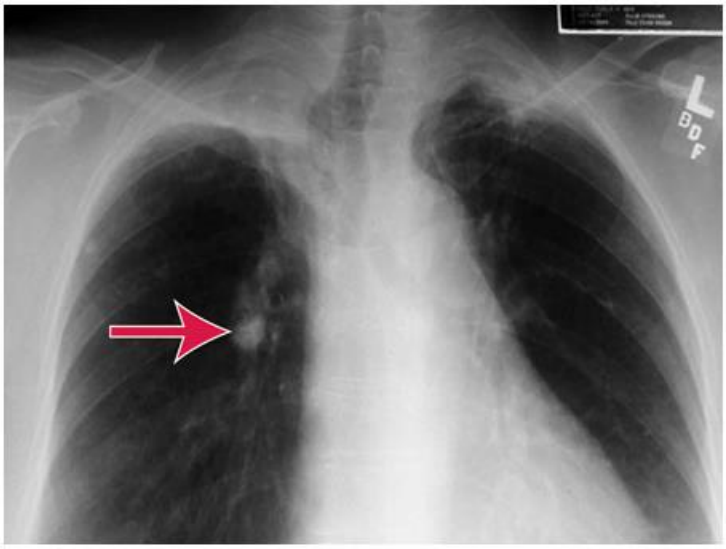
TUBERCULOSIS

ONE-THIRD OF THE WORLD'S POPULATION HAS TUBERCULOSIS AND THUS IT REMAINS AN IMPORTANT INFECTIOUS DISEASE

Table 70-1 Patients with a High Prevalence of Tuberculosis
Immigrants from high-prevalence countries
Patients with the human immunodeficiency virus
Residents and staff of prisons or shelters for the homeless
Alcoholics and illicit drug users
Elderly and nursing home patients

PATHOPHYSIOLOGY:

- Mycobacterium tuberculosis is a slow-growing aerobic rod that settles in areas of high oxygen content and blood flow
- Transmission occurs thorugh in halation of droplet nuclei into the lungs → people with active TB who excrete stainable mycobacteria in saliva or sputum are the most infectious
- Once organisms reach the lungs → may survive and be transported to regional lymph nodes → hosts cell-mediated immunity is further activated → granulomas (tubercles) may form → these are a sign of primary infection and may progress to caseation and necrosis/calcification → GHON FOCI



Ghon focus depicted by arrow

- If tubercle fails to contain the infection → spread by haematogenous, lymphatic or direct mechanical routes

- In immunocompromised hosts, progression of early active disease is more frequent
    - Only 5-10% of otherwise healthy patients go on to develop active post-primary disease, whereas it is as high as 20% in those with HIV and children (those with HIV have risk of 7-10% per year)
    - As host defense system weakens, latent infection may progress to active TB
    - Other groups at risk of reactivation → carcinoma (solid organ), leukaemia, transplantation, CRF requiring dialysis

CLINICAL FEATURES:

PRIMARY TUBERCULOSIS:

- Initial infection is usually asymptomatic
- When infection is active → fever, malaise, weight loss and chest pain
- In immunocompromised, primary infection may be rapidly progressive and fatal

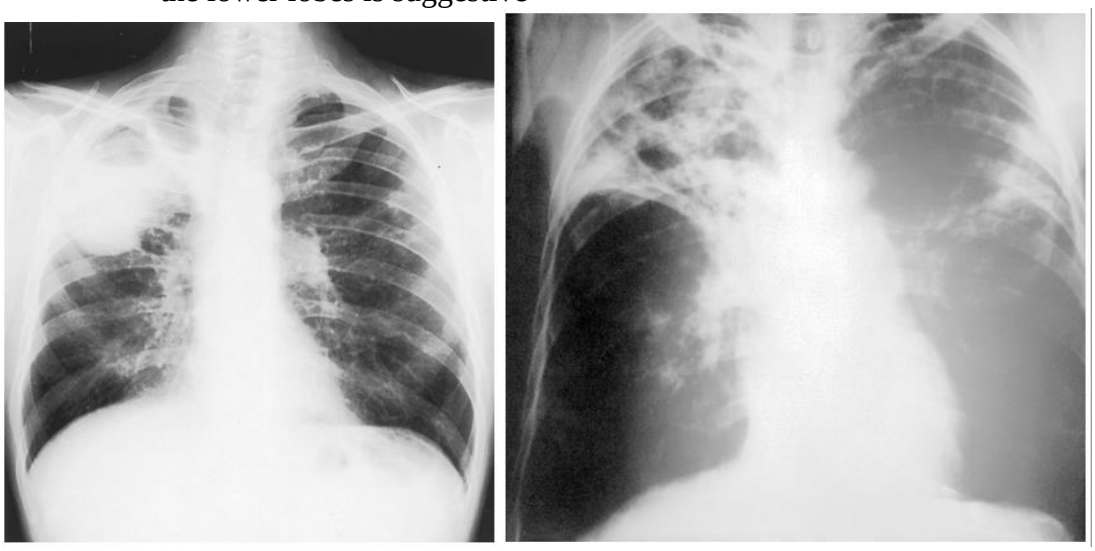
REACTIVATION TUBERCULOSIS:

