Objectives

When you have completed this unit you should be able to:
- Give reasons why tuberculosis is an important and dangerous disease.
- Describe primary tuberculous infection of the lung.
- List the complications of primary tuberculous infection.
- Diagnose tuberculosis.
- Perform and interpret a Mantoux skin test.
- Treat tuberculosis.
- List ways to prevent tuberculosis.

INTRODUCTION

8-1 What is tuberculosis?

Tuberculosis is a chronic infectious disease. Tuberculosis is often referred to as TB and may involve most organs of the body, but especially the lungs.

8-2 What causes tuberculosis?

Tuberculosis is caused by a bacillus called Mycobacterium tuberculosis. The TB bacillus (tuberculous bacillus) is a long, thin bacteria.

NOTE Mycobacterium tuberculosis was first described by Robert Koch in 1882.

8-3 How is tuberculosis spread from person to person?

Tuberculosis is usually spread when an infected person talks, coughs, spits, laughs, shouts, sings or sneezes. This sends a spray of very small droplets into the air (i.e. airborne droplet spread). Live TB bacilli (plural of bacillus) from the patient’s lungs then float in the air and may be breathed in by other people. The inhaled TB bacilli can cause an infection of the lung. Tuberculosis is usually spread from adults with untreated tuberculosis of the lungs (pulmonary tuberculosis). Therefore, a child (the contact) with tuberculosis almost always has been in close contact with an adult with pulmonary tuberculosis (the source). It is less common for a child to catch tuberculosis from another child as children usually do not cough up TB bacilli in such large numbers. Adults with untreated tuberculosis are a danger to children in the family.

NOTE TB bacilli in unpasteurised cow’s milk can be drunk and cause infection of the tonsils or gut, but this is very uncommon in South Africa.

Tuberculosis in children is usually spread from an adult with untreated pulmonary tuberculosis.
8-4 Do all children infected with *Mycobacterium tuberculosis* develop tuberculosis?

No. Most children infected with TB bacilli (i.e. *Mycobacterium tuberculosis*) do not develop tuberculosis (TB disease) because their immune system is able to control the infection and kill most of the TB bacilli. Therefore, the natural immune response protects most children with TB infection from developing tuberculosis.

**NOTE** Young children infected before 3 years of age and immunocompromised children have a much greater chance (20–50%) of developing tuberculosis after infection with TB bacilli.

8-5 Is tuberculosis common?

Infection with TB bacilli is very common, and it is estimated that almost 50% of South Africans have been infected. Most infections take place during childhood. However, only about 10% of all people with TB infection progress to tuberculosis (TB disease) during their lifetime. Therefore, TB infection is far more common than tuberculosis.

Tuberculosis is uncommon in most developed countries. However, tuberculosis is common in developing countries such as South Africa where the incidence has increased rapidly in the last few years. Tuberculosis is particularly common in the Western Cape and KwaZulu-Natal.

**Most TB infection occurs during childhood.**

**NOTE** It is estimated that 10 million new cases of tuberculosis occur worldwide each year with 3 million deaths due to TB. About 40 South Africans die of TB each day. With the AIDS epidemic this figure is rising rapidly.

8-6 In which communities is tuberculosis common?

In poor, disadvantaged communities where overcrowding, undernutrition and HIV infection are common. Tuberculosis is a disease of poverty. Tuberculosis may be spread in any overcrowded spaces such as homes, schools, churches, buses, clinics and trains. TB infection is usually caught from a family member, friend or neighbour.

**Tuberculosis is usually seen in poor communities.**

**NOTE** About 95% of new TB cases and 99% of TB deaths worldwide are in developing countries. In developed countries TB is virtually confined to poor, overcrowded environments and ethnic minorities.

8-7 Why is tuberculosis an important disease?

Because it is an important cause of illness and death in many poor countries.

8-8 Which infected children are at greatest risk of developing tuberculosis?

A child can only develop tuberculosis if the child is exposed to TB bacilli. Therefore, the more tuberculosis there is in the community, the higher is the risk that children will become infected. However, some children are at a particularly high risk of developing tuberculosis if they become infected with TB bacilli:

- **Children exposed to large numbers of TB bacilli:** Children living in poor, overcrowded, poorly ventilated conditions are at great risk of becoming infected. They are often exposed to large numbers of TB bacilli due to many adults with untreated pulmonary tuberculosis.
- **Children with a weak immune system:** In these children infection with TB bacilli may progress to tuberculosis because they have an inadequate immune system which is unable to control the infection.
Therefore, tuberculosis is most common when a child with a weak immune system is exposed to a large number of TB bacilli.

8-9 Which children have a weak immune system?

Young children under 3 years have an immature (weak) immune system which is unable to control severe infections. The younger the child, the less mature the immune system.

Some older children have an immune system which has been weakened by illness, malnutrition or drugs:

- Children with HIV infection
- Children recovering from measles or whooping cough
- Malnourished children
- Children on large doses of steroids

Severe tuberculosis itself weakens the immune system.

8-10 What is primary tuberculosis of the lung?

Tuberculous infection usually starts when TB bacilli are inhaled into the lung. During the first 6 weeks of infection the immune system is unable to control the TB bacilli, which multiply and cause a small, local area of inflammation in the lung. From here TB bacilli also spread along the lymphatics to the local lymph nodes (hilar nodes) at the place where the main bronchi divide into branches. After 6 weeks the immune system usually becomes active and kills most of the TB bacilli. As a result, the primary infection is asymptomatic in most children and does not cause clinical illness. Primary tuberculosis is common.

NOTE The primary infection in the lung, together with the infected regional lymph nodes, is called the primary complex (Ghon complex). Often primary infection of the lung can only be recognised by the presence of a positive skin test. Mild flu-like symptoms may sometimes occur.

Inhaling tuberculous bacilli into the lung results in a primary infection.

