Cortical blindness
Cortical blindness occurs following severe brain insults such as meningitis or cerebral malaria. The pupillary light reflex is normal, but the child cannot see. In some cases the vision gradually improves with time.

Management of blindness
- In the majority of cases, management is with rehabilitation and education rather than medical treatment.
- Cataracts and glaucoma in particular must be recognised and diagnosed early to preserve and save as much sight as possible.
- Most blind children have some sight and should have an opportunity to use low-cost visual aids. Simple aids, manufactured locally, may enable children to read and so transform their opportunities for education. These aids may consist of a strongly positive lens worn as spectacles or used as a stand magnifier.

Squint
Squint, or misalignment of the eyes (also known as strabismus), is common in children. When assessing a child for squint, consider the following:
- Does the child really have a squint? Look at the corneal light reflexes. If the reflection of light is in the same position in each eye, there is no squint, but if one is asymmetrical then that eye is squinting.
- Does the squint alternate? Cover the non-squinting eye. If the squinting eye moves to look at the light or object being held, and if the child can use either eye to fixate, then the squint alternates. This means that the vision is fairly good in each eye, and the treatment of the squint is purely cosmetic.
- If the squint does not alternate, is there any disease in the squinting eye? Test the pupillary light reflex and then dilate the pupils with mydriatic eye drops. Look for diseases such as cataract, retinal scar and in particular retinoblastoma. Refer the child for treatment if you find cataract or an abnormality in the retina. Treatment for retinoblastoma is urgent enucleation.
- Is there a refractive error, such as hypermetropia (long sight) or myopia (short sight)? This requires refraction tests.
- Is the squinting eye amblyopic (i.e. is there poor vision in the squinting eye)? At first, squints cause double vision (diplopia), which the child finds confusing. As time passes, the visual acuity in the squinting eye becomes permanently suppressed. The treatment for amblyopia is to force the child to use the squinting eye by wearing an occlusive patch over the healthy eye for about 1 hour a day for several weeks.

Amblyopia only develops in young children, and it can only be treated in children under 5 years of age. Surgery may be required, but should not be considered until eye disease and refractive errors have been excluded and amblyopia has been treated.

5.16 Neurological disorders

5.16.A Coma

Primary assessment and resuscitation
Coma is a medical emergency that requires immediate assessment and detection of reversible causes. Initial quick resuscitative measures are paramount, before undertaking a full clinical assessment of the child.

History
A detailed history should be taken from the parent or carer, with a focus on the following:
- possible cause of coma
- onset and progression of unconsciousness
- extent of injury
- signs of deterioration or recovery
- past medical history.

Examination
Clinical examination is directed towards identifying signs suggesting the following:
Section 5.16

- cause or causes
- extent of injury
- level of consciousness.

A general examination should be undertaken guided by the history and presumptive cause of coma. Identify immediate reversible causes of coma, such as hypoglycaemia, hyperglycaemia, trauma and seizures, and treat them accordingly (see Table 5.16.A.1). Look for rashes (e.g. purpura of meningococcal infection), tick bites, signs of trauma, evidence of ingestion of drugs or chemicals, and evidence of organ failure.

**TABLE 5.16.A.1 Causes of coma**

<table>
<thead>
<tr>
<th>Trauma</th>
<th>Head injury (consider child abuse)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure</td>
<td>Overt seizures, status epilepticus, subclinical seizures, post-ictal state</td>
</tr>
<tr>
<td>Infections</td>
<td><strong>Bacterial (meningitis):</strong> Streptococcus pneumoniae, Haemophilus influenzae, Neisseria meningitidis, streptococci (group B), Pseudomonas species, tuberculosis</td>
</tr>
<tr>
<td></td>
<td>Consider cerebral abscess</td>
</tr>
<tr>
<td></td>
<td><strong>Viruses:</strong> herpes simplex, Japanese B virus (JBV), herpes zoster</td>
</tr>
<tr>
<td></td>
<td><strong>Acute spirochaetemia:</strong> syphilis, Lyme disease, leptospirosis</td>
</tr>
<tr>
<td></td>
<td><strong>Parasitic:</strong> malaria, rickettsial</td>
</tr>
<tr>
<td></td>
<td><strong>Fungal:</strong> Cryptococcus neoformans</td>
</tr>
<tr>
<td>Metabolic</td>
<td><strong>Hypoglycaemia:</strong> Excess insulin or metabolic disorders</td>
</tr>
<tr>
<td></td>
<td><strong>Hyperglycaemia:</strong> Diabetic ketoacidosis</td>
</tr>
<tr>
<td></td>
<td><strong>Hypoxaemia</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Electrolyte imbalance:</strong> hyponatraemia or hypernatraemia</td>
</tr>
<tr>
<td></td>
<td><strong>Severe dehydration</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Severe malnutrition</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Organ failure:</strong> Liver failure, renal failure, Addison’s disease, respiratory failure</td>
</tr>
<tr>
<td></td>
<td><strong>Drugs:</strong> Opiates, salicylates, organophosphates, benzodiazepines, thiazines, aluminium in patients undergoing dialysis, barbiturates, antidepressants</td>
</tr>
<tr>
<td></td>
<td><strong>Other:</strong> Porphyrias, Reye’s syndrome</td>
</tr>
<tr>
<td>Poisoning</td>
<td><strong>Alcohol, recreational drugs, accidental/deliberate poisoning</strong></td>
</tr>
<tr>
<td>Tumours</td>
<td><strong>Primary:</strong> medulloblastoma, astrocytoma</td>
</tr>
<tr>
<td></td>
<td><strong>Secondary:</strong> leukaemias, sarcomas</td>
</tr>
<tr>
<td>Vascular</td>
<td><strong>Haemorrhage (subdural/subarachnoid), hypertension, hypotension, thrombosis, aortic stenosis, cardiac asystole, vacuities and collagen vascular syndromes</strong></td>
</tr>
<tr>
<td>Shock syndromes</td>
<td><strong>Sepsis, trauma, burns, peritonitis</strong></td>
</tr>
</tbody>
</table>

**Causes of coma**

The following features found on examination may be indicative of specific causes.

- **Pulse:** bradycardia may indicate raised intracranial pressure (RICP) or reflect the effects of poisons or drug overdose.
- **Blood pressure:** hypertension may indicate hypertensive encephalopathy or signs of RICP; hypotension occurs in shock.
- **Temperature:** this may indicate sepsis.
- **Respiratory pattern:** this may be irregular due to brainstem lesion or RICP, rapid due to acidosis or aspirin ingestion, or slow due to opiate ingestion.
- **Pupil size and reactivity:** pupil may be small due to opiate ingestion, or large due to amphetamine ingestion or RICP; pupils may be unequal and/or unreactive due to RICP.
- **Skin rashes:** these may be due to infections (e.g. meningococcal septicaemia, dengue fever).
- **Breath odour:** this may be caused by diabetic ketoacidosis, alcohol ingestion, or inborn errors of metabolism.
- **Hepatomegaly:** this may indicate Reye’s syndrome or other metabolic disorders.

- **Fundi:** Papilloedema may indicate RICP; dilated veins may indicate RICP; retinal haemorrhages may indicate trauma or malaria; and exudates, retinal whitening and orange coloration of vessels may indicate other signs of malaria retinopathy.
- **Posture/oculocephalic reflexes** (see Figure 5.16.A.2): these are abnormal in RICP.

**Neurological examination**

The purpose of the neurological examination is not only to identify features of raised intracranial pressure (including herniation syndromes), focal deficits (e.g. space-occupying lesions) and lateralising signs (hemiplegic syndromes), but also to establish a baseline for comparison on subsequent evaluations. Examination may also help to provide prognostic information.

**Level of consciousness**

Many methods exist for establishing the level of consciousness. Two that are commonly used are the AVPU system, and coma scales.
AVPU system
A = Alert
V = Response to Voice command
P = Response to Pain
U = Unresponsive

In this test:
- 'A' means that the patient is awake, alert and interacting with the environment.
- 'V' means that the patient appears to be asleep, but when spoken to opens their eyes.
- 'P' indicates that there is no response to a voice, but a painful stimulus will produce some response (e.g. a withdrawal).
- 'U' indicates that the patient is completely unresponsive to any stimulus.

Figure 5.16.A.1 shows sites for the application of a painful stimulus in order to elicit a response.

Coma scales
These have been devised to measure the depth of coma and improve agreement between clinicians. Coma scales can also be used to monitor progression or regression of the depth of coma. Although many different versions exist, the most widely used ones are the paediatric modification of the Glasgow Coma Scale (for children between the ages of 4 years and 15 years) and the Adelaide Coma Scale (for children under 4 years of age).

Pupillary reactions
Use a bright torch and from the side shine the light on the cornea of each eye in turn. Observe for pupillary size...
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(constricted or dilated) and the reaction to light (normal, sluggish or non-reactive). While doing this test consider the effect of drugs used in treatment (e.g. benzodiazepines).

**Ocular movements**
- Eyelid response.
- Corneal response.

**Oculocephalic reflexes (doll’s head manoeuvre)**
In the normal state while turning the head sharply to one side, the eyes move to the opposite side. In the abnormal state the eyes only partly deviate or remain fixed (see Figure 5.16.A.2).

*Before performing this test it is important to check that there is no cervical injury.*

**Oculo-vestibular or caloric response**
Tilt the head forward at 30 degrees, and instil ice cold water in the ear. In the normal state the eyes turn to the side of the stimulus (see Figure 5.16.A.2). This manoeuvre tests brainstem function.

*Before doing this test it is important to ascertain that the tympanic membrane is intact and there is no wax in the external meatus.*

**Motor function and activity**
Observe for tremors, abnormal movements and tone. The presence of hypertonia or hypotonia indicates a neuromuscular problem. Exaggerated deep tendon reflexes and clonus may indicate an upper motor neuron type lesion, whereas their absence may indicate a lower motor neuron type problem.

Abnormal postures in an unconscious patient (e.g. decerebrate or decorticate rigidity) may indicate brain damage at cerebral or cortical level (see Figure 5.16.A.3).

**Respiratory pattern**
Abnormal variations in breathing pattern may be difficult to identify in children. The following may be sought for:
- irregular: consider seizures
- Cheyne–Stokes: raised intracranial pressure, cardiac failure
- Kussmaul breathing: acidosis, central neurogenic hyperventilation, midbrain injury, tumour or stroke

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![IMAGE](a) Doll’s head manoeuvre
![IMAGE](b) Ice-water caloric response

**FIGURE 5.16.A.2** Oculocephalic reflex (doll’s head manoeuvre) and oculo-vestibular response (ice-water caloric response).

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![IMAGE](a) No response. (b) Decorticate. (c) Mixed decorticate/decerebrate. (d) Decerebrate.

**FIGURE 5.16.A.3** Abnormal postures elicited in an unconscious patient by a painful stimulus. (a) No response. (b) Decorticate. (c) Mixed decorticate/decerebrate. (d) Decerebrate.
Investigations
These are guided by the presumptive clinical diagnosis. Essential tests may include the following:
- Clinical chemistry for blood glucose, electrolytes, creatinine, urea, blood gases and liver function tests (including clotting profile).
- Blood film for malarial parasites.
- Haematological parameters such as full blood count and peripheral blood film. Toxicological tests for salicylates, organophosphates, opiates, alcohol and paracetamol.
- Blood cultures.
- Lumbar puncture if there is a high index of suspicion of central nervous system infection. This should be delayed if there are features suggestive of raised intracranial pressure, the child is too sick, there is infection at the puncture site, there is a bleeding tendency or there is rash of meningococcal septicaemia. The child should be given antibiotics to cover the possibility of bacterial meningitis, and lumbar puncture should be deferred until a later date.
- Chest X-ray if there is suspicion of tuberculosis or severe pneumonia.

If facilities are available, consider the following:
- Computerised tomography (CT) scan or preferably magnetic resonance imaging (MRI) scan. These are particularly useful for detecting space-occupying lesions and traumatic injury. Contrast dye should be given if an infection or a tumour is suspected.
- Plasma ammonia level and plasma and CSF lactate levels.
- Urine and plasma for organic and amino acids.

Other investigations (if available)
These will depend on the cause of the coma, and include the following:
- Hormonal assays: thyroid hormones, cortisol, ketosteroids (adrenal insufficiency);
- Electroencephalography (EEG): this may be helpful in detecting seizures or encephalitis. It may also be useful in establishing the prognosis;
- Evoked potential responses: these may help to detect brainstem lesions;
- Neuroimaging: magnetic resonance angiography or MRI or CT scan;

Differential diagnosis
A simple way to establish a cause would be to determine whether it is primarily intra- or extracranial. Intracranial conditions may be subdivided into those with or without focal signs. Extracranial causes include encephalopathies arising from metabolic derangements or exogenous toxins. The common causes are listed in Table 5.16.A.1.

Management
The prognosis depends on the aetiology, age of the patient, and level of consciousness at presentation. The presumptive cause of coma guides the treatment and the initial response to appropriate interventions.

See subsequent subsections and disease-specific sections (e.g. meningitis (Section 5.16.B), malaria (Section 6.3.A.d), tuberculosis (Section 6.1.N)). Consider the following interventions for general coma management.