- When latent infection progresses to active TB, symptoms may be systemic or pulmonary
- Most common symptom is fever → night sweats, malaise, fatigue and weight loss
- Productive cough with haemoptysis may occur
- Although most cases of TB are pulmonary (80%), 20% are extrapulmonary → adrenal glands, bones, joints, GIT, GU tract, lymph nodes, meninges, pericardiaum, peritoneum and pleura → most commonly in lymph nodes
- Pericarditis and peritonitis as result of TB often needs biopsy
    - Complications of TB pericarditis → tamponade and constrictive pericarditis

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS:

- DIAGNOSIS IS A CHALLENGE
- Variable presentation and time to culture makes diagnosis in ED difficult
    - If suspected at triage → institute isolation until excluded
- LOW RISK CRITERIA:
    - CXR → absence of cavitation/apical infiltrate
    - Non-immigrant
    - No weight loss
    - No prior history of TB/mantoux positive
    - Not homeless
    - Not recently incarcerated
        - If above all negative → NPV of 99.7%
- SKIN TESTING:
    - MANTOUX → relies on delayed type hypersensitivity reaction triggered in those with past infection → dependent on extent of skin induration at test site

        - HIV positive may lose ability to mount reaction (false negative)
        - BCG → false positive
- CXR IN TB:
    - Used to screen for disease
    - Cavitary or noncavitary lesions in the upper lobe or superior segment of the lower lobes is suggestive



    - In primary disease → parenchymal infiltrates in any area of the lung may be found
    - Younger patients are more likely to have enlarged hilar lymph nodes, whereas adults more often have parenchymal anomalies and effusion
    - In latent disease → hilar nodules or fibrotic nodules may be seen
- CULTURES:
    - Still considered gold standard
    - Staining of sputum specimin with ZIEHL-NIELSEN → acid fast bacilli diagnostic
        - Approximately 60% of culture-positive cases will have smears in which AFB are seen → lower in HIV
    - Sputum culture (LOWENSTEIN-JENSEN MEDIUM) → takes 4-8 weeks for culture and sensitivity

TREATMENT:

- Because of the possibility of drug reesistance, the treatment of active TB involves use of a combination of antimycobacterial medications

Standard short-course therapy consists of 2 months treatment with isoniazid, rifampicin, pyrazinamide and ethambutol followed by 4 months of isoniazid and rifampicin. This is *only* suitable if:

- organisms are susceptible to isoniazid, rifampicin and pyrazinamide
- the patient is able to tolerate all drugs in the regimen and there is full adherence to treatment
- there is no evidence of disseminated or central nervous system TB
- extensive cavitation is not present on the initial chest X-ray
- response to treatment is satisfactory.

Daily or intermittent (three-times-weekly) regimens can be used, but intermittent regimens are only recommended if DOT is available and the patient is HIV negative. Intermittent therapy should commence after an initial intensive daily regimen of at least 2 weeks.

Drug dosages should be reviewed regularly as weight may change significantly during therapy.

For the daily regimen, use:

isoniazid 300 mg (child: 10 mg/kg up to 300 mg) orally, daily for 6 months [Note 1] [Note 2]

PLUS

rifampicin 600 mg (adult less than 50 kg: 450 mg) (child less than 50 kg: 10 mg/kg up to 450 mg; 50 kg or more: 10 mg/kg up to 600 mg) orally, daily for 6 months

PLUS

ethambutol (adult and child 6 years or more) 15 mg/kg orally, daily for 2 months [Note 3]

PLUS

pyrazinamide (adult and child) 25 to 40 mg/kg up to 2 g orally, daily for 2 months [Note 4].