8-11 Can the primary infection cause illness due to spread of the infection within the lung?

Unfortunately, yes. Tuberculosis is a very unpredictable disease as there are a number of different ways that the primary infection can spread in the lungs:

1. Usually the primary infection heals and does not spread, as the TB bacilli have been contained by the natural immunity. These children do not develop tuberculosis.
2. In some children, especially those with a weak immune system, the body is unable to control the primary infection. The TB bacilli at the site of the primary infection multiply and spread to cause progressive lung infection (tuberculous pneumonia).
3. TB bacilli may multiply in the regional lymph nodes, causing them to rapidly enlarge and compress the bronchus or trachea. Clinically this may present as wheezing or stridor with either collapse or hyperinflation of a lobe or the whole lung.
4. The TB bacilli often remain dormant (inactive or ‘sleeping’) for many months or even years after the primary infection. The body has been able to control but not kill all the TB bacilli. If the child’s immune system later becomes weakened by malnutrition or another infection, such as HIV or measles, the TB bacilli may reactivate (multiply) and a local area of tuberculosis pneumonia will develop. Pulmonary tuberculosis due to reactivation of dormant TB bacilli may only present years after the primary infection. This is in contrast to progressive tuberculosis, which usually develops within the first year after the primary infection.
5. ‘Adult type’ TB is usually seen in older children, especially adolescents. The area of tuberculous pneumonia may ‘break down’ and rupture into a bronchus. An infected lymph node can also erode into a bronchus. The TB bacilli can now spread along the bronchi to other parts of the lung. This occurs most commonly in the upper parts of the lung and results in an air filled cavity (a hole) containing caseous (dead) tissue which contains huge numbers of TB bacilli. This adult form of pulmonary tuberculosis (‘open tuberculosis’) is very infectious as many TB bacilli enter the airways. From here they are then coughed into the air where they may be breathed in and infect the lungs of other people. Adult pulmonary TB is usually the source of TB infection in children.

6. Damage to the large airways by tuberculosis can result in bronchiectasis.

7. Tuberculous infection may also spread into the pleura causing an effusion.

8. Once the TB bacilli have spread beyond the primary infection (spread into the lung or enlarged lymph nodes) the child will become ill. Prompt diagnosis and urgent treatment is very important in these children with pulmonary tuberculosis.

8-13 Can tuberculous infection spread from the lung to other parts of the body?

- Yes. Infection with TB bacilli can spread from the lung, via the blood stream (TB bacteraemia,) to most organs of the body (extrapulmonary tuberculosis). The TB bacilli usually spread at the time of the primary lung infection. Sometimes tuberculosis of other organs presents soon after the primary lung infection. However, the TB bacilli often remain dormant in these organs for many months or years before they start to multiply and cause local tuberculosis. This reactivation of TB bacilli is usually due to weakening of the immune system.

- TB bacilli can also spread to other organs via the lymphatics. Spread from the hilar lymph nodes is usually up to the cervical lymph nodes or down to the abdominal lymph nodes. Lymph nodes in the axilla or groin may also be involved. Tuberculosis of organs other than the lungs is not infectious to other people.

8-14 Which other organs can be involved in tuberculosis?

Although the lung is the most common organ to be infected by TB bacilli, tuberculosis can involve any other organ of the body (extrapulmonary tuberculosis). The organs which are most commonly infected via the blood stream in children are:

- The meninges (tuberculous meningitis)
- Bones, especially the spine (tuberculous osteitis)
- Joints, especially the hip joint (tuberculous arthritis)

**NOTE** The abdomen, skin, tonsils, pericardium, bone marrow, middle ear and genitalia are less common sites of tuberculosis in children. Tuberculosis of the kidney usually only follows...
5 or more years after the primary infection and therefore is uncommon in childhood.

8-15 What are the most common complications of primary tuberculosis in children?
The most common complications of primary tuberculous infection in children are:

- Pulmonary spread (tuberculous pneumonia)
- Airway compression by hilar or mediastinal lymph nodes
- Pleural effusion
- Tuberculosis of the cervical lymph nodes
- Tuberculous meningitis
- Miliary tuberculosis

Note: Fifty percent of children with miliary TB are under 2 years of age and 80% are under 5 years. Thirty percent of these children will also have meningeal involvement.

8-16 How is tuberculosis diagnosed?
The suspected diagnosis of tuberculosis is often difficult to prove. The following are used clinically to diagnose tuberculosis in children:

1. There is often a history of an adult in the home with infectious pulmonary tuberculosis in the last 6 months (a history of contact).
2. The child often comes from a poor, overcrowded environment and has a weak immune system (young, undernourished or infected with HIV or measles).
3. There are clinical signs and symptoms of tuberculosis.
4. The tuberculin skin test is usually positive (but often negative in children with malnutrition or HIV infection).
5. The chest X-ray is usually abnormal.
6. TB bacilli (*Mycobacterium tuberculosis*) may be found in the sputum, gastric aspirate or other body fluids.
7. A high index of suspicion is very important in the early diagnosis of tuberculosis, as tuberculosis may present in many different ways.

8. Identifying the person who is the source of tuberculosis is also important.

The diagnosis of tuberculosis in children usually depends on a history of contact, clinical signs, tuberculin skin test and chest X-ray.

Note: A number of new methods, such as PCR for *Mycobacterium*, promise quick, sensitive and accurate methods of diagnosing tuberculosis.

8-17 What are the clinical signs and symptoms of tuberculosis?
The early signs and symptoms of tuberculosis are often vague and non-specific making the diagnosis difficult. These general signs and symptoms are caused by tuberculosis at any site in the body:

- Failure to thrive with poor weight gain or weight loss. This may be first noticed when the child’s weight is plotted on the Road-to-Health Card.
- Feeling generally unwell with loss of appetite, apathy and fatigue (feeling weak and tired).
- A fever for more than 2 weeks, often with sweating, especially at night.
- Lymphadenopathy, especially in the neck. There may also be an enlarged liver and spleen.

