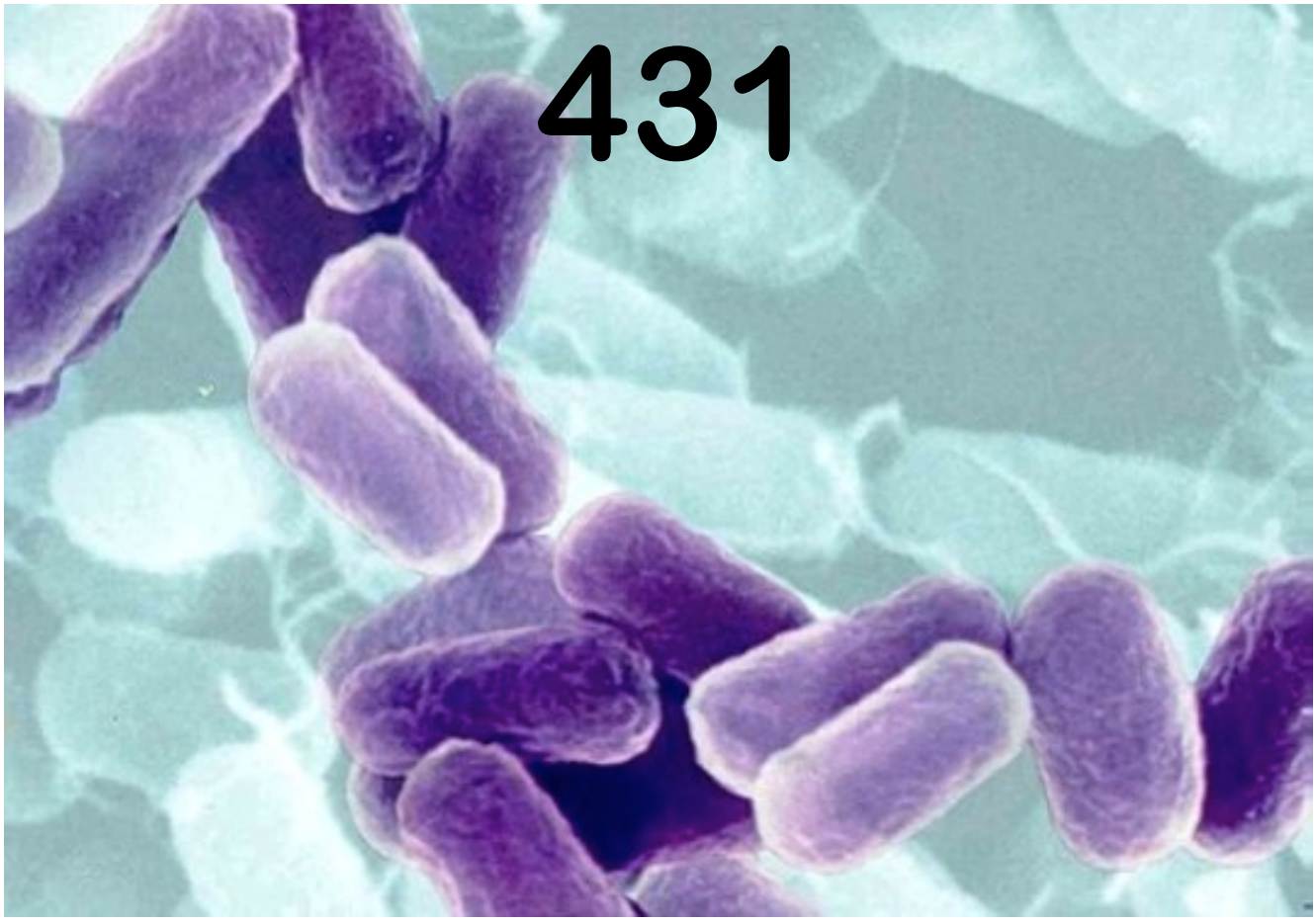
MICROBIOLOGY TEAM 431



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Tuberculosis

Curable if treated
Fatal if untreated (major cause of death)

Epidemiology:

- Affects 1/3 of humans (as latent)
- Worldwide (mostly in developing countries)
-ALL AGES
-AIRBORNE TRANSMISSION BY DROPLETS
-Reservoir: patients with OPEN TB (organism will come out as they cough)
-People at risk: doctors, nurses, micro lab workers, Diabetics, HIV, renal failure …etc

