Chapter 21

Mycobacteria (2)

Atypical Mycobacteria

-- These are those Mycobacteria which differ significantly from ***M. tuberculosis*** and therefore also called **Mycobacteria other than Tuberculosis (MOTTS).**

-- There are **four groups** based on **rate of growth** and **production of pigment** under certain conditions.

-- **Groups I-III are slow growers** but **Group IV are rapid growers** and produce visible colonies within 7 days.

-- **Group I** produce **yellow orange colonies in light** only (**photochromogens**).

-- **Group II** do so **chiefly in darkness** (**scotochromogens**).

-- **Group III do not produce pigment** (**nonchromogens)**.

Group I (photochromogens)

M. kansasii causes **lung disease resembling TB**.

Due to antigenic similarity, **tuberculin skin test is often positive**.

It is **susceptible** to standard antituberculous drugs.

M. marinum causes **fish tank granuloma**.

These lesions occur in the skin at the site of abrasions incurred at **swimming pools** and **aquariums**.

Treatment with **tetracyclines** is effective.

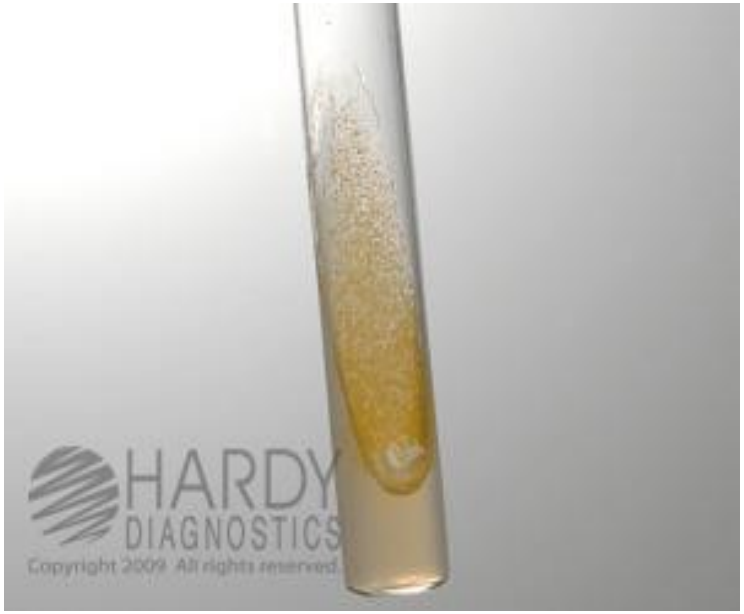
Group II (schotochromogens)

M. scrofulaceum causes **scrofula**, a granulomatous cervical adenitis usually in children (***M. tb*** can also cause this disease).

The organism enters through the **oropharynx** and infects the draining **lymph nodes**.

Its natural habitat is **environmental water** sources.

Scrofula can often be cured by **surgical excision** of the affected lymph nodes.



Group III (non chromogens)

-- ***M. avium-intracellulare*** complex (**MAI, MAC**) is composed of two species, ***M. avium*** and ***M. intracellulare*** .

-- These two species are **very difficult to distinguish from each other** by standard laboratory methods.

-- They cause **pulmonary disease clinically indistinguishable from tuberculosis** primarily in **immunocompromised patients** such as those with AIDS who have **CD4 cell counts of less than 200/µl**.

-- **MAI** is the most common cause of disease in **AIDS** patients.

-- They are **highly resistant to antituberculous drugs**, and a combination of up to 6 drugs may be required.

-- Current drugs of choice are **clarithromycin** plus one or more of the following: **ethambutol, rifabutin or ciprofloxacin**.

Group IV (rapidly growing Mycobacteria)

-- ***M. fortuitum - chelonei*** complex is composed of two **similar species**, ***M. fortuitum*** and ***M. chelonei*** .

-- These are **saprophytes** and rarely cause human disease.

-- These occur chiefly in **immunocompromised patients** and patients with **indwelling catheters** and **prosthetic hip joints**.

-- **Skin** and **soft tissue infections** occur at the site of puncture wounds.

-- They are **often resistant to antituberculosis drugs** and therapy with multiple drugs plus **surgical excision** may be required for effective treatment.

-- Current drugs of choice are **amikacin plus doxycycline**.

-- ***M. abcessus*** is another **rapidly growing saprophyte** that may cause **chronic lung infections**, and **infections of skin, bone and joints**.

It is **highly antibiotic resistant**.

-- ***M.smegmatis*** is a **rapid grower** which is **not associated** with human disease.