The later signs of tuberculosis usually depend on which organ or organs are infected (e.g. meningitis or abdominal distension).

Suspecting tuberculosis is the first step in making the diagnosis.

Note: Lymphadenopathy usually consists of a number of mildly tender or non-tender nodes stuck together (matted).

Phlyctenular conjunctivitis (a patch of conjunctivitis at the junction of the sclera and cornea) and erythema nodosum (raised, tender, purple patches on the shin) should always suggest TB.
8-18 What are the signs and symptoms of pulmonary tuberculosis?

- In addition to the early, general signs and symptoms, the most important sign of pulmonary tuberculosis is a persistent, cough lasting 3 weeks or more. The cough may be dry or productive. Shortness of breath, fast breathing and chest pain (usually older children) may also be present. Unlike adults, blood stained sputum is uncommon in children with pulmonary tuberculosis.
- The enlarged hilar nodes may press on a bronchus causing wheezing, coughing or stridor. The wheeze does not respond to inhaled bronchodilators.

**A persistent cough lasting longer than 3 weeks is an important symptom of pulmonary tuberculosis.**

8-19 How can a clinical diagnosis of pulmonary tuberculosis be confirmed?

A chest X-ray is very important in confirming a clinical suspicion or diagnosis of pulmonary tuberculosis. In children, tuberculosis is often diagnosed on a chest X-ray.

**A chest X-ray is an important way of diagnosing pulmonary tuberculosis.**

**NOTE** In children with HIV infection, other HIV related lung conditions may present with a similar X-ray appearance. This makes interpretation more difficult. If pneumonia does not respond to a weeks course of antibiotics, always suspect TB.

8-20 What are the signs of tuberculosis on a chest X-ray?

In children the following are the most common chest X-ray (radiographic) features:

- The site of the primary infection in the lung cannot usually be seen on a chest X-ray. However, the associated hilar lymphadenopathy (enlarged lymph nodes where the main bronchi enter the lung) is seen, often with widening of the mediastinum. A lateral chest X-ray will make it easier to see hilar adenopathy.
- The enlarged hilar lymph nodes may partially or completely compress a bronchus resulting in an area of over-expansion (air trapping), collapse or consolidation.
- Miliary tuberculosis presents with multiple small spots (nodular pattern) evenly spread through both lungs.
- A pleural effusion, especially in older children.
- A cavity may form within the area of pneumonia, especially in adolescents. This is usually seen in the upper lobes of the lungs.

In young children the interpretation of a chest X-ray may be difficult. A good chest X-ray is important to both diagnose tuberculosis and monitor the response to treatment. Some children with tuberculosis may have a normal chest X-ray, e.g. infants with tuberculous meningitis, bone tuberculosis or any other form of extrapulmonary tuberculosis.

8-21 What is a tuberculin skin test?

This is a skin test done with tuberculin which contains protein from TB bacilli. Usually PPD (i.e. Purified Protein Derivative) is the form of tuberculin which is used. It does not contain live TB bacilli. The most accurate method of tuberculin skin testing is the Mantoux test, when a small amount of PPD is injected into the skin (intradermally). If a large area of swelling (induration) develops after 2 to 3 days at the injection site, the test is said to be positive. A positive skin test indicates that the child is infected, or has previously been infected with the TB bacillus, or been given BCG. As a result the child has now developed a sensitivity (an ‘allergy’) to the PPD.

The Tine test is also used but is not as accurate as a Mantoux test.

**NOTE** The induration at the site of the skin test is due to delayed sensitivity to the PPD, which develops at the time of the primary infection or the BCG immunisation. This indicates a good cellular immune response. The effect of BCG
on the tuberculin skin test, however, does not last more than 2 years. Other signs of more marked sensitivity to *Mycobacterium tuberculosis* include phlyctenular conjunctivitis and erythema nodosum.

8-22 How is the Mantoux skin test done?

A 1 ml syringe and size 26 needle are used to inject 0.1 ml of tuberculin (PPD) into the skin (*intradermally*) over the inner side of the left forearm. It is very important that the tuberculin is injected into the skin and not under the skin (subcutaneously). If the tuberculin is correctly injected into the skin a raised, pale weal of 5 to 10 mm is formed. If no weal is raised, the tuberculin has been injected too deep in error.

Incorrect injection under the skin may make the result difficult to interpret.

8-23 How should you read a Mantoux skin test?

The Mantoux skin test must be read 2 to 3 days (48 to 72 hours) after it is done. The widest transverse diameter (across the arm) of induration (raised, swollen, thickened area of skin) is measured. It is important that the induration and not the area of redness is measured. The diameter of the induration is best measured with a ruler. The result should be reported in millimeters and not simply as positive or negative. The interpretation is as follows:

1. If the diameter of induration is 0 to 4 mm the test is negative.
2. A diameter of induration of 5 to 9 mm is intermediate and may be due to BCG or TB infection. In a healthy HIV negative child this usually indicates that BCG has been given. However, in HIV infected or severely malnourished children, it may indicate tuberculosis.
3. A diameter of induration of 10 mm or more is positive and indicates infection with TB bacilli.

A Mantoux skin test of 10 mm or more indicates tuberculous infection. However, an induration between 5 and 9 mm cannot differentiate between children who have a tuberculous infection and those who have had BCG in the past 2 years. Furthermore, a result of 10 mm or more cannot differentiate between a recent healed TB infection and active tuberculosis. It is unfortunate that BCG may confuse the interpretation of the Mantoux skin test in the first 2 years. It is important to understand that a positive Mantoux test suggest tuberculous infection but does not necessarily mean that the child has tuberculosis.