Immediate general management: overview – see relevant sections for detail
ABC support of vital functions (see Section 1.11)
- Support respiration if respiratory effort is not adequate to maintain the desired oxygen saturation and/or carbon dioxide excretion.
- Support circulation to maintain adequate cerebral perfusion (aim to keep systolic blood pressure at normal values for age, and avoid hypotension).
- Assess for and treat hypoglycaemia (see Section 5.8.B)
- Maintain normoglycaemic state: be cautious about administering insulin to hyperglycaemic patients, as hyperglycaemia may be stress induced.
- Assess and maintain electrolyte balance: avoid hyponatremia: use Ringer-lactate or Hartmann’s solution, both with added glucose (50 mL of 50% glucose in 500 mL of crystalloid gives a 5% solution, 100 mL gives a 10% solution). If possible keep serum sodium levels in the normal range (135–145 mmol/litre).
- Treat seizures if present and give prophylactic anti-convulsants if the child has repeated seizures (see Section 5.16.E and 5.16.D).
- Treat for meningitis if this is an acute illness (see Section 5.16.B).
- Treat for cerebral malaria if history and test confirm (see Section 6.3.A.d).
- Insert a nasogastric tube to aspirate the stomach contents. Perform gastric lavage in circumstances such as drug or chemical ingestion.
- Assess for and treat hypoglycaemia (see Section 5.8.B)
- Regulate the body temperature (avoid hyperthermia, i.e. temperature > 37.5°C).
- Undertake appropriate medical management of raised intracranial pressure.
- Support ventilation (maintain a pCO$_2$ of 3.5–5.0 kPa).
- Reduce raised intracranial pressure by using the following:
  - Mannitol: 250–500 mg/kg, i.e. 1.25–2.5 mL/kg of 20% IV over 15 minutes; repeat as required based on response and clinical signs (maximum total dose 2 grams/kg);
  - Hypertonic saline: 3 mL/kg of 3% sodium chloride as required, to a maximum increase of plasma sodium level of 10 mmol/litre.
- Dexamethasone (for life threatening cerebral oedema surrounding a space-occupying lesion):
  - Child under 35 kg: 20 mg initially then 4 mg 3 hourly for 3 days, then 4 mg every 6 hours for 1 day, then 2 mg every 6 hours for 4 days then decrease by 1 mg daily.
  - Child over 35 kg: 25 mg initially, then 4 mg 2 hourly for 3 days, then 4 mg 4 hourly for 1 day, then 4 mg 6 hourly for 4 days then decrease by 2 mg daily.
- Catheterisation for bladder care and urine-output monitoring.
- Plan for continued regular clinical assessment, mainly nursing observations of pulse, respiration, blood pressure and level of consciousness.

Intermediate general management
- Prevent the child from falling out of the bed.
- Nutritional support: give enteral nutrients to prevent malnutrition during periods of unconsciousness.
- Skin care: prevent bed sores by turning the patient.
- Use eye padding to avoid xerophthalmia.
Neurological impairment and hearing loss.

Clinical

Diagnosis of meningitis

- In infants and children: fever, neck stiffness, bulging fontanelle (in infants), vomiting, headache, altered consciousness and possibly convulsions. In meningococcal meningitis there may be a maculopapular or petechial rash.

- In neonates: signs are more subtle and non-specific and include poor feeding, hyper- or hypothermia, convulsions, apnoea, irritability and a bulging fontanelle.

Pathogens that cause meningitis

- Worldwide, the commonest pathogens are Streptococcus pneumoniae, Haemophilus influenzae and Neisseria meningitidis. Local incidence varies, and in many countries has been altered by vaccine availability.

- Neonatal meningitis is most commonly caused by group B streptococcus (Streptococcus agalactiae) and E. coli. Other coliforms and streptococci, as well as Neisseria meningitidis and Listeria monocytogenes, may also occur. Listeria monocytogenes and Group B streptococci cause both early and late neonatal infections, and may have a better prognosis than infections caused by coliforms. Neonatal meningitis has a poorer prognosis than most community-acquired meningitis of later childhood.

Long-term management

Provide rehabilitation, family education and support for disabilities that may arise. Seizures need to be looked for and treated.

Cerebral malaria (see Section 6.3.A.d)

In endemic areas, malaria is by far the commonest cause of coma. The majority of children affected are in the second year of life. Onset of coma is dramatic: the child may be well in the morning and comatose by the evening. The fatality rate is high even after prompt administration of antimalarial drugs. Neurological sequelae (i.e. hemiplegia, spasticity, blindness, deafness) may occur.

The incidence of bacterial meningitis is about ten times higher in resource-limited than in well-resourced countries, and the outcome is worse. Mortality is reported to be 12–44% in resource-limited countries, and less than 5% in well-resourced countries. In the former, sequelae are under-reported and frequent (20%), including significant neurological impairment and hearing loss.

Other pathogens

Consider tuberculous meningitis in children who do not respond to the initial antibiotics, particularly if two or more of the following are present: history more than 7 days, HIV known or suspected, patient remains unconscious, CSF has a moderately high white blood cell count (typically > 300–500/mL, mostly lymphocytes), elevated protein levels (0.8–4 grams/litre) and low glucose levels (< 1.5 mmol/litre), Chest X-ray suggests tuberculosis, optic atrophy, focal neurological deficit or extrapyramidal movements (see Section 6.1.N).

Children with HIV are more prone to meningitis and septicaemia caused by Streptococcus pneumoniae and Salmonella species, and relapse is more frequent. Non-typhoidal Salmonella (NTS) meningitis is common in post-malarial anaemia and malnutrition, and requires lengthy antibiotic treatment (at least 1 month).

Fungal infections (e.g. Cryptococcus neoformans),
phenicol resistance is emerging. Intermediate penicillin resistance may occur and chloramphenicol is widespread in Asia and some parts of Africa, and third-generation cephalosporins are again in bacterial meningitis where there is delay in presentation and antibiotics have already been given some hours earlier. There is no evidence that corticosteroids are helpful in bacterial meningitis where there is delay in presentation and antibiotics have already been given some hours earlier. Steroids are generally not indicated in meningococcal disease.

Do not use steroids in the newborn or in children younger than 3 months, or in patients with suspected cerebral malaria or viral encephalitis.

**Nursing and ongoing care**

**Monitoring**
- Careful observation is essential.
- Raised ICP and shock are the most severe complications. Early recognition and treatment are essential.
- Daily weights and urine specific gravity aid the assessment of fluid requirement.
- Temperature, pulse, blood pressure, capillary refill time (normal value is less than 3 seconds), respiratory rate

**TABLE 5.16.B.1 Bacterial meningitis: typical findings in cerebrospinal fluid**

<table>
<thead>
<tr>
<th>Condition</th>
<th>White cell count (&lt;10^9/L)</th>
<th>Cell differential</th>
<th>Protein (g/litre)</th>
<th>Glucose (mmol/litre)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>0.5</td>
<td>PMN ≤ 2 but &lt; 15 in neonate</td>
<td>&lt; 0.5</td>
<td>Two-thirds blood glucose</td>
</tr>
<tr>
<td>Acute bacterial</td>
<td>100 to &gt; 300,000</td>
<td>Mostly PMN. Monocytes in Listeria infection</td>
<td>&gt; 1.0</td>
<td>&lt; 2.5</td>
</tr>
<tr>
<td>Meningitis*</td>
<td></td>
<td>Lymphocytes early but also PMN</td>
<td>&gt; 1.0</td>
<td>&lt; 2.5, Usually 0</td>
</tr>
<tr>
<td>Tuberculous</td>
<td>50–500 sometimes higher</td>
<td>Mostly lymphocytes PMN early in the disease</td>
<td>&gt; 0.5</td>
<td>Normal</td>
</tr>
<tr>
<td>Meningitis</td>
<td>usually &lt; 500</td>
<td>WBC and RBC</td>
<td>RBC/WBC =500/1</td>
<td>Increases by 0.001 g/L per 1000 RBC</td>
</tr>
<tr>
<td>Cerebral abscess</td>
<td>10–200</td>
<td>PMN or lymphocytes</td>
<td>&gt; 1.0</td>
<td>Normal</td>
</tr>
<tr>
<td>Traumatic tap</td>
<td>WBC and RBC</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Bacterial meningitis can occur without a pleocytosis. Partial treatment will alter these findings. PMN, polymorphonuclear granulocytes; WBC, white blood cell count; RBC, red blood cell count.

mostly in children with HIV, often cause severe headache without neck stiffness. Lumbar puncture may improve symptoms.

**Therapy**

Antibiotic choices depend upon activity against the infecting organism, CSF penetration, cost and availability of the antibiotic, route of administration, and local patterns of antibiotic resistance (see Tables 5.16.B.2, 5.16.B.3 and 5.16.B.4). If national guidelines are available they should be followed. The degree of diagnostic certainty is also important, especially in the case of meningitis with minimal rash, as treatment should be given for all the common causes of bacterial meningitis according to the child’s age group.

It is important to know the antimicrobial sensitivities in the local area. Antimicrobial resistance has emerged among the three major bacterial pathogens that cause meningitis outside the neonatal period. In the meningococcus, intermediate penicillin resistance may occur and chloramphenicol resistance is emerging. Haemophilus influenzae infections are also frequently beta-lactamase resistant, and chloramphenicol resistance has been described. Third-generation cephalosporins are therefore the drugs of choice for both organisms, although if they are precluded on the basis of cost, chloramphenicol (plus penicillin or ampicillin) is an alternative. Pneumococci resistant to penicillin and to chloramphenicol are widespread in Asia and some parts of Africa, and third-generation cephalosporins are again the drugs of choice. However, pneumococcal resistance to third-generation cephalosporins may occur. Treatment of these strains requires the addition of vancomycin or rifampicin to therapy with third-generation cephalosporins.

Third-generation cephalosporins (ceftriaxone or cefotaxime) may be necessary first-choice antibiotics in some areas. In neonates, cefazidime, which is also active against Pseudomonas infections, may be the most suitable drug.

The antibiotic regimen should be rationalised once culture and sensitivity results for the infecting organism become available.

During confirmed epidemics of meningococcal meningitis and where there are other signs such as petechial rash, lumbar punctures are unnecessary. If resources are very limited, oily chloramphenicol (100mg/kg IM) as a single dose of up to 3 grams can be curative. If the oily dose is too large for one buttock, divide it into two doses. Alternatively, single-dose IM ceftriaxone, 100mg/kg up to 4 grams, may be recommended.

**Duration of therapy**

Neonates require 14–21 days of treatment. In infants and children, a 10-day course is usually adequate for pneumococcal and Haemophilus infections, and a 7-day course for meningococcal infections. Seven days of ceftriaxone treatment is usually sufficient. Where antibiotic availability is very limited, some authors have used 5–7-day courses of ceftriaxone for uncomplicated meningococcal, pneumococcal or Haemophilus meningitis in infants and children.

**Corticosteroids**

Dexamethasone may reduce the incidence of neurological sequelae and deafness in bacterial meningitis, although studies in resource-limited countries have been inconclusive. The usually recommended dose of dexamethasone is 0.15mg/kg four times daily for 4 days (or if this is not available, prednisolone 2mg/kg per day for 4 days). The first dose should be given concurrently with, or a maximum of 4 hours after, first antibiotic administration. There is no evidence that corticosteroids are helpful in bacterial meningitis where there is delay in presentation and antibiotics have already been given some hours earlier. Steroids are generally not indicated in meningococcal disease.
and effort, conscious level and pupillary responses should be monitored frequently after admission (4- to 6-hourly), particularly in patients with meningococcal disease (see Section 6.1.G). Pulse oximetry is valuable (if available) for monitoring oxygenation and for identifying early evidence of respiratory compromise.

- A critical care pathway is an ideal way of incorporating observations, treatment and laboratory findings on one chart. Doses and treatments can be standardised and incorporated on the chart.
- Ideally, if available, monitor electrolytes (sodium, potassium, calcium and magnesium, urea and/or creatinine) and replacement of fluid deficits (hyponatraemia due to excessive IV administration of hypo-osmolar solutions is common, and can predispose to seizures). Monitoring of full blood count and coagulation screen should be undertaken regularly if these are initially abnormal.

Supportive care

Fluids

Maintenance fluids should be given once any shock or dehydration has been corrected, initially by the IV route but later by nasogastric tube or orally. The degree of dehydration may be underestimated, and deep breathing may be a sign of acidosis. Low serum sodium levels often occur in meningitis. Avoid over-hydration by maintaining careful fluid balance, and in particular avoid IV fluids with low sodium levels such as 5% glucose. Use Hartmann’s solution with added glucose (5–10%) or a similar proprietary fluid. If electrolytes are being measured, maintain serum Na⁺ in the high normal range and above 135 mmol/litre.

Fluid balance

Urine output should be monitored, particularly in the unconscious child. Weighing nappies can be useful in the infant or young child. Catheterisation, unless undertaken in an aseptic way, can lead to urinary tract infection and is unwise if resources are limited.

Cerebral support

Seizures must be controlled with anticonvulsants, but there are no data to support routine use of prophylactic anticonvulsants (see Section 5.16.D and Section 5.16.A on seizures and coma).

- If there is a high fever (> 39°C), apply temperature reduction methods, including paracetamol.
- Blood glucose levels must be monitored every 4 hours, particularly in the infant and young child. Hypoglycaemia must be considered in any child with seizures or altered consciousness and corrected as follows: give 2–5 mL/kg of 10% glucose IV and recheck blood glucose levels 30 minutes later. If they remain low (less than 2.5 mmol/litre), repeat the IV glucose dose (5 mL/kg) and ensure that glucose is included in any infusion.

Gastric and airway protection

A nasogastric tube may be helpful in unconscious children or in those who are vomiting, in order to protect the airway. A small amount of milk (1 mL/kg/hour) passed down this nasogastric tube may prevent gastric erosions. Gastric protection may also be provided by using drugs such as ranitidine or omeprazole (if available).

Nutritional support

A nasogastric tube should be inserted if the child is unable to feed orally after 24 hours. Continue expressed breast milk if the child is breastfed, or give milk feeds 15 mL/kg every 3 hours.

Bedside care

Turn an unconscious child 2-hourly, keeping them dry, and prevent overheating. Insert a nasogastric tube if there is persistent vomiting.

- Include the mother or family members in progress reports, and make them part of the caring team.