It is part of **normal flora of smegma**.

Mycobacterium leprae

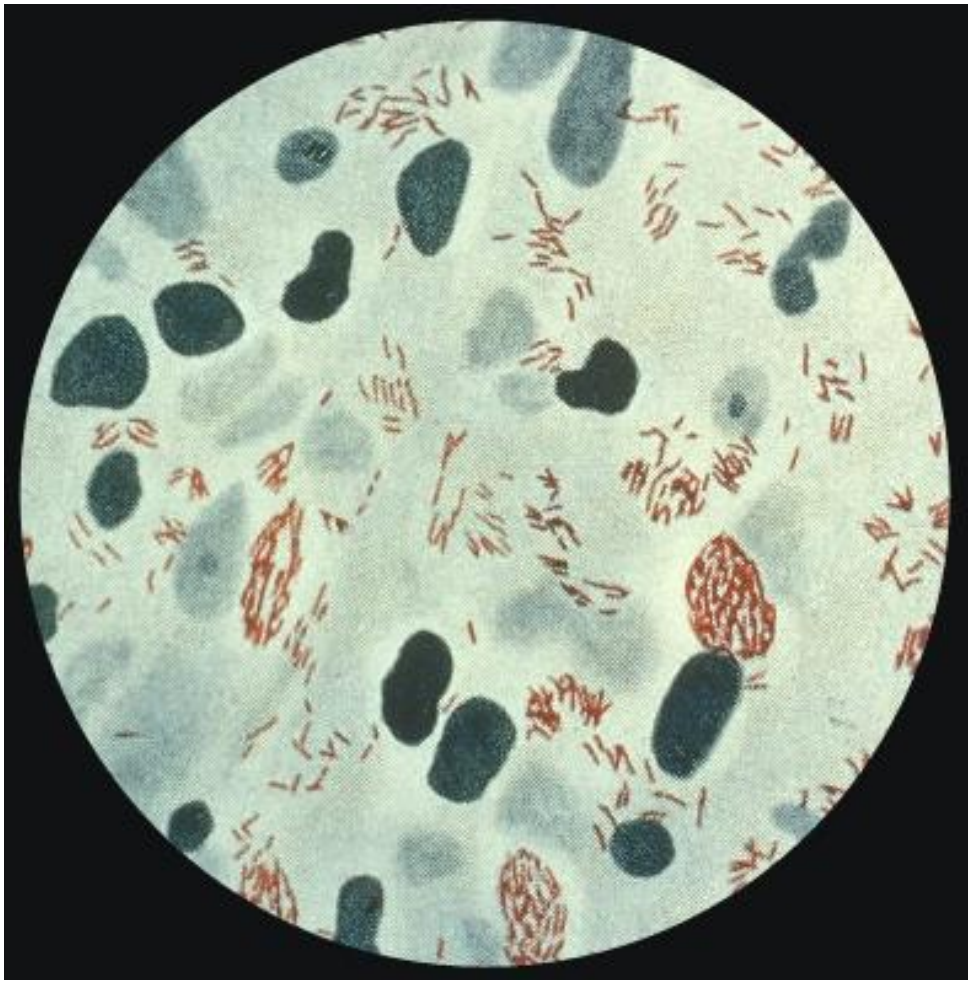
It causes **leprosy** (**Hansen's disease**).

Important Properties

-- ***M. leprae*** has **not been grown in the laboratory**, either on artificial media or in cell culture.

-- It **can be grown in experimental animals** such as **mice** and **armadillos**.

-- Appearance in tissues is similar to ***M. tuberculosis***



-- **Humans are the natural hosts** but armadillo appears to be natural host in some areas of US.

-- The **optimal temperature is 30°C** so it **preferentially grows in the skin and superficial nerves.**

-- It is the **slowest growing human pathogen** with a doubling time of **14 days.**

-- This means that **antibiotic therapy has to be continued for a very long time, usually several years**.

Transmission

-- Infection is acquired by **prolonged contact with patients with lepromatous leprosy**, who discharge the organism in large numbers in **nasal secretions** and from **skin lesions**.

-- The disease occurs **world wide** with most cases in **tropical areas of Asia and Africa.**

Pathogenesis

-- The organism replicates **intracellularly**, typically within **skin histiocytes, endothelial cells** and the **Schwann cells of nerves**.

-- **Nerve damage** is caused by **direct contact** with the bacterium and damage caused by **CMI (cell mediated immunity) attack on nerves**.