A positive Mantoux skin test indicates tuberculous infection but not necessarily tuberculosis.

**Note:** An area of induration of 5 to 9 mm may also indicate infection with a non-tuberculous *Mycobacterium*.

8-24 Does a negative Mantoux test exclude infection with tuberculous bacilli?

No. Although a negative Mantoux test suggests that there is no tuberculosis, the test may be negative (less than 5 mm induration) in spite of active infection with TB bacilli if the child’s immune system is not reacting to the tuberculin. Therefore, the test may be falsely negative, even though the child has tuberculosis, in:

- Early tuberculous infection (the Mantoux skin test becomes positive only 6 weeks to 3 months after the TB infection)
- Very young children
- Children with severe malnutrition
- HIV infection and AIDS
- After measles infection (for about 6 weeks)
- Children with severe tuberculous disease

**Note:** The test may also be falsely negative if the PPD is old or inactive, or if poor technique was used in doing the test.

The Mantoux test may be falsely negative in children with severe malnutrition, HIV infection, severe tuberculosis or after measles.
New blood tests may help to differentiate between TB and BCG infections.

8-25 How can tuberculosis bacilli be identified?

The most accurate way of diagnosing tuberculosis is to identify TB bacilli. Unfortunately this is not always possible in a child and the diagnosis often has to be made on the history, clinical examination, chest X-ray and Mantoux skin test alone. TB bacilli may be identified by either:

- Seeing TB bacilli
- Growing TB bacilli

In adults, TB bacilli are usually identified in a stained sample (smear and direct microscopy) of sputum (not saliva). A special stain is used to identify the bacteria as TB bacilli. The sputum is collected at a TB clinic and the test done at the nearest laboratory. The result can be obtained in a few hours. Patients who have TB bacilli identified by a ‘positive TB stain’ on a smear of their sputum are called ‘smear positive’.

When staining for TB bacilli with Ziehl-Nielsen stain, the stained bacilli are said to be ‘acid-fast’. Therefore, TB bacilli are often called ‘acid-fast bacilli’ or ‘AFBs’. The greater the concentration of AFBs in the sputum, the greater is the infectious risk to others. Sometimes TB bacilli can also be seen in other body fluids such as CSF or a pleural aspirate, in fine needle aspirates of a lymph node, or in histological specimens obtained through open biopsy.

TB bacilli can also be grown (cultured). Unfortunately this is more difficult and expensive and may take many weeks. Therefore, in most poor countries tuberculosis in adults is confirmed with a sputum smear. TB culture and sensitivity testing is important in communities where multidrug resistance is common.

A definite diagnosis of pulmonary tuberculosis in adults is usually made by identifying TB bacilli in their sputum.

8-26 Which adults with tuberculosis are most infectious?

Patients with untreated pulmonary tuberculosis (‘cavitary’ or ‘open TB’). These patients are highly infectious to others as they cough up large numbers of TB bacilli.

8-27 How can a sample of sputum be obtained in a child?

In older children and adults the patient can be asked to cough up a sample of sputum. However, younger children under 6 years of age are usually unable to cough up sputum to examine, as sputum is swallowed. If a sputum sample is needed in a child, it is easier to take a sample of gastric fluid which contains swallowed sputum. The gastric aspirate is best collected early in the morning before the first feed, the child having been nil per mouth for 6 hours. As gastric fluid is highly acid, 4% sodium bicarbonate in an equal volume to the gastric aspirate should be added to the specimen to neutralize the acid. Otherwise the TB bacilli will be killed before they can be cultured.

As children usually cough up or swallow far fewer TB bacilli than adults do, positive cultures are less common in children. Therefore, diagnosing tuberculosis in children is often done without obtaining a sputum sample.

A useful method of promoting coughing and sputum collection in a child can be performed before a meal. A puff of inhaled bronchodilator is given using a spacer followed 10 minutes later by 5 ml hypertonic saline (5% saline) also by nebuliser. This is followed by chest physiotherapy to loosen the mucus and promote coughing.

8-28 What is miliary tuberculosis?

If the primary tuberculous infection spreads (disseminates or seeds) into the bloodstream, TB bacilli can be carried to many organs other than the lungs. Tuberculosis affecting many different organs at the same time is called miliary tuberculosis.
8-29 How is miliary tuberculosis diagnosed?

Miliary tuberculosis is usually seen in young children under 2 years of age or children with a weak immune system due to HIV infection or severe malnutrition. Miliary tuberculosis presents with the general signs and symptoms of tuberculosis (fever, lethargy, weakness and weight loss). In addition, these children often have an enlarged liver and spleen. Miliary tuberculosis usually develops soon after the primary infection when TB bacilli ‘seed’ to many organs. The chest X-ray shows many small spots of pneumonia (‘a snow storm’ appearance).

8-30 What are the signs and symptoms of tuberculous meningitis?

Tuberculous meningitis usually occurs a few months after the primary TB infection, especially in small children below 3 years of age. It is the most dangerous complication of pulmonary tuberculosis. The TB bacilli reach the meninges via the blood stream, usually from the lungs. Most children with tuberculous meningitis have a positive Mantoux skin test, an abnormal chest X-ray and a history of contact with an adult suffering from pulmonary tuberculosis, but all of these could be absent.

For the first few days and weeks the child is generally unwell with fever and lethargy. Then signs of meningitis appear (headache, irritability, vomiting and neck stiffness) followed by confusion, a depressed level of consciousness, convulsions and neurological signs (weakness or paralysis). The classical signs of meningitis are often not present for the first few days. The risk of permanent brain damage (hydrocephalus, paralysis, deafness, blindness, convulsions and mental retardation) or death is high, especially if the diagnosis is made late. However, recovery can be complete with early treatment.

