Tuberculosis (TB):

Tuberculosis (TB), which is one of the oldest diseases known to affect humans, is a major cause of death worldwide. This disease is caused by bacteria of the *Mycobacterium tuberculosis* complex and usually affects the lungs, although other organs are involved in up to one-third of cases. If properly treated, TB caused by drug-susceptible strains is curable in virtually all cases. If untreated, the disease may be fatal within 5 years in 50–65% of cases. Transmission usually takes place through the airborne spread of droplet nuclei produced by patients with infectious pulmonary TB.

**Epidemiology:**

Tuberculosis (TB) is caused by infection with *Mycobacterium tuberculosis* (MTB), which is part of a complex of organisms including *M. bovis* (reservoir cattle) and *M. africanum* (reservoir human). *M. tuberculosis* is a rod-shaped, nonspore-forming, thin aerobic bacterium. Mycobacteria, including *M. tuberculosis*, are often neutral on Gram's staining. However, once stained, the bacilli cannot be decolorized by acid alcohol; this characteristic justifies their classification as acid-fast bacilli. The impact of TB on world health is significant; in 2006, there were an estimated 9.2 million new cases, 14.4 million prevalent cases and 1.5 million deaths attributable to TB. Furthermore, it is estimated that around one-third of the world's population has latent TB. The majority of cases occur in the world's poorest nations, who struggle to cover the costs associated with management and control programmes. (WHO) in 2009; 95% of cases were reported from developing countries. The resurgence of TB has been largely driven in Africa by HIV disease, and in the former Soviet Union and Baltic states by lack of appropriate health care exacerbated by social and political upheaval. The risk of acquiring *M. tuberculosis* infection is determined mainly by exogenous factors. Because of delays in seeking care and in making a diagnosis, it is generally believed that, in high-prevalence settings, up to 20 contacts may be infected by each AFB-positive case before the index case is found to have TB.

**Reasons for the increasing incidence of TB**

- **Developed countries**
  1. Immigration from high-prevalence areas
  2. Human immunodeficiency virus (HIV)
  3. Social deprivation (homelessness, poverty)
  4. Increasing proportion of elderly
  5. Drug resistance

- **Developing countries**
  1. Ineffective control programmes
  2. Lack of access to health care
  3. Poverty, civil unrest
  4. HIV
  5. Population increase
6. Drug resistance

Factors increasing the risk of TB

1-Patient-related
1. Age (children > young adults < elderly)
2. First-generation immigrants from high-prevalence countries
3. Close contacts of patients with smear-positive pulmonary TB
4. Overcrowding (prisons, collective dormitories); homelessness (doss houses and hostels)
5. Chest radiographic evidence of self-healed TB
6. Primary infection < 1 year previously
7. Smoking: cigarettes

2-Associated diseases
1. Immunosuppression: HIV, anti-TNF therapy, high-dose corticosteroids, cytotoxic agents.
2. Malignancy (especially lymphoma and leukaemia)
3. Type 1 diabetes mellitus
4. Chronic renal failure
5. Silicosis
6. Gastrointestinal disease associated with malnutrition (gastrectomy, jejuno-ileal bypass, cancer of the pancreas, malabsorption)
7. Deficiency of vitamin D or A
8. Recent measles: increases risk of child contracting TB

Pathology and pathogenesis:

*M. bovis* infection arises from drinking non-sterilised milk from infected cows. *M. tuberculosis* is spread by the inhalation of aerosolised droplet nuclei from other infected patients. Once inhaled, the organisms lodge in the alveoli and initiate the recruitment of macrophages and lymphocytes. Macrophages undergo transformation into epithelioid and Langhans cells which aggregate with the lymphocytes to form the classical tuberculous granuloma. Numerous granulomas aggregate to form a primary lesion or 'Ghon focus' (a pale yellow, caseous nodule, usually a few mm to 1-2 cm in diameter), which is characteristically situated in the periphery of the lung. Spread of organisms to the hilar lymph nodes is followed by a similar pathological reaction; the combination of a primary lesion and regional lymph nodes is referred to as the 'primary complex of Ranke'. Reparative processes encase the primary complex in a fibrous capsule limiting the spread of bacilli: so-called latent TB. If no further complications ensue, this lesion eventually calcifies and is clearly seen on a chest X-ray. However, lymphatic or haematogenous spread may occur before immunity is established, seeding secondary foci in other organs including lymph nodes, serous membranes, meninges, bones, liver, kidneys and lungs, which may lie dormant for years. The only clue that infection has occurred may be the appearance of a cell-mediated, delayed-type hypersensitivity reaction to tuberculin, demonstrated by tuberculin skin testing. If these reparative processes fail, primary progressive disease ensues. The estimated lifetime risk of developing disease
after primary infection is 10%, with roughly half of this risk occurring in the first 2 years after infection.

