I. TB – global vs. US incidence
   A. ~1/3 of the world’s population is infected with TB—mostly SE Asia, India and Africa
   B. In 2016, 10.4 million people around the world became sick with TB disease. There were 1.7 million TB-related deaths worldwide
   C. But only ~10,000 new US cases per year (~0.1% of the world’s new cases) in 2016
   D. And ~65% of the new US cases are among recent US immigrants
   E. TB is a leading killer of people who are HIV co-infected

II. Know the difference between TB infection and disease.
   A. Only ~7-10% of TB infected people will develop disease in their lifetimes
   B. 90-93% of all (non-HIV-infected) people will not progress to disease
   C. Much different for TB infected HIV/AIDS patients — 10%/year will develop active disease (either progression of primary infection or reactivation of latent infection).

III. Persons who are more likely to be infected with TB (overlapping exposure groups)
   A. Close contacts of an active case
   B. Foreign-born persons from areas where TB is common
   C. Medically underserved, low income populations
   D. Residents of long-term care facilities
   E. Persons who inject drugs
   F. Migrant farm workers and homeless persons
   G. Occupationally exposed persons - e.g., health care workers

IV. TB Transmission
   A. Almost exclusively airborne
   B. Close contacts are at greatest risk
   C. AIDS: TB is the only opportunistic bacterial infection of AIDS patients that is transmitted to other people
   D. Nosocomial - (infection in healthcare setting)
   E. Extrapulmonary TB is rarely contagious – (i.e., cough is the common route of transmission)
   F. Transmission by ingestion - very rare now that milk pasteurization is used

V. TB Pathogenesis (“buzz words” that link pathogenesis/pathology and radiology)
   A. “Droplet nucleus” - airborne particle that results in alveolar macrophage access of infection
B. “Bacteremic phase” - Regional lymph node and blood-borne spread from primary alveolar site of infection

C. “Ghon focus” - primary site of infection on x-ray; lung periphery

D. “Ranke complex” - Ghon focus/complex + calcification of lymph nodes

E. **Cell-mediated immunity** - mycobacterial antigens → lymphoproliferation, cytokine production, granuloma formation → *both antimicrobial effect and tissue damage*

F. “Primary” TB infection – results in either:
   1. Latent TB (clinically silent infection) - 90-93%; only 7-10% of immunocompetent people progress to active TB disease in their lifetimes
   2. Primary progression to active TB disease (almost exclusively in HIV/AIDS/immunosuppressed patients)

G. “Secondary” infection = reactivation of latent infection, resulting in clinically apparent disease – as a result of waning immunity (with age) or immunosuppression (HIV/AIDS or treatment-related) → development of pulmonary (80-90%) or extrapulmonary (10-15%) disease, which results in:
   1. Upper lobe lung infiltration, often with cavity formation (cellular immune response cause tissue destruction)
   2. Extrapulmonary reactivation disease – uncommon but possible any site infected during the initial, blood borne spread of TB during primary infection (e.g., meningitis, pericarditis, genitourinary TB, bone involvement)

VI. TB Diagnosis

A. **Medical history** - nonspecific symptom complex (cough, fever, fatigue)

B. **Physical examination** – nonspecific; or there may be *NO* abnormal physical findings

C. Radiographic or CT scan examination - upper lung field infiltrates, cavities, ± lesions in other organs (with extrapulmonary TB)
Extrapulmonary TB (XPTB)

1. Source – sites that progress from the original, bacteremic phase of infection – brain, epiphyses of long bones, kidneys, vertebral bodies, lymph nodes

2. Incidence ~ 15% of immunocompetent patients have only XPTB; disseminated infection and XPTB are at least twice as common in in AIDS

3. Sites of infection:
   a. CNS – peak incidence in children, 0-4 yrs old
   b. Pericarditis
   c. Osteomyelitis – Spine = “Pott’s disease”; lower thoracic and upper lumbar
   d. Peritonitis
   e. GU/Gyne – symptoms are usually local; genital without renal involvement more common in females; most common presentation in men is scrotal mass

E. Differential diagnosis of TB

1. Medical history – check for evidence of TB exposure; risk groups

2. Physical exam – nothing specific to help with DDX

3. Other chronic granulomatous infections
   a. Nontuberculous mycobacterial infections
   b. Fungal infections – e.g., endemic fungi, like Histoplasmosis, Blastomycosis

F. Immunological evidence of TB infection (delayed hypersensitivity response)

1. **PPD** skin test reaction (tuberculin reaction)

2. **Quantiferon assay** (is replacing the PPD skin test, in clinical practice) – essentially an interferon gamma production assay that asks whether the patient’s blood lymphocytes have “immunological memory” for selected TB antigens (encoded by TB virulence genes in the “region of difference”)

G. Microbiology

1. Sputum **AFB smears and cultures from otherwise sterile sites**

2. Multiple **culture** techniques:
   a) Solid media (L/J, 7H11 agar media) → “rough, nonpigmented” colonies – not done much any more in diagnostic micro. labs
   b) Liquid media → rapid detection (BACTEC, MGIT) – replacing solid medium in most laboratories (“positive” vials often being “shipped out” to reference labs for identification)
3. HPLC - mycolic acids → speciation – decreasing use; was in common use, but is labor intensive and is being replaced by molecular diagnostics

4. Molecular diagnostics – **standard of practice**
   a) Sputum – **nucleic acid amplification test** (NAAT) increasingly available and the standard of practice for rapid diagnosis
   b) Culture identification – molecular probes have replaced HPLC

VII. Antibiotic susceptibility testing – should be done for **all** first time positive cultures

VIII. **Contrast of nontuberculous mycobacterial (NTM) infections with TB**
   A. NTM infections are **environmental** (not human) in origin
   B. NTM infections (non-HIV) usually “require” some type of underlying, predisposing lung problem, whereas TB does not require a predisposing condition to cause disease.
   C. NTM infections can be caused by **direct inoculation** (e.g., from an environmental source) or **contamination at surgery**.
   D. Like TB, NTM infections elicit cellular immune responses and can cause granulomatous reactions (both protective and tissue destructive).
   E. NTM infections are usually **restricted to the lung** (or contaminated non-lung site) and rarely cause disseminated disease – **EXCEPT** in HIV/AIDS patients, where disseminated M. avium complex (DMAC) infection can occur.
   F. NTM **do not cause latent infection** – chronic infections, yes; true latency, where reactivation from a quiescent state occurs later in life, probably not.
   G. NTM lab **diagnosis / culture methods are similar to those used for TB**.
   H. BUT, skin testing and Quantumteron testing are **not available** or useful to NTM.
   I. **Radiographic presentations may be different** from TB – related to type of underlying lung disease

IX. Supplementary Reading (URLs with excellent TB-related links)
   A. World Health Organization Global TB Program - [http://www.who.int/gtb/](http://www.who.int/gtb/)