Complications

- Convulsions with or without hypoglycaemia (see Sections 5.16.D and E for management of convulsions).
- If fever does not settle within 48 hours and if the child’s condition deteriorates or is not improving, repeat lumbar puncture and review the CSF findings, and consider drug resistance and tuberculous meningitis.
- If the fontanelle is patent, monitor the head circumference daily to detect hydrocephalus. Consider a head ultrasound scan to look for ventriculitis, ventricular dilatation, subdural effusion or brain abscess. In older children, computed tomography or magnetic resonance imaging may be helpful for assessing the size and position of any intracranial lesion (if available and if intervention is possible).
- Aspiration pneumonia may occur in the unconscious child.
- Hydrocephalus, deafness, visual loss, epilepsy and neurological deficits may develop and be evident either early in disease or at follow-up. Around 20% of cases worldwide will develop serious sequelae.

Follow-up

- Undertake hearing tests in all children, and neurological assessments and head circumference measurements (in infants) on discharge from hospital and at post-discharge visits 1 month and 6 months after recovery. In the absence of effective treatment, a deaf child will require training in lip-reading and sign language, and they and their family will need significant support.
- New sequelae are unlikely to develop after discharge, but may have been missed.
- Physiotherapy may be required if neurological sequelae have resulted in contractures.

Immunisation to prevent meningitis

Highly effective protein-conjugated polysaccharide vaccines are available against Haemophilus influenzae and several serogroups of Streptococcus pneumoniae and Neisseria meningitidis. They are effective in young infants as well as in older children and adults. If they are unavailable, plain polysaccharide vaccines against Neisseria meningitidis and Streptococcus pneumoniae may be provided. Vaccine availability may be limited in low-income countries.
### TABLE 5.16.B.2 Antibiotic choices by age group for immediate treatment and where the infecting organism is not known

<table>
<thead>
<tr>
<th>Age group</th>
<th>Probable pathogen</th>
<th>Antibiotics of choice</th>
<th>Alternative antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonates</td>
<td>Gram-negative bacteria</td>
<td>Ampicillin plus third-generation cephalosporin: cefotaxime/ceftriaxone</td>
<td>Penicillin (but use ampicillin if Listeria is suspected) plus gentamicin or ceftazidime</td>
</tr>
<tr>
<td></td>
<td>Group B streptococci</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Listeria</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neisseria meningitidis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Streptococcus pneumoniae</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Haemophilus influenzae</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 month to 5 years</td>
<td>Neisseria meningitidis</td>
<td>Third-generation cephalosporin: cefotaxime/ceftriaxone</td>
<td>Chloramphenicol plus ampicillin Add vancomycin or rifampicin if there is S. pneumoniae resistance</td>
</tr>
<tr>
<td></td>
<td>Streptococcus pneumoniae</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Haemophilus influenzae</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children over 5 years</td>
<td>Neisseria meningitidis</td>
<td>Third-generation cephalosporin: cefotaxime/ceftriaxone</td>
<td>Chloramphenicol plus ampicillin Add vancomycin or rifampicin if there is S. pneumoniae resistance</td>
</tr>
<tr>
<td></td>
<td>Streptococcus pneumoniae</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For all age groups, if there is no improvement after the third day, look for evidence of cerebral abscess or subdural effusions, where relevant. These would manifest as continuing fever, localising neurological signs or decreased consciousness. Ultrasound or CT (if available) would be helpful. Seek neurosurgical advice (if available). Repeat the lumbar puncture, looking for evidence of improvement such as a reduced white cell count or increased CSF glucose levels. Add in a third antibiotic. Consider other sites of infection, such as cellulitis, pneumonia with empyema, arthritis or osteomyelitis.

Give all antibiotics parenterally (IV or IM) for at least 3 days. Chloramphenicol can then be given orally if the child is significantly improved.

The IM route may be used if the IV route cannot be accessed. High oral doses of chloramphenicol can be used if there is no alternative, but are not recommended for infants under 3 months of age.

### TABLE 5.16.B.3 Antibiotic therapy in bacterial meningitis where the infecting organism is known

<table>
<thead>
<tr>
<th>Organism</th>
<th>Antibiotics of choice</th>
<th>Alternative antibiotics</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>Ceftriaxone/cefotaxime</td>
<td>Ampicillin plus chloramphenicol*</td>
<td>10–14 days</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>Ceftriaxone/cefotaxime</td>
<td>Ampicillin/benzylpenicillin plus chloramphenicol*</td>
<td>10–14 days</td>
</tr>
<tr>
<td>Neisseria meningitidis</td>
<td>Ceftriaxone/cefotaxime</td>
<td>Benzylpenicillin plus chloramphenicol*</td>
<td>7 days</td>
</tr>
<tr>
<td>Gram-negative bacilli (including <em>E. coli</em>)</td>
<td>Ceftriaxone/cefotaxime with or without gentamicin</td>
<td>Ampicillin plus gentamicin or chloramphenicol*</td>
<td>At least 21 days²</td>
</tr>
<tr>
<td><em>Salmonella enteritidis</em></td>
<td>Ceftriaxone/cefotaxime plus IV ciprofloxacine (if available)</td>
<td>Meropenem or chloramphenicol* plus ampicillin (may be incomplete cover and excess mortality compared with cephalosporins)</td>
<td>At least 21 days²</td>
</tr>
<tr>
<td><em>Listeria monocytogenes</em></td>
<td>Ampicillin plus gentamicin</td>
<td></td>
<td>10–14 days</td>
</tr>
<tr>
<td>Group B streptococcus</td>
<td>Benzylpenicillin plus gentamicin or ceftriaxone/cefotaxime</td>
<td></td>
<td>10–14 days</td>
</tr>
<tr>
<td><em>Staphylococcus species</em></td>
<td>Flucloxacillin plus gentamicin</td>
<td>Flucloxacillin plus chloramphenicol*</td>
<td>10–14 days</td>
</tr>
</tbody>
</table>

* Chloramphenicol should be used with caution in children under 3 months of age. Monitoring of serum levels is advisable in this group.

† *Streptococcus pneumoniae* infections that are resistant to penicillins and cephalosporins are increasingly prevalent. If resistance is suspected, add either rifampicin or vancomycin (see doses below).

² Gram-negative infections are difficult to treat and have a high rate of sequelae. A repeat lumbar pucture to ensure response to antibiotics may be indicated if the clinical picture is not improving.

The choice of antibiotic depends on local antibiotic resistance patterns, national guidelines and drug availability.

Give all antibiotics parenterally for at least 3 days.

Once culture and sensitivity results are available, empirical antibiotics should be changed accordingly.

Do not delay antibiotic therapy if cephalosporins are unavailable; use the next most appropriate antibiotic combination.
Bacterial meningitis: prophylaxis for contacts
*Neisseria meningitidis*
Give rifampicin to all household contacts for 2 days as follows: adults, 600 mg twice daily; children aged 1 month to 12 years, 10 mg/kg twice daily; neonates, 5 mg/kg twice daily (see Section 6.1.G for alternative antibiotics and vaccination regimes).

In many countries, rifampicin is protected from use in any disease other than TB. In this case consider giving ciprofloxacin orally as a single dose as follows: adults, 500 mg; children aged 5–12 years, 250 mg; children aged 1 month to 5 years, 125 mg.

*Haemophilus influenzae*
Give rifampicin to all non-vaccinated household contacts for 4 days at the doses stated above.

### TABLE 5.16.B.4 Bacterial meningitis: antibiotic doses

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Route</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>IV</td>
<td>100 mg/kg/4–6 hourly (max. single dose 2 g every 4 hours)</td>
</tr>
<tr>
<td>Benzylpenicillin</td>
<td>IV</td>
<td>50 mg/kg/4 hourly (max. single dose 2.4 g)</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>IV</td>
<td>50 mg/kg/6 hourly (max. daily dose 12 g)</td>
</tr>
<tr>
<td>Ceftriazone</td>
<td>IV or IM</td>
<td>80 mg/kg/24 hours once daily* (max. single dose 4 g) large doses preferably IV</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>Oral</td>
<td>25 mg/kg 6 hourly*</td>
</tr>
<tr>
<td></td>
<td>IM</td>
<td>An oil preparation of chloramphenicol is available and is usually used in a single dose of 50–100 mg/kg with a maximum dose of 3 g. The dose may be repeated after 24 hours. It is recommended only if more suitable alternatives are unavailable</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Flucloxacillin or cloxacillin N 50 mg/kg 6 hourly (max. dose 8 g/day)</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>IV or IM</td>
<td>1 month-12 years 2.5 mg/kg 8 hourly† (see Section 3.4 for neonatal doses)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>IV</td>
<td>10 mg/kg 8 hourly (10 mg/kg/12 hourly in the neonate)</td>
</tr>
<tr>
<td>Meropenem</td>
<td>N</td>
<td>1 month to 12 years body weight &lt; 50 kg; 40 mg/kg 8 hourly; body weight &gt; 50 kg; 2 g every 8 hours (maximum single dose 2 g) by slow IV injection over 5 minutes 12–18 years 2 g every 8 hours</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>N</td>
<td>15 mg/kg loading dose and then 10 mg/kg 6 hourly‖ (total daily dose should not exceed 2 g)</td>
</tr>
</tbody>
</table>

* Ideally, 80 mg/kg 12-hourly should be given for the first two doses, followed by 80 mg/kg/24 hours.
† Although not recommended in children under 3 months old or in malnourished children, the evidence for this is slight.
‖ Monitoring of drug levels is strongly advised if at all possible, with adjustment of doses.

For doses in the neonatal period, see Section 3.4

### 5.16.C Encephalitis

**BOX 5.16.C.1 Minimum standards**
- ABCD and intensive care.
- Lumbar puncture, basic clinical chemistry and haematology.
- Temperature control.
- Anticonvulsants.
- Antiviral and antibiotic drugs.

**Introduction**

Encephalopathy refers to a clinical syndrome of reduced consciousness for which there may be a variety of causes. Encephalitis is an inflammatory process involving primarily the brain parenchyma, but sometimes also the meninges (meningoencephalitis) or spinal cord (encephalomyelitis). Primary encephalitis refers to cases in which the causative agent invades and replicates within the nervous system, whereas in post-infectious encephalitis the clinical manifestations appear to be caused by an immunological response to the agent. In practice it can be difficult to differentiate between the two entities. This subsection focuses on primary infectious encephalitis.

**Aetiology**

- In many instances no specific aetiological agent can be identified.
- Geographical location and seasonal variation influence the frequency of infection with specific organisms.
- Viruses are the responsible pathogen in the majority of cases (see Table 5.16.C.1).
- Arboviruses are an important cause of encephalitis worldwide, but the major contributor within the arbovirus group, the Japanese encephalitis virus (JEV), is limited to Asia and the Pacific Rim.
- Enteroviruses are a common seasonal cause of encephalitis in Europe and the USA. In the last decade there have been periodic large outbreaks of enterovirus 71 infections in Asia, and the overall incidence of enterovirus 71 is increasing in this region.
### TABLE 5.16.C.2  Suggested investigations in children with acute encephalitis, with reference to differential diagnosis

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Relevance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood glucose levels</td>
<td>Hypoglycaemia (common in infants and children with severe infections and poor oral intake/vomiting)</td>
</tr>
<tr>
<td></td>
<td>Hyperglycaemia (diabetes)</td>
</tr>
<tr>
<td></td>
<td>Metabolic encephalopathies, inborn errors of metabolism</td>
</tr>
<tr>
<td>Full blood count, blood film</td>
<td>Cerebral malaria (in endemic regions, returning travellers, etc.)</td>
</tr>
<tr>
<td>Urea and electrolytes</td>
<td>Hyponatraemia, syndrome of inappropriate secretion of antidiuretic hormone</td>
</tr>
<tr>
<td>Liver function tests</td>
<td>Reye’s syndrome, metabolic encephalopathies</td>
</tr>
<tr>
<td>Arterial blood gas</td>
<td>To assess severity, particularly in individuals with brainstem compromise</td>
</tr>
<tr>
<td>Ammonia</td>
<td>Reye’s syndrome, metabolic encephalopathies</td>
</tr>
<tr>
<td>Blood culture and Widal test</td>
<td>Typhoid and other septicaemias may have encephalopathic features</td>
</tr>
<tr>
<td>Acute and convalescent serology</td>
<td>To include locally relevant pathogens (e.g., Japanese encephalitis serology in Asia) and those suggested by history and examination (e.g., measles, mumps, varicella, HSV, Mycoplasma, Legionella)</td>
</tr>
<tr>
<td>Toxicology</td>
<td>Heavy metals, pesticides</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate</td>
<td>Collagen vascular disorders</td>
</tr>
<tr>
<td>Autoantibodies</td>
<td>Collagen vascular disorders</td>
</tr>
<tr>
<td>Cerebrospinal fluid (CSF)</td>
<td>Bacterial meningitis</td>
</tr>
<tr>
<td>Examination and culture</td>
<td>Tuberculous meningitis</td>
</tr>
<tr>
<td>CSF PCR</td>
<td>Intracranial haemorrhage</td>
</tr>
<tr>
<td></td>
<td>HSV</td>
</tr>
<tr>
<td></td>
<td>Enterovirus 71</td>
</tr>
<tr>
<td>Electroencephalography (EEG)</td>
<td>Status epileptic</td>
</tr>
<tr>
<td>Neuroimaging (with contrast enhancement)</td>
<td>Space-occupying lesion (malignancy, brain abscess)</td>
</tr>
<tr>
<td></td>
<td>Tuberculous meningitis</td>
</tr>
<tr>
<td></td>
<td>Intracranial haemorrhage</td>
</tr>
</tbody>
</table>

- Herpes simplex type 1 (HSV-1) causes sporadic encephalitis worldwide.
- Spirochaetal infections including syphilis, leptospirosis and Lyme disease are a well-recognised cause of meningoencephalitis. Other organisms such as *Brucella* are occasionally implicated. *Mycoplasma pneumoniae* is an important and treatable cause. Neurological
Clinical features

Presentation

The following clinical manifestations commonly occur, whatever the aetiological agent:

- An acute systemic illness with fever, headache, nausea and vomiting.
- Generalised seizures, less commonly focal.
- Behavioural or personality changes.
- Deteriorating conscious level, confusion and drowsiness, lapsing into coma.
- Neck stiffness is common but not invariable.
- Signs of involvement of any part of the nervous system may be present (e.g. hemiparesis, ataxia, myelitis, movement disorder, brainstem abnormalities).
- A rash may point to a specific diagnosis (e.g. measles, VZV, enteroviruses).
- Presentation may be subtle and/or subacute in immunocompromised individuals.
- Signs of raised intracranial pressure (ICP) may be present. The possible contribution of raised ICP to the clinical picture should always be considered, as this may be amenable to treatment.