-In KSU: 32-64/100.00 people affected

MYCOBACTERIA: Rod shaped
Not movable
Does NOT form spores

Contains high lipid concentration (**MYCOLIC ACID**) in the cell wall which resist staining (CANT USE GRAM STAIN) ➔ called acid alcohol fast (AFB) because it resists decolorization

Stain with : Ziehl Neelson Stain (ZN) = AFB stain

AFB= ACID FAST BACILLI

STRICT AEROBES
Slow growing (2-8 weeks)
Multiply intracellulary (cell mediated immunity required)
➔ Delayed hypersensitivity reaction

ORGANISM CAUSING TUBERCULOSIS: [[Mycobacterum tuberculosis complex]]

1.**M.tuberculosis (human)**
2.M.bovis (bovine “animals”) not frequent anymore due to milk pasteurization
3.M.africanum
4.M.BCG strains (used for vaccination, but if low immunity: TB disease my occur)

PATHOGENESIS

1. Mycobacterium is acquired by airborne droplets ➔ reaching the alveoli ➔ taken up by Alveolar macrophages.
2. Activates the cell mediated immunity (CMI) ➔ control multiplication of organism BUT DOESN’T KILL IT
3. GRAMULOMA is formed and the organism lives in a dormant state (latent TB = no Symptoms)
4. CMI causes destruction ➔ result in a disease

PRIMARY TUBERCULOSIS:

(1st exposure to mycobacteria) = In patients not previously infected

Inhale bacteria ➔ phagocytosis by macrophages ➔ lymph nodes calcify and produce:
GHON focus "primary complex"

At the periphery of the mid area of lung

Microscopy: Granuloma
Clinically: No Symptoms/Minor illness

Nonpulmonary TB
TB that spreads from pulmonary infection to other organs

Ex: TB of lymph nodes (cervical, mesenteric)
TB of meningitis (very dangerous)
TB of bone & joints
Genitourinary TB
Miliary TB: spreads to blood and other organs
Soft tissue TB (cold abscess): NO inflammation with caseation

Caseation: due to delayed hypersensitivity reaction.
Contains many bacilli, enzymes. 02, N2
➔➔ necrotic center of granuloma which appears as cheesy material

SECONDARY TUBERCULOSIS:

[[Reactivation]]
occurs later in life & is more common in the lungs
occurs in immunocompromised patients
lesions localized in apices of lungs
Infectious (to other people) and symptomatic

Microscopy: many bacilli, large are of caseous Necrosis ➔ cavity (open tb) with granuloma
Clinically: fever, weight loss, weakness, cough, Hemoptysis (cough with blood)

Source of secondary TB:

Endogenous: reactivation of old TB

Exogenous: re-infection of previously sensitized patient

Tuberculin skin test (Mantoux Test)

- Uses PPD: purified protein derivative
- expressed by tuberculin unit

- Results show when lymphocytes produce CMI which appears as skin INDURATION.
- Not specific: may not differentiate between active and past infection
  But is used with individuals with recent contact with infected cases (relative screening)
- Low level activity may be induced by environmental mycobacteria & previous vaccination

Method of Tuberculin skin test

- Mantoux Test (takes 2-10 weeks after inhaling the organism to become positive)
- Heaf Test (Screening) "Used if there is a large number of people, like in schools"

((Intradermal injection of 0.1 ml of PPD, 5TU "Tuberculin Unit". Read after 48-72 hours))

Positive Tuberculin skin test

If induration is more than 5mm TB is POSITIVE in:
*Recent contact with active TB.
*A person with HIV or high risk of HIV.
*Chest w-ray is consistent with healed TB.

If induration is more than 10 mm TB is POSITIVE in:
*IV drug users
*HIV seronegative patients
*Medical conditions, eg. Diabetes, Malignancy.
*Residents & employee at high risk.
*Patients from country with high incidence.
*Children more than 4yrs or exposed to adult high risk group.
*Mycobacteriology lab workers

If induration is more than 15mm TB is POSITIVE in:
*any persons including those with no risk factors for TB.

Negative Tuberculin skin test

NO INDURATION.
Either to:

*No previous Infection.
*Pre-hypersensitivity stage.
*Lost TB sensitivity with loss of Ag.

(AIDS patients are susceptible to infection.)

