Tuberculosis

- Causative organism -*Mycobacterium tuberculosis*

  - Strict aerobe

  - Pathogenic strains---hominis, bovis, avium, murine & cold blooded vertebrate strain

  - Epidemiology

  - poverty, crowding, chronic debilitating disease

  - AIDS

Koch’s bacillus

- small slender, rod like bacillus, 4um non-motile, aerobic
- high lipid content
- divides every 16 to 20 hours, an extremely slow rate
- stains very weakly Gram-positive or does not retain dye due to the high lipid & mycolic acid content of its cell wall
- can withstand weak disinfectant and survive in a dry state for weeks.
- demonstrated by
    - Ziehl Neelsen staining
    - Fluorescent dye method
    - Culture in LJ media
    - Guinea pig inoculation

Current Situation

- Two to three million people around the world die of TB each year.
- Someone is infected with TB every second.
- One third of the world population is infected with TB
- Twenty three countries in south east Asia and sub Saharan Africa account for 80% total cases around the world.
- Number of new cases of TB correlates with economic conditions: the highest incidences are seen in Africa, Asia, and Latin America
- 70% untreated actively infected individuals die.

Modes of transmission

- Inhalation
- Ingestion
- Inoculation
- Transplacental route

Spread

- Local
- Lymphatic
- Haematogenous
- By natural passages

Pathogenesis

- Anti- mycobacterial CMI, confers resistance to bacteria→dev of HS to tubercular Ag
- Bacilli enters macrophages
- Replicates in phagosome by blocking fusion of phagosome & lysosome, continues for 3 weeks →bacteremia but asymptomatic
- After 3 wks, T helper response is mounted by IL-12 produced by macrophages
- T cells produce IFN, activates macrophages → bactericidal activity, structural changes
- Macrophages secrete TNF→ macrophage recruitment, granuloma & necrosis

Fate of granuloma

- Caseous material undergo liquefaction---cold abscess
- Bones, joints, lymph nodes & epididymis---sinuses are formed & sinus tract lined by tuberculous granulation tissue
- Dystrophic calcification

Types of TB

- Primary Pulmonary TB
- Secondary TB (miliary, fibrocaseous, cavitary)
- Extra-pulmonary TB (bone, joints, renal, adrenal, skin…)

Primary TB

- Infection in an individual who has not been previously infected or immunised
- Primary complex

  Sites--- lungs, hilar lymph nodes

  - tonsils, cervical lymph nodes
  - small intestine, mesenteric lymph nodes

Primary TB

In the lung, Ghon's complex has 3 components:

- Pulmonary component

  - Inhalation of airborne droplet ~ 3 microns.

  - Bacilli locate in the subpleural mid zone of lung

  - Brief acute inflammation – neutrophils.

