

THE GENUS
MYCOBACTERIUM

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- **Aerobic bacilli** – non spore forming, non motile
- **Cell wall** – rich in lipids
- **Acid-fast bacilli**
- **Very slow growing**

Mycobacteria: Properties

- **Most slow growing bacteria**
- **Doubling time about one day
(20 hours)**
- **Gram-positive, but don't Gram stain**
- **Mycolic acid cell wall**
 - acid fast staining
- **Positive 'Acid-fast bacilli'**

Generative (or doubling) time

- It is the time, covering the beginning of division of the mother cell up to the formation of two new cells.
- The average generative time is about 20 – 30 minutes in a majority of medically important bacteria.
- They are some exceptions among pathogenic bacteria:
 - *Mycobacterium tuberculosis* has the generative time about 18 hours,
 - *Mycobacterium leprae* has even much longer generative time than other species (10 – 20 days).

- The mycobacteria, or acid-fast bacilli, are responsible for tuberculosis and leprosy and a number of saprophytic species occasionally cause opportunist disease.
- There are about 50 species of mycobacteria, which are divisible into two major groups, the slow and rapid growers, although the growth rate of the latter is slow relative to that of most other bacteria.
- The leprosy bacillus has never convincingly been grown in vitro.

Mycobacterium tuberculosis

- *Mycobacterium tuberculosis* causes the infectious disease tuberculosis (TB).
- Rod-like obligate aerobe with filaments.

- *Mycobacterium tuberculosis* infects 1.7 million people world-wide and causes 3 million deaths each year, the most for any single infectious disease.

- After inhalation of the tubercle bacilli, the initial lesion appears as an area of nonspecific pneumonitis. Delayed hypersensitivity develops in 2 to 4 weeks resulting in granulomatous inflammation and the characteristic tubercles. The pulmonary focus and the granulomatous lesion in the hilar lymph node are known as **the primary complex**.
- The next stage in the inflammatory process consists of caseation necrosis. The caseous lesions heal by fibrosis and calcification. The healed primary complex is referred to as **the Ghon focus**. In a small minority of individuals, the infection is not brought under control and the primary lesions become larger, coalesce, and liquefy. When this material is released, a cavity is formed in the lung.

- Most tuberculosis in adults is secondary to reactivation of long-dormant foci remaining from the primary infection. The foci are usually located in the lung.
- By the time disease is recognised, liquefaction of the caseous lesion has occurred and the resulting cavity provides a favourable site for the rapid proliferation of bacilli. These may then be transmitted to other individuals via droplet nuclei produced by aerosols of infected sputum.

- Almost every organ in the body may be the site of extrapulmonary tuberculosis. The genitourinary, bones, joints, pleura, and peritoneum are most commonly involved. Extrapulmonary manifestations may also occur as a result of reactivation of dormant lesions seeded during the primary infection.
- HIV patients are particularly prone to reactivation of pulmonary TB, the extent of which depends on the amount of immunosuppression. HIV-positive individuals may also acquire new infection from others in their environment.

Mycobacterium tuberculosis

- Tuberculosis is a chronic granulomatous disease.
- Mammalian tuberculosis is caused by four very closely related species:
 - *Mycobacterium tuberculosis* (the human tubercle bacillus)
 - *Mycobacterium bovis* (the bovine tubercle bacillus)
 - *Mycobacterium microti* (the vole tubercle bacillus)
 - *Mycobacterium africanum*

- *M. tuberculosis* causes tuberculosis but other species of mycobacteria also cause infection in the lungs. These are called the "atypical mycobacteria", "non-tuberculous mycobacteria" or "mycobacteria other than tuberculosis - MOTT".
- Tuberculosis is a killer and ranks as one of the most serious infectious diseases of the developing world. This has become particularly obvious in patients with AIDS.
- Tuberculosis is primarily a disease of the lungs but may spread to other sites or proceed to a generalized infection ("miliary tuberculosis").
- Infection is acquired by inhalation of *M. tuberculosis* in aerosols and dust. Airborne transmission of tuberculosis is efficient because infected people cough up enormous number of mycobacteria.

