 2
- Legs flexed and abducted, arms slightly flexed = 3
- Full flexion of arms and legs = 4.

Square window: Flex the hand at the wrist. Exert pressure sufficient to get as much flexion as possible. The angle between the thumb and the anterior aspect of the forearm is measured and scored:

- > 90° = –1
- 90° = 0
- 60° = 1
- 45° = 2
- 30° = 3
- 0° = 4.

Arm recoil: With the infant supine, fully flex the forearm for 5 seconds, then fully extend by pulling the hands and release. Score the reaction:

- Remains extended 180°, or random movements = 0
- Minimal flexion, 140–180° = 1
- Small amount of flexion, 110–140° = 2
- Moderate flexion, 90–100° = 3
- Brisk return to full flexion, < 90° = 4.

Popliteal angle: With the infant supine and the pelvis flat on the examining surface, the leg is flexed on the thigh and the thigh is fully flexed with the use of one hand. With the other hand the leg is then extended and the angled scored:

- 180º = –1
- 160º = 0
- 140º = 1
- 120º = 2
- 100º = 3
- 90º = 4
- < 90º = 5.

Scarf sign: With the infant supine, take the infant's hand and draw it across the neck and as far across the opposite shoulder as possible. Assistance to the elbow is permissible by lifting it across the body. Score according to the location of the elbow:

- Elbow reaches or nears level of opposite shoulder = –1
- Elbow crosses opposite anterior axillary line = 0
- Elbow reaches opposite anterior axillary line = 1
- Elbow reaches midline = 2
- Elbow does not reach midline = 3
- Elbow does not cross proximate axillary line = 4.

Heel to ear: With the infant supine, hold the infant's foot with one hand and move it as near to the head as possible without forcing it. Keep the pelvis flat on the examining surface. Score as shown in Table 3.3.1 above.

After assigning the score for the physical and neurological criteria, the sum of the two scores is then used to assess the gestation based on Table 3.3.2.

TABLE 3.3.2 Assessment of gestation from total score

Total score	Gestational age (weeks)
–10	20
–5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

Low birth weight and/or preterm infants

Infants with birth weight in the range 2.25–2.5 kg

- These infants are normally strong enough to start feeding themselves. They need to be kept warm and closely observed for infection, but otherwise no special care is required.

Infants with birth weight in the range 1.75–2.25 kg

- These infants sometimes need extra care, but can normally stay with their mothers to receive feeding and warmth, especially if skin-to skin contact can be maintained. Close monitoring by a healthcare worker is required.
- Feeds can be started within 1 hour of delivery. Many of these infants will be able to suck and can be breastfed. Those who cannot breastfeed should be given expressed breast milk with a cup. When the infant is sucking well from the breast and gaining weight on a daily basis, they can be weaned off cup feeds.
- These infants should be reviewed at least twice a day to assess their feeding ability, fluid intake and the presence of any **danger signs** (*see* Box 3.3.1 below), including signs of serious bacterial infection. Such problems will necessitate close monitoring in a neonatal nursery (if available) in a similar way to the very low birth weight. The risk of keeping the child in hospital (including hospital-acquired infections) should be considered.

Infants with birth weight below 1.75 kg

- These infants are at risk of hypothermia, apnoea, hypoxaemia, sepsis, feed intolerance and necrotising enterocolitis. The smaller the infant, the greater these risks. All infants with a birth weight below 1.75 kg should be admitted to a special care or neonatal intensive care unit (if available).

Other treatments for low-birth-weight and/or preterm infants

Oxygen

Oxygen should be administered via nasal cannulae, nasal prongs or a head box if there are signs of respiratory distress, such as moderate to severe recession (preterm infants may show mild recession with normal breathing), and definitely in the presence of cyanosis. **Pulse oximetry to measure oxygen saturation is a vital part of oxygen usage in the preterm infant.** Retinopathy of prematurity (ROP), previously known as retrolental fibroplasia, which leads to lifelong blindness in many cases, is caused by high blood levels of oxygen saturation in the preterm infant. There is no good evidence for the optimum oxygen saturation for preterm infants. On the one hand it is important to avoid hypoxia, which would lead to brain damage, as the infant is likely to have respiratory problems from surfactant deficiency, and on the other hand unrestricted oxygen may cause ROP, which would lead to blindness. Current advice is that the infant born at or before 32 weeks' gestation or weighing less than 1500 grams at birth should have a target oxygen saturation of 86–92%, which is higher than the oxygen saturation to which the fetus is exposed *in utero*.

Prevention of hypothermia

To prevent hypothermia, nurse the infant in skin-to-skin contact between the mother's breasts ('kangaroo care')

or clothed in a warm room, or in an incubator. A hot water bottle wrapped in a towel can be useful for keeping the infant warm if no power for heating is available, but take care not to burn the infant. Aim for an axillary temperature of 36.0–36.5°C, with the feet warm and pink. When the mother is asleep or if she is ill, a clean incubator can be used. Incubators should be washed with disinfectant between infants, and should be of a basic design that can be used appropriately by the staff available.

Fluids

It is best to give fluids enterally. However, if the infant is not well enough (e.g. due to severe respiratory distress), give IV fluids (*see* Section 3.4). Initially, consider giving approximately 2–4 mL of expressed breast milk every 1 to 2 hours through a nasogastric tube. This can be adjusted depending on the weight and the amount of IV fluids that the infant is receiving. With increasing age and weight gradually increase the volume and timing of each feed (the maximum time interval between feeds should not exceed 4 hours). The total fluid intake of enteral feeds plus IV fluids per 24 hours should adhere to the following fluid management guidelines:

- 60 mL/kg on day 1
- 80–90 mL/kg on day 2
- 100–120 mL/kg on day 3
- 120–150 mL/kg on day 4
- 150–180 mL/kg thereafter.

Some infants can be fed with a cup. Use only expressed breast milk if possible. If 2–4 mL per feed is tolerated (i.e. there is no vomiting, abdominal distension, or gastric aspirates of more than half the feed) the volume can be increased by 1–2 mL per feed each day. Ideally, aim to have feeding established in the first 5 to 7 days so that the IV fluids can be tapered off. Reduce or withhold feeds if signs of poor tolerance occur. As the infant grows, recalculate the feed volume based on the higher weight. Feeds may be increased over the first 2 weeks of life to 150–180 mL/kg/day based on a 3- to 4-hourly feeding pattern.

How to give gastric feeds (see also Section 8.5 on gastric tube management)

Place the baby's lips on the breast even though he or she is unable to suck or attach before each feed. Place expressed breast milk (EBM) in the syringe. Only use fresh milk or milk that has been stored in a refrigerator, and that has not been out of the fridge for more than 1 hour in a hot climate. Check that the tube is in the stomach before every feed or administration of enterally given drugs. Also check that there is not more than 10% of the previous feed in the stomach by gentle aspiration using a 2- or 5-mL syringe. Connect the syringe containing EBM and remove the plunger, giving the milk by gravity over 10–15 minutes per feed. Only if the feed does not flow in should you gently push with the plunger for a few seconds only to get it started. Never push the whole feed in. Observe the infant closely during the feed for signs of respiratory distress that might be due to lung aspiration. Replace the tube every 7 days, or sooner if it is blocked.