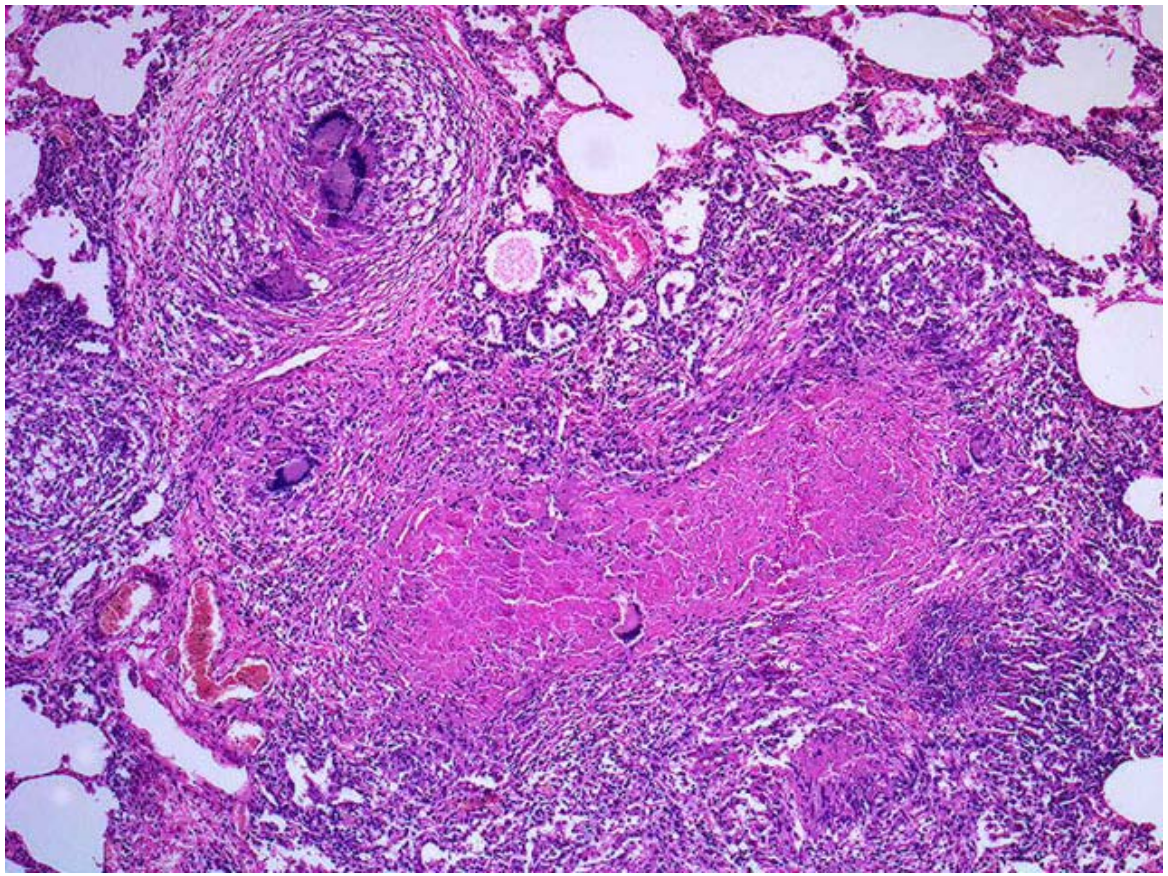
  - 5-6 days- invoke granuloma formation.

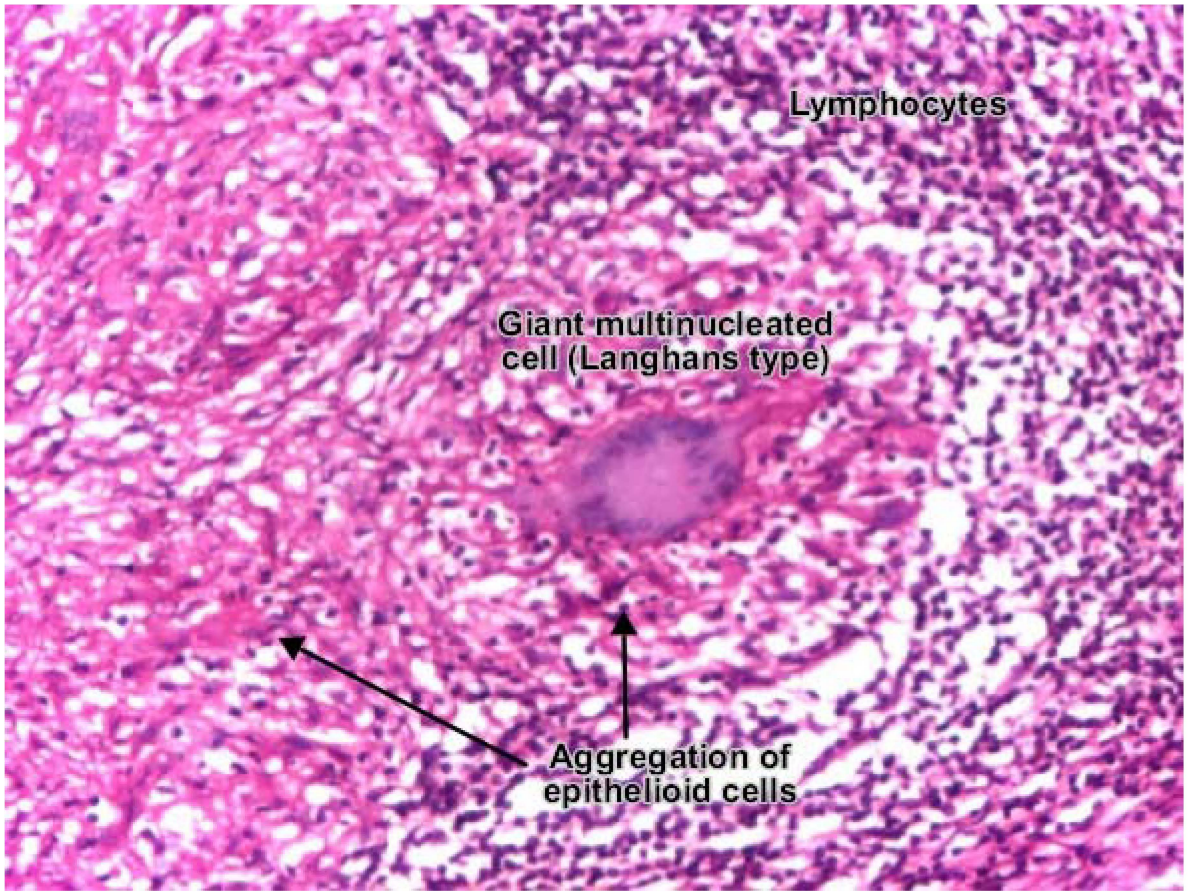
  - 2 to 8 weeks – healing – single round ;1-1.5 cm- Ghon focus.

