5.3 Lung disorders

5.3.A Pneumonia

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

Acute respiratory infection

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

- Acute upper respiratory infection (AURI): above the vocal cords and epiglottis. These infections include colds, tonsillitis and otitis media. They are not life-threatening, but may lead to disability (e.g. otitis media is a leading cause of deafness in resource-limited countries) and complications (e.g. rheumatic fever following streptococcal pharyngitis).

- Acute lower respiratory infection (ALRI): below and including the vocal cords and epiglottis. These infections include croup (and other infectious causes of upper airway obstruction), pneumonia and bronchiolitis. Acute upper airway obstruction is described in Section 5.1.

Importance of acute respiratory infection

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

Immunisation

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

Management of the child with acute upper respiratory infection

Coryza or pharyngitis

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

Presentation

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

Treatment

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

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

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

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

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

- age under 1 year
- malnutrition
pneumonia as a complication of infection with measles, pertussis, malaria or HIV.

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

The following clinical features should be recorded:

- The presence of cyanosis, which is best seen in the lips or tongue. It may be missed if the lighting is poor or if the child is anaemic (e.g. due to co-infection with malaria), and it can be difficult to detect in black children. Cyanosis is a late sign of respiratory problems, and if possible oxygenation should be assessed with a pulse oximeter. Normal saturation at sea level (SaO₂) is greater than 94%.
- Inability of the child to drink.
- The presence of chest wall indrawing (an inward motion of the lower chest wall when the child breathes in).
- The presence of grunting (expiratory braking).
- The presence of hyperinflation (asthma or bronchiolitis).
- Elevated respiratory rate. Respiratory rate is measured over 1 minute, using a suitable timing device. The respiratory rate in children varies with age. Table 5.3.A.1 lists the abnormal values for respiratory rate for various age groups.

<table>
<thead>
<tr>
<th>Age</th>
<th>Abnormally fast breathing</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2 months</td>
<td>≥ 60 breaths/minute</td>
</tr>
<tr>
<td>2–12 months</td>
<td>≥ 50 breaths/minute</td>
</tr>
<tr>
<td>12 months to 5 years</td>
<td>≥ 40 breaths/minute</td>
</tr>
</tbody>
</table>

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

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

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

Features of pneumonia include the following:

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

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

- consolidation or effusion/empyema
- wheeze
• bronchiolitis (hyperinflation with crackles at the lung bases)
• alveolitis (e.g. in HIV-induced Pneumocystis pneumonia) with end-inspiratory crackles.
• pericardial involvement (rare)
• pneumothorax (rare).

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

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

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

Table 5.3.A.2 gives guidelines for the assessment and treatment of acute respiratory infection. Children with the following features should be managed differently, as described elsewhere in this book:
• stridor (see Section 5.1.A)
• wheeze (see Sections 5.2.A and 5.2.B)
• severe malnutrition (see Section 5.10.B)
• signs suggesting meningitis (see Section 5.16.B).

**Diagnosis of severe pneumonia**

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

**In addition, some or all of the other signs of pneumonia may be present, such as the following:**
• fast breathing:
  - age < 2 months: ≥ 60 breaths/minute
  - age 2–11 months: ≥ 50 breaths/minute
  - age 1–5 years: ≥ 40 breaths/minute
• nasal flaring
• grunting (in young infants)
• lower chest wall indrawing
• chest auscultation signs of pneumonia:
  - decreased breath sounds
  - bronchial breath sounds
  - crackles
  - abnormal vocal resonance (decreased over a pleural effusion, and increased over lobar consolidation)
  - pleural rub.

Obtain a chest X-ray and SaO2 (if available).