Give enteral feeds only if there is no abdominal distension or tenderness, bowel sounds are present, meconium has been passed, and there is no apnoea, low aspirates, no vomiting and adequate stool output.

TABLE 3.3.3 Guide to volumes of each feed given every 3–4 hours at different infant weights

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
Total (mL/kg/day)	60	80	100	120	140	150	160	170
1.25–1.4 kg	10	15	18	20	22	24	25	≥26
1.5–1.9 kg	15	17	19	21	23	25	27	≥27
2.0–2.4 kg	20	22	25	27	30	32	35	≥35
≥2.5 kg	25	28	30	35	35	≥40	≥45	≥50

Blood glucose levels

Check blood glucose levels every 6 hours until enteral feeds are established, and immediately if there are any danger signs of infection.

Infection or feed intolerance

Observe carefully and constantly for infection or feed intolerance.

Apnoea

Monitor for apnoea, ideally with a pulse oximeter (which are now affordable and available in many resource-limited countries), supplemented by close visual monitoring of the infant by the mother or a close relative.

Discharge and follow-up of low-birth-weight infants

Discharge when:

- there are **no danger signs** (*see* Box 3.3.1), including signs of serious infection
- the infant is gaining weight (at least 20 grams per day for 3 consecutive days) on breastfeeding alone

BOX 3.3.1 Danger signs associated with infection in the neonate

Common danger signs

- Infant feeding less well than before.
- Infant lying quietly and making few spontaneous movements.
- Hypothermia or fever > 38ºC.
- 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

- Low respiratory rate (< 20 breaths/minute) or apnoea.
- Jaundice.
- Abdominal distension.

- the infant is able to maintain temperature in the normal range (36–36.5°C axillary) in an open cot or with skin-to-skin care
- the mother is confident and able to take care of the infant.

Low-birth-weight infants should be given all scheduled immunisations by the time of discharge from the health facility or soon after.

Counsel the parents before discharge on:

- exclusive breastfeeding
- keeping the infant warm
- the danger signs that necessitate seeking care (*see* Table 3.3.4), plus advice on when to return for healthcare
- basic life-saving manoeuvres to use in the event of an emergency, particularly mouth-to-mouth and nose ventilation if prolonged apnoea occurs.

Low-birth-weight infants should be followed up at regular intervals following discharge for weighing, assessment of feeding, and assessment of general health until they have reached 2.5 kg in weight.

TABLE 3.3.4 Danger signs for parents of discharged newborns

Seek advice immediately if any of the following occur:	Seek advice very quickly if any of the following occur:
Convulsion(s)	Infant refuses feeds
ANY bleeding	Minor diarrhoea or vomiting
Severe diarrhoea or vomiting	Minor breathing problems
Infant appears unresponsive	Infant is less active/interested
Severe breathing problems	Infant feels abnormally hot
Infant feels cold	Jaundice

Enteral feeding for the newborn infant in hospital

Type of milk

Breast milk will provide the nutrients required by almost all infants. However, for preterm infants the following supplements are needed:

Vitamin D supplementation

Term breastfed infants generally do not need extra vitamin D. However, this is only true if the mother has an adequate vitamin D status. Maternal vitamin D deficiency during pregnancy and lactation is common in resource-limited countries, contributing to the low vitamin D content of breast milk. Newborn infants of mothers who have dark skin or wear concealing clothes are also at greater risk of vitamin D deficiency at birth.

Large amounts of calcium and phosphorus are transferred from the mother to the infant during the last 3 months of pregnancy, helping the infant's bones to grow. Therefore a preterm infant may not receive sufficient amounts of calcium and phosphorus for this purpose. Vitamin D helps the body to absorb calcium from the intestines and kidneys. Very preterm infants require adequate vitamin D supplements. Liver problems such as cholestasis and prolonged use of diuretics or steroids may also cause problems with blood calcium levels.

Therefore, without further supplementation, preterm and also some full-term breastfed infants may be at risk of vitamin D deficiency. This risk may be minimised either by supplementing the mother with large amounts of vitamin D (4000 IU/day) during pregnancy and lactation, or by supplementing the infant directly (400 IU/day) during the period of lactation.

Phosphorus supplements

These may be needed in the case of very small infants, who can become hypophosphataemic (i.e. with plasma phosphorus levels of < 1.5 mmol/litre). If untreated, this may result in metabolic bone disease. The addition of a concentrated phosphorus salt (50 mg/kg/day of phosphorus) to feeds will prevent this. Adding 0.05 mL/kg of a 4 mmol/mL phosphorus solution to each of eight feeds per day will give 50 mg/kg/day of supplemental dietary phosphorus.

Vitamin A supplementation

In resource-limited countries, vitamin A supplementation of the newborn infant reduces mortality. Preterm infants are at high risk of vitamin A deficiency. This important subgroup of our infant population is not only born with inadequate body stores of vitamin A, but is also often unable to tolerate routine oral supplementation. Vitamin A supplementation programmes significantly reduce infant mortality as well as the incidence of xerophthalmia, respiratory infection, and morbidity from gastrointestinal disease. Oral supplementation of 4000 IU/kg/day has been recommended for very-low-birth-weight (VLBW) (< 1500 grams at birth) infants from establishment of full enteral feeding until discharge from the neonatal unit. Supplementing term newborn infants with vitamin A (100 000 IU as a single dose) within 48 hours of birth reduces infant mortality by almost 25%, with those of low birth weight deriving the greatest benefit. Alternatively, **a single dose of 200 000 units can be given to all postpartum mothers within 6 weeks of delivery, when the likelihood of pregnancy is very low, and when infants benefit most from the presence of vitamin A in breast milk**.

Vitamin K

All neonates should be given vitamin K 1 mg IM within 1 hour of birth. Those who require surgery, those with birth trauma, those who are preterm and those exposed before birth to maternal medication (that can interfere with vitamin K) are at high risk of bleeding and must be given vitamin K. If the need for surgery only becomes apparent some time after birth, we suggest that a repeat dose should be given before surgery.

Multivitamin preparation

A multivitamin preparation (preferably containing adequate vitamins A and D) for preterm infants may be commenced from 3 weeks of age. A supply of vitamin D (400 IU/day) is particularly important for bone mineralisation.

Iron supplements

Iron supplements for preterm infants are usually commenced from about 6 weeks of age. Preterm infants have reduced iron stores compared with term infants, especially if the umbilical cord is clamped early. The daily dietary iron supplementation is 2–4 mg/kg of elemental iron, up to a maximum of 16 mg/day.

Breast milk banking

The WHO recommends that low-birth-weight babies who cannot be fed their own mother's breast milk should receive donor milk. The high maternal mortality and morbidity in low-income countries mean that there are many infants who cannot be put to the breast within a few hours of birth, and donor milk is suitable for them. In addition, there is evidence that human donor milk reduces the incidence of severe infection and necrotising enterocolitis (NEC) in low-birth-weight babies, compared with formula milk.

It is possible to establish safe donor milk banks in resource-limited settings, provided that there is a microbiology laboratory able to process donor samples, and a power supply to keep the banked milk frozen. A nurse or other staff member must be trained in good hand hygiene, and the importance of labelling and storage. Only simple equipment is needed.