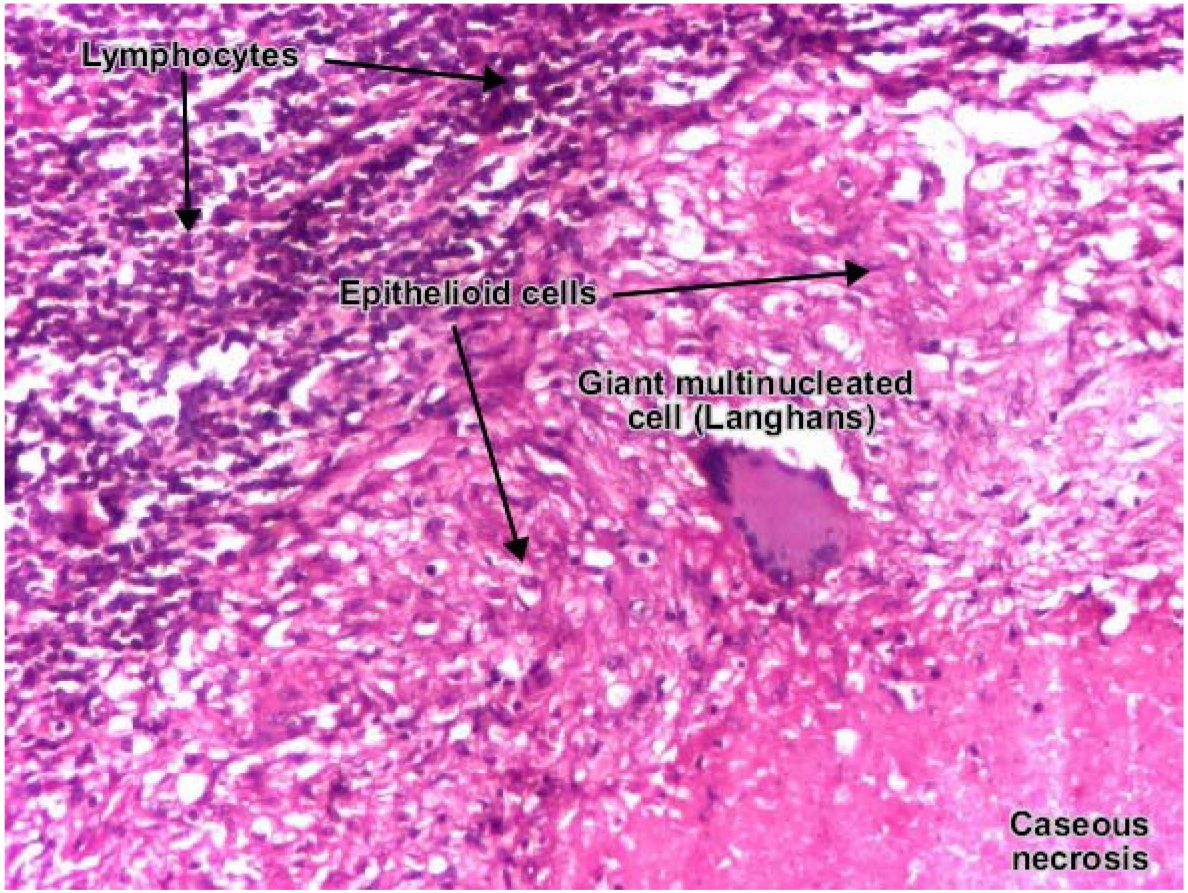
- Lymphatic vessel component
- Lymph node component