[Induration: Stiffness]

Laboratory diagnosis of TB

1. Specimens (v.imp for TB because bacteria are usually small in number):
*3 early morning urine.
*Bone, joint aspirate.
*Lymph nodes, pus or tissues NOT swab.
*Cerebrospinal fluid (CSF) for TB meningitis
*3 early morning sputum samples (or induced cough), or bronchial lavage, or gastric washing(infants). For Pulmonary TB.
*Repeat Sample

2. Direct microscopy of specimen
Z-N or (Auramine) stain

3.Culture (Sometimes smear is negative so we take culture to make sure)
*the gold standard test for identification and sensitivity.
*Media used: **Lowenstein-Jensen media** (L J).
*Media contains: eggs, asparagin, glycerol, pyruvate/ malachite green.
*Colonies appear in LJ media after 2-8 weeks as eugenic, raised,buff,adherent growth enhanced by glycerol (in M.TB) or by pyruvate (in M.bovis).
*Other media plus LJ media may be used, Such as: Fluid media (middle Brook), MGIT (mycobacteria growth indicator test), Automated methods :- eg. Bactec MGIT, PCR: molecular test directly from specimen (CSF), and Measurement of interferon –gamma (IF-γ) secreted from sensitized lymphocytes challenged by the same mycobacterial proteins in a patient previously exposed to disease, will produce interferon gamma. Has a **specific** significance than tuberculin skin test

Identification of Tb:

*Morphology , growth at 37C + 5 -10 % CO2
*Biochemical tests : Niacin production & Nitrate test.
*Sensitivity testing.
*Guinea pig injection [rarely done].

Management of tb

1. Isolation for 10-14 days, till the patient is not infectious (for smear positive cases i.e. > 1000 organisms / ml of sputum considered infectious case). Then he continues treatment at home.
2. Triple regimen of therapy (3 drugs combined) to prevent resistant mutants, cover strains located at different sites of the lung, and To prevent relapse.
3. Treatment must be guided by sensitivity testing.

First line treatment

***Isoniazide (INH)**
***Rifampicin (RIF)**
***Ethmbutol (E)**
***Pyrazinamide (P)**
*Streptomycin (S)
INH+ RIF +P for 2 months then continue with INH+RIF for 4-6 months. Multidrug resistant TB is resistance to **INH & RIF**.

*Directly Observed Therapy (DOT). [Important for every patient to make sure they take their drugs]

Second line treatment

Used if the bacteria was resistant to first line drugs. More toxic than the first line drugs.

*PASA (Para-Amino Salicylic acid).
*Ethionamide
*Cycloserine,
*Kanamycin,
*Fluroquiolones

Prevention of TB:

*Tuberculin testing of herds.
*Slaughter of infected animals.
*Pasteurization of milk to prevent bovine TB.
*Recognition of new cases.
*Prophylaxis with INH for family and close contacts to patients with TB.
*Follow up cases.
*Immunization with BCG to all new borne.

Summary:

Mycobacterium tuberculosis* aerobic
Transmission: airborne (droplets hang in the air for long periods)
Very infectious (dangerous)
Affects all organs (respiratory system TB is most infectious)
ACID FAST BACILLI
ZN STAIN for staining * * * * (they don't lose the dye when you wash it out)
Activates cell mediated immunity
GHON FOCUS: Lesion in lung from PRIMARY TB (asymptomatic)
Laboratory TB: CULTURE but it is slow growing
Media used: lowenstein Jensen media
TREATMENT* *
Multi resistant TB (MRTB): resistant to INH & RIF

Review Questions:

1. Which one of the following is a feature of Primary TB?

   A. It is a reactivation of old TB
   B.It is more common in the apecis of the lung
   C. Lymph nodes calcify and produce GHON focus
   D. None of the above

2. Which one of the following is true about Mantoux skin test?

   A. It does not indicate whether it is a new infection of a reactivation of an old one.
   B. It is used for a large group of people.
   C. It is an intramuscular injection.
   D. All of the above

3. Sputum specimen is taken early in the morning because:

   A. Sputum is dry in the morning.
   B. There is a larger number of bacteria in sputum before eating
   C. There are no bacteria is the sputum at night.
   D. None of the above.

4. Which one of the following is a drug for first line treatment of TB?

   A. Isoniazide.
   B. Ethionamide.
   C. Cycloserine.
   D. All of the above.

Answers:

1. C
2. A
3. B
4. A