Examination of the cerebrospinal fluid (CSF) obtained by lumbar puncture is helpful in making the clinical diagnosis. The diagnosis is only confirmed by finding TB bacilli (by staining or culture) in the CSF.

**Note** In TB meningitis the CSF typically has a markedly raised protein, low sugar and low chloride, with a dominance of lymphocytes and total cell count usually below 500/ul. In early TB meningitis the CSF may be normal. The Gram stain is negative. Unfortunately TB bacilli are rarely seen while the culture takes a few months.

All children with suspected tuberculous meningitis must be referred urgently to hospital for investigation and treatment (and treatment preferably started immediately).

8-31 What are the signs and symptoms of abdominal tuberculosis?

Abdominal tuberculosis usually results from spread of TB bacilli via the lymphatics from the chest. TB infection from the abdominal lymph nodes can then spread to the omentum, peritoneum, liver and other abdominal organs. These children present with the general signs of tuberculosis, i.e. fever, lethargy and weight loss. They may also have diarrhoea, abdominal pain and a distended (swollen) abdomen due to ascites or enlarged abdominal lymph nodes.

**Note** *Mycobacterium bovis* may also cause abdominal TB due to drinking unpasteurised milk from a cow with tuberculosis. This causes a primary TB infection of the gut. It also gives a positive Mantoux skin test.

8-32 What are the signs of tuberculous infection of the peripheral lymph nodes?

Peripheral lymphadenopathy (enlarged lymph nodes) is common in tuberculosis. Enlarged TB lymph nodes in the neck (cervical, submandibular) are usually due to spread of infection via the lymphatics from the chest. Axillary and inguinal lymph nodes are less commonly affected.

Peripheral TB lymph nodes are typically non tender (unless secondarily infected) and often matted (stuck together). In the neck the lymph nodes enlarge and fuse together becoming stuck to the skin. They may become fluctuant or even ulcerate through the skin to form a chronic sinus.
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**Note** Rarely human or bovine TB may cause a primary infection of the tonsil with enlarged cervical nodes. TB adenitis with ulceration through the skin is called scrofula.

**Enlarged lymph nodes in the neck may be caused by tuberculosis.**

**8-33 How is tuberculosis affected by HIV infection and AIDS?**

- Increasing numbers of adults and children have both HIV infection and untreated tuberculosis. As adults are highly infectious, more infants (both HIV positive and negative) are becoming infected with TB bacilli.
- HIV infection weakens the immune system. This increases the risk that the child will develop severe tuberculosis. Previous asymptomatic primary tuberculous infection may become reactivated resulting in tuberculosis. With damage to the immune system by HIV, previously well controlled TB bacilli can become active and multiply rapidly.
- Tuberculosis may be the first serious infection in an HIV infected child and be the first indication that the child is HIV infected.

**Tuberculosis is a very common complication and cause of death in children and adults with HIV infection.**

HIV infection makes the diagnosis of TB more difficult. The Mantoux skin test may be falsely negative and the chest X-ray confusing. While a smear may be negative, TB bacilli can still be grown in the sputum.

**8-34 How does tuberculosis affect HIV infection and AIDS?**

Tuberculosis weakens the patient’s immune system and enables HIV infection to progress more rapidly to AIDS.

**Every child with tuberculosis should be screened for HIV infection.**

**8-35 How can tuberculosis be prevented?**

1. By improving the standard of living and preventing overcrowding
2. By diagnosing and treating adults with pulmonary tuberculosis
3. By immunising all newborn infants with BCG
4. By keeping children away from adults with untreated tuberculosis
5. By screening children who have come into close contact with an adult with pulmonary tuberculosis and giving chemoprophylaxis to all TB exposed children under 5 years of age
6. By monitoring weight gain (Road-to-Health Card) to identify children with failure to thrive. Preventing malnutrition and giving routine vitamin A helps prevent the progression of TB infection to tuberculosis (TB disease).
7. By preventing the spread of HIV infection and HIV) is a major problem in South Africa.
- Most children with both HIV and tuberculous infections will respond as well to the standard antituberculosis treatment as children who are not infected with HIV.

**HIV infection weakens the immune system and allows previously dormant tuberculosis bacilli to become active, resulting in tuberculosis.**

- Due to their weak immune system, tuberculosis of organs other than the lungs is more common in children with HIV infection, e.g. miliary tuberculosis or tuberculous meningitis and even chronic otitis media due to TB bacilli.
- The recent increase in deaths due to tuberculosis in many developing countries is largely due to the spread of HIV infection. Tuberculosis is a very common complication of HIV infection and many children with HIV infection will develop pulmonary tuberculosis. Co-infection (TB and HIV) is a major problem in South Africa.
8-36 What is the value of BCG immunisation?

Immunisation with BCG gives some protection against infection with wild TB bacilli. BCG gives good protection against miliary tuberculosis and tuberculous meningitis, especially in well nourished children. Unfortunately, BCG immunisation does not give total protection against tuberculosis. BCG should be given to all infants at birth.

BCG should still be given to newborn infants who have HIV positive mothers. However, BCG should not be given to children with clinical signs of HIV infection. Side effects from BCG are more common in HIV infected children.

Immunisation against measles and diphtheria also helps reduce the risk of tuberculosis.

8-37 How is the diagnosis of tuberculosis classified in children?

2. Probable tuberculosis: The chest X-ray suggests tuberculosis in a child who is failing to thrive, has a chronic cough, has a positive Mantoux skin test and/or has a history of contact with an adult suffering from untreated tuberculosis.
3. Confirmed tuberculosis: In addition to the above, TB bacilli are seen or grown from the sputum or any other body fluid.

Unfortunately the diagnosis of tuberculosis is often only suspected or probable and cannot be confirmed. These infants need to be treated as if they had confirmed tuberculosis.

8-38 What is the management of tuberculosis?