**Clinical features:**

**pulmonary disease:** Primary TB refers to the infection of a previously uninfected (tuberculin-negative) individual. A few patients develop a self-limiting febrile illness but clinical disease only occurs if there is a hypersensitivity reaction or progressive infection. Progressive primary disease may appear during the course of the initial illness or after a latent period of weeks or months

- **Clinical presentations of pulmonary TB**
  1. Chronic cough, often with haemoptysis
  2. Pyrexia of unknown origin
  3. Unresolved pneumonia
  4. Exudative pleural effusion
  5. Asymptomatic (diagnosis on chest X-ray)
  6. Weight loss, general debility
  7. Spontaneous pneumothorax

**Post-primary pulmonary TB:** Post-primary disease refers to exogenous ('new' infection) or endogenous (reactivation of a dormant primary lesion) infection in a person who has been sensitised by earlier exposure. It is most frequently pulmonary and characteristically occurs in the apex of an upper lobe where the oxygen tension favours survival of the strictly aerobic organism. The onset is usually insidious, developing slowly over several weeks. Systemic symptoms include fever, night sweats, malaise, and loss of appetite and weight, and are accompanied by progressive pulmonary symptoms. Very occasionally, this form of TB may present with one of the complications. **Radiological changes** include ill-defined opacification in one or both of the upper lobes, and as progression occurs, consolidation, collapse and cavitation develop to varying degrees. It is often difficult to distinguish active from quiescent disease on radiological criteria alone, but the presence of a miliary pattern or cavitation favours active disease. In extensive disease, collapse may be marked and result in significant displacement of the trachea and mediastinum. Occasionally, a caseous lymph node may drain into an adjoining bronchus resulting in tuberculous pneumonia.

- **Chest X-ray:** major manifestations and differential diagnosis of pulmonary TB.
• **Features of primary TB**

• **Infection (4-8 weeks)**

1. Influenza-like illness
2. Skin test conversion
3. Primary complex

• **Disease**

1. Lymphadenopathy: hilar (often unilateral), paratracheal or mediastinal
2. Collapse (especially right middle lobe)
3. Consolidation (especially right middle lobe)
4. Obstructive emphysema
5. Cavitation (rare)
6. Pleural effusion
7. Endobronchial
8. Miliary
9. Meningitis
10. Pericarditis

• **Hypersensitivity**

1. Erythema nodosum
2. Phlyctenular conjunctivitis
3. Dactylitis

**Cryptic TB**

1. Age over 60 years
2. Intermittent low-grade pyrexia of unknown origin
3. Unexplained weight loss, general debility (hepatosplenomegaly in 25-50%)
4. Normal chest X-ray
5. Blood dyscrasias; leukaemoid reaction, pancytopenia
6. Negative tuberculin skin test
7. Confirmation by biopsy (granulomas and/or acid-fast bacilli demonstrated) of liver or bone marrow

**Miliary TB:** Blood-borne dissemination gives rise to miliary TB, which may present acutely but more frequently is characterised by 2-3 weeks of fever, night sweats, anorexia, weight loss and a dry cough. Hepatosplenomegaly may develop and the presence of a headache may indicate coexistent tuberculous meningitis. Auscultation of the chest is frequently normal, although with more advanced disease widespread crackles are evident. Fundoscopy may show choroidal tubercles. The classical appearances on chest X-ray are of fine 1-2 mm lesions ('millet seed') distributed throughout the lung fields, although occasionally the appearances are coarser. Anaemia and leucopenia reflect bone marrow involvement. 'Cryptic' miliary TB is an unusual presentation sometimes seen in old age.

**Clinical features:**
**Extrapulmonary disease**
Extrapulmonary tuberculosis accounts for about 20% of cases in those who are HIV-negative but is more prevalent in HIV-positive individuals. In order of frequency, the extrapulmonary sites most commonly involved in TB are the lymph nodes, pleura, genitourinary tract, bones and joints, meninges, peritoneum, and pericardium. However, virtually all organ systems may be affected.