Milk can be collected from lactating mothers who are known to have tested negative to HIV and syphilis, and are non-smokers. Ideally they have also been screened for hepatitis infections. Milk is collected by hand expression under supervision (as 'drip milk' is lower in calories than expressed milk). A 1-mL aliquot from each donor's sample is sent to the microbiology lab. If colony-forming organisms are grown, the whole sample is discarded. Milk can be stored in a refrigerator while awaiting the microbiology results.

Milk is pasteurised by heating for 30 minutes at 62.5°C, and then cooled and frozen. Pasteurised frozen milk can be stored for up to 6 months from the date of collection. Supplementary formula feeding for the infants of mothers who cannot provide breast milk, or whose mothers have died, may be needed after discussion with the infant's carers.

Fluid and electrolyte management for the neonate in hospital

When giving fluid or blood intravenously, best practice is to use an in-line infusion chamber/burette to avoid fluid overload.

Fluid requirements

Body water content is high at birth and urine output is low for the first few days. Therefore giving large volumes of fluid in the first few days may make an infant oedematous and worsen any respiratory disease. **A simple general rule** is to start an ill newborn infant who cannot take enteral fluids (breast milk) on 60 mL/kg/day IV as 10% dextrose solution, increasing in daily steps of 20–30 mL/kg/day to a maximum of 140–180 mL/kg/day. However, in a small-for-gestational-age infant it may be necessary to begin with 70–90 mL/kg/day in order to meet the glucose requirements.

Ideally, use a 100-mL paediatric intravenous burette where 60 drops = 1 mL and therefore 1 drop/minute = 1 mL/hour.

So for an infant weighing 1.8 kg on day 1: 1.8 × 60 = 108 mL.

In each hour the fluid will be 108 ÷ 24 = 4.5 mL, which corresponds to 9 drops every 2 minutes.

The rate of insensible water loss (mainly through the skin) is high in some circumstances, particularly in infants under 29 weeks' gestation or when an overhead heater (radiant warmer) rather than an incubator is used. Helpful measures for reducing insensible water loss in such cases include the following:

- Place the infant from below the neck in a clean plastic bag to maintain humidity. Maintaining humidity helps to keep very premature infants warm by reducing evaporative heat loss.
- Clothe the infant, or wrap the body below the head with bubble wrap or aluminium kitchen foil (with the shiny side facing inward towards the infant).
- When an overhead heater is used, the infant should not be covered, and the heater output must be adjusted in direct response to the infant's skin temperature (typically achieved by a continuous temperature probe servo system). Alternatively, a plastic bag over the infant's body from the neck down can help to preserve heat.
- In the first week of life, high rates of insensible water loss will be reflected by high rates of weight loss (more than 10% of birth weight), and often an increase in the plasma sodium concentration to 150 mmol/litre or higher. If either occurs, the infant is dehydrated and fluid intake should be increased by 30 mL/kg/day. When nursing a low-birth-weight infant under an overhead heater, it is advisable to add an extra allowance of 30 mL/kg/day right from the start (i.e. start on day 1 at 90 mL/kg/day rather than 60 mL/kg/day).

Note, however, that even 30 mL/kg/day might not be enough to meet the insensible losses of a very preterm infant (29 weeks or less) under a radiant heater. Such infants are much better nursed in closed incubators.

In very-low-birth-weight infants, enteral feeds should be advanced slowly in 20–30 mL/kg/day increments. Infants who are being enterally fed but who are unable to breastfeed can be given expressed breast milk by orogastric tube or cup. A general plan for fluid enhancement is as follows:

- day 1: 60 mL/kg/day
- day 2: 85 (range 80–90) mL/kg/day
- day 3: 110 (range 100–120) mL/kg/day
- day 4: 135 (range 120–150) mL/kg/day
- day 5 and thereafter: 165 (range 150–180) mL/kg/day.

Monitor the fluid intake by weighing the infant daily and recording the frequency of urine output.

To weigh the baby, first place a blanket in the scales, set them to zero and then place the baby naked in the scales and cover the infant with the blanket to keep them warm. Fluid intake may need to be adjusted frequently to maintain fluid balance. Urine output can be monitored by measuring the difference between wet nappies (diapers) and a dry one using accurate scales. Generally expect at least eight wet nappies in a 24-hour period. Look out for signs of fluid overload (oedema) or dehydration. If possible measure the plasma electrolytes, but remember that these cannot be interpreted without information on body weight and urine output.

Electrolyte requirements when giving IV fluids

Sodium requirements

Infants over 48 hours of age need some sodium supplementation in a dose of 2–3 mmol/kg/day. This can most easily be given by adding 20 mL/kg of normal saline (0.9%) to the daily requirement of 10% glucose to make up the

total daily fluid volume needed. This gives approximately 3 mmol of sodium per kg.

Adding sodium is open to many errors. Ready-made neonatal fluids are available in some countries, and may be used to avoid this problem in some situations. The sodium requirements of very preterm infants may be much higher, as urinary sodium losses may approximate 10 mmol/kg/day in those of 29 weeks' gestation or less.

Sodium can be commenced on the third day of life (after 48 hours) in infants receiving intravenous fluids, but if there is respiratory distress it is wise to wait until the diuresis associated with recovery begins (this is often delayed until the third or fourth day of life).

Potassium requirements

Potassium supplementation in a dose of 1–2 mmol/kg/day will meet requirements and can be provided by adding mathematically correct and smal amounts of potassium chloride to a 10% glucose fluid. If IV potassium is given, the plasma potassium concentration must be monitored daily. Potassium can be added to fluids but this should be done very carefully. **Remember that too much IV potassium can be fatal.** The concentration of KCl in peripheral IV solutions should never exceed 40 mmol/litre. **Do not add KCl until the urine output is well established.**

Remember that it is best to give potassium and calcium supplements orally, unless very low serum values are identified.

Glucose requirements

Infusing glucose at the following rates will match the normal hepatic glucose output and therefore maintain the blood glucose concentration at an acceptable level:

- term infant: 3–5 mg/kg/minute
- preterm, appropriate weight for gestation: 4–6 mg/kg/minute
- small for gestational age: 6–8 mg/kg/minute.

A solution of 10% glucose at 60 mL/kg/day will give 4 mg (0.22 mmol) glucose/kg/minute.

These infusion rates provide minimal glucose requirements to maintain a normal blood glucose level, but higher rates will be required for growth. Consider hyperinsulinism as a cause of the problem if an infant requires higher rates of infusion to maintain normoglycaemia. Always use 5% or ideally 10% glucose/dextrose for peripheral IV infusions; an umbilical venous catheter will be needed if high glucose requirements or limits on fluid volume necessitate a more concentrated solution which will be damaging to thin peripheral veins.

Composite maintenance fluid

An alternative way to make a simple composite maintenance fluid is by adding the following to give a total volume of 100 mL:

- 1/5 dextrose saline (0.18% normal saline with 5% dextrose) = 71 mL
- 7.4% KCl = 2 mL
- 10% calcium gluconate = 2 mL
- 25% dextrose = 25 mL
- **Total volume = 100 mL.**

Each 100 mL of the above solution would contain dextrose 10%, KCl 2 mEq, Ca 2 mEq and sodium 2.5–3 mmol. **Any such mixture must be prepared under sterile conditions.**

Remember that KCl should not be added until urine output is well established.