1. Multi-drug treatment with 3 or 4 drugs is essential to make sure that the tuberculosis is cured and that resistance to the anti-TB drugs does not develop.
2. The most important aspect of treating a child with tuberculosis is to ensure that the medicine is taken correctly and regularly. This is often difficult as the treatment takes many months. It is essential that the health care workers at the clinic develop a good working relationship with the mother and child.
3. While ill children need hospitalisation, most children with tuberculosis can be treated from a clinic.
4. The child's general nutritional status must be improved as most children with tuberculosis are underweight for age. The Road-to-Health Card is a valuable way of monitoring the child's weight gain.
5. If children are infected with both HIV and TB, both infections should be treated. These children have a damaged immune system and their HIV infection should be correctly managed with prophylactic co-trimoxazole and antiretroviral therapy if they qualify.

8-39 What drugs are used to treat tuberculosis in children?

Because the TB bacillus rapidly becomes resistant to 1 antituberculous drug if it is given on its own, multiple drug therapy is used. Usually 3 or more drugs are given together. The drug combination usually given consists of:

- Rifampicin
- Isoniazid (INH)
- Pyrazinamide (PZA)

All 3 drugs are usually given together before breakfast. It is very important that the drugs are taken regularly and correctly. Hospitalisation and bed rest are usually not needed. With
correct treatment more than 90% of children with tuberculosis can be cured.

Children with miliary TB or TB meningitis must be hospitalised. A fourth antituberculous drug is added (preferably ethionamide, otherwise ethambutol or streptomycin). These drugs are given at higher doses in TB meningitis and miliary TB.

**NOTE** Usually added pyridoxine is not needed.

### 8-40 What is short course treatment of tuberculosis?

The cure rate of tuberculosis has improved with shorter, well monitored courses of anti-TB drugs. This method is better than previous longer courses where compliance was poor and many patients did not take their medication regularly or stopped treatment too soon. Short course treatment is more cost effective with better patient compliance. However it must be well managed.

With short course treatment from a clinic, the anti-TB drugs are usually given on 5 days of the week only (Monday to Friday). Most children can be treated with combination tablets (rifampicin, INH and pyrazinamide or rifampicin and INH alone). Usually all 3 drugs are given for 2 months (the initial phase) and then only rifampicin and isoniazid are taken for a further 4 months (continuation phase). See Table 8.1 for the usual 6 month treatment regimen.

### 8-41 How is the response to treatment monitored?

Once the child has been on triple drug treatment for a few weeks the signs and symptoms of TB should gradually improve and the child should start to gain weight. A definite improvement in the chest X-ray may be seen in early infections after a month. However, the X-ray changes may take months to improve in extensive pulmonary TB.

**NOTE** The results of sensitivity tests are usually available by the end of the initial 2 month period of treatment.

### 8-42 What are the side effects of antituberculous drugs?

Unfortunately, all anti-TB drugs have side effects. In children these are fortunately not as severe as in adults. The organ most commonly

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<td>5 times per week</td>
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**Table 8.1:** The usual 6-month treatment regimen for tuberculosis. $R =$ Rifampicin; $H =$ INH; $Z =$ Pyrazinamide.
affected by anti-TB drugs is the liver. Nausea and skin rashes may occur. The urine is often stained orange when rifampicin is given.

**Note** All 3 antituberculous drugs (RMP, INH and PZA) may cause a drug induced hepatitis. INH may cause a peripheral neuropathy, but this is very uncommon in children.

**8-43 What is the most common cause of failure to cure tuberculosis?**

Failure to take the anti-TB drugs correctly as prescribed (non-compliance). If doses of the drugs are missed repeatedly, the tuberculosis will not be cured and drug resistance may develop. Resistance to both INH and rifampicin is called multidrug resistant (MDR) TB. This is very difficult to treat. In multidrug resistance, the TB bacilli continue to multiply and are not killed by the usual combination of anti-TB drugs. Multidrug resistant TB develops because of incorrect treatment or poor adherence. Multidrug resistant TB can be transmitted to close contacts, including children and is becoming a major problem in some regions.

**Note** Resistance to 3 or more antituberculous drugs is called extreme drug resistant (EDR) TB. It is usually fatal.

If the treatment is stopped too soon the tuberculosis can also return (relapse). In many poor countries it is common for TB patients not to complete their full course of treatment. Once they feel well again they stop their treatment. As a result, relapse of TB occurs and many people die of TB.

**8-44 What is the DOTS strategy?**

‘DOTS’ stands for Directly Observed Treatment – Short course. With the DOTS strategy the patient is given the anti-TB drugs by some responsible person in the community who observes the patient swallowing every dose of the medication. The treatment supporter does not have to be a health professional. With adults, it is best if the treatment supporter is not a family member. This ensures good compliance without the patient having to go to the clinic for every dose. If DOTS is correctly used, the failure rate of treatment is greatly reduced and over 85% of patients should be cured. The general public can play an important role in the control of TB by supporting DOTS (i.e. DOTS supporters). The cure rate for TB without DOTS in poor countries may be as low as 40%.

**Note** The DOTS strategy consists of 5 main points: Government commitment to sustained TB control activities; case detection by sputum smear microscopy among symptomatic patients; self-reporting to health services; standardized treatment regimens of 6 to 8 months for at least all confirmed sputum smear positive cases, with directly observed treatment (DOT) for at least the initial 2 months; a regular, uninterrupted supply of all essential anti-TB drugs; and a standardized recording and reporting system that allows assessment of treatment results for each patient and of the TB control programme overall. DOTS was introduced to South Africa in 1996.

**With DOTS a responsible person must see the patient take the tablets.**

**8-45 When are anti-tuberculous drugs given prophylactically to young children?**

The following children should be given prophylactic (preventative) treatment:

- Clinically well, asymptomatic children under 5 years of age who have been in the same home as someone who has smear-positive pulmonary TB. These young children are at very high risk of developing TB themselves as they have an immature immune system.
- Children under 5 years who have a positive Mantoux skin test (10 mm or more), who
are clinically well and have not recently been treated for TB.
• HIV positive children who are in contact with adults with smear-positive tuberculosis.

