Progression to active TB disease

Risk factors for developing TB disease.

In most individuals with LTBI, the combination of macrophages, dendritic cells and T cells is sufficient to maintain a controlled, asymptomatic infection. In a subset of hosts, for reasons that are not completely clear, the infection can progress to clinical disease, in as early as weeks or as long as decades.

- HIV
  - TNF - tumour necrosis factor, neutralizing antibodies and inborn errors in immunity. The role of TNF in containing *M. tuberculosis* infection was experimentally demonstrated in mice in the early 1990s and confirmed in observational studies that showed an increased risk of active TB disease in patients receiving anti-TNF treatments. However, further investigation has shown that TNF mechanisms are complex.
  - Inborn errors in immunity
### TB risks factors: population attributable fraction

<table>
<thead>
<tr>
<th>TB risk factor</th>
<th>Relative risk for active TB disease</th>
<th>Weighted prevalence (22 HBCs)</th>
<th>Population Attributable Fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV infection</td>
<td>8.3</td>
<td>1.1%</td>
<td>7%</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>3.0</td>
<td>17.2%</td>
<td>25%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3.0</td>
<td>3.4%</td>
<td>6%</td>
</tr>
<tr>
<td>Alcohol use (&gt;40g / d)</td>
<td>2.9</td>
<td>7.9%</td>
<td>13%</td>
</tr>
<tr>
<td>Active smoking</td>
<td>2.6</td>
<td>18.2%</td>
<td>23%</td>
</tr>
<tr>
<td>Indoor air pollution</td>
<td>1.5</td>
<td>71.1%</td>
<td>26%</td>
</tr>
</tbody>
</table>

HBC = 22 high-burden countries with >80% of the global new TB cases

\[
P_{AF} = \frac{P \times (RR-1)}{P \times (RR-1) + 1}
\]

Anyone with symptoms of TB or a positive skin test reaction should be evaluated for TB disease

1. The medical history. A medical history is the part of a patient's life history that is important for diagnosing and treating the patient's medical condition. It includes social, family, medical, and occupational information about the patient.

To obtain a medical history, the clinician should ask whether the patient has:

- a. Been exposed to a person who has infectious TB
- b. Symptoms of TB disease
- c. Had TB infection or TB disease before
- d. Risk factors for developing TB disease
Diagnosis of TB Disease

Previous TB infection or TB disease. During the medical history, the clinician should ask the patient whether he or she has ever been diagnosed with or treated for TB infection or disease.

- Patients known to have a positive skin test reaction probably have TB infection.

- If they were infected within the past 2 years, they are at high risk for TB disease.

- Patients who have had TB disease before should be asked when they had the disease and how the disease was treated.

- If the regimen prescribed was inadequate or if the patient did not follow the recommended treatment, TB may recur, and it may be resistant to one or more of the drugs used.
Symptoms of TB disease

- People with TB disease may or may not have symptoms.
- Most patients with TB disease have one or more symptoms that led them to seek medical care.
- Occasionally, TB is discovered during a medical examination for an unrelated condition (for example, when a patient is given a chest x-ray before undergoing surgery).
- Usually, when patients do have symptoms, the symptoms have developed gradually, and they have been present for weeks or even months.

Pulmonary TB disease usually causes one or more of the following symptoms:
  - Coughing
  - Pain in the chest when breathing or coughing
  - Coughing up sputum (phlegm from deep in the lungs) or blood
Occasionally patients may present massive haemoptysis due to erosion of a bronchial artery.

The majority of patients has only minimal constitutional manifestations (Baydur, 1977, Weir, 1985)
The general symptoms of TB disease (pulmonary or extrapulmonary) include
  - Weight loss
  - Fatigue
  - Malaise
  - Fever
  - Night sweats

The symptoms of extrapulmonary TB disease depend on site of disease. For example, TB of the spine may cause pain in the back; TB of the kidney may cause blood in the urine. All of these symptoms may be caused by other diseases, but they should prompt the clinician to suspect TB disease.
Radiology. Primary Tuberculosis (1)

- **Chest radiography** remains the mainstay of diagnosis; however, normal radiographic findings may be seen in up to 15% of patients with proved tuberculosis.
- **At radiology**, primary tuberculosis manifests as four main entities:
  1) parenchymal disease,
  2) lymphadenopathy,
  3) miliary disease,
  4) pleural effusion

**1) Parenchymal Disease**
- Typically, homogeneous parenchymal consolidation in any lobe;
- Predominance in the lower and middle lobes is suggestive of the disease
- In approximately two-thirds of cases, the parenchymal focus **resolves without sequelae at conventional radiography**; however, this resolution can take up to 2 years.
- In the remaining cases, a radiologic scar persists that can **calcify in up to 15% of cases**, an entity that is known as a **Ghon focus**.
- Cavitation is uncommon in primary TB, seen only in 10-30% of cases
- **Tuberculomas** can cavitate and undergo calcification.

http://pubs.rsna.org/doi/full/10.1148/rg.275065176
2) **Lymphadenopathy.**
- Lymphadenopathy is seen in up to 96% of children and 43% of adults.
- Lymphadenopathy is typically unilateral and right sided, involving the hilum and right paratracheal region, it is bilateral in about one-third of cases.
- It is usually seen in the elderly, infants, and immunocompromised persons, manifesting within 6 months of initial exposure.