Drug use in the newborn infant

Relatively few drugs are needed to deal with most common neonatal emergencies.

The IV route should be used if the infant is already being given IV fluids, as this will reduce the amount of pain to which the child is subjected. There are dangers associated with rapid administration or breaking into an existing IV line, leading to an increased risk of sepsis. Erecting an IV line merely to administer drugs also risks exposing the child to dangerous fluid overload, unless a syringe pump can be used to control the rate at which fluid is infused.

Common emergency problems that require hospital care in the first month of life

Many emergencies can be prevented by attention to good feeding practices, providing adequate warmth and preventing infection. The more preterm or low birth weight the infant, the more likely it is that the following complications will occur:

- feeding difficulties
- poor temperature control, especially hypothermia
- infection – prevention and early recognition and safe management are essential
- polycythaemia
- respiratory distress and apnoeic attacks
- bleeding
- jaundice and neonatal anaemia
- reduced conscious level and seizures, including hypoglycaemia
- surgical problems.

Feeding difficulties

Infants born after 34 weeks are generally mature enough to suck and swallow well, but may be less demanding of feeds than term infants. Attention to the following can help all newborn infants, especially those born preterm, to establish breastfeeding:

- Encourage early and prolonged skin contact.
- Encourage small frequent feeds by waking the infant every 2 to 3 hours and putting them to the breast.
- If the infant will not latch on and suck, the mother can be encouraged to express breast milk and offer it to the infant by cup and/or spoon or if not accepted by orogastric or nasogastric tube.
- If an otherwise well infant on breast milk feeds is experiencing inadequate growth, an inadequate milk supply may be the problem. There are several possible causes for this, which can usually be identified by listening to the mother and then watching the infant feed. A relaxed mother will have a good 'let-down' reflex which gives the infant the more calorie-rich hind milk as well as the fore milk. The mother can tell when she has 'let down' by a tingling feeling in her breasts, and the infant starts to swallow rapidly. The infant must latch on properly for feeding to be successful, and this may need some assistance from the midwife. The best way to increase the milk supply for a hungry infant who is not thriving is to increase the feed frequency. Breast milk works on

a demand-and-supply system, so the more the infant demands, the more the breast supplies. If the infant is not feeding vigorously enough to increase the milk supply, the mother should express milk after feeding and give it to the infant as described above.
- Avoid giving formula or breast milk by bottle. A small feeding cup (about the size of a medicine measuring cup, with a smooth rim) or a spoon can be used to feed the infant.
- Give expressed breast milk via orogastric or nasogastric tube if the infant is too unwell to suck or drink from a cup.
- As the infant becomes stronger, encourage a transition to demand breastfeeding.

Feeding problems

- **Ingested meconium/blood.** Infants who have swallowed a lot of meconium or blood before birth may retch and appear distressed after birth. Such problems almost always settle within a few hours without any intervention.
- **Uncoordinated feeding.** Infants born before 32 weeks' gestation often have difficulty sucking and swallowing in a coordinated way. Most will initially need some tube feeds. They are not likely to start gaining weight until they are taking at least 120 mL/kg of milk a day. Infants need to be fed regularly at least once every 4 hours, day and night. Breast milk can be supplemented with formula milk at this time if donor milk is not available. However, every effort needs to be made to sustain the mother's lactation by expression and by keeping the mother in hospital to be near her infant.
- **Regurgitation.** Hurried frequent feeding may cause regurgitation. A poorly developed cough reflex can cause the infant to inhale milk into the lung, resulting in possible pneumonitis and even pneumonia. Newborn infants benefit from frequent small feeds every 2 to 3 hours. Feeds should be increased gradually over the first 3 to 5 days of life. Patience is required. Dehydration (and the risk of hypoglycaemia) need to be monitored, and can be prevented during this period by giving supplemental gastric or IV fluids so that total fluid intake (i.e. taking the gastric/IV and the oral intake together) does not fall below 120 mL/kg per day.
- **Feeding tubes.** Tube feeding is the best option for infants who have not yet developed a coordinated suck and swallow reflex. Nasogastric tubes are popular, easier to secure and less easily pushed out by the infant's tongue, but they can almost completely block one nostril, significantly increasing the work of breathing. Therefore orogastric tubes are preferred if respiratory distress is present. Alternatively, a fine-bore nasogastric tube can be left in place and changed as required (up to a maximum of 7 days). Small frail infants should be handled as little and as gently as possible, and can be left lying undisturbed in their cots during a tube feed so long as the head end of the cot is elevated 25 cm.

Temperature control and hypothermia prevention and treatment

Hypothermia can be due to a cold environment, but remember that **starvation** or **serious infection** can present as hypothermia.

Normal temperatures for newborn infants are **36.5–37.5°C (axillary)** if measured over 3 minutes, and lower (around **36.0–36.5°C**) if measured over at least 1 minute. Rectal thermometers are difficult to use and can be dangerous. If the trunk is cold, the infant is almost certainly hypothermic.

Use a **low-reading digital thermometer**, not a mercury thermometer. If the axillary temperature is less than 32°C, hypothermia is severe; if it is in the range 32–35.9°C the infant has moderate hypothermia. If the infant's temperature does not register on the normal thermometer, assume that they have hypothermia.

Hypothermia can be prevented by the following measures:
- Dry the infant well immediately after birth and place them in skin-to-skin contact with the mother. This is especially important for low-birth-weight infants who do not have other complications. For those with medical problems, warm the infant by skin-to-skin care. If there are adequate resources and staff, an overhead radiant heater **or** an air-heated incubator (set at 35–36°C) can be used.
- 'Kangaroo care' (skin-to-skin contact with the mother between her breasts and covered with a blanket) is the most effective method for all infants, especially for those of low-birth-weight. Randomised trials in both well-resourced and resource-limited countries have shown significant advantages to this technique for the infant and the mother, including an increased prevalence of breastfeeding, a reduced incidence of apnoea and a reduced risk of infection. Take care when examining the infant not to allow the temperature to fall (ideally room temperature in the hospital ward should be higher than 25°C).
- A cot heated **with a hot-water bottle with the top screwed in tightly and wrapped in a clean towel** can be just as effective if the above are not available. Ordinary domestic radiant heaters or electrical blower type heaters can also be effective.
- Cover the infant's head with a warm woollen hat and dress them in **warm, dry clothes**. Keeping the nappy dry is also very helpful.
- Avoid overheating by monitoring the axillary temperature 4- to 6-hourly.
- Feed the infant 2-to 3-hourly, and continue with 4-hourly feeds during the night.
- Avoid washing the infant before they are 24 hours of age.
- Do not leave the infant where there are any draughts.
- The infant should sleep either with or next to the mother during the night.

The development of incubators earlier in the twentieth century significantly reduced the mortality of preterm infants, but they are expensive, and require regular maintenance, thorough cleaning and sufficient numbers of trained staff. The nursing of infants in incubators is covered by standard texts, but Table 3.3.5 gives the settings from which to start, adjusting the incubator temperature up or down to maintain the infant's axillary temperature at 36.0–36.5°C.