Ghon’s complex

Pulmonary Tuberculosis




Lymphocytes
Giant multinucleated cell (Langhans type)
Aggregation of epithelioid cells


Lymphocytes
Epithelioid cells
Giant multinucleated cell (Langhans)
Caseous necrosis

Fate of primary tuberculosis

- Lesions heal by fibrosis, may undergo calcification, ossification
  - a few viable bacilli may remain in these areas
  - bacteria goes into a dormant state, as long as the person's immune system remains active
- Progressive primary tuberculosis: primary focus continues to grow & caseous material disseminated to other parts of lung
- Primary miliary tuberculosis: bacilli may enter circulation through erosion of blood vessel
- Progressive secondary tuberculosis: healed lesions are reactivated, in children & in lower resistance

Secondary tuberculosis

- Post-primary/ reinfection/ chronic TB
- Occurs in immunized individuals.
- Infection acquired from
  - endogenous source/ reactivation
  - exogenous source/ reinfection
- **Reactivation-** when immune system is depressed
  - Common in low prevalence areas.
  - Occurs in 10-15% of patients
  - Slowly progressive (several months)
- **Re-infection -** when large innoculum of bacteria occurs
  - In areas with increased personal contact

Secondary TB

- Sites- Lungs

  1-2 cm apical consolidation with caseation
- Other sites - tonsils, pharynx, larynx, small intestine & skin

Fate of secondary tuberculosis

- Heal with fibrous scarring & calcification
- Progressive secondary pulmonary tuberculosis:
  - fibrocaseous tuberculosis
  - tuberculous caseous pneumonia
  - miliary tuberculosis

Fate of secondary tuberculosis

- Fibrocaseous tuberculosis:

  - massive caseation which may break into a bronchus to produce- cavitary/open TB,

  - endobronchial or endotracheal TB

  - or remain as soft caseous lesion- non-cavitary

Complications:

  a) aneurysm of arteries– hemoptysis

  b) bronchopleural fistula

  c) tuberculous empyema

- Tuberculous caseous pneumonia: caseous material may spread to rest of the lung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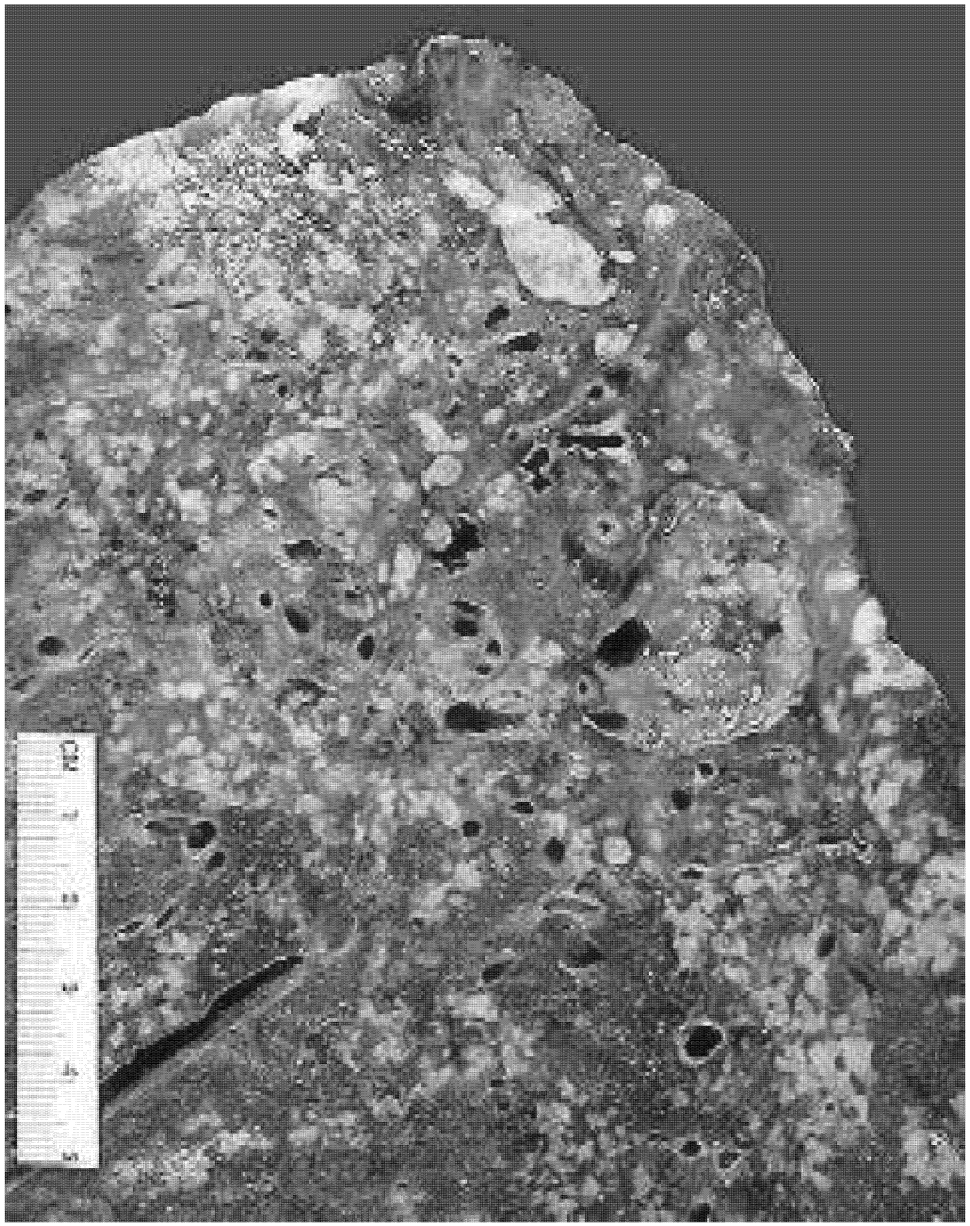
Miliary TB