- More prolonged therapy is recommended for immunocompromised patients ro for those with extrapulmonary disease → may be modified once susceptibilities are known
- Side effects or interactions can be significant, although often it is efficacious and safe

Table 70-4 Dosages and Common Side Effects of Some Drugs Used in Tuberculosis (Adults)*

Drug	Daily (maximum)	Three Times Weekly DOT (maximum)	Two Times Weekly DOT (maximum)	Potential Side Effects and Comments
Isoniazid	5 milligrams/kg PO* (300 milligrams)	15 milligrams/kg PO (900 milligrams)	15 milligrams/kg PO (900 milligrams)	Hepatitis, peripheral neuropathy, drug interactions.
Rifampin (RIF)	10 milligrams/kg PO* (600 milligrams)	10 milligrams/kg PO (600 milligrams)	10 milligrams/kg PO (600 milligrams)	Hepatitis, thrombocytopenia, GI disturbances, drug interactions.
Rifapentine	Not given daily	Not given three times weekly	600 milligrams PO twice weekly in adults; not approved in children <12 y old	Hepatitis, thrombocytopenia, exacerbation of porphyria. Centers for Disease Control and Prevention recommended for continuation therapy only for human immunodeficiency virus–negative patients.
Rifabutin	5 milligrams/kg PO (300 milligrams)	5 milligrams/kg PO (300 milligrams)	5 milligrams/kg PO (300 milligrams)	Similar to RIF, used for patients who cannot tolerate RIF.
Ethambutol	15–20 milligrams/kg PO (1.6 grams)	25–30 milligrams/kg PO (2.5 grams)	50 milligrams/kg PO (2.5 grams)	Retrobulbar neuritis, peripheral neuropathy.
Pyrazinamide	15–30 milligrams/kg PO (2 grams)	50 milligrams/kg PO (3 grams)	50 milligrams/kg PO (2 grams)	Hepatitis, arthralgia, hyperuricemia.

- A portion of patients will clinically worsen after initiation of treatment for TB → paradoxical reaction or immune reconstitution disease → seen most often in those with HIV → thought to be due to improvement in the body's ability to mount an inflammatory response as mycobacteria are cleared

- Majority are able to be treated initially as outpatients → institute home isolation procedures → do NOT institute in ED unless physicans are directed to do so by health care professionals
- Admit if patient appears toxic, hypoxic or SOB or if patient is noncompliant or if diagnosis is uncertain

SPECIAL POPULATIONS:

PATIENTS WITH TB AND HIV:

- TB (pulmonary and extrapulmonary) can often be the initial manifestion of immunodeficiency
- It is an AIDS-defining illness
- Even with retroviral treatment, the risk of active TB is twice that of the general population
- As part of initiating TB treatment, should offer HIV testing
- Longer treatment time recommended, but generally effective
- Also beware use of rifampicin as it interacts heavily with antiretrovirals
- Higher mortality rate has been reported

PATIENTS WITH MULTI-DRUG RESISTANT TB:

- DEFINED AS RESISTANCE TO AT LEAST ISONIAZID AND RIFAMPICIN → often coinfected with HIV and there was a high mortality rate → majority of cases in those born overseas, often as a result of inadequate drug therapy or noncompliance with initial treatment
- EXTENSIVE DRUG RESISTANT TB → resistance to isoniazid and rifampicin PLUS RESISTANCE TO ANY FLUOROQUINOLONE
- Initial treatment involves at least four oral agents plus one injectable drug (amikacin, spectinomycin or capreomycin) for 3-6 months → then continue effective oral agents for 15-18 months

CHILDREN WITH TB:

- Occurs in the same risk groups as in adults, but kids have several unique aspects
    - More likely to progress to early active disease
    - Symptoms are more subtle
    - May even be asymptomatic with abnormal radiographs
    - Those <5 may present as military TB
    - Usually not infectious due to their weaker cough and lower number of AFB
    - Lower mycobacterial load results in lower rates of treatment failure and relapse but the rates of progressive disease and extrapulmonary dissemination remains higher in patients <4 years old

MILIARY TB:

- Initially a historical description used to describe th gross appearance of the lung during disseminated TB → MILLET SEEDS

- Now it refers to disease that results from wide haematogenous spread during the primary infection or secondary seeding of multiple organs in the very young or immunocompromised host
- High mortality rate (up to 30%)
    - When it presents during primary Tb, it is generally more rapid and severe → associated with multi-organ failure, shock and ARDS
    - Signs of multi-system disease should cause one to suspect miliary disease