3) **Miliary tuberculosis**
- It is uncommon but carries a poor prognosis.
- It represents haematogenous dissemination of an uncontrolled tuberculous infection.
- It is seen both in primary and post-primary tuberculosis.
- Although implants are seen throughout the body, the lungs are the easiest location to the image.
- The classic radiographic findings of evenly distributed diffuse small 2-3-mm nodules, with a slight lower lobe predominance, are seen in 85% of cases.
- CT is more sensitive than conventional radiography, with nodules seen in a random distribution.
Pleural Effusion.

- A pleural effusion is seen in approximately one-fourth of patients with proved primary tuberculosis.
- The effusion is often the sole manifestation of TB and usually manifests 3-7 months after initial exposure.
- Pleural effusions are more frequent in adults, seen in 30-40% of cases, and a very uncommon finding in infants.
- The effusion is usually unilateral, and complications are rare (eg, empyema formation, fistulization, bone erosion).
- Residual pleural thickening and calcification can result. Ultrasonography (US) often demonstrates a complex septated effusion.
• Postprimary tuberculosis remains primarily a disease of adolescence and adulthood
• The term postprimary tuberculosis is generally used to refer to both reinfection with and reactivation of tuberculosis.
• Primary tuberculosis is usually self-limiting, whereas postprimary tuberculosis is progressive, with cavitations, hematogenous dissemination of the disease as well as disease spread throughout the lungs.
• Healing usually occurs with fibrosis and calcification.
• The earliest finding in parenchymal disease is poorly defined consolidation, in the apical and posterior segments of the upper lobes.
• Cavities are usually multiple and occur within areas of consolidation.
• Resolution can result in emphysematous change or scarring.
• A minority of cavities demonstrate air-fluid levels; however, these findings can indicate the presence of superinfection.
• If there is airway disease and, in particular, endobronchial spread of infection, tree-in-bud opacities may develop.
Consolidations, cavities typically in the apical and posterior segments of the upper lobes.

Rarely in the lower and middle lobes.
Primary Tuberculosis

- CONSOLIDATION, LATER CASEATION
- UNILATERAL HILAR ADENOPATHY
- EFFUSION (UP TO 40%) in adolescents and young adults
Primary TB infection
Acute hematological dissemination
Miliary tuberculosis
Post Primary Tuberculosis Reactivation TB

- Apical pleural scarring
- Bronchiectasis
- Cavity indicates active disease
- Apical consolidation
- Scarring elevates hilar vessels
Tuberculoma

- Tuberculomas are persistent nodules or mass-like lesions which can be seen in both primary TB and PPT.
- Pulmonary tuberculomas can range in size from being subcentimetric to 5 cm in diameter, and may be solitary or multiple.
- They are most often the result of healed primary TB and are usually smooth-walled and sharply defined.
- The majority of these lesions remain stable in size and may calcify. Nodular or diffuse calcification can be seen in 20-30% of tuberculomas.
- Cavitation is seen in 10-50% of cases.
- In 80% of cases, small round opacities (satellite lesions) may be observed in the immediate vicinity of the main lesion.
Post primary TB.
Rigid fibrous cavern, unfavorable course of TB

Develops slowly, 2 years
Usually smear and culture posit, epidemiologically dangerous

Male, 62 y
Tuberculous Spondylitis

[Image: Close-up of a diseased bone, likely from Tuberculous Spondylitis, provided by Yale Rosen from USA. Uploaded by CFCF via Wikimedia Commons]
Tuberculous Spondylitis
Male, 23 a.,  MDR-TB
Tuberculous Spondylitis

Thoracic spine showing collapsed vertebrae from infection with tuberculosis.

Photo by Brian Spatola. Wikimedia Commons
Osteoarticular TB

- Characteristically a monoarthritis affecting large weight-bearing joints.

- The imaging findings are similar to those of other infectious and inflammatory arthritides and are, therefore, nonspecific.

- These findings include osteopenia, synovitis and other soft-tissue swellings, marginal erosions, and varying degrees of cartilage destruction.

- Joint space narrowing occurs with highly variable rapidity but is usually delayed.

- As with any chronic infection, synovial involvement in the young results in hyperemia and epiphyseal overgrowth, most commonly in the knee.

- With progression of infection, bone sequestration and sinus formation can develop. The end result is usually fibrous ankylosis of the joint.