- Millet like, yellowish, firm areas without caseation
- Extensive spread through lympho-hematogenous route
- Low immunity
- Pulmonary involvement via pulmonary artery
- Systemic through pulmonary vein:
  - LN: scrofula, most common
  - kidney, spleen, adrenal, brain, bone marrow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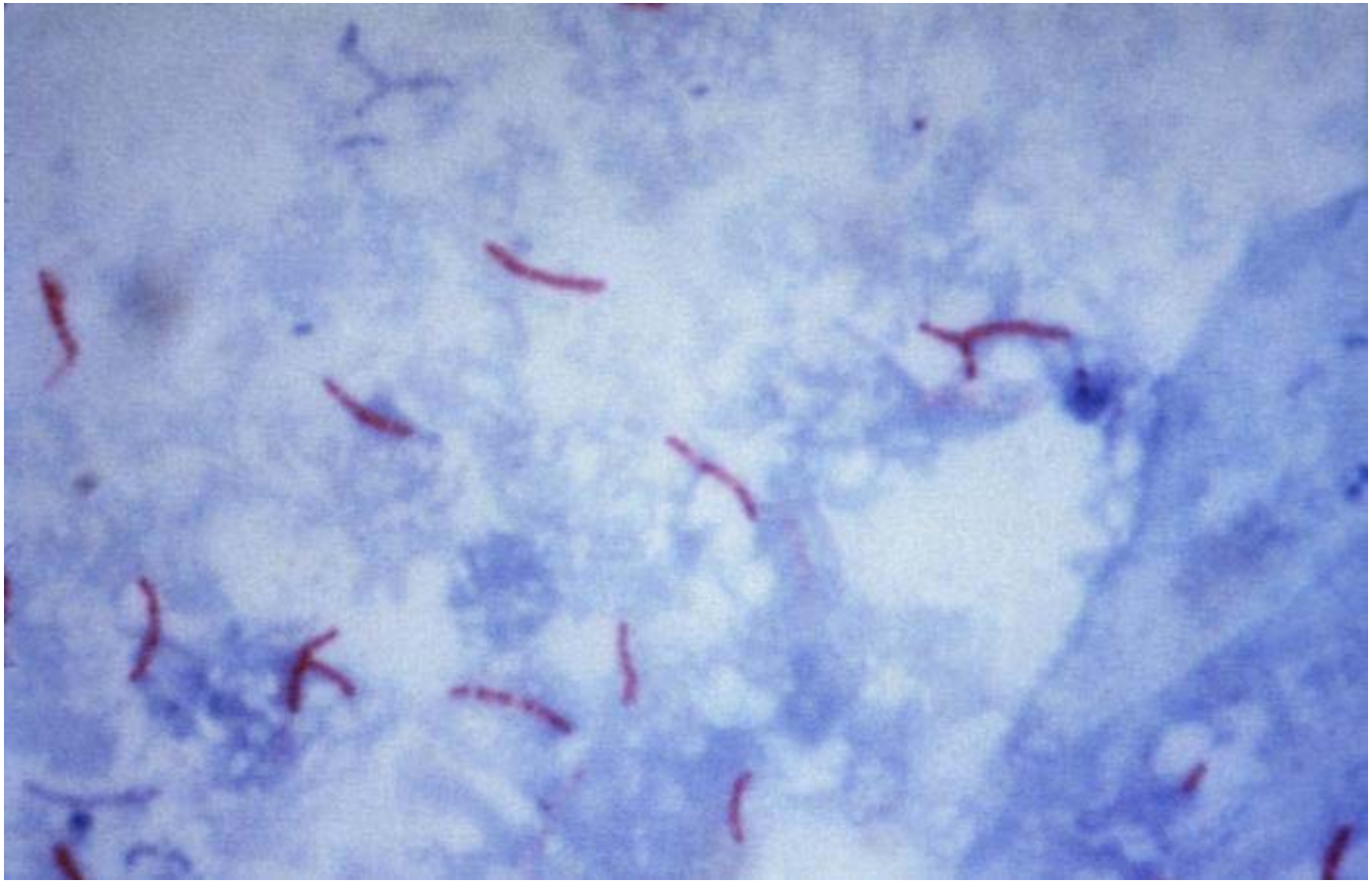
Signs and Symptoms of Active TB

- Pulmonary- cough, hemoptysis, dyspnea
- Systemic:
- fever
- night sweats
- loss of appetite
- weight loss
- chest pain, fatigue
- If symptoms persist for at least 2 weeks, evaluate for possible TB infection.