**Systemic presentations of extrapulmonary TB.**

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**Lymphadenitis:**
Lymph nodes are the most common extrapulmonary site of disease. Cervical and mediastinal glands are affected most frequently, followed by axillary and inguinal; more than one region may be involved. Disease may represent primary infection, spread from contiguous sites or reactivation. Supraclavicular lymphadenopathy is often the result of spread from mediastinal disease. The nodes are usually painless and initially mobile but become matted together with time. When caseation and liquefaction occur, the swelling becomes fluctuant and may discharge through the skin with the formation of a 'collar-stud' abscess and sinus formation. Approximately half of cases fail to show any constitutional features such as fevers or night sweats. The tuberculin test is usually strongly positive. During or after treatment, paradoxical enlargement, development of new nodes and suppuration may all occur but without evidence of continued infection; rarely, surgical excision is necessary. In non-immigrant children in the UK, most mycobacterial lymphadenitis is caused by opportunistic mycobacteria, especially of the *M. avium* complex.

**Gastrointestinal disease:**
making up 3.5% of extrapulmonary cases in the United States. TB can affect any part of the bowel and patients may present with a wide range of symptoms and signs. Upper gastrointestinal tract involvement is rare and is usually an unexpected histological finding in an endoscopic or laparotomy specimen. Ileocaecal disease accounts for approximately half of abdominal TB cases. Fever, night sweats, anorexia and weight loss are usually prominent and a right iliac fossa mass may be palpable. Up to 30% of cases present with an acute abdomen. Ultrasound or CT may reveal thickened bowel wall, abdominal lymphadenopathy, mesenteric thickening or ascites. Barium enema and small bowel enema reveal narrowing, shortening and distortion of the bowel with caecal involvement predominating. Diagnosis rests on obtaining histology by either colonoscopy or mini-laparotomy. The main differential diagnosis is Crohn's disease. Tuberculous peritonitis is characterised by abdominal distension, pain and constitutional symptoms. The ascitic fluid is exudative and cellular with a predominance of lymphocytes. Laparoscopy reveals multiple white 'tubercles' over the peritoneal and omental surfaces. Low-grade hepatic dysfunction is common in miliary disease when biopsy reveals granulomas. Occasionally, patients may be frankly icteric with a mixed hepatic/cholestatic picture.

**Pericardial disease:**
Disease occurs in two forms: pericardial effusion and constrictive pericarditis. Fever and night sweats are rarely prominent and the presentation is usually insidious with breathlessness and abdominal swelling. Coexistent pulmonary disease is very rare, with the exception of pleural effusion. Pulsus paradoxus, a raised JVP, hepatomegaly, prominent ascites and peripheral oedema are common to both types. Pericardial effusion is associated with increased pericardial dullness and a globular enlarged heart on chest X-ray. Constriction is associated with a raised JVP, an early third heart sound and, occasionally, atrial fibrillation; pericardial calcification occurs in around 25% of cases. Diagnosis is on clinical, radiological and echocardiographic grounds. The effusion is frequently blood-stained. Open pericardial biopsy can be performed where there is diagnostic uncertainty. The addition of corticosteroids to
antituberculosis treatment has been shown to be beneficial for both forms of pericardial disease.

**Central nervous system disease:**
Meningeal disease represents the most important form of central nervous system TB. Unrecognised and untreated, it is rapidly fatal. Even when appropriate treatment is prescribed, **mortality rates of 30% have been reported and survivors may be left with neurological sequelae documented in 25% of treated cases.** Since meningeal involvement is pronounced at the base of the brain, paresis of cranial nerves (ocular nerves in particular) is a frequent finding. The ultimate evolution is toward coma, with hydrocephalus and intracranial hypertension. AFB are seen on direct smear of CSF sediment in **up to one-third of cases, but repeated lumbar punctures increase the yield.** Culture of CSF is diagnostic in **up to 80% of cases** and remains the gold standard. Polymerase chain reaction (PCR) has a sensitivity of up to 80%

**Bone and joint disease:**
The spine is the most common site for bony TB (Pott's disease), which usually presents with chronic back pain and typically involves the lower thoracic and lumbar spine. The infection starts as a discitis and then spreads along the spinal ligaments to involve the adjacent anterior vertebral bodies, causing angulation of the vertebrae with subsequent kyphosis. Paravertebral and psoas abscess formation is common and the disease may present with a large (cold) abscess in the inguinal region. CT and/or MRI are valuable in gauging the extent of disease, the amount of cord compression, and the site for needle biopsy or open exploration if required. The major differential diagnosis is malignancy, which tends to affect the vertebral body and leave the disc intact. Important complications include spinal instability or cord compression. TB can affect any joint, but most frequently involves the hip or knee. Presentation is usually insidious with pain and swelling; fever and night sweats are uncommon. Radiological changes are often non-specific, but as disease progresses, reduction in joint space and erosions appear.

