Tuberculosis

Definitions

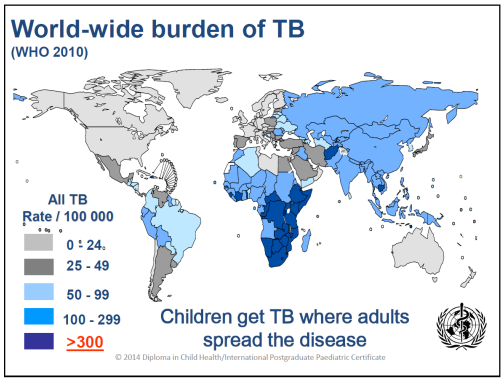
TB exposure: 5%→infection. Incubation. 2-3wk. Mantoux +ve after 2-3mo.
Latent TB infection (LTBI): Positive Mantoux but asymptomatic, normal CXR
TB Disease/Active TB: Symptomatic or positive CXR. It may be: Primary or Secondary.
Primary infection: First infection – usually lung. *Miliary TB:* multiorgan dissemination.
Secondary (reactivation) infection: ↓immune fn e.g. malnutrition, AIDS, immunosuppressants

Pathophysiology

- Chronic granulomatous disease caused mostly by Mycobacterium tuberculosis (MTB). Occ. M. bovis or M. africanum. Aerobic, non-sporing, bacilli. Slow-growing & hardy.
- Humans only known reservoirs of M. tuberculosis infection.
- Primary infection results from aerosol distribution from infected individuals.
- Alveolar macrophages unable to destroy MTB but infected macrophages reach regional LN and beyond (kidney, bones, meninges, apical posterior areas of the lung) where cell-mediated immune response initiated & terminates growth of MTB in ~2-3 weeks by CD8 suppressor T cells in lung → caseating granulomas (tubercules). Hence site of 1st infection usually heals with caseation & encapsulation but can grow & cause symptoms.
- Initial infection site+adjacent LN = primary complex (or Ghon focus). May be calcified.
- Most people infected with M. tuberculosis do not go on to have active disease.
- Disease may result from:
    - Progression of 1° complex → hilar & mediastinal ↑LN & bronchial collapse.
    - Spread by progressive caseation and cavitation through the adjacent bronchi.
    - Spread through the bloodstream and lymphatics occurs more often in children and can progress to miliary TB (when several organs or tissues are infected).
    - Bacteria released into the bloodstream can produce disseminated disease meningeal, skeletal, pleural, cutaneous, genitourinary, gastrointestinal TB.
    - Reactivation of TB that has remained dormant (usually in post. apical lung).
- Time-line – greatest risk of progressive disease is <1yr from infection.
    - 1-3m: Cell-mediated response (necessary for pos Mantoux), 2-6m:Milliary TB or TB meningitis, 4-10m:LN disease/pleural effusion, 10m-years: Adult-like disease.

Epidemiology

Prevalence: ~1/3 world population infected.
↑Incidence. Active TB incidence: 9x10^{6} cases/yr.
2nd commonest cause of infectious death.



Risk Factors

- Close contact with TB-infected adult: especially household & ED healthcare workers.
- Ethnic minority groups
- Poverty, malnutrition, homeless, alcoholics and IVDU
- HIV Positive and other immunocompromised patients
- Elderly patients - latent TB may reactivate in elderly patients.
- Other conditions: Smoking, debilitating disease, DMs, ESRF, silicosis, and gastrectomy
- Children<5y: particularly susceptible to mycobacterial infection as immuno-immature
- Vertical transmission to babies of infected mothers.

Presentation

- Insidious onset.
- Primary infection usually asymptomatic.
- Secondary infection may be non-specific, need high index of suspicion
- TB can affect all organs and body systems.
- Extra-pulmonary TB more common in children/immunosuppressed

General symptoms: fatigue, malaise, fever, weight loss, anorexia, failure to thrive, PUO.
Pulmonary: Chronic cough with purulent±bloodstained sputum. May → lobar collapse, bronchiectasis, pleural effusion, pneumonia.
GUS: "sterile" pyuria. There may be kidney lesions, salpingitis, abscesses and infertility in females and swelling of the epididymis in males.
MSK: arthritis, osteomyelitis and abscess formation (e.g. vertebral - Pott's disease).
CNS: tuberculous meningitis and tuberculomas.
GIT: mainly ileocaecal lesions but occasional peritoneal spread causes ascites
LN: hilar, paratracheal, cervical, or superficial node involvement. Scrofula.
Skin: Erythema nodosum, erythema induratum.