TABLE 3.3.5 Incubator temperature guidelines

Weight of baby (grams)	Day 1	Day 2	Day 3	Day 4 and subsequently
< 1200	35.0°C	34.0°C	34.0°C	33.5°C
1200–1500	34.0°C	34.0°C	33.5°C	33.5°C
1500–2500	33.5°C	33.0°C	32.0°C	32.0°C
> 2500	33.0°C	32.5°C	31.0°C	30.5°C

Do not use antipyretic drugs to control fever in a newborn infant. Instead control the environment (e.g. remove some clothes, adjust incubator temperature) and always consider the possibility of serious infection.

Prevention of neonatal infection

A newborn infant with risk factors for infection (membranes ruptured more than 18 hours before delivery, mother with fever > 38°C before delivery or during labour, or foul-smelling/purulent amniotic fluid) should be treated with prophylactic antibiotics (ampicillin and gentamicin IM or IV) for at least 2 days. After 2 days the infant should be reassessed and treatment continued if there are signs of sepsis (or a positive blood culture).

Simple measures that can prevent infection in the newborn include the following:

- Ensure a **clean delivery environment** for the mother and infant, including disinfectant cream for all maternal vaginal examinations (e.g. Hibitane cream).
- **Good cord care:** the WHO recommends that the cord be kept clean and dry. It should not be covered. Local applications of creams, ointments, etc. are generally not required except in high-risk settings, where application of an antiseptic is recommended. An antiseptic solution or cream such as 4% chlorhexidine has recently been shown to reduce omphalitis and resulting neonatal mortality. It should be applied immediately after birth and for several days thereafter if possible, preferably after every nappy change. Similarly, there is extensive successful experience with the application of surgical spirit or iodine solution to the cord.
- **Exclusive breastfeeding.**
- Strict procedures for **hand washing** or the use of hand sprays or hand rubs for all staff and for families before and after handling infants.
- **Not using water for humidification** in incubators (where *Pseudomonas* can easily colonise).
- **Cleaning incubators with an antiseptic before use** (if skin-to-skin mother care is not possible).
- **Strict sterility for all invasive procedures.**
- **Sterile injection practices.**
- **Remove intravenous drips** when they are no longer necessary.
- **Keep invasive procedures (e.g. blood sampling, unnecessary IV cannulation) to a minimum**, only undertaking them when they are essential.

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 labour and delivery. The most frequently observed organisms vary from one part of the world to another. Gram-negative enteric bacteria (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.* Rarely *Listeria monocytogenes* is isolated from newborn infants with sepsis, especially when there are foodborne epidemics.

Maternal risk factors for early-onset sepsis

These include the following:

- maternal fever (especially 38°C or higher) before delivery or during labour
- pre-labour rupture of membranes
- prolonged rupture of membranes (18 hours or longer)
- preterm labour
- maternal bacteriuria during pregnancy (including *E. coli* and group B beta-haemolytic streptococcus)
- prior infected infant (group B beta-haemolytic streptococcus).

Early-onset sepsis in the newborn usually results from bacteria acquired from the mother at or shortly before delivery. These infants mostly present with respiratory distress, and have bacteraemia or pneumonia. 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 ones 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 due to 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, 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 can be directed accordingly. (For details of treatment of sepsis, *see* Section 3.4.)

Laboratory evaluation of the unwell infant

In an infant who is generally unwell with no clinically obvious infective focus, the following investigations should be performed:

- **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. The results can be assessed at 48 hours.

- **White blood cell and differential cell count are not helpful in most situations.**
- **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.
- **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 after the onset of an infection if this is present.
- **Blood glucose concentration.**
- **Serum bilirubin concentration:** if the infant appears jaundiced.
- **Surface cultures (ear canal, umbilical stump) and gastric aspirate cultures:** these do not correlate with either the likelihood of sepsis or the causative agent in septic infants. **These cultures should not be obtained.**
- **Midstream or suprapubic aspirate of urine for culture:** This procedure is of little value in the infant with suspected sepsis shortly after birth, but may be positive 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.

In seriously sick 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 if needed (see above), can be performed once the infant is stable and antibiotics have been started. (For details of treatment of sepsis, *see* Section 3.4.)

Infants who are vulnerable to maternal factors

The infant of a diabetic mother

If a diabetic mother is poorly controlled, her infant may be large for gestational age, putting him or her at risk of slow progress in labour and perhaps shoulder dystocia. At birth, the infant, although large, behaves in a similar manner to a preterm infant. There is a major risk of hypoglycaemia, caused by the intrauterine over-stimulation of the infant pancreas to produce abnormally high levels of insulin. The infant must be monitored at least hourly for hypoglycaemia in the first 6 hours, and should then be monitored 4-hourly for hypoglycaemia, which should be treated as described above with an infusion of 10% dextrose. The infant of a diabetic mother has immature lung maturation and is liable to surfactant deficiency (*see* Section 3.4), poor feeding and jaundice. Polycythaemia is also more likely.

The infant of a mother who is dependent on alcohol or drugs of addiction

These infants have been exposed to significant levels of narcotic drugs or alcohol *in utero*, causing an increased risk of congenital abnormalities and of abnormal neurological development and behaviour during childhood. Soon after birth they may show hyper-irritability and convulsions, requiring treatment and gradually reducing sedation as they are 'weaned off' the addictive drugs to which they have been exposed. These infants are also at risk of having been exposed to bloodborne viruses such as HIV and hepatitis B and C.

Birth injuries

Swellings around the head

- The commonest is a **caput succedaneum**, which is oedematous tissue over the occiput present after a vaginal delivery. This usually resolves within a few days and is of no consequence, requiring no intervention.
- A **cephalhaematoma** is a lateral (sometimes bilateral) fluctuant swelling, well circumscribed by the sutures. It does not cross the midline and anatomically represents a sub-periosteal haemorrhage. There may be an associated skull fracture, but neither this nor the swelling itself usually needs treatment. The only important complication can be worsening of jaundice as the blood is degraded and reabsorbed. **Never aspirate blood from a cephalhaematoma, as this can cause a serious infection.**
- A **subaponeurotic haemorrhage** (bleeding between the skull periosteum and the scalp aponeurosis) is the least common but most dangerous scalp swelling. It represents haemorrhage beneath the aponeurosis of the scalp. Onset and progression is often insidious, with progressive pallor due to significant haemorrhage. The boggy swelling of the head, extending from above the eyes to the occiput, may only be noticed after the infant has developed hypovolaemic shock. The infant may develop bruising behind the ears and around the eyes. This must be recognised early, as these infants often need urgent transfusion. Injection of vitamin K should be given.

Nerve palsies

- **Facial nerve palsies** are sometimes associated with forceps delivery. They usually resolve within a few days, requiring little intervention.
- **Brachial plexus trauma** may follow shoulder dystocia or a difficult breech delivery, and reflects traction injury to the upper roots of the brachial plexus. The arm is flaccid and the wrist flexed. This can most clearly be demonstrated by eliciting an asymmetric Moro reflex. Look for signs of respiratory distress, as the phrenic nerve on the same side is sometimes affected. An X-ray should be obtained to exclude a pseudoparesis associated with clavicular fracture or syphilitic osteitis. The humerus should also be included in the X-ray to rule out **humeral fractures**, which may occasionally be present. Most brachial plexus palsies resolve within 3 to 4 weeks of delivery, but rarely they can be permanent. Once fractures have been ruled out, the mother can be shown how to perform passive movements to reduce the possibility of joint contractures developing. Refer

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

World Health Organization (2012) *Born Too Soon: The Global Action Report on Preterm Birth*. www.who.int/pmnch/media/news/2012/preterm_birth_report/en/index.html

3.4 Neonatal illnesses and emergencies

Sepsis in the neonate

Recognising and treating neonatal infection

Bacterial sepsis (septicaemia) 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 than before
- infant lying quiet and making few spontaneous movements
- hypothermia or fever > 38ºC
- 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.