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

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

<table>
<thead>
<tr>
<th>Sign or symptom</th>
<th>Classification</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central cyanosis and/or SaO2 &lt; 90%</td>
<td>Severe pneumonia</td>
<td>Admit to hospital&lt;br&gt;Give IV/IM appropriate antibiotics*&lt;br&gt;Give oxygen&lt;br&gt;Manage the airway&lt;br&gt;Treat high fever if present&lt;br&gt;If the child has HIV infection, refer to specific guidelines (and see Section 6.2.D)</td>
</tr>
<tr>
<td>Severe respiratory distress (e.g. head nodding, gasping, chest wall indrawing, grunting)</td>
<td>Severe pneumonia</td>
<td>Admit to hospital&lt;br&gt;Give IV/IM appropriate antibiotics*&lt;br&gt;Give oxygen&lt;br&gt;Manage the airway&lt;br&gt;Treat high fever if present&lt;br&gt;If the child has HIV infection, refer to specific guidelines (and see Section 6.2.D)</td>
</tr>
<tr>
<td>Fast breathing as below under ‘pneumonia that is not severe’</td>
<td>Pneumonia that is not severe</td>
<td>Home care (but depends on home circumstances and overall clinical state of the child)&lt;br&gt;Give an appropriate antibiotic*&lt;br&gt;Advise the mother when to return if treatment fails on amoxicillin and more appropriate second-line treatment is needed&lt;br&gt;Follow up in 2 days</td>
</tr>
<tr>
<td>Decreased breath sounds and/or bronchial breathing</td>
<td>Pneumonia that is not severe</td>
<td>Home care (but depends on home circumstances and overall clinical state of the child)&lt;br&gt;Give an appropriate antibiotic*&lt;br&gt;Advise the mother when to return if treatment fails on amoxicillin and more appropriate second-line treatment is needed&lt;br&gt;Follow up in 2 days</td>
</tr>
<tr>
<td>Crackles in the lung fields</td>
<td>Pneumonia that is not severe</td>
<td>Home care (but depends on home circumstances and overall clinical state of the child)&lt;br&gt;Give an appropriate antibiotic*&lt;br&gt;Advise the mother when to return if treatment fails on amoxicillin and more appropriate second-line treatment is needed&lt;br&gt;Follow up in 2 days</td>
</tr>
<tr>
<td>Vocal resonance and percussion suggesting consolidation and/or effusion</td>
<td>Pneumonia that is not severe</td>
<td>Home care (but depends on home circumstances and overall clinical state of the child)&lt;br&gt;Give an appropriate antibiotic*&lt;br&gt;Advise the mother when to return if treatment fails on amoxicillin and more appropriate second-line treatment is needed&lt;br&gt;Follow up in 2 days</td>
</tr>
<tr>
<td>Pleural rub</td>
<td>Pneumonia that is not severe</td>
<td>Home care (but depends on home circumstances and overall clinical state of the child)&lt;br&gt;Give an appropriate antibiotic*&lt;br&gt;Advise the mother when to return if treatment fails on amoxicillin and more appropriate second-line treatment is needed&lt;br&gt;Follow up in 2 days</td>
</tr>
<tr>
<td>Inability to drink, vomiting, reduced consciousness</td>
<td>Pneumonia that is not severe</td>
<td>Home care (but depends on home circumstances and overall clinical state of the child)&lt;br&gt;Give an appropriate antibiotic*&lt;br&gt;Advise the mother when to return if treatment fails on amoxicillin and more appropriate second-line treatment is needed&lt;br&gt;Follow up in 2 days</td>
</tr>
</tbody>
</table>

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

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

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

Give oxygen if the child shows any of the following:
- Restlessness (if oxygen makes the child more comfortable)
- Severe chest wall indrawing
- A breathing rate of more than 70 breaths/minute (in a child aged 2 months to 5 years)
- Grunting (in an infant under 2 months of age)
- Gaspings
- If a pulse oximeter is available, SaO2 of less than 94% (at sea level; lower values will be normal at high altitude, and normal values of SaO2 should be known for healthy local children in your area if it is at high altitude). Aim to maintain SaO2 in the range 94–98%.

Give oxygen until the signs of hypoxia (e.g. severe lower chest wall indrawing, high breathing rates and/or SaO2 < 94% in air) are no longer present.

**Oxygen delivery**

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

Figure 5.3.A.4 shows the delivery of oxygen through nasal cannulae. A mask should be used to give high-flow oxygen during resuscitation.

![Nasal cannulae for delivering oxygen. The cannula has been taped to the child’s cheeks, close to the nostrils. The tubing is run under the child’s shirt to stop them pulling it, and leads to the low-flow meter and oxygen concentrator or cylinder. A flow splitter may be used.](image)

**Antibiotics**

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

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

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

**Symptomatic and supportive treatment for children with all degrees of pneumonia**

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

**Fever:**
- Remember that fever may not be simply due to the child’s pneumonia. Consider other diagnoses, such as malaria.
- If the child has fever (~39°C or ~102.2°F) that appears
to be causing distress, give paracetamol oral or rectally, 10–15 mg/kg 4- to 6-hourly.
- Remove by gentle suction under direct observation any thick secretions in the throat which the child cannot clear.
- Ensure daily maintenance fluids appropriate for the child's age, but avoid over-hydration.
- Encourage breastfeeding and oral fluid intake.
- If the child cannot drink, insert a nasogastric tube and give maintenance fluids in frequent small amounts. If the child is taking fluids adequately by mouth, do not use a nasogastric tube, as it increases the risk of aspiration pneumonia. Encourage eating as soon as food can be taken. When the child is recovering, nutritional rehabilitation may be necessary.