Currently, prophylaxis consists of INH for 6 months. The treatment is given daily for 5 days a week using the same dose as for short course treatment. Children of 5 and older, who have been in close contact with an adult with untreated pulmonary TB, or have a positive Mantoux, are not given prophylaxis, as they are at far less risk of developing tuberculosis. However, they should be followed and treated if they develop any early signs of TB.

Prophylactic treatment is given to well children under 5 years of age who have been in close contact with someone with untreated tuberculosis.

8-46 What is the management of a newborn infant if the mother has tuberculosis?

1. If the mother has untreated pulmonary tuberculosis, or has not been on treatment for at least 4 weeks before delivery, the infant should have prophylactic treatment. The same will apply if another family member has active pulmonary tuberculosis. Usually INH 5 mg/kg/day is given. Some services use INH plus rifampicin.
2. The mother should be allowed to care for and breastfeed her infant. The infant need not be isolated but can stay with the mother. The mother must receive a full course of treatment.
3. BCG should not be given at birth (as the BCG bacillus could be killed by the anti-TB drugs).
4. At 3 months, a Mantoux skin test must be done:
   • If the infant is thriving and the skin test is negative, the infant has not been infected with TB bacilli. BCG should now be given after the prophylactic treatment has been stopped for 3 days. No further treatment is needed.
   • A Mantoux skin test of 5 mm or more indicates that the infant has been infected by TB bacilli despite the prophylactic treatment. Do not give BCG but treat the child for tuberculosis.

**Note** Prophylactic treatment of newborn infants remains controversial. The choice of 1 or more drugs and the duration of treatment is still debatable. Therefore, some authorities use both INH and rifampicin for 3 months.

8-47 Is tuberculosis a notifiable disease?

Yes. All cases of tuberculosis must be notified to the local health authority. The healthcare worker who makes the diagnosis is responsible for the notification. The local health authority should now look for the person who is the source of the infection and also screen contacts for tuberculosis.

8-48 Should adults with tuberculosis be isolated?

After 2 weeks of the correct treatment, patients with pulmonary tuberculosis are no longer infectious to others even though TB bacilli may still be seen on a smear. Isolation of patients with tuberculosis is, therefore, usually not necessary. Younger children usually do not develop ‘adult type tuberculosis’ with cavities and, therefore, are less infectious to others. As a result, most children with tuberculosis do not need to be isolated.

8-49 How can tuberculosis be controlled in a community?

1. By the early identification, referral and correct treatment of adults with tuberculosis (especially if smear-positive)
2. By looking for family members, friends or care givers with untreated tuberculosis (TB contacts) when a child is diagnosed with tuberculosis. It is important to look for the source of infection.
3. By bringing any child who has been in contact with a smear-positive tuberculosis to clinic for assessment and possible prophylactic treatment. This is particularly
important in children under 5 years of age and those with HIV infection.

4. By improving general nutrition and preventing overcrowding (good housing)

5. By immunising all infants with BCG, measles and pertussis vaccine

6. By routinely monitoring weight gain in children with the Road-to-Health Card

7. By using the DOTS strategy

8. By reducing the transmission of HIV to children and correctly treating children with symptomatic HIV infection

9. By notifying all cases of tuberculosis

8-50 What are the main responsibilities of the staff in a primary care TB clinic?

1. Identifying adults and children with tuberculosis or at high risk of having tuberculosis

2. Referring them for correct diagnosis

3. Making sure that patients take their treatment correctly

4. Looking for other cases of tuberculosis in the home

5. Finding children under 5 years who need prophylactic treatment

6. Supporting the family of a patient with tuberculosis

CASE STUDY 1

A 7-year-old child presents at a local clinic with a history of a persistent, dry cough for the past month. He has a poor appetite, has lost weight recently and reports that he sweats a lot at night. Examination reveals a thin child with an expiratory wheeze. A BCG scar is noted over his right upper arm. His mother says she and her 5 children live with her father in a 2 roomed house. The grandfather is also unwell and has been coughing and complaining of chest pain for the past few months. She is unemployed and the whole family live on the grandfather’s pension. The child is sent for a chest X-ray and Mantoux skin test.

1. Why should you suspect that this child has pulmonary tuberculosis?

The symptoms of chronic cough for a month, poor appetite, weight loss and night sweats are strongly suggestive of tuberculosis. They live in poor, overcrowded conditions and the grandfather’s history also suggests tuberculosis. The child has probably been infected by the grandfather who could have smear-positive pulmonary tuberculosis.

2. Would BCG immunisation not protect this child from tuberculosis?

BCG immunisation gives partial protection against tuberculosis, especially tuberculous meningitis and miliary tuberculosis. However, an immunised child can still become infected particularly if they are undernourished or exposed to large numbers of TB bacilli. Therefore, this child may have tuberculosis even though he has been immunised with BCG.

3. How can the suspected diagnosis of tuberculosis be confirmed in this child?

A chest X-ray should be taken and a Mantoux skin test performed. The grandfather should also be investigated for tuberculosis.

4. What are the typical chest X-ray findings of tuberculosis in a child?

Usually an area of pneumonia (consolidation) is seen together with a widened mediastinum due to enlarged hilar and mediastinal lymph nodes.

5. What is the probable cause of the wheeze?

Either a wheeze or stridor can be caused by pressure of enlarged lymph nodes on the airway. This is common in children with pulmonary tuberculosis. The wheeze seldom responds to inhaled bronchodilators.
6. How would you interpret a Mantoux skin test with an area of induration of more than 15 mm across?