Severity ranges from a mild illness with fever, a single brief seizure and confusion lasting for 2–3 days, to a more prolonged illness with a fluctuating level of consciousness and evolution of neurological signs over several weeks. Occasionally the course may be fulminating, with death occurring within a few days.

Diagnosis

The following investigations (see Table 5.16.C.2) should be considered in all cases but may be constrained by lack of resources. Efforts should be directed towards identifying those diseases that are treatable, common locally, or indicated by specific details in the history.

CSF examination and culture provide valuable diagnostic information, but if the child shows evidence of raised ICP, has signs suggestive of a space-occupying lesion or has cardiovascular compromise, lumbar puncture may be contraindicated. Lumbar puncture should be deferred until considered clinically safe, and antimicrobial therapy should be prescribed empirically, directed towards the common pathogens and antibiotic sensitivity patterns in the region.

Typical findings in the CSF in viral encephalitis are documented in Table 5.16.C.3, together with characteristic features on EEG and neuroimaging. In general it is possible to differentiate between viral and bacterial CNS infections on the basis of the CSF picture. If there is doubt, however, empirical antibiotic therapy should be given pending CSF culture results (see Section 5.16.B). Alternatively, if the child is stable, the lumbar puncture should be repeated after 24–48 hours while observing the clinical condition closely.

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF microscopy and biochemistry</td>
<td>Rarely may be normal</td>
</tr>
<tr>
<td></td>
<td>Usually lymphocyte-predominant pleocytosis (from a few to several thousand white blood cells/mm³)</td>
</tr>
<tr>
<td></td>
<td>In early disease, polymorphonuclear cells may predominate</td>
</tr>
<tr>
<td></td>
<td>Mildly elevated or normal protein levels</td>
</tr>
<tr>
<td></td>
<td>Normal CSF/plasma glucose ratio</td>
</tr>
<tr>
<td></td>
<td>Absence of microorganisms on Gram stain</td>
</tr>
<tr>
<td></td>
<td>Esosinophilia suggests parasitic infection</td>
</tr>
<tr>
<td></td>
<td>India-ink stain: cryptococcus</td>
</tr>
<tr>
<td></td>
<td>Normal CSF opening pressure (&lt; 25 cmH₂O)</td>
</tr>
<tr>
<td>Electroencephalography (EEG)</td>
<td>Virtually always abnormal</td>
</tr>
<tr>
<td></td>
<td>Diffuse slow waves; occasionally unilateral patterns may suggest particular causative agents, such as HSV (see below) or subacute sclerosing panencephalitis</td>
</tr>
<tr>
<td>Neuroimaging: CT or MRI</td>
<td>May be normal</td>
</tr>
<tr>
<td></td>
<td>Cerebral oedema is common</td>
</tr>
<tr>
<td></td>
<td>Features may suggest particular causative agents (e.g. HSV, Japanese encephalitis virus)</td>
</tr>
</tbody>
</table>

Management

In the majority of cases no specific treatment is available, and management is primarily supportive.

- Provide bed rest, and analgesia for headaches. Care is needed with sedation, as a deterioration in conscious level may be obscured and/or respiratory depression may occur.
- Antipyretics may be used to alleviate distress, but are no longer recommended solely to reduce the temperature.
- Ensure adequate oxygenation (SaO₂ > 94%).
- Regularly monitor electrolytes and review fluid balance.
- Fluid restriction may not be appropriate if the cardiac output is low. Aim to keep the serum sodium level (and other electrolytes) within the normal range. Consider the possible causes of hyponatraemia (e.g. vomiting/gastrointestinal losses, excessive hypotonic intravenous fluids, over-hydration, syndrome of inappropriate secretion of antidiuretic hormone) and act accordingly.

- Critically ill children, particularly those with evidence of brainstem involvement or raised ICP, should be managed in an intensive-care unit if possible. Assisted ventilation and cardiovascular support should be...
Enterovirus 71

Features of specific viral infections that cause encephalitis

**Enterovirus 71**
- There have been recurrent outbreaks in Asia since the 1990s, and a rising prevalence in the region.
- Children under 5 years of age are most commonly affected.
- These infections can be associated with hand, foot and mouth disease (HFMD) (with vesicular lesions on the hands, feet or mouth) or herpangina (mouth ulcers).
- Neurological involvement includes aseptic meningitis, acute flaccid paralysis, Guillain–Barre–type illness and brainstem encephalitis (cerebral deep sensory changes, myoclonic jerks and autonomic disturbance). The onset of neurological problems is commonly within the first 3 days of illness.
- Diagnosis is primarily clinical, but viral culture on throat, rectal or vesicle swabs provides supportive evidence. If available, PCR is advisable to identify the specific serotype of enterovirus.
- Children affected with brainstem encephalitis are at risk of cardiopulmonary complications such as shock, pulmonary oedema and/or haemorrhage. They should be managed in a paediatric intensive care unit if possible.
- Polyclonal IgG (2 grams/kg in 24 hours) may be given when there is neurological involvement, although there is no direct evidence to support this therapy at present. There are potential adverse effects, such as anaphylaxis, and IVIG should only be administered with cardiac monitoring facilities.
- High-level supportive care is necessary for patients with cardiopulmonary compromise, but there is a high case fatality and morbidity in this group.

**Japanese encephalitis virus**
- This is the most common cause of encephalitis worldwide. There are an estimated 50,000 cases and 15,000 deaths each year.
- It is currently limited to Asia and the Pacific Rim, but there is evidence that previously non-endemic regions such as Tibet have cases.
- The virus is transmitted by Culex mosquitoes, with an enzootic cycle involving pigs and birds.
- Most infections are asymptomatic (200–300 asymptomatic cases for every case of encephalitis).
- Extrapyramidal and brainstem involvement is common in patients with encephalitis. Patients may have Parkinsonian features acutely, with some later developing choreoathetoid movement disorders. Gradual improvement over several months is usual in survivors.
- Myelitis may occur, usually accompanied by some encephalitic features. The prognosis for recovery from myelitis is poor.
- Diagnosis rests on IgM/IgG capture ELISA in serum and CSF. Viral isolation is difficult, as the viraemia is short-lived.
- Thalamic, basal ganglia and brainstem lesions are often apparent on CT or MRI imaging (if available).
- There are no specific features on EEG.
- Treatment is supportive only, but effective vaccines are available.
- The prognosis is poor. Up to 30% of patients with encephalitis die in the acute stage. Neurological sequelae are common in survivors, but do tend to improve with time.

**Herpes simplex virus**
- This causes sporadic encephalitis worldwide.
- Encephalitis is more frequently a manifestation of recurrent than primary infection. There is no correlation between the presence of herpetic skin lesions and the diagnosis of HSV encephalitis.
- Seizures (both focal and generalised) are a prominent feature.
- Personality changes, temporal lobe phenomena, and dysphasia are also common.
- CSF findings:
  - Lymphocytic pleocytosis: < 50 to 2000/mm³.
  - Red blood cells are present in CSF in more than 80% of cases, reflecting haemorrhagic necrosis.
  - Protein levels are usually moderately elevated, but may reach very high levels as the disease progresses (3–5 grams/litre).
  - Up to 25% of cases may have a relatively low CSF glucose concentration.
Occasionally the CSF is entirely normal in early disease.

- Diagnosis is by polymerase chain reaction (PCR) or serology on CSF. Viral isolation is difficult.
- If the initial CSF-PCR is negative but there are ongoing clinical features suggestive of HSV infection (e.g., deteriorating level of consciousness, focal seizures), a repeat lumbar puncture more than 72 hours after the onset of neurology is advisable. Early CSF for PCR may be falsely negative.
- EEG may show a typical pattern of multifocal periodic lateralising episodic discharges (PLEDs) on a slow background, often with a temporal lobe focus.
- CT and MRI (if available) may show lesions (often haemorrhagic) in the temporal lobes. In early disease, scans may be normal.
- Treatment is with high-dose IV aciclovir for 21 days as an infusion over one hour (neonate to 3 months 20 mg/kg; 3 months–12 years 500 mg/m² (see Section 9 for chart on surface area); 12–18 years 10 mg/kg. All doses given 8 hourly: in older child use ideal weight for height if obese).
- Treatment may be stopped if the patient is diagnosed with a clear alternative cause of the encephalitis.
- In those with a definitive diagnosis, it is advisable to have a negative CSF PCR at the end of the treatment course.
- Early diagnosis and treatment improve the outcome significantly. HSV is a possibility in all patients with encephalitis, although in areas of the world where other pathogens such as enterovirus 71 encephalitis are endemic, HSV is responsible for only a very small minority of the total number of cases. If resources permit, start aciclovir (at the dosage stated above) in all cases without a definitive diagnosis and continue until HSV has been excluded, or an alternative diagnosis has been reached.
- Mortality can still be up to 20%, with around 15% of cases left with severe sequelae. Relapses occur occasionally, but these are less likely to occur if treatment is continued for 21 days.

**Varicella zoster virus (VZV)**

- VZV infection usually only results in mild encephalitides, with acute cerebellar ataxia as the main feature. Seizures and coma are rare, and the prognosis is good.

**Measles (see Section 6.2.E)**

- Acute encephalitis may occur 6–8 days after the onset of the rash, and may be severe, with up to 10% mortality and frequent sequelae.
- Delayed chronic encephalitis may also occur in the form of subacute sclerosing panencephalitis (SSPE), presenting with cognitive deterioration and myoclonic jerks. In such cases the EEG shows stereotypic polyphasic complexes on a background of excess slow activity.

**Rabies (see Section 6.2.H)**

- Saliva (plus virus) from an infected mammal enters via a bite, skin abrasion, or rarely through intact skin or mucous membranes.
- The incubation period varies from a few days to many months. A history of animal bite may not be elicited at the time of presentation.
- There is an initial prodrome of fever and malaise lasting a few days, followed by a second phase of excitement, hyperacusis, hydrophobia and pharyngeal spasms.
- Lastly, a paralytic phase occurs (rarely this may be the only manifestation).
- Death is inevitable once neurological signs are apparent.
- Effective prevention is available with the human diploid cell vaccine, and should be combined with passive immunisation if exposure has occurred.

**Other organisms**

**Mycoplasma**

- Neurological involvement occurs in up to 7% of infections.
- Both direct invasion of CNS and immune-mediated disease occur.
- Aseptic meningitis, transverse myelitis and Guillain–Barré syndrome are the most common manifestations.
- Diagnosis is by complement fixation titres (if available).
- If the diagnosis is suspected, treat intravenously or enterally if tolerated, with erythromycin, 12.5 mg/kg/ dose 6-hourly for 10 days. However, this is not effective for the immune-mediated disease.

**Cryptococcus**

- This can cause acute fulminant meningoencephalitis in immunocompromised children.
- It may present more subtly in an immunocompetent child.
- Consider when there is prolonged headache, fever, vomiting and focal neurology.
- It is important to have a baseline CSF opening pressure (provided that there are no contraindications).
- There may be normal CSF biochemistry and cell count.
- Diagnosis is based on India ink smear or CSF culture or rapid antigen assay in CSF or serum.
- Start with a 2-week induction treatment phase of an IV infusion over 4–6 hours of amphotericin 250 micrograms/kg once daily as tolerated to 1.5 mg/kg once daily (after a test dose of 100 micrograms/kg to be included in the first calculated dose) plus flucytosine 25 mg/kg/every 6 hours, or fluconazole 6–12 mg/kg/day up to a maximum of 800 mg/day.
- Children with HIV may require higher doses of amphotericin (up to 5 mg/kg/day).
- Amphotericin therapy requires pre-hydration and close supervision for toxicity, including hepatic and renal function tests, electrolyte monitoring and regular full blood counts.
- In settings where amphotericin is not available, fluconazole 12 mg/kg/day up to 1200 mg/day with or without flucytosine 100 mg/kg/day or fluconazole 12 mg/kg/day up to 1200 mg/day alone may be used.
- Initial treatment should be followed by an 8-week consolidation phase using fluconazole 6–12 mg/kg/day, up to a maximum of 400–800 mg/day.
- For the maintenance treatment phase, fluconazole 6 mg/kg/day up to a maximum of 200 mg/day is used.
- Raised intracranial pressure may develop during treatment, and prompt recognition is important. If identified, repeated therapeutic lumbar punctures can be helpful in controlling headache and limiting the development of ventricular dilatation, blindness and cranial nerve palsies.
- In HIV-infected individuals, consider antiretroviral therapy...
once antifungal treatment is established, but there is a risk of immune reconstitution syndrome.

