Outline

I. Microbiological Characteristics

- Causes tuberculosis (TB); most TB is pulmonary, but non-pulmonary TB is also common
- Other mycobacteria are called non-tuberculous mycobacteria (NTM)
- MTBC discovered by Robert Koch in 1882; genome was sequenced in 1998
- All Mycobacteria are aerobic acid fast bacilli (AFB), including NTM
- All Mycobacteria have a waxy cell surface, due to the presence of mycolic acid, so the Gram stain is ineffective; they stain with acid-fast stains such as Ziehl-Neelsen (ZN) or Auramine stains.
- MTBC is a slow grower, taking weeks to culture on solid agar. Many NTMs are rapid growers.

II. General Information

- TB is endemic in Singapore. There were 1,251 new cases of active TB among residents in 2022.
- The incidence in 2022 was ~31 cases per 100,000/year: it was 300/100,000/yr in the 1960s.
- It remains this high in some surrounding countries, so immigrants are screened for active TB.
- Latent TB: ~90-95% of new infections are controlled by the immune system and don't cause active disease; these are 'latent TB' cases. Approximately 10% of these latent infections progress to active disease, most within two years of infection, but some decades later.
- Treating latent TB prevents progress to active TB, so contact tracing aims to detect new latent TB
- TB is more common in the elderly, as ~30% have latent TB, reflecting untreated infection decades earlier when rates were high. Immuno-senescence allows progression to active TB.
- Immunocompromised patients are at a higher risk of developing active TB after infection.
- Transmission is 'airborne', after close and prolonged exposure to an infectious individual with untreated, active pulmonary TB.
- Multi-drug resistant TB is far more difficult to treat and has far lower cure rates, with death rates as high as 40-58%.
- World Tuberculosis (TB) Day falls on 24 March.

III. Clinical Features

Symptoms associated with TB: cough, fever, night sweats, loss of weight, loss of appetite, fatigue

Pulmonary TB	Extrapulmonary TB
• Prolonged cough (> 3 weeks) • Chest pain • Haemoptysis (coughing up blood)	• Lymphadenitis (enlargement in lymph nodes) • Pleural effusion • Osteomyelitis (infection of the bone) • Meningitis • Gastrointestinal involvement

IV. Detection and Diagnosis Methods for Active TB – 'Disease'

- Chest X-ray; abnormalities are not specific to TB, but a clear CXR has a high NPV
- Sputum for pulmonary TB; other relevant specimens, such as CSF, tissue, pus, urine
- AFB stains (smears) have low sensitivity, ~30-50%. Note NTM also stain positive.
- TB culture. Most sensitive method, over 95% sensitive. Enables susceptibility testing.
- Nucleic acid amplification tests (NATs), usually PCR, often include a test for Rifampicin susceptibility. NATs are ~60% sensitive in 'smear negative' TB, and ~100% in 'smear positive' TB. NATs are not sensitive enough for a negative result to exclude TB in smear-negative TB, so always do TB culture: culture is both more sensitive, and enables comprehensive susceptibility testing.

V. Treatment Options

- Must not only prescribe an appropriate regimen but also assess adherence of the patient to the regimen. Non-adherence due to adverse reactions and prolonged therapy is a major problem as it leads to possible treatment failure and acquired drug resistance.
- Traditional drug therapy for new cases has a two month intensive phase with four first-line drugs (Isoniazid (INH), rifampicin, pyrazinamide, and ethambutol or streptomycin), followed by a four month continuation phase (with Isoniazid and rifampicin).
- In uncomplicated, drug-susceptible TB cases, six months of drug therapy is sufficient.
- Shorter alternative regimens are becoming available, with new drugs.
- Latent TB is treated with a simpler shorter schedule.
- Directly Observed Treatment (DOT) is recommended for all TB patients. DOT allows for closer monitoring, thus ensuring adherence to treatment, preventing development of drug resistance. DOT is available at the TB Control Unit (TBCU) and polyclinics.
- Patients are non-infectious after two weeks' treatment; issue MC for at least two weeks.
- Follow-up appointments should be at no longer than monthly intervals for patients on TB treatment. Patients should be assessed for clinical response to treatment, adherence to therapy and any adverse drug effects, particularly hepatitis.
- Response to treatment is best monitored bacteriologically with repeat sputum examination at the very least at two months (end of intensive phase) and at the end of treatment.
- All TB cases should be referred to the TBCU for contact tracing.

VI. Detection and Diagnostic Methods for Latent TB

Using tests for immunological memory of past infection

- TST – tuberculin skin test (Mantoux test); suffers from false positives due to prior BCG vaccine.
- IGRA - Interferon gamma release assays (Quantiferon or T-Spot TB). Much more specific.
- Neither tell you when infection was acquired, so treatment of latent TB depends on the doctor's opinion on whether infection was acquired recently or in the distant past.

VII. Pathweb Links

Tuberculosis in the testes
Tuberculosis in the larynx
Tuberculosis in the spleen – miliary tuberculosis
Tuberculosis in the small intestine
Tuberculosis in the spleen
Tuberculosis in the mesenteric lymph nodes
Tuberculosis in the lungs with lymph nodes
Tuberculosis in the lungs
Tuberculosis in the lungs with cavitation
Tuberculosis with primary complex in the lungs and lymph nodes

References

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2. Ministry of Health, Singapore. (2023). Update on Tuberculosis Situation in Singapore. https://www.moh.gov.sg/news-highlights/details/update-on-tuberculosis-situation-in-singapore-2023 (Accessed 25 September 2023).

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