**Genitourinary disease:**
Fever and night sweats are rare with renal tract TB and patients are often only mildly symptomatic for many years. Haematuria, frequency and dysuria are often present, with sterile pyuria found on urine microscopy and culture. In women, infertility from endometritis, or pelvic pain and swelling from salpingitis or a tubo-ovarian abscess occur occasionally. In men, genitourinary TB may present as epididymitis or prostatitis.

- **Chronic complications of pulmonary TB**

- **Pulmonary**
  1. Massive haemoptysis
  2. Cor pulmonale
  3. Fibrosis/emphysema
  4. Atypical mycobacterial infection
  5. Aspergilloma
6. Lung/pleural calcification
7. Obstructive airways disease
8. Bronchiectasis
9. Bronchopleural fistula

• **Non-pulmonary**
  1. Empyema necessitans
  2. Laryngitis
  3. Enteritis*
  4. Anorectal disease*
  5. Amyloidosis
  6. Poncet's polyarthritis

**Diagnosis:**
Specimens required

**Pulmonary**

Sputum (induced with nebulised hypertonic saline if not expectorating) At least 2 but preferably 3, including an early morning sample.

  - Bronchoscopy with washings or BAL
  - Gastric washing* (mainly used for children)

**Extrapulmonary**

  - Fluid examination (cerebrospinal, ascitic, pleural, pericardial, joint): yield classically very low
  - Tissue biopsy (from affected site); also bone marrow/liver may be diagnostic in patients with disseminated disease

**Diagnostic tests**

  - **Circumstantial** (ESR, CRP, anaemia etc.)
  - **Tuberculin skin test** (low sensitivity/specificity; useful only in primary or deep-seated infection)
  - **Stain**
    - Ziehl-Neelsen
  - Auramine fluorescence
  - **Nucleic acid amplification** (These systems permit the diagnosis of TB in as little as several hours, with high specificity and sensitivity approaching that of culture.)
  - **Culture**
    - Solid media (Löwenstein-Jensen, Middlebrook)
    - Liquid media (e.g. BACTEC or MGIT = mycobacteria growth indicator tube)
  - **Response to empirical antituberculous drugs** (usually seen after 5-10 days)

Determinations of ADA and IFN-gamma levels in pleural fluid may be useful as adjunct tests in the diagnosis of pleural TB; the utility of these tests in the diagnosis of other forms of
extrapulmonary TB (e.g., pericardial, peritoneal, and meningeal) is less clear. IGRAs are more specific than the TST as a result of less cross-reactivity due to BCG vaccination and sensitization by nontuberculous mycobacteria. The presence of an otherwise unexplained cough for more than 2-3 weeks, particularly in an area where TB is highly prevalent, or typical chest X-ray changes should prompt further investigation.

Direct microscopy of sputum is the most important first step. The probability of detecting acid-fast bacilli is proportional to the bacillary burden in the sputum (typically positive when 5000-10 000 organisms are present). By virtue of their substantial lipid-rich wall, tuberculous bacilli are difficult to stain. The most effective techniques are the Ziehl-Neelsen and rhodamine-auramine stains. A positive smear is sufficient for the presumptive diagnosis of TB but definitive diagnosis requires culture. Smear-negative sputum should also be cultured, as only 10-100 viable organisms are required for sputum to be culture-positive. A diagnosis of smear-negative TB may be made in advance of culture if the chest X-ray appearances are typical of TB and there is no response to a broad-spectrum antibiotic. MTB grows slowly and may take between 4 and 6 weeks to appear on solid medium such as Löwenstein-Jensen or Middlebrook. Faster growth (1-3 weeks) occurs in liquid media such as the radioactive BACTEC system or the non-radiometric mycobacteria growth indicator tube (MGIT). The BACTEC method is commonly used in developed nations and detects mycobacterial growth by measuring the liberation of $^{14}$CO$_2$, following metabolism of $^{14}$C-labelled substrate present in the medium. New strategies for the rapid confirmation of TB at low cost are being developed; these include the nucleic acid amplification test (NAT), designed to amplify nucleic acid regions specific to MTB, and has the potential to provide a simple, non-invasive test which does not require a laboratory or highly skilled personnel. The diagnosis of extrapulmonary TB can be more challenging. There are generally fewer organisms (particularly in meningeal or pleural fluid), so culture or histopathological examination of tissue is more important. In the presence of HIV, however, examination of sputum may still be useful, as subclinical pulmonary disease is common.