**Human angiostrongylus**
- This is predominantly found in the Pacific Islands and Asia, where it is the most common cause of eosinophilic meningoencephalitis.
- The main mode of infection is via consumption of raw snails or other molluscs, freshwater prawns, frogs and contaminated vegetables.
- The hands may become contaminated with larvae that are then directly carried to the mouth by small children.
- Presentation is commonly with acute severe headache, low-grade fever, cranial nerve involvement, visual disturbances, paraesthesia or hyperaesthesia, and raised intracranial pressure.
- Peripheral blood eosinophilia may be very marked.
- Eosinophils are also seen in the CSF. Organisms may invade both the meninges and the brain parenchyma, especially involving the posterior fossa.
- Diagnosis is primarily clinical, relying on a history of likely ingestion of contaminated food, with typical clinical findings and an eosinophilic CSF picture. Serological tests are available, but may be normal in the early stages, and are also difficult to interpret because there is great cross-reactivity with other parasites.
- MRI (if available) may show multiple micronodular enhancing lesions.
- In many cases the symptoms spontaneously resolve within several weeks (mean period of 20 days).
- It is rarely fatal, and sequelae are usually minimal. A minority of patients have persistent paraesthesia and weakness associated with chronic infection.
- Provide analgesia for headache: consider giving a 2-week course of albendazole and prednisolone orally, but the evidence for treatment regimes in children is lacking, and most cases resolve with time.

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**5.16.D Epilepsy**

### 5.16.D.1 Minimum standards

- Anticonvulsants: phenobarbitone, phenytoin, sodium valproate, carbamazepine, ethosuximide.
- Temperature control.
- Prednisolone.
- EEG and neuroimaging with CT and MRI (if available).

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**Introduction**

Epilepsy is a symptom caused by a central nervous system (CNS) disorder, and is usually defined as the occurrence of two unprovoked seizures. In over 70% of cases a cause cannot be identified (idiopathic epilepsy), although genetic causes may be important, as there is often a family history. Most children with epilepsy live in disadvantaged communities where the incidence rates are estimated to be twice those in western countries, and where more than 70% of affected individuals are untreated.

The impact of epilepsy on children and families is wide-ranging. To reduce disability, management is best shared with other healthcare workers who can visit the family closer to home, such as community doctors, and healthcare or disability workers.

**Confirming the diagnosis of epilepsy**

There is no justification for a trial of anti-epileptic drugs if the diagnosis is unclear. The diagnosis of epilepsy is purely a clinical one, and is usually based on a good history or eyewitness account or ideally a video (often taken with a mobile phone) of an event.

Important features of the seizures include the following:
- Timing and duration
- Provocation factors
- The early phase of the attack; look for localising features
- Movements
- Sensory symptoms

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**Role of investigations**

The history and sometimes the examination will usually indicate the cause. Children can be managed without the need for an electroencephalogram (EEG) or neuroimaging. EEG and neuroimaging (preferably an MRI scan, but sometimes a CT scan may be informative) should be reserved for intractable cases or those with neurological signs suggesting a space-occupying lesion. Such problems, and the imaging needed to identify them, will usually require the support of a specialised neurosurgical centre, at least one of which should exist in every country.

**Prognostic features of epilepsy**

When a syndrome cannot be identified precisely, the features in Table 5.16.D.2 can serve as a guide to the prognosis.

Once the diagnosis and prognosis have been assessed, draw up a problem list as follows:
- What effect does the epilepsy have on the development of the child?
- Are learning or motor problems present?
- Is the child attending school and getting opportunities to play with other children?
- Are there any behavioural problems?

**Selecting appropriate anti-epilepsy drugs**

Phenobarbitone, phenytoin, carbamazepine and sodium valproate should be available.

Convulsive status epilepticus (see Section 5.16.E).
Section 5.16

How to start treatment

- Monotherapy is the aim, to reduce the side effects and interactions.
- Try to avoid using drugs that impair development (e.g. phenobarbitone, except in infancy).
- If possible, always prescribe the same brand, as there may be pharmacodynamic differences.
- Always start in low doses to minimise side effects and increase the likelihood of compliance.
- Remember to warn the child and their family about any likely side effects, especially if they are temporary, such as drowsiness.
- Increase the drug dose gradually (every 2–4 weeks) until the seizures stop or are significantly reduced, or side effects become significant (see Table 5.16.D.3).

How to monitor treatment

- Case notes should record the diagnosis, problem list, dates and types of seizures, indication for treatment,
past treatment with response and side effects of treatment, and information that has been given to the child and their parents or carers.

- Hand out medical cards to be kept as a seizure diary, reminder of prescription and clinic dates. Graphic symbols can be used for the illiterate.
- Regularly review the child to check on their progress. Review them more often if seizure control has not been achieved, or if side effects or drug changes.

**When to change treatment**

- Consider changing treatment if side effects are troublesome.
- Introduce the second anti-epileptic drug in the normal way, first checking for possible drug interactions. Once established, begin to withdraw the first anti-epileptic gradually. If seizure control is not achieved with mono-therapy, seek a specialist referral.

**When and how to stop treatment**

In children with a good prognosis, 12–24 months of freedom from seizures is associated with a 70% risk of continuing seizure remission. Withdrawal must be a gradual and closely monitored process. If seizures recur after a decrease in drug dose, they usually remit once the last decrease has been reversed. The withdrawal period depends on the drug (e.g. phenobarbitone over 4–6 months, carbamazepine over 2–3 months).

**Whom to refer**

This depends upon local facilities. One-third of patients will be intractable to treatment with first-line anti-epileptic drugs. Some of them may not have epilepsy, and others may have syndromes with a poor prognosis. They will require specialist assessment and treatment advice. Epilepsy may also be a part of complex developmental disorders involving the CNS, and these children may also benefit from specialist input.

**TABLE 5.16.D.3 Doses of common anti-epileptic drugs**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual dose</th>
<th>Side effects and toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>1 month–12 years initially 5 mg/kg at night or 2.5 mg/kg twice daily increasing to 5 mg/kg three times a day Maximum dose 20 mg/kg per day 12–18 years initially 100–200 mg 1–2 times daily increasing to 200–400 mg two or three times daily Maximum up to 1.8 mg daily</td>
<td>Ataxia, diplopia, aplastic anaemia (bruising, mouth ulcers)</td>
</tr>
<tr>
<td>Phenobarbamide</td>
<td>One month to 12 years initial dose 1.5 mg/kg twice daily increasing to 2.5–4 mg/kg/day once or twice daily 12–18 years 60–180 mg once daily</td>
<td>Drowsiness, agitation, rashes, developmental impairment</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>1 month–12 years initial dose 1.5–2.5 mg/kg twice daily then increasing to 2.5–5 mg/kg twice daily 12–18 years initial dose 75–150 mg twice daily increasing to 150–200 mg twice daily (max 300 mg twice daily)</td>
<td>Gum hypertrophy, hirsutism, acne, ataxia, diplopia, nystagmus, neuropathy, choreoathetosis, encephalopathy, lymphoma, megaloblastic anaemia</td>
</tr>
<tr>
<td>Sodium valproate</td>
<td>1 month–12 years initial dose 5–7.5 mg/kg twice daily increasing to 12.5–15 mg/kg twice daily 12–18 years initial dose 300 mg twice daily increasing to 0.5–1 g twice daily</td>
<td>Nausea, epigastric pain, alopecia, weight gain, tremor, hepatitis, pancreatitis, encephalopathy</td>
</tr>
</tbody>
</table>

**Social issues**

**Promoting social integration**

Children need to participate as fully as possible in the normal activities of their peers, at school, at play, in the home and preparing for employment. Community workers should be involved in the wider management, and parents’ fears and anxieties discussed.

**Supporting parents**

Parents often tend to overprotect their children who have epilepsy, and may lack confidence in dealing with seizures. In many societies epilepsy carries a stigma. Opportunities to discuss first aid, behaviour and other concerns are vital, and can be provided by healthcare workers or parent groups.

**First-aid advice**

The general theme to be emphasised is that children with epilepsy should be encouraged to live as full and normal a life as possible. There are very few absolute restrictions, but these include climbing trees or riding bikes or motorcycles. Children should be accompanied when swimming or when near to hazards such as stoves and fires. During a convulsion, place the child in the recovery position, protect them from hard or sharp objects in the vicinity, and cushion their head. Do not put anything in their mouth or try to restrain their limbs. Let them recover by themselves. They may need to rest or sleep, but keep them under observation because they may start convulsing again. As a rough guide, a convolution that does not stop spontaneously within about 10 minutes is likely to continue for longer, and may need intervention with anti-epileptic drugs given IV, rectally or buccally. The use of rectal diazepam at home by parents and carers is described later in this subsection.

**Febrile seizures**

A febrile seizure is a seizure that occurs in children aged between 6 months and 7 years with febrile illness not caused by an intracranial disease. The commonest age of onset is 14–18 months. Febrile seizures are common, occur in 2–5% of all these children, and account for about one-third of all childhood seizures.
Clinical presentation
Febrile seizures are usually brief, generalised, clonic or tonic-clonic convulsions lasting less than 10 minutes with minimal post-ictal confusion or weakness. About 20% of febrile seizures are complex (i.e. focal), or last longer than 15 minutes, or occur more often than once in 24 hours. Complex febrile seizures may suggest an underlying central nervous system cause and are associated with a poorer outcome (cognitive impairment or epilepsy).

Febrile seizures occur while the child has a recognisable infection, most commonly an upper airway infection or a viral illness such as gastroenteritis. Other causes include pneumonia, urinary tract infections and after vaccinations. Shigellosis, roseola infantum and malaria have an unusually high incidence of seizures. Most children have a core temperature of 38–41°C, but it may occur at the onset of the febrile illness, and the child may have a normal temperature at the time of seizure.

An increased frequency of febrile seizures occurs in the children of parents and siblings who have had febrile seizures, and siblings with epilepsy.

Identify the cause
Check blood glucose levels (by finger-prick test if available), take a careful history and examine the patient thoroughly, especially with regard to alertness and ability to play, looking for common and serious sites of infection. Where relevant, look at rapid test or film for malaria parasites, and full blood count. Consider urinalysis, lumbar puncture, cultures of blood, urine, pharyngeal swab and cerebrospinal fluid, and relevant X-rays in children whose history and examination offer clues to serious infection. A lumbar puncture is mandatory if meningitis is thought to be a possibility (unless there is evidence of raised intracranial pressure, when IV antibiotics should be given until meningitis can be excluded; see Section 5.16.A and Section 5.16.B).

Differential diagnosis
Exclude the following:
- meningitis
- encephalitis
- acute encephalopathies of metabolic or toxic origin
- cerebral malaria
- electrolyte disorders
- hypoglycaemia
- anoxia
- trauma
- haemorrhage
- tumour.

Other entities that can be confused with febrile seizures include the following:
- febrile delirium (in which the patient is speaking but not making sense)
- febrile rigors (in which the patient is shaking with a fine tremor).

Treatment
No treatment is necessary in simple self-limiting febrile seizures provoked by a minor febrile illness. Advice to parents should consist of the following:
- Reassurance that the condition is almost always benign and that the large majority of children stop having seizures after 5 or 6 years of age, while many have only one seizure.
- Practical demonstration of the recovery position for use if a further seizure occurs (see Section 5.16.E).
- Advice to seek medical help if a further seizure occurs, both in case it is prolonged (less than 5% of cases, but see below) and, importantly, so that the source of the provoking infection can be identified.

Sequelea
- About one-third of children with febrile seizures will have another febrile seizure.
- Around 3% will have at least one afebrile seizure.
- Around 2% may develop epilepsy (recurrent afebrile seizures).
- Approximately 65% of children with simple febrile seizures will have no further seizures by 7 years of age.
- Recurrent seizures tend to re-occur, particularly in children aged less than 1 year at the onset of the febrile convulsions or those with a positive family history.

Risk of later epilepsy
The risk factors for the development of epilepsy are as follows:
- complex febrile seizures
- previous abnormal neurological function
- multiple febrile seizures
- family history of epilepsy
- age less than 1 year at the first seizure.

Long-term care: home treatment
- Rectal diazepam for parents to administer if there are prolonged seizures (2.5 mg for children under 1 year, 5 mg for those aged 1–3 years, 10 mg for those aged over 3 years). The parents must also be taught what to do if their child stops breathing (i.e. they should be equipped with a bag and mask and shown how to use it).
- Oral or rectal paracetamol to prevent or treat febrile seizures.
- Advice to parents as described above.
5.16.E Convulsive status epilepticus

Introduction
Convulsive status epilepticus (CSE) is a life-threatening condition in which the brain is in a state of prolonged electrical discharge. It is defined as a generalised convulsion lasting for more than 30 minutes, or recurrent convulsions which occur very frequently over a 30-minute period, where the patient does not regain consciousness between seizures.

The duration of the convulsion is highly relevant, as the longer the duration of the episode, the more difficult it becomes to control it. Convulsions that persist for longer than 10 minutes are much less likely to stop spontaneously. Therefore it is usual practice to institute anticonvulsant treatment when the episode has lasted for 5 minutes or more.

Common causes of convulsions in children
These include the following:
- Fever with a predisposition to febrile convulsions (usually between the ages of 6 months and 6 years)
- Meningitis
- Epilepsy
- Hypoxia
- Metabolic abnormalities
- Abrupt withdrawal of anti-seizure medication, especially phenobarbitone
- An acute cerebral event or injury (e.g. haemorrhage, trauma)
- Ingestion of medication.

Tonic–clonic status occurs in approximately 5% of patients with epilepsy. Up to 5% of children with febrile seizures will present with status epilepticus. The mortality rate of status epilepticus can be high (up to 20% in adults), especially if treatment is not initiated quickly. However, with optimal management and adherence to a structured and standardised management plan, the mortality in children is much lower and patients can survive with minimal or no brain damage.