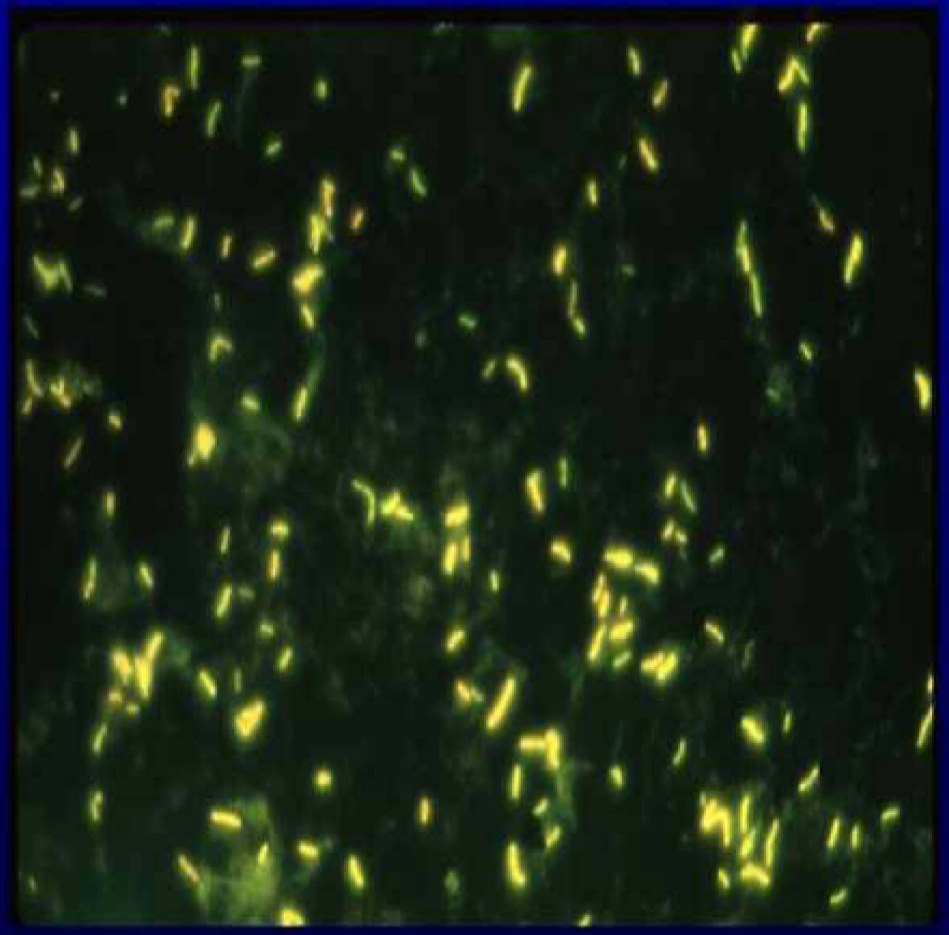
Diagnosis

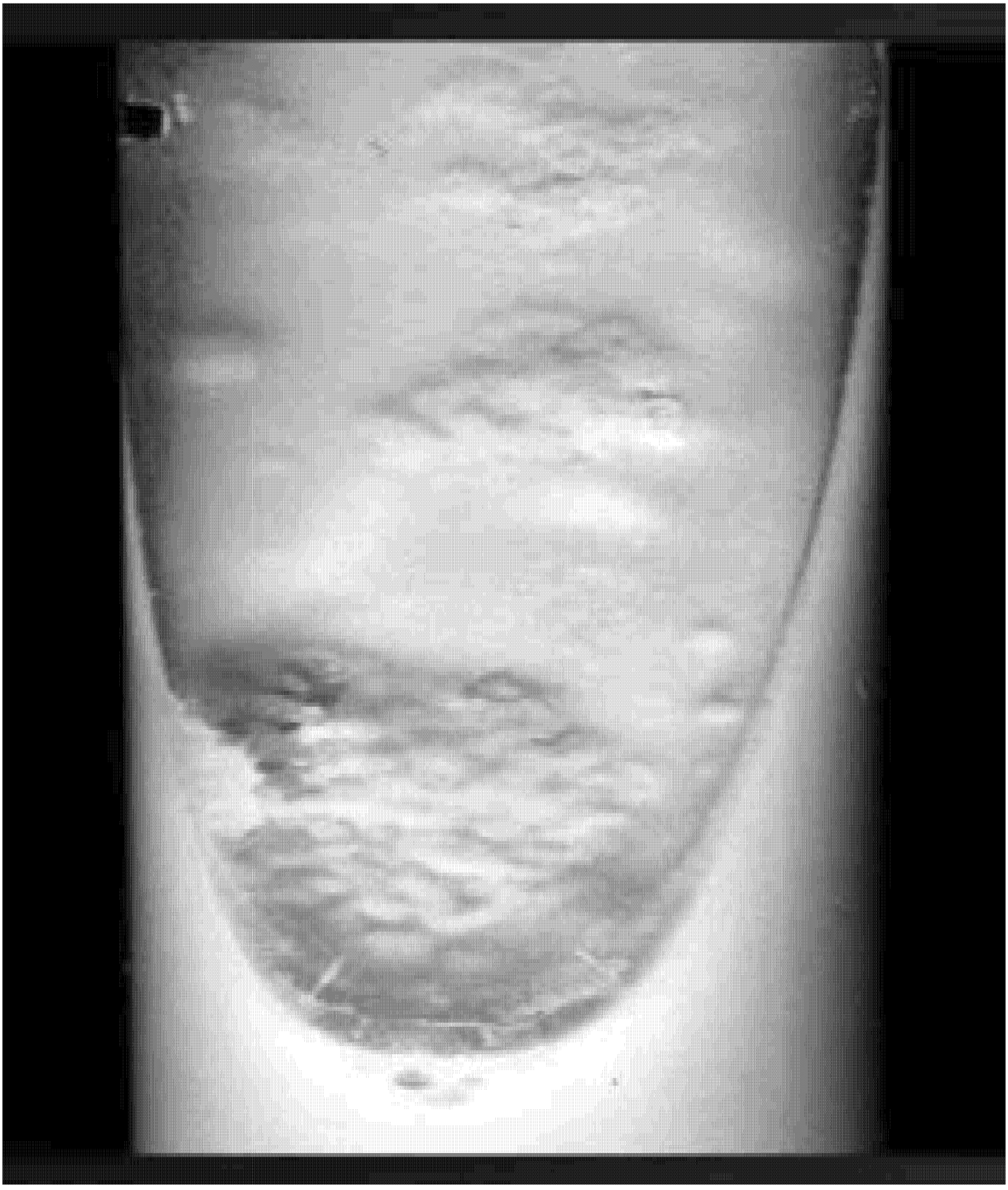
- Sputum- Ziehl Neelsen stain – 10,000 bacilli, 60% sensitivity
  - release of acid-fast bacilli from cavities intermittent.
  - 3 negative smears : low infectivity
- Culture most sensitive and specific test.
  - Conventional Lowenstein Jensen media- 10 wks.
  - Liquid culture: 2 weeks
- Automated techniques within days
  - PCR should only be performed by experienced laboratories (10 bacilli)
- PPD for clinical activity / exposure sometime in life
- X-ray chest
- FNAC