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 cloxacillin or flucloxacillin if there are signs suggesting that *Staphylococcus aureus* is a cause (e.g. skin pustules, abscess, 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 is generally unhelpful in this setting.**
- **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 > 38ºC
- 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 septicaemia 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 sterilise 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 days 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* **ceftriaxone**) intravenously using the dose regimen 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 blood cell count is ≥ 25 cells/mm^3), 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 septicaemic 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 ceftriaxone 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 septic 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/mm^3) 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 intra-ventricular 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-osmolarity 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.

The infant of a mother with tuberculosis (*see* Section 2.8.G)

- If the mother has active lung tuberculosis and was treated for less than 2 months before birth, or was diagnosed with tuberculosis soon after birth, the infant should be evaluated for congenital tuberculosis.
- Women with tuberculosis who have been treated appropriately for 2 or more weeks and who are not considered contagious can breastfeed. Reassure the mother that it is safe for her to breastfeed her infant.
- Do not give the tuberculosis vaccine (BCG) at birth. Instead give prophylactic isoniazid 5 mg/kg body weight orally once daily. Separation is not necessary unless the mother (or household contact) has possible multi-drug-resistant tuberculosis.
- At the age of 6 weeks, re-evaluate the infant, noting weight gain and taking an X-ray of the chest if possible. Congenital TB is most often intra-abdominal, so look for signs suggesting this. If there are any signs or findings suggestive of active disease, start full anti-tuberculosis treatment according to national guidelines. If at the age of 6 weeks the infant is doing well and tests are negative, continue prophylactic isoniazid to complete 6 months of treatment.
- Delay BCG vaccination until 2 weeks after treatment is completed. If BCG vaccine has already been given, repeat it 2 weeks after the end of the isoniazid treatment.
- If the mother is suspected of having multi-drug-resistant tuberculosis, an expert in tuberculosis disease treatment should be consulted.

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 0.9% 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 diplococci) 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 gonococcus), 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 chlamydia 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. cephalexin 25 mg/kg 6–12-hourly for 7 days) may also be used if extensive pustules are found. If septicaemia is suspected, septic investigations and IV antibiotics after hospitalisation may be needed. Sometimes staphylococcal pustules can be difficult to distinguish from **erythema toxicum** (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 aminoglycoside) 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.

Warning: Excess and inappropriate antibiotic usage, besides being costly and generating a lot of nursing work, also leads to multi-drug resistance. Excess use can cause overt *Candida* infection (thrush), and also risks the eventual emergence of multi-drug-resistant organisms, especially in a hospital setting. The widespread use of ampicillin has caused many coliform organisms to become increasingly resistant to this antibiotic, while units that use cefotaxime extensively are starting to encounter serious *Enterobacter* and other multi-drug-resistant Gram-negative sepsis.

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 (with phenoxymethylpenicillin) 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 as 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 3.4.1 Antibiotics and other drugs for use in the neonatal period

Drug	Route	Single dose	Frequency	Postnatal age	Gestation
Ampicillin	IV, IM	50–100 mg/kg	12 hourly	< 7 days	Any
		50–100 mg/kg	8 hourly	7–21 days	Any
		50–100 mg/kg	6 hourly	> 21 days	Any
	Reduce dose frequency in severe renal impairment and birth asphyxia *Use higher doses in case of suspected Group B strep infection or meningitis*				

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

(*continued*)

Drug	Route	Single dose	Frequency	Postnatal age	Gestation
Miconazole	Oral gel		6 hourly		
	Skin ointment		6 hourly		
	This controls infection with Candida *('thrush') better than topical nystatin* *Use for at least 7–10 days*				
0.5% Aqueous Gentian violet	Apply		Once daily for 4 days		
Oral nystatin drops	PO	1 mL	6 hourly		
	Can be used to reduce heavy intestinal tract carriage				
Nevirapine	*See* Section 2.8.C for details on its use.				
Paraldehyde	Rectal	0.2 to 4 mL/kg	(***loading dose***)		
		Can repeat once 4–5 hours later			
	Use injection rectally or ready-diluted rectal solution *Dilution with an equal volume of olive oil or any edible oil* *If using a plastic syringe administer immediately* *IM injections may cause sterile abscessed (maximum 1 mL at one site)*				
Phenobarbitone	IV, IM, PO	20 mg/kg	(***loading dose***)	*followed by maintenance 12–24 hours later*	
	Slow IV over 5 minutes. Loading dose may be repeated by at 10 mg/kg if clinically indicated				
		3–5 mg/kg/24 hours	Once daily	*Once daily generally but with time may need to be give 12 hourly*	
	Monitor plasma levels *Therapeutic range: 15–30 mg/L although increasing up to 40 mg/L should be considered in resistant seizures*				
Phenytoin	IV, PO	15–20 mg/kg	(***loading dose***)		
	Give IV infusion over 20–30 minutes diluted in 10 mL of normal saline				
		1.5–3 mg/kg	12 hourly		
	Slow IV over 20–30 minutes *Usual maximum dose 7.5 mg/kg 12 hourly* *Therapeutic range 5–17 mg/L*				
	Oral dose is poorly absorbed particularly in premature infants *Wide variation in levels, so monitor and adjust dose and interval accordingly* *Measure trough level. May not reach steady state for up to 14 days*				
Procaine penicillin	IM	10 mg/kg	Single dose		
	Give to asymptomatic babies born to mothers with evidence of untreated syphilis				
		100 mg/kg	Once daily		
	Babies thought to be infected at birth are often give once daily for 10 days ***Never give this drug IV*** *Rarely repeated IM injections can cause a sterile abscess with subsequent muscle fibrosis and atrophy* *Alternatively* *IM or IV benzylpenicillin for 10 day (as specified above) is just as effective* Babies born to mother fully treated for syphilis need not further treatment after birth *(Maternal treatment = 1.8 grams or 2.4 mega units of benzathine benzylpenicillin at least 4 weeks before birth*				
Zidovidine	*See* Section 2.8.C for details on its use.				

Polycythaemia

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.