Evaluation and immediate management of status epilepticus
During a seizure:
- Turn the child on their side.
- Adopt an ABC approach. It is vital to ensure satisfactory respiration and circulation and to exclude or treat hypoglycaemia before giving anti-epileptic drugs.
- Ensure that the airway is patent and that there is adequate respiratory effort and circulatory volume. Institute corrective measures immediately if these are required.
- If available, administer oxygen via a mask.
- Check glucose levels and treat if they are low (< 2.5 mmol/litre or 45 mg/dL). If in doubt or unable to check the levels, it is safer to treat as if hypoglycaemia is present and give 10% dextrose IV 2–5 mL/kg as an initial bolus and, if safe to do so, follow this with an infusion containing a glucose-containing fluid to avoid the risk of rebound hypoglycaemia.
- If the seizure has lasted more than 5 minutes (or if the duration is not known), prepare for anticonvulsant treatment. Short recurrent seizures lasting less than 5 minutes should also be treated (see Figure 5.16.E.1).
- A self-inflating bag with non-return valve (e.g. Ambubag) and a suitably sized face mask must be available in case excessive respiratory depression is caused by benzodiazepines (see Section 1.12).
- Treat the fever (if present) with exposure, tepid sponging and rectal paracetamol (40 mg/kg loading dose, 20 mg/kg if less than 3 months of age).

Drugs
Lorazepam (intravenous or intra-osseous route)
Lorazepam is a benzodiazepine with a fast onset of action and a longer duration of effect (12 hours). It can be used with diazepam (which is less than 1 hour). It produces less respiratory depression than other benzodiazepines, and is less likely to require additional anticonvulsants to stop the seizure. However, absorption from the rectal route is poor. Lorazepam is not available in every country, but is no more expensive than diazepam.

Dose: 50–100 micrograms/kg/dose by IV or intra-osseous route (the dose can be repeated after 10 minutes if necessary).

Midazolam (buccal application)
Midazolam is an effective fast-acting anticonvulsant that has an onset of action within minutes but has a shorter lasting effect (15–20 minutes). Most children do not convulse again once the seizure has been terminated.

Buccal midazolam is twice as effective as rectal diazepam, but both drugs produce the same degree of respiratory depression. This occurs only in about 5% of patients, is short-lived, and is usually easily managed with bag-valve-mask ventilatory support.

Midazolam can be given by the buccal or IV route. However, the ready-made buccal midazolam may not be available in some countries. In such situations the standard IV preparation can be used instead via the buccal route. Simply draw the required dose in a syringe using a needle so as to filter off any glass fragments, and after removing the needle apply the drug on the buccal mucosa between the lower lip and the gum.

**BOX 5.16.E Minimum standards**
- ABC and high-dependency care.
- Anticonvulsants:
  - lorazepam
  - phenobarbitone
  - phenytoin
  - paraldehyde
  - diazepam
  - midazolam
  - thiopentone.
- Temperature control.
- Mannitol.
- Dexethasone.
- Mannitol.
Dose:
- 500 micrograms/kg/dose (maximum 10 mg) with buccal application (the dose may be repeated).

**Diazepam**
Diazepam is an effective, commonly used, readily available and fast-acting anticonvulsant with similar characteristics to midazolam. It is widely used, but may now be superseded by the more effective lorazepam or buccal midazolam where the latter is available. The rectal dose is well absorbed.

Dose:
- 500 micrograms/kg/dose rectally
- 200–300 micrograms/kg/dose by the IV or intra-osseous route (the dose may be repeated).

**Lorazepam (intranasal route)**
This has been found to be safer than IM paraldehyde, and is also easier and less painful to access. It is directly instilled into one nostril, with the patient in a supine position, drop by drop over 30–60 seconds.

Dose: 50–100 micrograms/kg/dose intranasally.

**Paraldehyde**
Paraldehyde is an effective and cheap anticonvulsant with a sustained level of effect and a good safety profile. However, it may be difficult to find in some countries. Paraldehyde takes 10–15 minutes to start to take effect, and its action is sustained for 2–4 hours.

It is generally given by the rectal route after mixing the required dose with an equal amount of any edible oil (e.g. olive oil). This mixture is then quickly pushed up the rectum using a simple feeding tube attached to a syringe.

Do not leave paraldehyde standing in a plastic syringe for longer than a few minutes, as the drug dissolves plastic. The IM route can also be used, but is very painful and can lead to abscess formation, so is better avoided. Paraldehyde causes little respiratory depression, but should not be used in patients with liver disease.

Dose: 0.4 mL/kg rectally (0.4 grams/kg).

**Phenytoin**
Phenytoin is a readily available anticonvulsant that can give very good results with little effect on respiration. It has a peak action within 1 hour, and a long half-life. Its action is therefore more sustained than that of diazepam.

It is administered as an IV infusion mixed with 0.9% sodium chloride solution up to a concentration of 10 mg/mL, given over a 20-minute period. Phenytoin can cause dysrhythmias and hypotension (especially if given rapidly), so it is important to monitor the electrocardiogram (ECG) and blood pressure if these are available. In addition, local irritation, phlebitis and dizziness may accompany IV administration.

If the child is known to be on oral phenytoin it is better to either avoid using phenytoin (use phenobarbitone instead) or use a lower loading dose (i.e. 10 mg/kg).

Dose: 20 mg/kg IV infusion given over 20 minutes (only use normal (0.9%) saline for dilution).

**Phenobarbitone**
Phenobarbitone is a time-tested anticonvulsant and readily available in many countries; the parenteral preparation is on the WHO essential drug list. It can be used to good effect in all age groups, and causes little respiratory depression. It is given by the IV route as a slow injection over 5–15 minutes, and can also be given by the IM route, although the absorption is variable. It has a sustained effect that lasts over 12–24 hours.

There is now evidence to suggest that phenytoin and phenobarbitone may have some synergistic effect when used sequentially. It is thought that one primes the brain in readiness for the other, thus producing a beneficial effect.

However, there is controversy about which drug should be used first.

Dose: 20 mg/kg IV infusion over 5–10 minutes.

**Thiopental**
Thiopental (thiopentone) sodium is a drug better used by experienced staff who are familiar with it (usually anaesthetists: see Section 1.24) and who are capable of intubating difficult cases. It is a general anaesthetic agent with no analgesic properties but with marked cardiorespiratory effects. It is usually given after paralysis and intubation in induction of anaesthesia. Other anti-epileptic medication must be continued. The child should not remain paralysed, as continued seizure activity cannot otherwise be monitored. A paediatric neurologist should continue to give clinical advice and support.

**General measures once seizures are controlled**
- Maintain a normoglycaemic state using 5% glucose-containing solutions (10% in young infants). Often children may show a hyperglycaemic pattern following seizures as a stress-induced response. This does not require correction with insulin.
- Normal maintenance fluid volume can be given to avoid hypoglycaemia and to maintain electrolyte balance. However, evidence of raised intracranial pressure or increased antidiuretic hormone secretion should necessitate fluid restriction.
- Assess and maintain electrolyte balance, maintaining serum sodium levels within the normal range (135–145 mmol/litre). Avoid hyponatraemia by using Ringer-lactate or Hartmann’s solution.
- Aspirate the stomach contents by inserting a gastrotomy tube, and perform gastric lavage or give charcoal (1 gram per year of the child’s age) if appropriate for specific drug ingestion.
- Regulate the temperature, ensuring that temperatures above 37.5°C are avoided.
- Treat raised intracranial pressure, if clinically present (see Section 5.16.K), as follows:
  - Support ventilation (maintain a pCO₂ of 4.5–5.5 kPa).
  - Maintain a 20-degree head-up position.
  - Give 20% mannitol, 250–500 mg/kg (1.25–2.5 mL/kg) IV over 15 minutes. This may be repeated on a 2-hourly basis as required.
  - Alternatively, hypertonic saline can be used (2.7% or 3% at a dose of 3 mL/kg). This may not be associated with a ‘rebound’ rise in pressure or induce a diuresis like mannitol but rather augments plasma volume.
  - Give dexamethasone, 50 micrograms/kg twice daily (for oedema surrounding a space-occupying lesion).
- Catheterise the bladder, as distension may aggravate raised intracranial pressure.
- Frequent reassessment of ABC is mandatory, as

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therapy may cause depression of ventilation or hypotension, especially if benzodiazepines or barbiturates have been used.

- If available, a standard EEG can be done to establish cessation of electrical seizure activity.

- Identify and treat the underlying cause of the convulsion.

- Following seizure control there are several regimes for continued drug control of the convulsions, but they are beyond the scope of this text.

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FIGURE 5.16.E.1 Algorithm for the treatment of status epilepticus in children.
5.16.F Neuropathies

**BOX 5.16.F Minimum standards**
- Muscle biopsy.
- Prevention of scoliosis.
- Prevention of muscle contractures.

**Introduction**
Neuropathies are diseases that affect the anterior horn cells and/or the peripheral nerves.

**Anterior horn cell disease**
The most common neuropathies are:
- Poliomyelitis (see Section 6.2.G)
  - spinal muscular atrophy.

**Spinal muscular atrophy**
This is a motor neuron disease of the spinal cord and brainstem, inherited as an autosomal-recessive disorder and associated with deletions of the survival motor neuron (SMN) and neuronal apoptosis inhibitory protein (NAIP) genes. It is the second commonest autosomal-recessive disorder after cystic fibrosis.

**Clinical features**
These children have delayed motor development but normal social, language and intellectual development. They are floppy and weak. The weakness is proximal more than distal, and affects the lower limbs more than the upper ones. The children are areflexic, and fasciculation of the tongue is diagnostic (observed with the tongue at rest in the mouth). There are three clinical subtypes based on severity.
- **Severe infantile type**: These infants never sit, crawl or walk. The onset is before or soon after birth. They have severe intercostal and bulbar weakness but the diaphragm is spared. Most die from respiratory failure before their second birthday.
- **Intermediate type**: These infants can sit but are unable to walk. They may or may not have respiratory and bulbar weakness, and this factor determines their prognosis. If it is absent, these children can survive into adulthood.
- **Mild type** (also known as Kugelberg–Welander type). The onset is later and these children can walk, but they do so late and with difficulty. Respiratory and bulbar weakness is not usually present. A coarse tremor of the hands is frequently seen in this and the intermediate form. This is a useful sign for distinguishing this type from muscular dystrophy, with which it is often confused (see Table 5.16.F.1).

**Diagnosis**
Since the discovery of the gene defect, muscle biopsy is rarely needed. Deletion of the SMN gene is found in almost all cases of spinal muscular atrophy of all three types. It can be detected rapidly by the polymerase chain reaction (PCR). Blood (2–5 mL in an EDTA tube), or DNA extracted from it, can be sent by post to a laboratory that will perform the test and confirm the diagnosis within a few days.

| TABLE 5.16.F.1 Comparison of spinal muscular atrophy (mild type) and Duchenne muscular dystrophy |
| --- | --- | --- |
| Feature | Spinal muscular atrophy | Duchenne muscular dystrophy |
| Motor milestones | Delayed | Normal or delayed |
| Hypotonia | +++ | +/-- |
| Pseudohypertrophy | +/-- | +++ |
| Hand tremor | +++ | -- |
| Tongue fasciculation | + | -- |
| IQ | Normal | Normal or low |
| ECG | Baseline tremor | R- and Q-wave changes |
| Creatine kinase | Normal or slightly raised (× 2) | Very high (× 100) |
| EMG | Chronic denervation | Myopathic |
| Muscle biopsy | Denervation | Dystrophic |

**Management**
Management is supportive. The most important complication in the intermediate form is the development of scoliosis. This can be delayed by getting the child to stand with support of lightweight callipers for as long as possible. If the child is confined to a wheelchair, a brace may be needed to control the scoliosis. Surgery (fusion of the spine) may be necessary. Children with symptoms of nocturnal hypoventilation (disturbed sleep, headaches, daytime drowsiness and poor concentration) may benefit from assisted non-invasive night-time ventilation with a nasal mask (see Section 8.2).

**Peripheral neuropathy**
The two commonest causes of peripheral neuropathy in children are Guillain–Barré syndrome (see Section 5.16.G) and hereditary motor and sensory neuropathy.

**Hereditary motor and sensory neuropathy**
This is the commonest chronic peripheral neuropathy in children. It is progressive, and there are several types, but the commonest is type I (peroneal muscular atrophy). It is dominantly inherited, and most children are asymptomatic until late childhood, when unsteady clumsy gait with frequent falls develops. There is weakness and wasting of the muscles of the anterior compartment of the leg. The parents
are often asymptomatic. The diagnosis is confirmed by the finding of very low motor conduction velocities in both the child and one of the parents, indicating demyelination. Type II is similar, but rare, and shows axonal rather than demyelinating changes in nerve conduction studies. There are no treatments for these diseases other than special boots and ankle orthoses to stabilise the ankle.

**Other peripheral neuropathies**

These include leukodystrophies (where peripheral nerve demyelination occurs as part of CNS demyelination), toxic neuropathy (due to glue or benzene sniffing, lead, or drugs) and diphtheria (see Section 6.1.C).

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**5.16.G Guillain–Barré syndrome**

**BOX 5.16.G Minimum standards**

- ABC resuscitation and emergency care.
- Lumbar puncture.

**Introduction**

This is the commonest peripheral neuropathy seen in childhood. It is a demyelinating neuropathy induced by an autoimmune process that is precipitated by a preceding viral or other infection. It has a peak incidence at around 8 to 9 years of age in well-resourced countries and 3 to 4 years of age in resource-limited ones, possibly due to overcrowding. Rarely, an acute axonal form occurs, especially in some countries, such as China.