-- There are **two** distinct types: **tuberculoid** and **lepromatous** with several intermediate forms.

Tuberculoid leprosy

-- The **CMI response to the organism limits its growth**, very few acid fast bacilli are seen and **granulomas containing giant cells form**.

-- **Main damage to nerves is due to CMI.**

-- The **CMI response** consists primarily of **CD4-positive cells** and a **Th-1 profile of cytokines namely γ-interferon, IL-2, and IL-12.**

-- The **lepromin skin test result is positive**. It is similar to tuberculin test.

-- An extract of ***M. leprae*** is injected **intradermally**, and induration is observed **48 hours** later in those in whom CMI response against the organism exists.

Lepromatous leprosy

-- **Cell mediated response to organism is poor.**

-- **The skin and mucous membrane lesions contain large number of organisms.**

-- **Foamy histiocytes** rather than granulomas are formed and **lepromin skin test is negative**.

-- The **nerve damage seems likely to be caused by direct contact** as there are many organisms and CMI response is poor.

Only the CMI to ***M. leprae*** is defective (patient is **anergic** to ***M. leprae***), that to other organisms is intact.

Humoral response is intact but the **antibodies are not protective**.

The T cell response consists primarily of **Th-2 cells**.

Clinical findings

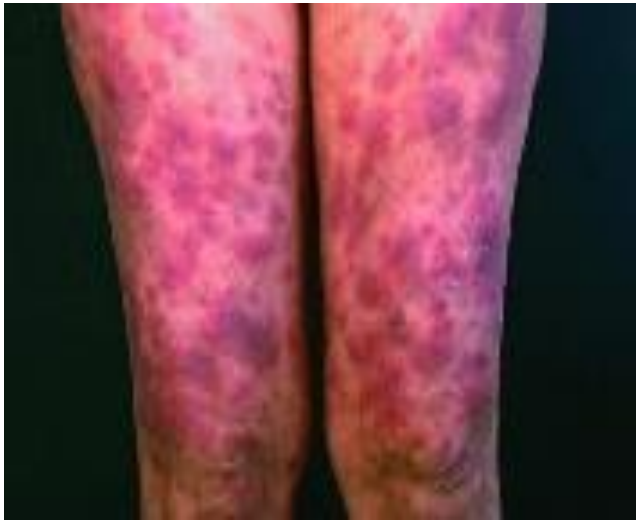
-- **The incubation period averages several years, and onset of disease is gradual.**

-- In **tuberculoid leprosy**, **hypopigmented macular** or **plaque-like skin lesions, thickened superficial nerves,** and **siginificant anesthesia** of the skin lesions occur.

-- In **lepromatous leprosy**, **multiple nodular skin lesions** occur resulting in typical **leonine (lion like**) facies.

-- After onset of therapy, patients of lepromatous leprosy often develop **erythema nodosum leprosum (ENL)** which is **an indication the CMI is being restored.**

-- **ENL is characterized by painful nodules, especially along the extensor surfaces of tibia and ulna, neuritis and uveitis.**



The **disfiguring appearance of disease** is due to:

1. **Skin anesthesia** that results in burns and other traumas which often become infected.

2. **Resorption of bone** that leads to loss of features such as the nose and finger tips.

3. **Infiltration of the skin and nerves** that leads to thickening and folding of the skin.

In most patients with a **single skin lesion**, the disease **resolves spontaneously**.

Patients with appearance in between tuberculoid and lepromatous form, may progress to **either extreme**.

Laboratory Diagnosis

-- **In lepromatous leprosy, bacilli are easily demonstrated by acid fast stain of skin lesions or nasal scrapings.**

-- Lipid laden macrophages called **"foam cells"** with many acid fast bacilli are seen in the skin.

-- In **tuberculoid leprosy**, there are **very few organisms** but appearance of **typical granulomas is diagnostic**.

-- Cultures or serological tests are **irrelevant**.

-- Diagnosis can be **confirmed by PCR**.

Treatment

-- Mainstay of therapy is **dapsone** (diaminodiphenylsufone).

-- Due to emergence of resistance**, combination therapy** with addition of **rifampin** and **clofazimine** for **lepromatous leprosy** and **rifampin** for **tuberculoid form** is recommended.

-- Treatment is given for **at least 2 years** or until the lesions are free of organisms.

-- **Thalidomide** is the treatment of choice for severe **ENL reactions**.

Prevention

-- **Isolation of all lepromatous patients**, coupled with **chemoprophylaxis with dapsone** for exposed children is required.

-- There is **no vaccine**.


Thank You!