Polycythaemia 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
- 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 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 **airway** is open and that it remains so. Thick secretions from the throat may be cleared by intermittent suction using direct observation
- 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 SaO_2 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 as are available are 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.**
  - **Nasal cannulae optimise the efficient use of the available oxygen supply.** They prevent wasting of oxygen, and also make it very much easier to move and handle the infant without disrupting the supply. However, they make it rather more difficult to quantify how much oxygen is needed to control cyanosis.
- Infants should ideally have their actual oxygen needs monitored and adjusted at regular intervals.
  - Measuring the inspired oxygen concentration needed is one way of assessing the infant's changing condition. This can be done using a combination of a pulse oximeter with an inspired oxygen monitor placed in a head box next to the infant's face.
  - A simpler alternative for achieving this objective involves titrating the oxygen flow to maintain saturation on the pulse oximeter in the range 92–96% for term infants and lower, at 86–92%, for preterm infants, as described earlier.
- Keeping the infant fully clothed with a pulse oximeter attached makes it possible to dispense with any other monitoring of pulse and respiration, thus keeping the infant warm with minimal handling.
- If assisted ventilation is available and there is very severe respiratory failure, an arterial or capillary blood gas measurement can be helpful for determining the severity of respiratory acidosis and the need for ventilator support such as nasal continuous positive airway pressure (nCPAP) or intubation and ventilation.
- Infants with serious respiratory distress should not be offered feeds until their condition has stabilised. Support expression of milk by the mother so that she is ready to provide breast milk when her infant has recovered. In such situations, IV infusion of 10% glucose (60 mL/kg/day) is safest. If there are no facilities for IV infusion, breast milk or 10% glucose may be given in limited quantities (up to 60 mL/kg/day) by orogastric tube. **Nasogastric tubes may 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.

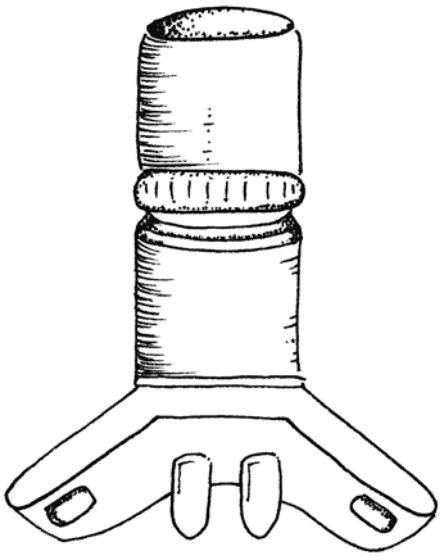


FIGURE 3.4.1 Nasal continuous positive airway pressure (CPAP) nasal prongs.

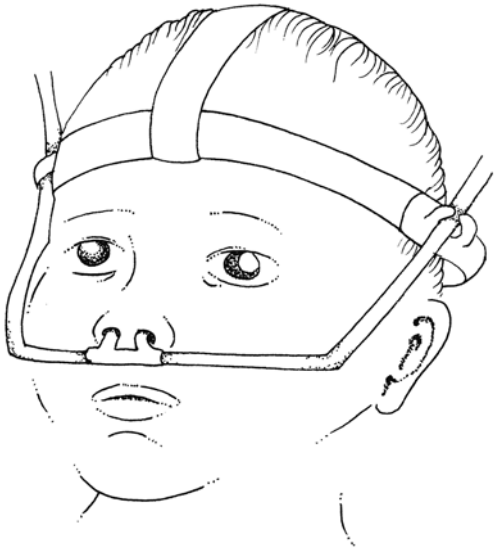


FIGURE 3.4.2 Nasal continuous positive airway pressure (CPAP) equipment in place.

Even though the 3-mm nasal cannulae that are normally used to provide supplemental oxygen can provide some CPAP, especially when higher flow rates are applied (6–8 litres/minute), there is a need for an air–oxygen blender to ensure that excessive and harmfully high concentrations of oxygen are not given. Humidification of the air–oxygen mixture is also required. Purpose-built CPAP systems with special nasal cannulae are better able to provide pressures of 5–8 cmH_2O (a system specially designed for resource-limited settings based on an oxygen concentrator has recently become available: www.diamedica.co.uk). In general, all that is then required is a controlled flow of blended humidified air and oxygen with a simple device for producing controlled adjustable CPAP. Regular nursing attention is necessary to make sure that the nasal cannulae remain correctly positioned and do not cause necrotic pressure damage to the nose. This is a skill that does not take long to acquire.

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

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 vasodilation, 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 unrelievable 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.

TABLE 3.4.2 Caffeine doses for apnoea of prematurity given intravenously or orally

Preparations	Each dose	Dose frequency	Notes on administration
Caffeine citrate	20 mg/kg	Loading dose	If oral dose is too large, divide into two and give 1 hour apart
	5–8 mg/kg maintenance	Once daily	
Caffeine base	10 mg/kg	Loading dose	Give IV loading dose over 30–60 minutes diluted as much as possible
	2.5–4 mg/kg maintenance	Once daily	

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 quantitating 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, and are an unreliable early indicator of the amount of 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 (phytomenadione or phytonadione) IV. If bleeding continues, give 20 mL/kg of fresh-frozen plasma (if available). Administer platelets if the count is < 60 000/mm^3. 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 sterilise 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.

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 previously had affected infants, or if she is known to have a hereditary haemolytic disorder, or if risk factors for infection or clinical signs of sepsis exist. Hepatosplenomegaly could be suggestive of congenital infection.

The following should suggest a high risk for haemolysis:

- red cell antibodies in the mother's blood
- a positive Coombs' or direct antiglobulin test on blood samples from the umbilical cord
- a packed cell volume > 65%, Hb > 220 g/litre
- a family history of G6PD deficiency or congenital spherocytosis
- a history of previous children being seriously jaundiced in the first week of life
- otherwise unexplained neonatal anaemia at birth (haemoglobin level < 140 g/litre or haematocrit < 40%).

Useful laboratory tests include the following:

- the mother's and infant's ABO and Rhesus blood groups. Save serum to cross-match if exchange transfusion is needed
- direct Coombs' test (if positive this indicates an isoimmune haemolytic anaemia)
- complete blood count and reticulocyte count (anaemia and reticulocytosis indicate haemolysis, high PCV suggests polycythaemia and/or abnormal white blood cells indicate possible infection)
- peripheral blood smear (abnormal red cell morphology and/or fragmented red cell forms suggest a specific red cell disorder and/or haemolysis)
- G6PD screen
- syphilis serology
- thyroid function tests (T_4, TSH)
- urine test for non-glucose-reducing substance (for possible galactosaemia)
- ultrasound scan of liver.

Treatment

The bilirubin treatment charts (*see* Table 3.4.3) show intervention levels for the two principal treatments (i.e. phototherapy and exchange transfusion). In general, the smaller the infant and the sicker the infant, the more urgent the need to intervene. Bilirubin in plasma is normally bound to albumin, but in a sick acidotic infant less binding occurs, and more 'free' bilirubin will be available to enter the central nervous system. Therefore consider intervening about 40 µmol/litres below the indicated line in such circumstances.

The specific bilirubin levels for which phototherapy and exchange transfusions need to be considered in infants born before 31 weeks' gestation are less certain. A frequently used guideline is to **initiate phototherapy when the bilirubin level approaches 85 µmol/litre/kg birth weight (which equals approximately 5 mg/dL/kg birth weight), and to consider an exchange transfusion for levels above 170 µmol/litre/kg birth weight (which equals approximately 10 mg/dL/kg birth weight)**.