**Clinical features**

The onset is usually acute. There is often a history of a preceding upper respiratory or gastrointestinal tract infection and insidious sensory symptoms (e.g. muscle tenderness, occasionally an unsteady gait, and frequent falls). The weakness starts in the lower limbs and ascends to affect the trunk, upper limbs, and the respiratory (intercostal and diaphragm) bulbar and facial muscles. It is usually symmetrical and affects both proximal and distal muscles, and may take 10–30 days to reach its maximum. Cranial nerve involvement often precedes respiratory difficulties. Reflexes are frequently absent. Sensory loss is minimal and of the ‘glove-and-stocking’ distribution. Ophthalmoplegia, papilloedema and bladder involvement rarely occur. Autonomic dysfunction occurs in many children, resulting in hypertension, hypotension and cardiac arrhythmias. In some patients the paralysis occurs rapidly with quadriplegia and respiratory paralysis within 2–5 days.

**Chronic inflammatory demyelinating polyradiculoneuropathy**

The disease may evolve into chronic inflammatory demyelinating polyradiculoneuropathy. This disease is similar to Guillain–Barré syndrome, consists of progressive or relapsing motor and sensory dysfunction, and lasts at least 2 months, with hyporeflexia of all four limbs. The importance of identifying this condition is that it responds to steroids (prednisolone 2 mg/kg/day).

**Diagnosis**

The diagnosis is confirmed by an abnormal nerve conduction stimulation, but a high CSF protein level and almost normal cell count are very suggestive. These findings are usually present after the first week of onset. Other causes of acute flaccid paralysis such as poliomyelitis in endemic countries need to be considered (see Table 5.16.G.1).

**Management**

Supportive care is the cornerstone of successful management of the acute patient. Of greatest concern is respiratory failure due to paralysis of the diaphragm (the muscle that is most important for breathing). Intubation may be needed if there is evidence of impending respiratory failure. The following steps in management should be taken:

- Admit the child to hospital to monitor for impending respiratory and bulbar paralysis and autonomic dysfunction.
- Measure the respiratory rate, heart rate and blood pressure, perform pulse oximetry and if possible measure vital capacity (or peak flow), and check airway protection frequently. Blood gas analysis may be helpful.
- If the vital capacity is less than 50% of normal for age and/or there is significant respiratory failure with hypoxaemia and hypercapnia, ventilate the child if possible.
- If bulbar and respiratory paralysis occurs, airway protection, tube feeding and ventilatory support will be necessary. Airway protection can be achieved by intubation or tracheostomy.
- Plasma exchange (also called plasmapheresis) and high-dose immunoglobulin therapy may lessen the severity of the illness and accelerate recovery in some patients, but are not widely available. These two treatments are equally effective, and a combination of the two is not significantly better than either alone. However, immunoglobulin is easier to administer.
- Children who require ventilation can be given high-dose human immune globulin if available (0.4 grams/kg IV over 6 hours daily for 5 days). This can be repeated if there is no response, if deterioration occurs or if there is a relapse.

**Prognosis**

Recovery is usually complete within 4–6 months in most children, but may take up to 2 years. About 5% of children will have minor motor sequelae, and around 2–3% will die from respiratory failure or autonomic dysfunction. Poor prognostic factors include onset of weakness within 8 days of preceding infection, rapid progression, cranial nerve involvement and a CSF protein level of > 800 mg/litre in the first week of the disease. The prognosis is generally better in children than in adults.
### TABLE 5.16.G.1 Other causes and features of acute flaccid paralysis

<table>
<thead>
<tr>
<th>Cause</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spinal cord</strong></td>
<td></td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>Preceding fever, headache and meningeal irritation, asymmetrical weakness, CSF pleocytosis</td>
</tr>
<tr>
<td>Enterovirus: Japanese B encephalitis</td>
<td>Similar to poliomyelitis</td>
</tr>
<tr>
<td>Trauma</td>
<td>History and evidence of trauma</td>
</tr>
<tr>
<td>Myelitis</td>
<td>Paraplegia, segmental sensory loss</td>
</tr>
<tr>
<td>Epidural abscess</td>
<td>Fever, vertebral tenderness</td>
</tr>
<tr>
<td><strong>Neuropathies</strong></td>
<td></td>
</tr>
<tr>
<td>Guillain–Barré syndrome</td>
<td>Symmetrical, areflexia, ascending weakness</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>Preceding history of diphtheric pharyngitis, cardiac involvement, deep sensation impaired</td>
</tr>
<tr>
<td>Botulism</td>
<td>Bulbar symptoms before onset of weakness, ophthalmoplegia</td>
</tr>
<tr>
<td>Tick paralysis</td>
<td>Rapid progressive paralysis, no sensory loss, normal CSF protein levels</td>
</tr>
<tr>
<td></td>
<td>Resolves quickly once tick has been removed</td>
</tr>
<tr>
<td><strong>Metabolic</strong></td>
<td></td>
</tr>
<tr>
<td>Acute intermittent porphyria</td>
<td>Family history, other symptoms</td>
</tr>
<tr>
<td>Hereditary tyrosinaemia</td>
<td></td>
</tr>
<tr>
<td><strong>Muscle</strong></td>
<td></td>
</tr>
<tr>
<td>Myasthenia gravis (rare but treatable)</td>
<td>Fluctuating weakness that is worsened by activity and better after rest</td>
</tr>
<tr>
<td></td>
<td>Tension test is positive</td>
</tr>
<tr>
<td>Acute viral myositis</td>
<td>Tender muscles, limp, fever, elevated muscle enzymes (creatine phosphokinase or aldolase)</td>
</tr>
<tr>
<td><strong>Other causes</strong></td>
<td></td>
</tr>
<tr>
<td>Organophosphate poisoning</td>
<td>History of exposure, excessive salivation, twitching of muscles, meiosis, tachycardia</td>
</tr>
</tbody>
</table>

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### 5.16.H Muscular dystrophy

**BOX 5.16.H.1 Minimum standards**

- Creatine kinase measurement.
- Prevention of scoliosis and contractures.
- Prednisolone.

**Introduction**

The muscular dystrophies are a group of inherited disorders that cause progressive muscle weakness and share a common pathological process of muscle fibre degeneration and fibrosis.

**Duchenne muscular dystrophy**

This is the most common muscular dystrophy, caused by deficiency of dystrophin, a structural protein found on the inner side of the sarcolemmal membrane. The deficiency is caused by deletions or point mutations of the dystrophin gene, which is located on the short arm of chromosome Xp21.

**Clinical features**

Duchenne muscular dystrophy is X-linked; it affects boys and is transmitted by females. Affected infants are normal in the first 2 years but will have very high serum creatine kinase levels. They usually present between 2 and 5 years of age with delayed walking, frequent falls, and difficulty in climbing stairs and in getting up from the floor. The weakness affects proximal more than distal muscles, and the pelvic girdle more than the shoulder girdle. The facial muscles are unaffected. Prominent calves and thighs are characteristic. With time, these children walk on their toes with marked lumbar lordosis and a waddling gait. The arm reflexes are lost early but ankle jerks are preserved. Once confined to a wheelchair, they rapidly develop contractures of the knees, hips and ankles and scoliosis. Intellectual impairment may occur or develop in some patients, often related to the onset of respiratory failure. The ECG shows dominant R waves in right-sided leads, deep Q waves in left-sided leads, and inverted T waves in most patients.

**Diagnosis**

The serum creatine kinase activity is very high (100 times normal). The electromyogram (EMG) is myopathic, and muscle biopsy shows dystrophic changes and absent...
dystrophin. Deletions in the dystrophin gene can be identified by the polymerase chain reaction (PCR) in DNA extracted from blood in 60–80% of patients.

Management
There is no effective drug treatment. A course of oral prednisolone (0.75 mg/kg/day) for 3–6 months can produce a small but significant improvement in muscle strength, but has many side effects, and these must be weighed against the slight benefit. Night splints to keep the ankles at 90 degrees may delay shortening of the tendo-achilles. When walking is becoming difficult, the fitting of lightweight callipers and intensive physiotherapy may keep the child ambulant for a few more years. Once the child is wheelchair-bound, a rigid seat and adequate postural support of the spine may prevent scoliosis.

Prognosis
The weakness is progressive, and by 10–12 years of age a wheelchair will be needed. Later, as respiratory muscle weakness develops, nocturnal hypoventilation may cause disturbed sleep and morning headaches (due to hypoventilation and carbon dioxide retention). Assisted non-invasive ventilation (using a nasal mask) at night will improve the child’s quality of life (see Section 8.2). Death occurs in the twenties from respiratory or cardiac failure.

Genetic counselling
An elevated creatine kinase activity (on three separate occasions) in female relatives indicates carrier status. Some will also have an abnormal muscle biopsy, with some fibres showing normal and others absent dystrophin. Normal creatine kinase and muscle biopsy does not exclude the carrier state. Prenatal diagnosis is possible in some but not all families, but requires specialised molecular genetic techniques.

5.16.I Breath-holding episodes

### 5.16.I.1 Minimum standards
- Haemoglobin measurement.
- Oxygenation measurement.

#### Introduction
Breath-holding episodes occur in about 4% of children under the age of 5 years. They typically start between the ages of 6–18 months, and usually cease before the age of 5 years. They are infrequent, usually occurring less than once a month, but occasionally occur more often. There are two types of episodes, which are differentiated by the presence of cyanosis or pallor. The underlying mechanism of the two types is different.

#### Type of episodes

**Cyanotic breath-holding episodes**
These are provoked by anger, frustration, fright or pain. The infant cries vigorously, holds their breath in expiration, goes blue, loses consciousness and becomes limp. Rarely this is followed by a brief stiffening of the body. The infant then starts breathing again and the attack ends. These attacks may be due to cerebral ischaemia from a sudden rise in intrathoracic pressure that impedes venous return. Intrapulmonary right–left shunting also plays a part.

**Pallid asystolic spells**
These are less common than the cyanotic type (about 20% of all cases), and may occur in the context of a minor illness. The attack is provoked by pain, usually from a mild injury on the head. The child cries, loses consciousness, develops marked pallor and goes stiff. Occasionally the child loses consciousness immediately after the injury without crying. A few clonic jerks (reflex anoxic seizures) may occur. These pallid spells are caused by vagal asystole, and can be induced by pressure on the eyeballs (oculo-cardiac reflex), although it is not necessary to elicit this reflex; and if thought to be important, this should only be done under controlled conditions with EEG and ECG monitoring. There is also a risk of damaging the eyeballs when pressing on them.
Diagnosis
The diagnosis is based on a careful history of the sequence of events. These attacks are frequently confused with epilepsy. In epilepsy, the cyanosis occurs after the tonic–clonic phase of the seizure. In breath-holding spells cyanosis occurs before but, more importantly, the diagnosis rests on the fact that the attacks are always precipitated by an appropriate stimulus. An EEG is not necessary except when the diagnosis is in doubt and epilepsy is suspected. An ECG must be done in pallid asystolic spells to exclude long QT interval syndromes. Always exclude anaemia, which is a well-documented cause of breath-holding episodes. Also exclude chronic hypoxaemia, which is also a cause from unrecognised cardiac or respiratory disease.

Prognosis
These attacks are frightening for the parents, but are harmless. They eventually cease with time, and if there is no underlying pathology they do not have any long-term effects. There is no risk of subsequent epilepsy. Some infants with the pallid type go on to develop faints in later childhood.

Management
The parents need to be given an explanation of these attacks and reassured about their harmless nature. There is no effective drug and no need for drug treatment. Treat anaemia and hypoxaemia if these are present.

5.16.J Migraine

Introduction
Migraine is a common cause of recurrent headaches in children. Its prevalence increases with age. It may be preceded by a history of recurrent abdominal pain and vomiting at a younger age (abdominal migraine, cyclical vomiting). The headache is typically throbbing in nature, temporal or frontal in location, more often bilateral than unilateral (in contrast to adult migraine), and commonly associated with nausea, vomiting, pallor and sometimes photophobia. It usually lasts for 1–3 hours, but sometimes persists for 24 hours, and it is relieved by sleep. Migraine is precipitated by stress (e.g. school examinations, family pressure, unrealistic expectations) and sometimes by hunger, fatigue, lack of sleep, exposure to sun, and some foods (e.g. chocolates, Coca-Cola, caffeinated drinks, nuts, cheese). A positive family history of migraine, especially on the maternal side, is found in over 90% of patients, and the diagnosis of migraine must be questioned in the absence of such a history. Between the attacks the child is well.

Classification of migraine
Migraine is classified into three types.

- **Common migraine:** There is no aura in this type. It is the commonest form in children, accounting for over 80% of children with migraine.
- **Classical migraine:** An aura precedes the headache, which is rare in children (about 10%). Visual aura include hemianopia (loss of half of the visual field), scotoma (small areas of visual loss), fortification spectra (brilliant white zigzag lines), blurred vision and flashes of lights. Occasionally sensory auras occur, consisting of paraesthesia round the mouth and numbness of the hands and feet.
- **Complicated migraine:** Rarely neurological signs occur during the headache and persist for varying periods after it. Ophthalmoplegic migraine (third cranial nerve palsy) is rare, and must be distinguished from a berry aneurysm or other space-occupying lesion compressing the third cranial nerve.

- **Hemiplegic migraine** is the occurrence of hemisindrome (weakness or numbness down one side of the body) with the headache. Recurrent attacks of hemiplegic migraine are rare in children, but occasionally, starting in infancy, a child may have alternating hemiplegia as a manifestation of migraine.
- **Basilar migraine** results from vasoconstriction of the basilar and posterior cerebral arteries. Symptoms include vertigo, tinnitus, diplopia, blurred vision, ataxia and occipital headaches. There is complete recovery after the attack. Minor head trauma may precipitate basilar migraine.

Management
A careful history and examination is essential to confirm the diagnosis of migraine. Investigations are rarely needed. Explanation of the attacks and the relatively benign nature and good prognosis will reassure the parents and the child, and by itself will lead to a reduction in frequency and severity of the headaches in over 50% of these children. Where possible, precipitating factors need to be identified and eliminated or reduced. In particular, dietary factors such as chocolate, Coca-Cola, caffeinated drinks and cheese should be avoided.