Management:
Chemotherapy:
A variety of highly effective short-course regimens are available; choice depends on local health resources and infrastructure. They are based on the principle of an initial intensive phase (which rapidly reduces the bacterial population), followed by a continuation phase to destroy any remaining bacteria. Treatment should be commenced immediately in any patient who is smear-positive, or who is smear-negative but with typical chest X-ray changes and no response to standard antibiotics. Quadruple therapy has become standard in the UK, although ethambutol may be omitted under certain circumstances. Fixed-dose tablets combining two or three drugs are generally favoured: for example, Rifater (rifampicin, isoniazid and pyrazinamide) daily for 2 months, followed by 4 months of Rifinah (rifampicin and isoniazid). Streptomycin is rarely used in the UK, but is an important component of short-course treatment regimens in developing nations. Six months of therapy is appropriate for all patients with new-onset, uncomplicated pulmonary disease. However, 9-12 months of therapy should be considered if the patient is HIV-positive, or if drug intolerance occurs and
a second-line agent is substituted. Meningitis should be treated for a minimum of 12 months. Pyridoxine should be prescribed in pregnant women and malnourished patients to reduce the risk of peripheral neuropathy with isoniazid. Where drug resistance is not anticipated, patients can be assumed to be non-infectious after 2 weeks of appropriate therapy. Most patients can be treated at home. Admission to a hospital unit with appropriate isolation facilities should be considered where:

1. there is uncertainty about the diagnosis,
2. intolerance of medication,
3. questionable compliance,
4. adverse social conditions or
5. a significant risk of multidrug-resistant TB (MDR-TB: culture-positive after 2 months on treatment, or contact with known MDR-TB).

In choosing a suitable drug regimen, underlying comorbidity (renal and hepatic dysfunction, eye disease, peripheral neuropathy and HIV status), as well as the potential for drug interactions, must be considered. Baseline liver function and regular monitoring are important for patients treated with standard therapy including rifampicin, isoniazid and pyrazinamide, as all of these agents are potentially hepatotoxic. Mild asymptomatic increases in transaminases are common but serious liver damage is rare. Patients treated with rifampicin should be advised that their urine, tears and other secretions will develop a bright orange/red coloration, and women taking the oral contraceptive pill must be warned that its efficacy will be reduced and alternative contraception may be necessary. Ethambutol should be used with caution in patients with renal failure, with appropriate dose reduction and monitoring of drug levels. Adverse drug reactions occur in about 10% of patients, but are significantly more common in the presence of HIV co-infection.

Corticosteroids reduce inflammation and limit tissue damage, and are currently recommended when:

1. treating pericardial or
2. meningeal disease,
3. in children with endobronchial disease.
4. They may confer benefit in TB of the ureter and fallopian tube,
5. pleural effusions
6. extensive pulmonary disease,
7. can suppress hypersensitivity drug reactions.

Surgery is still occasionally required (e.g. for massive haemoptysis, loculated empyema, constrictive pericarditis, lymph node suppuration, spinal disease with cord compression), but usually only after a full course of antituberculosis treatment. The effectiveness of therapy for pulmonary TB may be judged by a further sputum smear at 2 months and at 5 months. A positive sputum smear at 5 months defines treatment failure. Extrapulmonary TB must be assessed clinically or radiographically as appropriate.

Control and prevention: The WHO is committed to reducing the incidence of TB by 2015. Important components of this goal include supporting the development of laboratory and
health-care services to improve detection and treatment of active and latent TB. Detection of latent TB Contact tracing is a legal requirement in many countries. It has the potential to identify the probable index case, other cases infected by the same index patient (with or without evidence of disease), and close contacts who should receive BCG vaccination or chemotherapy. Approximately 10-20% of close contacts of patients with smear-positive pulmonary TB and 2-5% of those with smear-negative, culture-positive disease have evidence of TB infection. Cases are commonly identified using the tuberculin skin test. An otherwise asymptomatic contact with a positive tuberculin skin test but a normal chest X-ray may be treated with chemoprophylaxis to prevent infection progressing to clinical disease. Chemoprophylaxis is also recommended for: children aged less than 16 years identified during contact tracing to have a strongly positive tuberculin test, children aged less than 2 years in close contact with smear-positive pulmonary disease, those in whom recent tuberculin conversion has been confirmed, and babies of mothers with pulmonary TB. It should also be considered for HIV-infected close contacts of a patient with smear-positive disease. Rifampicin plus isoniazid for 3 months or isoniazid for 6 months is effective. 

