Medical Bacteriology- Lecture 10

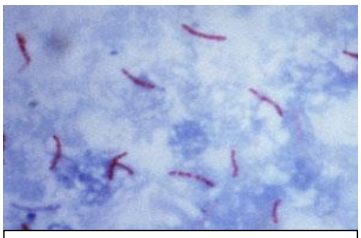
Mycobacterium

Actinomycetes

Nocardia

Mycobacterium

Characteristics



***M. tuberculosis* acid fast stain.**

- Large, very weakly gram positive rods
- **Obligate aerobes**, related to Actinomycetes
- Catalase positive
- Non spore forming
- Non motile
- **very slow growing- slow generation time (14-15 hours), colonies appears by (2-8 wks)**
- **Acid fast bacteria** (**Ziehl-Neelsen stain)**
- **facultative intracellular parasite**, usually of macrophages
- **rich in lipids -** Mycolic acids in (***Mycobacteria, Nocardia)***
- Egg yolk agar and Lowenstein- Jensen agar (Selective media)
- More resistant to chemical agents than other bacteria
- Many non-pathogenic mycobacteria are parts of human normal flora

Medically important species:

•***M. tuberculosis*** is cause agent of **tuberculosis in humans**.

•***M. bovis*** is the agent of **TB in cows** and **rarely in humans** (Both cows & humans can serve as reservoirs). Humans can infected by the consumption of unpasteurized milk. This route of transmission can lead to the development of **extra pulmonary TB.**

•***M. leprae*****,** the causative agent of **leprosy.**

Human Tuberculosis

- **Tuberculosis (TB)** is the leading cause of death in the world.
- Most people with TB infection have a positive reaction to the **tuberculin skin test** (purified protein derivative).
- **Incubation period:** 4-6 weeks.
- **The disease manifests with (low fever, night sweating, headache, cough with expectoration, significant weight loss, fatigue and weakness).**
- **Contagious**
- **Disease progression depends on** (Strain of MTB - Prior exposure - Vaccination - Infectious dose - Immune status of the host)
- **Source of infection:** Tuberculous patients
- **Route of infection**: **Respiratory TB**; transmitted via Inhalation of airborne droplets.

  Extra-pulmonary TB; Ingestion of contaminated milk
- ***Bacille Calmette-Guerin* (BCG- vaccine); live strain of *M. bovis*** developed by Calmette and Guerin for use as an **attenuated vaccine** to prevent tuberculosis and other mycobacterial infections.

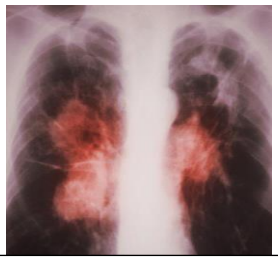
Stages of the Tuberculosis Disease

1) Droplet nuclei (Primary nodule) (tubercle): Inhalation air droplet (one droplet nuclei contains no more than 3 bacilli). Droplet nuclei are so small that they can remain air-borne for extended periods of time.

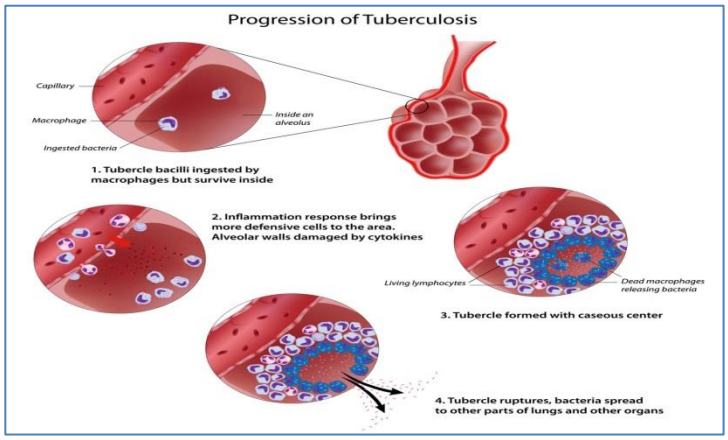
2): (Tissue necrosis): Begins 7-21 days after initial infection. **MTB multiplies within macrophages** until the macrophages burst.

3) (Consolidation): The individual becomes **tuberculin-positive**. The host developing a cell mediated immune response. An antibody will not control of a MTB infection because MTB is intracellular and if extracellular, it is resistant to complement killing due to the high lipid concentration in its cell wall. at this stage that **tubercle formation** begins. The center of the tubercle is characterized by **semi-solid or "cheesy" necrosis**". MTB cannot multiply within these tubercles because of the low pH. MTB can, however, persist within these tubercles for extended periods. **(most contagious).**

4) (Calcification): MTB uses macrophages to replicate, and the tubercle grows. The growing tubercle may invade a bronchus. If this happens, MTB infection can spread to other parts of the lung. **(X-rays positive)**.



X-Ray positive during Calcification stage



Cell Wall Structure of *M. tuberculosis*

- It is **unique among prokaryotes**, and it is a major determinant of virulence for the bacterium

The cell wall complex contains

- **Peptidoglycan**
- **Complex lipids** (consists of three major components, **mycolic acids, cord factor & wax-D**)

• **Mycolic acids:** found in cell walls of ***Mycobacterium, Corynebacterium and Nocardia***- **(a significant determinant of virulence**)- prevent attack of the mycobacteria by cationic proteins, lysozyme and oxygen radicals in the phagocytes.