Acute attack
Rest and sleep in a quiet darkened room is usually preferred by patients. A simple analgesic alone or in combination with a non-steroidal anti-inflammatory agent is often all that is required, and if given at the onset will abort or reduce the severity of the headaches. Paracetamol (20 mg/kg per dose, repeated every 6 hours as necessary) and ibuprofen (5 mg/kg per dose) are useful agents.

If nausea and vomiting are troublesome, an anti-emetic may be prescribed, such as metoclopramide. Aged 5–9 years 2.5 mg and 9–18 years 5 mg three times daily orally or 100–150 microgram/kg slowly (over 2 minutes) by IV injection (maximum 1 mg). Children weighing over 60 kg can have metoclopramide orally 10 mg three times daily.

Prochlorperazine is also useful, 200 micrograms/
kg (maximum 12.5 mg) orally IM or IV immediately, then 100 micrograms/kg per dose 6- to 8-hourly, orally or rectally. Prochlorperazine is not licensed for use in children who weigh less than 10 kg. Extrapyramidal side effects may occur.

The triptans (sumatriptan, zolmitriptan and rizatriptan) are serotonin-receptor agonists and are highly effective for the acute attack, but their use in children under 12 years of age awaits further evaluation. The dose of sumatriptan for adults is 50–100 mg orally as soon as possible after onset. It must not be used for basilar or hemiplegic migraine.

**Prophylactic treatment**

If the headaches are frequent (at least three to five per month) and troublesome, continuous prophylaxis is required, usually for a period of 1 year. If the headaches recur, the course of treatment is repeated. The drug of choice for children is propranolol, but pizotifen and clonidine have both been tried in children, with varying degrees of success.

- Propranolol is a beta-blocker, and can be given to children over 2 years of age (the dose for children aged 2–12 years is 200–500 micrograms/kg three times daily orally; for children over 12 years it is 20–40 mg two to three times daily). **Propranolol must not be given to children with asthma or diabetes, and it may cause depression.**

- Clonidine can be given at a dose of 2 micrograms/kg every 8 hours (maximum dose 200 micrograms/day).

- Pizotifen is given for children aged 5–10 years at an initial dose of 500 micrograms, increasing to 1 mg at night or 500 micrograms 8-hourly. For children aged 10–12 years give 1 mg at night or 500 micrograms 8-hourly. For children aged 12–18 years give 1.5 mg at night, increasing to 1.5 mg 8-hourly. It may cause weight gain.

**Prognosis of migraine**

The prognosis is generally good. About 50% of children with migraine will undergo spontaneous prolonged remission after the age of 10 years. In most children the headaches are infrequent and rarely interfere with schooling or daily activities. In some the headaches are frequent and troublesome, and these will require prophylactic treatment.

### 5.16.K Neurosurgical disorders

<table>
<thead>
<tr>
<th>BOX 5.16.K.1 Minimum standards</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Maternal folic acid before and during pregnancy.</td>
</tr>
<tr>
<td>- Dexamethasone and mannitol.</td>
</tr>
<tr>
<td>- High-dependency care.</td>
</tr>
<tr>
<td>- Antibiotics.</td>
</tr>
<tr>
<td>- Anticonvulsants.</td>
</tr>
<tr>
<td>- Shunts.</td>
</tr>
<tr>
<td>- Regional/national centre (with CT and MRI scanning facility).</td>
</tr>
</tbody>
</table>

**Introduction**

Every country needs at least one hospital equipped to manage children with neurosurgical problems. The central and essential component of accurate assessment of the most frequently encountered intracranial neurosurgical emergencies is the prompt identification of the presence of raised intracranial pressure (ICP). Once this is recognised and controlled, the precise diagnosis of the site and cause can await sophisticated neuroimaging by ultrasound examination, computed tomography (CT) or magnetic resonance imaging (MRI).

**Raised intracranial pressure**

The signs and symptoms are different for pre-speech and younger infants compared with older children.

**Babies and children under 2 years**

The signs and symptoms are as follows:

- abnormally rapid head growth
- separation of cranial sutures
- bulging of the anterior fontanelle (note that the anterior fontanelle usually closes by 18 months of age)
- dilatation of scalp veins

By 2–12 years is 200–500 micrograms/kg three times daily. It is important to note that features may be non-specific (as in irritability and vomiting), that there may be marked fluctuations in the younger child’s condition from minute to minute and from hour to hour, and that frank unconsciousness occurs relatively late, often being preceded by apnoea. Decerebrate attacks can be mistaken for epileptic seizures; in the former, the child extends all four limbs and trunk, whereas in the latter, flexion of the upper limbs is more usual and there are clear tonic-clonic phases.

**Older children**

The signs and symptoms are as follows:

- headaches
- vomiting
- loss of postural control of the trunk
- falling vision
- diplopia
- neck pain and extension
- decerebrate attacks
- irregular rate and rhythm of breathing, usually with slowing of the respiratory rate
- irregular heart rate, usually with bradycardia, but occasionally with tachycardia
- decerebrate attacks.

- irritability
- vomiting
- loss of truncal tone
- fluctuating level of responsiveness
- irregular rate and rhythm of breathing, usually with slowing of the respiratory rate
- irregular heart rate, usually with bradycardia, but occasionally with tachycardia
- decerebrate attacks.

- head pain
- neck pain and extension
- decerebrate attacks
- irregular rate and rhythm of breathing, usually with slowing of the respiratory rate
- irregular heart rate, usually with bradycardia, but occasionally with tachycardia, and mounting hypertension with widening pulse pressure
- diminishing level of consciousness.
The most urgent features are failing vision, neck pain and extension, decerebrate attacks, diminishing level of consciousness and cardiorespiratory failure, as they all indicate incipient terminal events. Failing visual acuity is also urgent, as it indicates severe papilloedema and a danger of permanent visual loss. The absence of papilloedema does not exclude raised intracranial pressure; its presence does indicate that there is a risk of permanent visual loss.

Accurate cerebral localisation on a clinical basis is difficult in children and virtually impossible in babies and young children, but the following can be fairly dependable features of a supra-tentorial mass lesion:
- dysphasia
- visual field defects
- epileptic seizures.

Unilateral pupillary dilatation indicates a mass ipsilateral to the dilated pupil, or on the side of the pupil that dilated first in the case of bilateral pupillary dilatation.

Management
Although the definitive solution is removal of the causative lesion, this will often have to await the availability of imaging by computed tomography and transfer to a neurosurgical facility. The emergency relief of raised intracranial pressure can be achieved by one or more of the following medical measures:
- dexamethasone by slow IV injection (500 micrograms/kg immediately and then 100 micrograms/kg every 6 hours)
- 20% manitol by IV infusion (250–500 mg/kg and repeated as required based on response and clinical signs; maximum total dose 2 grams/kg infusion over 20 minutes).
- alternatively, hypertonic saline can be used (2.7% or 3% at a dose of 3 mL/kg). This may not be associated with a rebound rise in pressure as may occur with manitol and does not induce a diuresis like mannitol but rather augments plasma volume.
- intubation and artificial ventilation to PaCO2 of about 4 kPa (if available).

In an extreme emergency, and faced with a rapidly deteriorating child with no immediate prospects of evacuation for neuroimaging and specialist neurosurgical care, the following measures can be employed if there is no history of head injury.

Babies
Trans-fontanelle needle tapping of the subdural space is undertaken, and if there is no subdural effusion, the needle is then advanced into the cerebral ventricle in the hope of finding and relieving hydrocephalus.

Infants and children
Right frontal burr-hole and ventricular drainage is undertaken (see below).

If there is a history of head injury, the procedure for ‘blind’ burr-holes is followed (see below).

Head injuries (see Section 7.3.C).

Intracranial abscesses
Spontaneous extradural, subdural or intracerebral abscesses most commonly arise in children as a complication of an acute, or very occasionally chronic, episode of infection in the paranasal sinuses or middle ear. The cardinal clinical features are as follows:
- raised intracranial pressure
- signs of focal neurological disturbance, including epileptic seizures
  - systemic signs of sepsis; these may be absent.

The diagnosis can be confirmed by CT scan with IV contrast enhancement (if available).

- Evacuation of pus is important both to relieve raised intracranial pressure and mass effect, and to provide material for accurate microbiological diagnosis. Intracerebral abscesses can often be drained satisfactorily by burr-hole aspiration, which may have to be repeated. Extracerebral subdural collections will usually require a major craniotomy.
- Raised intracranial pressure will usually be very severe, and may require the use of manitol.
- Pending microbiological diagnosis, or in the absence of such support, the most useful antibiotics are a combination of cefuroxime (IV 60 mg/kg 6-hourly for 3 days, then 25 mg/kg 6-hourly) and metronidazole (7.5 mg/kg by IV infusion over 20 minutes every 8 hours) for a minimum of 3 weeks. A further 6 weeks of an appropriate oral antibiotic, such as amoxicillin, is usually necessary.
- Amoxicillin route: oral:
  - Dose: 1 month to 18 years of age, 40 mg/kg daily in 3 divided doses maximum dose 1.5 g daily in 3 divided doses.
- An ENT surgeon may need to drain fronto-ethmoid sinuses or mastoids to prevent recurrence.

Hydrocephalus
Hydrocephalus can be diagnosed by trans-fontanelle ultrasound in infants with an open anterior fontanelle, and by CT (if available) in older infants and children. CT will also demonstrate the likely cause.

- The emergency relief of hydrocephalus, or suspected hydrocephalus, is by trans-fontanelle needle drainage in babies, or by burr-hole drainage and insertion of an external ventricular drain in older children.
- The best site for burr-hole drainage is on the right coronal suture in the mid-orbital line. The landmarks for trans-fontanelle puncture are the same as for subdural puncture (see above), but the needle is angled more steeply. Most babies will tolerate venting of up to 50 mL of CSF. Following withdrawal of the needle, the skin puncture is closed with a suture to prevent external leakage of CSF.
- It is important to have the CSF examined by a microbiology laboratory, remembering that sub-acute, partially treated, ‘neglected’ pyogenic meningitis and tuberculous meningitis can present with hydrocephalus.
- Definitive treatment may involve removal of the obstructing lesion in the case of a tumour or other mass, or establishment of a permanent CSF diversion by inserting an implanted ventriculo-peritoneal shunt.
- Shunt blockage is common and must be diagnosed quickly. The symptoms of shunt blockage are essentially those of raised intracranial pressure, and require urgent attention if death or disability is to be avoided. The most reliable eye sign is loss of upward gaze. Blockages
usually affect the ventricular end of the catheter rather than the peritoneal end. Many children develop abdominal distension after shunting. This is due to the unusual load of CSF. In the absence of vomiting and constipation, it should be treated conservatively.

- Shunt infections can present acutely with features of cerebral irritation, fever and seizures if there is major ventriculitis occurring within a few days of insertion; however, this is relatively rare. The only method that is guaranteed to eliminate shunt infection is removal of all components, including any loose or retained fragments from earlier procedures, interval external drainage, appropriate antibiotics and shunt reinsertion through fresh incisions. As with all serious infections, success is dependent upon accurate microbiological diagnosis. The most frequently encountered organisms are *Staphylococcus epidermidis* and *Staphylococcus aureus*. The most useful antibiotic is vancomycin by IV injection children 1 month to 18 years 15 mg/kg every 8 hours to a maximum daily dose of 2 grams. The duration of treatment depends on how rapidly the CSF becomes sterile, but a minimum of 7 days is recommended.

### Myelomeningocele

Myelomeningocele is the commonest major congenital malformation compatible with survival. Its incidence has been progressively falling for 20 years. Although there are regional variations, the overall frequency is 0.7–0.8 per 1000 live births. The object of management in the immediate postnatal period is the prevention of infection of the central nervous system. This is achieved by early closure of the lesion.

- The level of the open lesion is noted and an assessment made of the sensorimotor level, the state of the sphincters, any orthopaedic deformity, and the presence of major hydrocephalus, as evidenced by signs of raised intracranial pressure (see above).
- The ideal is to achieve closure within 24 hours of birth. The majority of lesions have adequate skin in the wall of the sac, as long as this is not unnecessarily sacrificed by a wide incision. The technique employed involves mobilisation of the neural plate, watertight dural repair and closure of the skin. While awaiting closure, the lesion should be protected with a dressing of moist sterile 0.9% saline, which must be replaced every few hours to prevent desiccation.
- Most babies will require surgical treatment for hydrocephalus in the first few weeks of postnatal life.

In children who are paralysed and without urinary or bowel control, the commitment is a lifelong one, and this is a challenge to families and healthcare systems. Before offering treatment to these children, it is important that their future prognosis and quality of life is discussed with the parents.

The aim should be to prevent as many as possible of these anomalies by adequate maternal nutrition prior to conception and during pregnancy. Folic acid taken prior to conception and for the first trimester of pregnancy abolishes 75% of cases of myelomeningocele and anencephaly. See Section 5.10.A.

### 5.17 Orthopaedic problems

#### 5.17.1 Minimum standards

- Antibiotics.
- X-rays.
- Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).
- Antituberculous drugs.
- Orthopaedic procedures.

### Infections

Paediatric musculoskeletal infections are a common presentation in resource-limited countries. Morbidity and mortality can be prevented by prompt diagnosis, antibiotics and surgery where indicated. Infection should be suspected in any child presenting with pain or swelling in the limbs, spine or pelvis.

### Pyomyositis

- Pus is present within skeletal muscle, most commonly in the thigh and gluteal regions.
- It is caused by bacterial infection of muscle, in nearly 70% of cases due to *Staphylococcus aureus*.
- It is common in the tropics, but exceedingly rare in the developed world.
- There may be a history of previous infection or trauma to the site.
- Signs include general malaise, swinging fever, decreased range of motion, fluctuant swelling in the later stages, and tenderness.