TABLE 3.4.3 WHO recommendations (2012) for phototherapy and exchange transfusion levels of unconjugated bilirubin

	Phototherapy		Exchange transfusion	
Age	Healthy newborns ≥ 35 weeks' gestation	Newborns < 35 weeks' gestation or any risk factors	Healthy newborns ≥ 35 weeks' gestation	Newborns < 35 weeks' gestation or any risk factors
Day 1	Any visible jaundice		260 mmol/litre (15 mg/dL)	220 mmol/litre (10 mg/dL)
Day 2	260 mmol/litre (15 mg/dL)	170 mmol/litre (10 mg/dL)	425 mmol/litre (25 mg/dL)	260 mmol/litre (15 mg/dL)
Day 3+	310 mmol/litre (18 mg/dL)	250 mmol/litre (15 mgd/L)	425 mmol/litre (25 mg/dL)	340 mmol/litre (20 mg/dL)

Phototherapy

This uses light in the blue-green region of the spectrum (**not ultraviolet**) to convert bilirubin to its water-soluble isomer **lumirubin**, 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 breastfeeds 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 rise 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 haemolyse
- 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 serves to identify most of these infants.

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). Twice this amount of blood will be required. Do not exceed this (usually 1 bag of whole blood = 450 mL). Do not use blood that is more than 4 days old.
2 Check that the blood has either the same ABO group as the infant or is blood group O Rhesus-negative and in addition is compatible with the mother's serum.
3 Ensure that the infant is closely monitored throughout the procedure.
4 This is a sterile procedure, so gloves and gowns must be worn and universal precautions applied.
5 Secure umbilical vein access. Pass the umbilical venous catheter (UVC) as described in Section 8.4.B, and check its position with an X-ray (if available). Ideally it should be positioned in the vena cava just outside the right atrium, 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.
6 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.
7 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.
8 Make sure that the total blood in and out is recorded. Plan to spend 1.5–2 hours on the procedure.
9 Decide on the size of aliquot you will be exchanging 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.

   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.
10 Send the first aliquot for measurement of bilirubin, electrolyte and calcium concentrations.
11 Halfway through the procedure check the blood glucose, calcium and potassium concentrations.
12 Measure them again, together with the bilirubin concentration, at the end of the procedure.
13 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.

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 hypo- 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.

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.

The neonate with anaemia

Causes of anaemia

These include the following:

- haemorrhage
- twin-to-twin transfusion
- feto–maternal transfusion
- placental abruption
- haemolysis due to
  - Rhesus 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 Rhesus-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 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.

TABLE 3.4.4 Differentiating between seizures and jitteriness

Well but jittery infant	Infant with clonic seizures
No abnormal eye movements	Abnormal eye movements
No apnoea	Apnoea
No colour changes	Pallor or cyanosis
No heart rate changes	Tachycardia
Easily triggered by handling and stopped by gentle passive flexion of the affected limb	Independent of handling
Rhythmical movements	Jerky with fast and slow components that are not equal

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 + HCO_3). Normal anion gap = 5–17 mEq/litre in neonates
- **maternal substance abuse**, particularly opiate withdrawal
- **tetanus** remains a problem in many low-resource countries.

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) may aid diagnosis and treatment
- 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:
  - phenobarbitone, 20 mg/kg over 5 minutes IV or IM
  - paraldehyde, 0.2 mL/kg IM or 0.4 mL/kg rectally
  - diazepam 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 SaO_2 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.

Emergency treatment of hypoglycaemia

Hypoglycaemia is a common cause of seizures in infants. Ideally, do a rapid bedside test for low blood glucose levels and act accordingly, but if this test is not available then a test dose of 2 mL/kg of 10% glucose should be given IV or, if venous access is not available, intra-osseously.

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. 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 over 5 minutes or rectally in a dose of 500 microgram/kg. The rectal dose can be repeated once after 10 minutes if the infant is still fitting.

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 phenobarbitone) 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,**

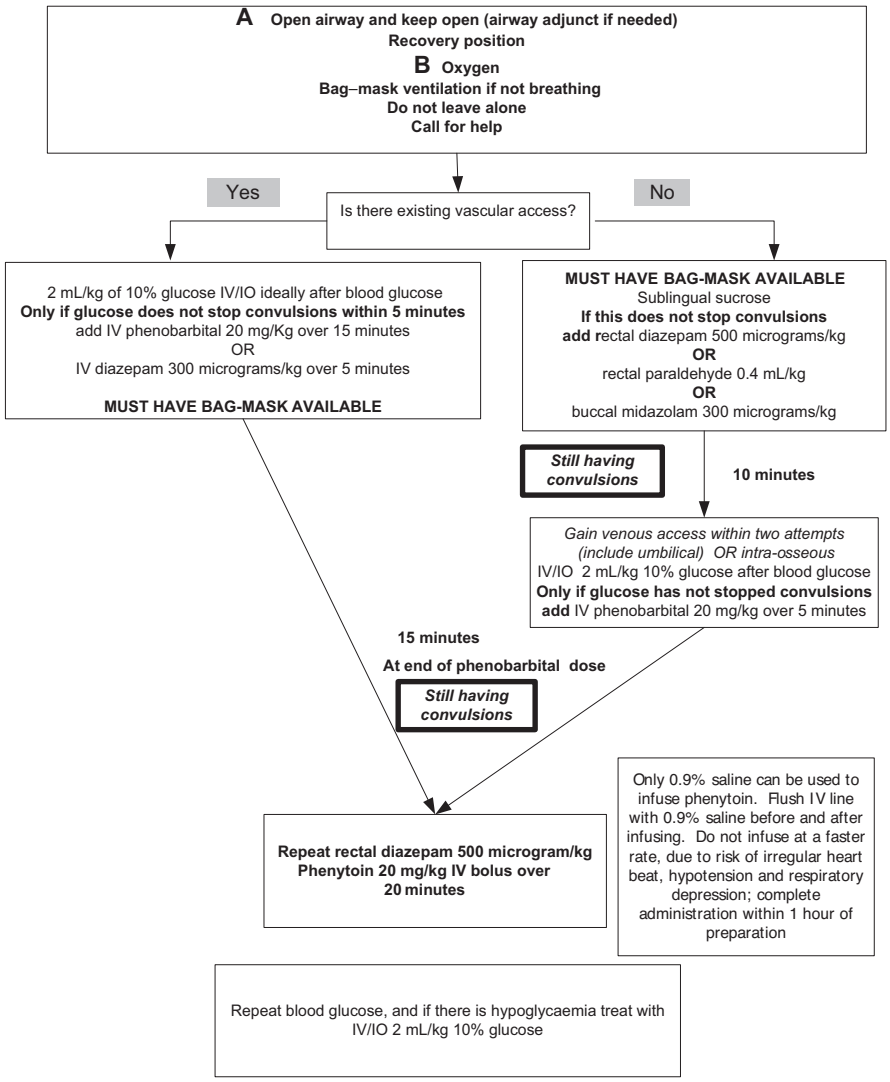


FIGURE 3.4.4 Pathway of care for a neonate who is having convulsions.

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 acidaemia, methylmalonic acidaemia, 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 intrauterine 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. Hypostop 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 spasm 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 irritant) 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 hyponatraemia, 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 3.4.5 Sarnat's grading of hypoxemic-ischaemic encephalopathy

	Mild (stage 1)	Moderate (stage 2)	Severe (stage 3)
Conscious level	Hyper-alert	Lethargic	Stuporose
Muscle tone	Normal	Hypotonic	Flaccid
Seizures	Rare	Common	Severe
Feeding	Sucks weakly	Needs tube feeds	Needs tube feeds or IV fluids
Respiration	Spontaneous	Spontaneous	Absent

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 stuporose 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 nasogastric 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.