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

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

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

Pneumonia that does not respond to standard antibiotics within 2 weeks

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

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

Staphylococcal pneumonia
Staphylococcal pneumonia is suspected if there is rapid clinical deterioration despite treatment, a pneumatocoele or necrotising pneumonia with effusion on chest X-ray, numerous Gram-positive cocci in a smear of sputum, or heavy growth of Staphylococcus aureus in cultured sputum or empyema fluid.

- Treat with cloxacillin (50 mg/kg IM or IV every 6 hours) and gentamicin (7.5 mg/kg IM or IV once a day) for at least 7 days.
- When the child improves, continue cloxacillin/flucloxacillin orally four times a day for a total course of 3 weeks. Note that cloxacillin can be substituted by another anti-staphylococcal antibiotic, such as oxacillin, flucloxacillin or dicloxacillin.

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

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

Management of ALRI in special circumstances

Management of the child under 6 months of age
Young infants with severe ALRI/pneumonia may not cough, but rather they may present with apnoea, poor feeding or hypothermia. Remember that in infants under 2 months of age, the abnormal respiratory rate cut-off is higher (> 60 breaths/minute). For infants aged 2–12 months the cut-off is > 50 breaths/minute.

- Some chest wall indrawing is normal during REM (dream) sleep.
- All infants with severe ALRI/pneumonia should be admitted to hospital for treatment.
- Bronchiolitis is a frequent cause, and usually involves hypoxaemia due to ventilation to perfusion mismatch. Oxygen is usually required. Additional respiratory support (see Section 5.2.A) may also be necessary, especially if there is apnoea or severe respiratory distress leading to exhaustion.
- Grunting (a short expiratory noise at the start of expiration) is common and usually an indication for oxygen.
- Avoid using chloramphenicol in infants under 2 months of age (there is a risk of development of “grey baby syndrome”). Use benzylpenicillin or ampicillin plus gentamicin instead.
- Respiratory infection in neonates may rapidly develop into septicaemia, shock and death, so it is essential to act quickly (see Section 3.4).

Further reading
5.3.B Pleural effusion, empyema and bronchiectasis

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

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

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

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

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

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

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

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

1. Select a drain, the largest that will comfortably pass through the intercostal space into the cavity by holding the tip of the tube in the forceps. Do not use the stylet, as this can damage the lung.
2. Position the child and locate the effusion in the same way as for the diagnostic tap.
3. Use sufficient local anaesthetic (1% lidocaine).
4. Make an incision in the skin and part the underlying muscle with artery forceps.
The mucus within the lumen then becomes dehydrated. Water moves from the airway lumen into the cell by osmosis. The cell cytoplasm has a high salt content, and chloride ions cannot leave the cell to enter the bronchial lumen. The cell with cilia, and this leads to bacterial colonisation of the airway, with chronic inflammation and neutrophil damage. There are also viscid secretions in the biliary tract, pancreas and reproductive system, causing poor fat digestion and very low fertility in male patients.

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

**Incidence**

The incidence of cystic fibrosis in countries such as the UK and the USA is around 1 in 2500 live births, and around 1 in 25 of the population are carriers. Very little is known about the incidence of cystic fibrosis in other countries, but it is estimated that at least 25% of the population are carriers. Very little is known about the incidence of cystic fibrosis in other countries, but it is estimated that at least 25% of the population are carriers.

**5.3.C Cystic fibrosis**

**BOX 5.3.C.1 Minimum standards**

- Diagnostic testing.
- Pancreatic enzyme supplements.
- Fat-soluble vitamins (A, D and E).
- Daily chest physiotherapy.
- Early use of antibiotics, including fluclaxacinil, amoxy-
  cillin, chloramphenicol, ciprofloxacin, gentamicin and
ceftazidine.

**Introduction**

Pathophysiology

In the cells lining the airways of patients with cystic fibrosis (CF), chloride ions cannot leave the cell to enter the bronchial lumen. The cell cytoplasm has a high salt content, and water moves from the airway lumen into the cell by osmosis. The mucus within the lumen then becomes dehydrated.

Sticky mucus interferes with the action of the respiratory cilia, and this leads to bacterial colonisation of the airway, with chronic inflammation and neutrophil damage. There are also viscid secretions in the biliary tract, pancreas and reproductive system, causing poor fat digestion and very low fertility in male patients.