Skin testing in TB: tests using purified protein derivative (PPD) Heaf test Read at 3-7 days

- Multipuncture method
- Grade 1: 4-6 papules
- Grade 2: Confluent papules forming ring
- Grade 3: Central induration
- Grade 4: > 10 mm induration

- Mantoux test Read at 2-4 days
  - Using 10 tuberculin units: Positive when induration 5-14 mm (equivalent to Heaf grade 2) and > 15 mm (Heaf grade 3-4)

False negatives Skin testing:
1. Severe TB (25% of cases negative)
2. Newborn and elderly
3. HIV (if CD4 count < 200 cells/mL)
4. Malnutrition
5. Recent infection (e.g. measles) or immunisation
6. Immunosuppressive drugs
7. Malignancy
8. Sarcoidosis

Tuberculin skin testing may be associated with false-positive reactions in those who have had a BCG vaccination and in areas where exposure to non-tuberculous mycobacteria is high. These limitations may be overcome by employing interferon-gamma release assays (IGRAs). These tests measure the release of IFN-γ from sensitised T cells in response to antigens. The greater specificity of these tests, combined with the logistical convenience of one blood test, as opposed to two visits for skin testing, suggests that IGRAs will replace the tuberculin skin test in low-incidence, high-income countries.

Directly observed therapy (DOT): Poor adherence to therapy is a major factor in prolonged infectious illness, risk of relapse and the emergence of drug resistance. DOT involves the
supervised administration of therapy thrice weekly and improves adherence. It has become an important control strategy in resource-poor nations. In the UK, it is currently only recommended for patients thought unlikely to be adherent to therapy: those who are homeless, alcohol or drug users, drifters, those with serious mental illness and those with a history of non-compliance. **Drug-resistant TB** Drug-resistant TB is defined by the presence of resistance to any first-line agent. **Multidrug-resistant (MDR)** TB is defined by resistance to at least rifampicin and isoniazid, with or without other drug resistance. **Extensively drug-resistant (XDR) TB** is defined by resistance to at least rifampicin and isoniazid, in addition to any quinolone and at least one injectable second-line agent. The prevalence of MDR-TB is rising, particularly in the former Soviet Union, Central Asia and Africa. It is more common in those with a prior history of TB, particularly if treatment has been inadequate, and those with HIV infection.

Diagnosis is challenging, especially in developing countries, and although cure may be possible, it requires prolonged treatment with less effective, more toxic and more expensive therapies. Mortality rate from MDR-TB is high and that from XDR-TB higher still.

**Factors contributing to emergence of drug-resistant TB:**
1. Drug shortages
2. Poor-quality drugs
3. Lack of appropriate supervision
4. Transmission of drug-resistant strains
5. Prior anti-tuberculosis treatment
6. Treatment failure (smear-positive at 5 months)

**Vaccines:** BCG (the Calmette-Guérin bacillus), a live attenuated vaccine derived from *M. bovis*, is the most established TB vaccine. It is administered by intradermal injection and is highly immunogenic. BCG appears to be effective in preventing disseminated disease, including tuberculous meningitis, in children, but its efficacy in adults is inconsistent and new vaccines are urgently needed. Current vaccination policies vary world-wide according to incidence and health-care resources, but usually target children and other high-risk individuals. BCG is very safe with the occasional complication of local abscess formation. It should not be administered to those who are immunocompromised (e.g. by HIV) or pregnant.

**Prognosis:** Following successful completion of chemotherapy, cure should be anticipated in the majority of patients. There is a small (< 5%) and unavoidable risk of relapse, which usually occurs within 5 months and has the same drug susceptibility. In the absence of treatment, a patient with smear-positive TB will remain infectious for an average of 2 years; in 1 year, 25% of untreated cases will die. Death is more likely in those who are smear-positive and those who smoke. A few patients die unexpectedly soon after commencing therapy and it is possible that some have subclinical hypoadrenalism that is unmasked by a rifampicin-induced increase in steroid metabolism. HIV-positive patients have higher mortality rates and a modestly increased risk of relapse.

By: Brwa