- Most human tuberculosis is caused by *M. tuberculosis* but some cases are due to *M. bovis*, which is the principal cause of tuberculosis in cattle and many other mammals.
- The name *M. africanum* is given to tubercle bacilli with rather variable properties and which appear to be intermediate in form between the human and bovine types. It causes human tuberculosis and is mainly found in Equatorial Africa.
- *M. microti* is seldom, if ever, encountered nowadays.

Anti-tuberculous agents

- The treatment of infection caused by *Mycobacterium tuberculosis* and other mycobacteria presents an enormous challenge to medicine and pharmaceutical industry.
- They grow and multiply extremely slowly and **effective inhibition takes months**.
- A number of anti-tuberculous agents are now available.
- Most are restricted to this use to prevent resistance emerging in other species and potentially being transferred to mycobacteria or because the toxicity of the drugs makes them unattractive for general use.

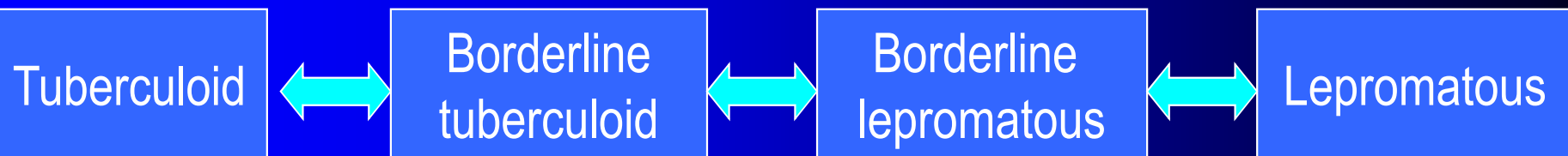
Treatment of TB

- Initiate four drugs
 - Isoniazid
 - Rifampin
 - Pyrazinamide
 - Ethambutol or Streptomycin
- Adjust regimen when drug susceptibility results known
- Total treatment usually 8 weeks of 4 drugs + 16 weeks of 2 drugs = 24 weeks total

Treatment regimens may vary between countries
in general

Mycobacterium leprae

- Acid fast bacilli
- Strict human pathogens
- Cannot be cultivated in-vitro
- Transmission - ? Air borne
- Low infectivity - prolonged contact required
- Spectrum of clinical presentations
 - dependent on host –parasite interactions



Mycobacterium leprae - pathogenesis

- *M. leprae* causes granulomatous lesions resembling those of tuberculosis, with epithelioid and giant cells but without caseation.
- The organisms are predominantly intracellular and can proliferate within macrophages, like tubercle bacilli.
- Leprosy is distinguished by its chronic slow process.
- The organism has a predilection for skin and nerves. In the cutaneous form of the disease, large firm nodules are distributed widely and on the face they create a characteristic leonine appearance. In the neural form, segments of peripheral nerves are involved, more or less at random, leading to localised patches of anaesthesia. The loss of sensation in the fingers increases the frequency of minor trauma, leading to secondary infection and mutilating injuries.

Treatment of leprosy

- Infection caused by *M. leprae* is characterized by persistence of the microorganism in the tissues for years, necessitates very prolonged treatment to prevent relapse.
- For many years **dapsone**, a sulphone derivative has been used. This drug has the advantage that it is given orally and it is cheap and effective.
- However, widespread use as monotherapy has resulted in the emergence of resistance and multidrug regimens are therefore preferable. **Rifampicin can be combined with dapsone.** Alternatively clofazime is active against dapsone-resistant *M. leprae*, but it is expensive.

- In addition to the tubercle and leprosy bacilli there are many species of mycobacteria that normally exist as saprophytes of soil and water.
- Some of these, termed environmental or „atypical“ mycobacteria, occasionally cause opportunist disease in animal and man.

Diseases due to atypical mycobacteria:

- skin lesions following traumatic inoculation of bacteria,
- localized lymphadenitis,
- tuberculosis-like pulmonary lesions,
- disseminated disease.