Investigations

Intradermal Tuberculin skin test (Mantoux): Purified protein derivative (PPD) reaction read at 48-72hr & indicates exposure (latent or present infection) if induration >5, 10 or 15mm depending on pre-test risk. False +ve if recent BCG or non-TB mycobacterial infection. False –ve if young child, immunosuppressed, infection<3mo,recent chickenpox/rubella, adult anergy.
Cultures

- Samples: 3+ spontaneous sputum samples for MC&S (incl an early morning sample) or, esp in children, induced sputum, gastric aspirate, NPA, BAL, or string test.
- Can do FNA or excision (not incision) biopsy
- Ziehl-Nielson stain and rapid direct microscopy for acid/alcohol fast bacilli
- Culture on a Lowenstein-Jensen slope (4-8wks)
- Antibiotic sensitivity cultures take a further 3-4 weeks.

CXR: Pulmonary TB is unlikely with a normal CXR.

- Primary TB – Normally base of upper lobe or top of lower lobe ± pleural effusion. Hilar LNs - Lateral XR may show nodes post & lat to trachea. (1° or Ghon Complex = calcified hilar LN+peripheral nodule).
- Reactivated TB - no pleural effusion and lesions in posterior apex. Patchy or nodular shadows, loss of volume, fibrosis ± cavitation, calcification.
- Miliary TB - uniform 1-2mm shadows throughout lung.

Non-respiratory TB:

- Consider biopsy and needle aspiration for MC&S
- Early morning urine for GUS disease.
- LP for meningitis
- CXR should be done for co-existing respiratory TB

Other tests:

- Serological tests have good negative predictive value except in HIV.
- Interferon-gamma release assays e.g. Quantiferon are similarly sens but more specific than Mantoux. Unaffected by BCG but still don't separate latent & active infection.
- PCR is possible (e.g.GeneXpert – 70% sens) but not widely available.

Management

Antituberculous drugs - Combination therapy to reduce resistance.

- All sites except CNS: quadruple Rx (isoniazid, rifampicin, pyrazinamide & ethambutol) x 2mo then (isoniazid and rifampicin) x 4mo.
- Meningitis: qradruple Rx x 2mo then (isoniazid and rifampicin) x 10mo. No evidence of need for intrathecal streptomycin.

First line drugs

- **Isoniazid**: Bactericidal. Renal excretion. **SE:** peripheral neuropathy (prophylactic pyridoxine if DM, alcoholics, malnourished, CRF or HIV), hepatitis
- **Rifampicin**: mycobacterial RNA polymerase inhibitor. Hepatic CP450 met & induction. **SE:** orange body fluids, ARF, thrombocytopaenic purpura, ↑metabolism of OCP, warfarin, sulphonylureas & steroids, hepatitis
- **Pyrazinamide**: Bacteriostatic. Renal excretion. **SE:** arthralgia, hepatitis, rash
- **Ethambutol**: Bacteriostatic. Excreted in urine and faeces. **SE:** ↓Visual acuity/fields, optic neuritis, colour blindness.

Second line drugs

- E.g. amikacin, capreomycin, cycloserine, macrolides (azithromycin, clarithromycin) and quinolones (moxifloxacin, levofloxacin). Streptomycin rarely used.

Steroids

- Give **prednisolone** 20-40mg [child 1-2mg/kg] PO OD x 2-3wk then taper if:
    - Meningitis, lobar collapse 2° to lymphadenopathy, renal or adrenal TB, moribund

Chemoprophylaxis for latent TB infection:

- **Isoniazid** x 6mo OR **isoniazid**+**rifampicin** x 3mo.

Multidrug resistant TB (MDR-TB)

- Long courses of triple therapy ± 2nd line drugs
- Consider surgical excision of lesions

Risk factors for drug resistance include:

- Previous treatment for TB
- Prior failure of TB treatment
- Contact with a known case of drug resistant TB
- Immigration from areas of high resistance
- HIV-positive status
- Age profile (highest rates are between ages 25 and 44)
- Male gender

Prognosis

- Prognosis very much depends on the extent and type of infection.
- Miliary TB, disseminated TB and tubercular meningitis are associated a poor prognosis.

Prevention

- Isolation, face mask use.
- Compliance & supervised treatment.
- Isoniazid preventative therapy (6mo) for children (close contact, asymptomatic AND <5y or immunocompromised)
- Public Health: Notification, contact tracing & Immigration screening.
- BCG vaccination. In high incidence areas BCG programme can be useful.
- Prevent/treat HIV early
- Post-exposure prophylaxis