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

**Diagnosis**

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

Sometimes a child who has had lobar pneumonia does not recover fully, and develops bronchiectasis in the affected lobe. There are other rare causes, such as some viral infections. Children with bronchiectasis usually cough and produce sputum every day. Their symptoms may become much worse at times due to secondary infection. The child may have finger clubbing, a hyperinflated chest and coarse crackles in many parts of the lung. Look for thickened bronchi and areas of consolidation on the chest X-ray.

**Treatment**

Bronchiectasis cannot be cured, although occasionally symptoms can be improved by removing the lung lobe that is most severely affected. The child and their parents must understand that daily treatment with chest physiotherapy and frequent courses of antibiotics will be needed. The use of physiotherapy is described in Section 8.3.
the frequency of the disorder in resource-limited countries. Diagnosis relies on the sweat test, which is difficult to perform where laboratory facilities are limited. The incidence of cystic fibrosis among black South Africans is thought to be between 1 in 700 and 1 in 14,000, with between 1 in 14 and 1 in 60 of the general population being carriers. In some well-resourced countries there is routine screening of newborn infants from heelprick blood samples.

**The CF gene**
The CF gene is on chromosome 7. The commonest mutation causing disease is DF508, and it occurs all over the world. It is as common in cystic fibrosis patients in North Africa as it is in those in Northern Ireland. Over 1,000 other mutations have been found, many of which are rare. The gene product is a protein which sits on the apical membrane of epithelial cells and regulates the movement of chloride ions. As cystic fibrosis is a recessively inherited condition, two abnormal genes, one from each parent, are required for the disease to occur, and then this protein is defective and chloride transport is disrupted.

**Presentation**

**Meconium ileus**
In the newborn period, babies may present with a triad of:
- failure to pass meconium in the first 24 hours
- abdominal distension
- vomiting.

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

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

**Differential diagnosis**
The differential diagnosis of chronic cough and failure to thrive includes the following:
- pulmonary tuberculosis
- bronchiectasis (especially following measles, which may also cause chronic diarrhoea)
- HIV infection.

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

**Figure 5.3.C.1** Differential diagnosis of the child with chronic cough and failure to thrive.
Diagnosing cystic fibrosis

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

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

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

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

**Fat-soluble vitamins**
The child should be given extra fat-soluble vitamins. Appropriate doses are vitamin E, 50 mg once daily in infants and young children (aged 0–5 years), 100 mg/day in older children (aged 5–12 years), and 200 mg/day in patients over 12 years of age. Vitamin E may be given as vitamin E suspension 100 mg/mL or as 50 mg tablets. Multivitamin drops, such as Abidec, which contains vitamin A 4000 units/6 mL and vitamin D2 400 units/6 mL, are also required. Abidec should be given as follows:
- 0.3 mL/day for newborn infants
- 0.6 mL/day for infants aged 1–12 months
- 1.2 mL/day for children over 1 year of age.

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

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

(For physiotherapy techniques, see Section 8.3)

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

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

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

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Dose</th>
<th>Number of doses/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 year</td>
<td>125 mg</td>
<td>4</td>
</tr>
<tr>
<td>1–6 years</td>
<td>250 mg</td>
<td>4</td>
</tr>
<tr>
<td>7–12 years</td>
<td>500 mg</td>
<td>4</td>
</tr>
<tr>
<td>&gt; 12 years</td>
<td>500–1000 mg</td>
<td>4</td>
</tr>
</tbody>
</table>

Amoxicillin or ampicillin

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Dose</th>
<th>Number of doses/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 year</td>
<td>125 mg</td>
<td>4</td>
</tr>
<tr>
<td>1–7 years</td>
<td>250 mg</td>
<td>4</td>
</tr>
<tr>
<td>&gt; 7 years</td>
<td>500 mg</td>
<td>4</td>
</tr>
</tbody>
</table>

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

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

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

Gentamicin

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

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

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

Ciprofloxacin

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

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

Ceftazidime

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

Other manifestations and complications of cystic fibrosis

In addition to those features mentioned above under clinical presentation, the following may occur:
- haemoptysis (not usually a major problem)
- pneumothorax (usually small because of chronic pleural thickening)
- bronchiectasis
- biliary cirrhosis, portal hypertension and oesophageal varices
- diabetes mellitus (requiring insulin)
- infertility (in men)
- women may become pregnant but will need careful management of their chest problems
- ‘meconium ileus equivalent’ (obstructed bowel occurring in older children)
- arthropathy.

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