A test of 10 mm or more would indicate tuberculosis, even if the child had received BCG.

7. What other diagnostic investigations should be done on the child?

The child should be able to cough up a sample of sputum. This should be stained and then examined for TB bacilli.

8. What medication should be given to this child to treat his tuberculosis?

Rifampicin, isoniazid and pyrazinamide are used for the first 2 months then only rifampicin and isoniazid continued for another 4 months. With short course treatment the drugs are given 5 times a week. It is very important that the drugs are given regularly and that doses are not missed.

9. Is tuberculosis a notifiable disease?

Yes. All forms of tuberculosis are notifiable in South Africa. This enables the local health authority to look for the person who is the source of the infection and to screen contacts for tuberculosis.

**CASE STUDY 2**

An 18 month old infant is brought to hospital with a 1 week history of fever and irritability. For the last 2 days the infant has been very drowsy, refuses feeds and does not want to play with her siblings. She has also vomited a few times. The mother reports that the child has not been immunized as she was born at home and lives far from the nearest clinic. The child has received no treatment or traditional medicine. A chest X-ray done at the clinic is normal.

1. What diagnosis should be suspected?

Tuberculous meningitis.

2. How can this diagnosis be confirmed?

By examining a sample of cerebrospinal fluid (CSF) obtained by lumbar puncture. If the child has tuberculous meningitis the fluid will be abnormal. Children with TB meningitis often have a normal chest X-ray. The typical signs of meningitis are often not present during the first few days of illness.

3. Which children are at most risk of tuberculous meningitis?

Children under 3 years of age who have not been immunized with BCG and are exposed to large numbers of TB bacilli. It would be important to ask if there is an adult in the home who may have untreated tuberculosis.

4. What are the dangers of tuberculous meningitis?

The child may die or suffer permanent brain damage. Hydrocephalus, paralysis, deafness, blindness, convulsions or mental retardation may result, especially if the diagnosis is only made when the child already has neurological signs. If diagnosed and treated early, the child may fully recover. The clinical presentation in this child suggests an early diagnosis.

5. How should this child be managed?

The child must be urgently referred to hospital for investigation and treatment. Treatment with anti-TB drugs will be needed for 6 months.

6. What other organs can be infected with the tuberculosis bacilli?

The lungs are the most common organs to be infected with tuberculosis. In children, tuberculous meningitis, abdominal tuberculosis, tuberculosis of the bones or joints, and tuberculous infection of the lymph nodes are less common. Almost any organ can be infected with tuberculosis.
CASE STUDY 3

A 16-year-old adolescent gives a history of feeling unwell and losing weight for the past 2 months. She also complains of a chronic loose cough and blood stained sputum. Her older brother was treated for tuberculosis for 2 months but stopped when the medicine ran out. He remained well for a while but is now coughing again. She has a younger brother who is well. The nurse at the clinic refers the patient to hospital for a chest X-ray as she suspects that she has tuberculosis.

1. How is tuberculosis spread?

Usually by breathing in TB bacilli that have been coughed into the air by an adult with untreated pulmonary tuberculosis.

2. What viral infections may weaken the immune system and increase the risk of tuberculosis?

HIV infection is a very important cause of damage to the immune system. Therefore children with HIV infection are at high risk of developing tuberculosis. A recent infection with measles can also damage the immune system.

3. What would you expect to see on this patient’s chest X-ray?

She probably has adult type pulmonary tuberculosis with cavities in an upper lobe. Patients with this type of tuberculosis are highly infectious as they cough up large numbers of TB bacilli. A stain of her sputum will probably be full of TB bacilli.

4. When was this child probably infected with the TB bacilli?

She could have had an asymptomatic primary tuberculosis infection a number of years ago, but recent infection transmitted from her older brother is more likely. If her tuberculosis was the result of reactivation from previous infection, it was because her immune system was able to stop the TB bacilli from multiplying at the time of the previous infection but it was not able to kill them. A few years later the TB bacilli started to multiply again causing pulmonary tuberculosis. This resulted in her becoming ill.

5. What is the best method to make sure that she takes her anti-tuberculosis treatment correctly?

DOTS (Directly Observed Treatment – Short course). It is best if every dose of medication is carefully supervised by a responsible person. It is not necessary to admit her to hospital for treatment. With DOTS she also need not visit the local clinic daily for her treatment.

6. How should the younger brother be managed?

The younger brother should be screened for tuberculosis. Any child in the home who is under 5 years of age and does not have tuberculosis should receive prophylactic treatment.

CASE STUDY 4

A 1-year-old child is seen by a general practitioner with a short history of fever and being generally unwell. On examination the child is obviously ill with an enlarged liver and spleen. The mother is also unwell with weight loss and chronic diarrhoea.

1. What is the probable diagnosis in this child?

Although a number of different infections can present in this way, miliary tuberculosis must be suspected.

2. What would be the appearance of a chest X-ray in miliary tuberculosis?

With miliary tuberculosis the chest X-ray shows numerous small spots throughout both lungs indicating a widespread pneumonia.
3. Would you expect the Mantoux skin test to be positive?

The Mantoux skin test may be positive. However, with miliary tuberculosis the Mantoux could be negative, as the severe infection weakens the immune system.

4. How did this child probably become infected with TB?

The mother probably has tuberculosis. The story of chronic diarrhoea suggests that she may also have AIDS. Tuberculosis and HIV infection often occur together.

5. How can a newborn infant be protected against infection if the mother has tuberculosis?

The infant should be started on prophylactic anti-TB treatment (usually INH alone or INH plus rifampicin) as soon as possible after delivery. Immunisation with BCG should be delayed until the treatment is completed.

6. Should a mother with tuberculosis be allowed to breastfeed her infant?

Yes, provided the infant is given prophylactic treatment. The mother must take her anti-TB medication correctly and need not be separated from her infant.