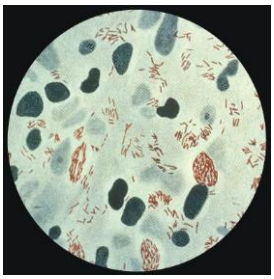
• **Cord Factor:** is toxic to host cells and inhibit PMN migration- most abundant in **virulent strains of MTB**.

• **Wax-D:** is the major component of Complete **Freund's adjuvant** (CFA). (*a solution of water-in-oil emulsion used as an immune-potentiate (booster). containing heat-killed mycobacterial cell wall components, is an effective means of active cellular and humoral antibody response*)

The benefits of high concentration lipids in *M. tuberculosis* cell wall :

Resistance to many antibiotics
Resistance to killing by acidic and alkaline compounds
Resistance to osmotic lysis by complement.
Resistance to lethal oxidations and survival inside of macrophages
Impermeability to stains, dyes and drying.

Mycobacterium leprae



- Gram positive
- **Acid fast bacilli**
- **Causes leprosy**
- non motile
- aerobic
- Mostly found in warm tropical countries
- **Obligate intracellular parasite- Cannot be cultivated in-vitro (**Not grown in non-living bacteriologic media).

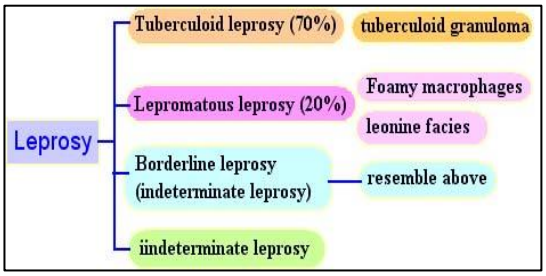
- **Characteristic lesions are grown in laboratory animals.**

  e.g. Foot pads of mice

  Armadillos

- Incubation period is months to years.
- Route of infection is through nasal mucus secretion
- Severe and permanent nerve damage

Types of Leprosy



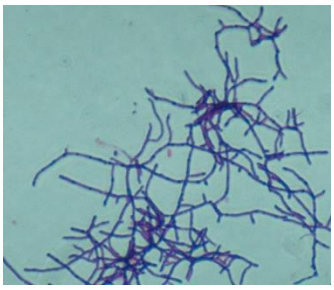
1- Tuberculoid; host is highly resistant, clinical abnormalities limited to a few peripheral nerves and adjacent skin areas, tuberculoid granuloma.

2- **Lepromatous;** host lacks resistance, all tissue affected, foam cell granuloma.

3- Intermediate.

MYCOBACTERIA ASSOCIATED WITH HUMAN DISEASE

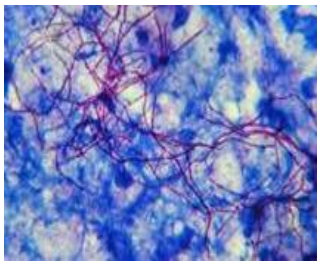
Mycobacterium	Environmental contaminant	Reservoir
M. tuberculosis	no	human
M. bovis	no	Human, cattle
M. leprae	no	human
M. kansasii	rarely	Water, cattle
M marinum	rarely	Fish, water
M scrofulaceum	possibly	Soil, water
M avium intracellulare	possibly	Soil, water, bird
M ulcerans	no	unknown
M fortuitum	yes	Soil, water, animal
M chelonae	yes	Soil, water, animal



Actinomycetes

- Gram positive bacilli
- **Branching filaments**
- facultative or strictly anaerobic- aerobic
- Actinomyces are morphologically similar to **Nocardia** except that they **Actinomyces are not acid-fast**
- Free living (soil)
- Normal flora of the upper respiratory, gastrointestinal and female genital tracts
- **Grow slowly in culture** (up to two weeks or more)
- *Human actinomyosis*
- causes infections that are slow to develop and tend to be; chronic, abscesses, dental caries
- Low virulence potential, causing opportunistic disease following disruption of mucosal barriers by trauma, surgery or infection
- Aerobic actinomycetes whose cell walls lack mycolic acid: **Streptomyces species** (produce antibiotics)

Nocardia



- Weakly gram positive bacilli
- **Branching long filamentous cells**
- **Acid fast**
- Common found in soil, aquatic environment, humans (oral flora) and animals
- Exogenous infections
- Cutaneous, sub- cutaneous, systemic lesions.
- Transmission (inhalation, skin). Most Nocardia infections are acquired by inhalation of the bacteria.
- 50% of patients are immunocompromised
- Treatment (long term antibiotics therapy)
- ***Nocardia madurae; causes*** **Madura foot**

Differences between the genera *Actinomyces* and *Nocardia*

Actinomyces species	*Nocardia* species
Facultative anaerobes	Strict aerobes
Grow at 35-37oC	Wide temp range of growth
Oral commensals	Environmental saprophytes
Non-acid-fast mycelia	Usually weakly acid-fast
Endogenous cause of Disease	Exogenous cause of disease

Review Questions

- What is the major phenotypic characteristic of Mycobacteria? (5 points)
- Mycobacteria contain three medically important species, write them and write its diseases?
- What is the human Tuberculosis stages, which is more Contagious, which one can be seen apparently under X- rays. What is the body sites that exposed for TB disease?
- What is the components of lipid layer on the Mycobacterial cell wall, what is the major virulence determinants of the lipid components. What is the benefits of Lipid layer?
- What is the types of *Mycobacterium leprae* diseases? Only points.
- *M. leprae* cannot be cultured in laboratory, because it cannot survive outside of mammalian cells. So, how it can be diagnosed?
- Give two examples of Branching bacteria? How can differ between them according to acid fast stain?
- What is the causative agent of; leprosy, tuberculosis, Madura foot?