AFB



Sputum - TB Auromine/Rhodamine





PPD Tuberculin Testing

- Read after 72 hours.
- Induration size - 5-10 mm
- Does not d/s b/w active and latent infection
- False +: atypical mycobacterium
- False - : malnutrition, HD, viral, overwhelming infection, immunosuppression
- BCG gives + result.

Tuberculosis

Atypical mycobacteria

- Photochromogens---M.kansasii
- Scotochromogens---M.scrofulaceum
- Non-chromogens---M.avium-intracellulare
- Rapid growers---M.fortuitum, M.chelonei

5 patterns of disease

- Pulmonary—M.kansasii, M.avium-intracellulare
- Lymphadenitis---- M.avium-intracellulare, M.scrofulaceum
- Ulcerated skin lesions----M.ulcerans, M.marinum
- Abscess---- M.fortuitum, M.chelonei
- Bacteraemias---- M.avium-intracellulare as in AIDS

7 A 32-year-old woman has had a chronic cough with fever for the past month. On physical examination, she has a temperature of 37.5°C, and on auscultation of the chest, crackles are heard in all lung fields. A chest radiograph shows many small, ill-defined nodular opacities in all lung fields. A transbronchial biopsy specimen shows interstitial infiltrates with lymphocytes, plasma cells, and epithelioid macrophages. Which of the following infectious agents is the most likely cause of this appearance?

(A) *Staphylococcus aureus*
(B) *Plasmodium falciparurn*
(C) *Candida albicans*
(D) *Mycobacteriurn tuberculosis*
(E) *Klebsiella pneumoniae*
(F) Cytomegalovirus

Infectious Granulomatous Diseases

Examples of Diseases with Granulomatous Inflammations

Disease	Cause	Tissue Reaction
Tuberculosis	*Mycobacterium tuberculosis*	Noncaseating tubercle (granuloma prototype): a focus of epithelioid cells, rimmed by fibroblasts, lymphocytes, histiocytes, occasional Langhans giant cell; caseating tubercle: central amorphous granular debris, loss of all cellular detail; acid-fast bacilli
Leprosy	*Mycobacterium leprae*	Acid-fast bacilli in macrophages; non-caseating granulomas
Syphilis	*Treponema pallidum*	Gumma: microscopic to grossly visible lesion, enclosing wall of histiocytes; plasma cell infiltrate; central cells are necrotic without loss of cellular outline
Cat-scratch disease	Gram-negative bacillus *Bartonella henselae*	Rounded or stellate granuloma containing central granular debris and recognizable neutrophils; giant cells uncommon