Diseases caused by acid-fast organisms, *Mycobacterium*, et al.

TB is due to acid-fast bacillus (?) and its relatives and is the **number one** infectious disease in the world today.
Tuberculosis, TB

- Historically, major impact disease
- 100 yrs ago TB was biggest human killer
  - many famous deaths
  - believed to be genetic
    • linked to genius
- Romanticism stopped with Koch’s work
- Predisposing factors
  - elderly, urban poor, malnourished, crowded living, occupational, immuno-compromised (AIDS)
- Eskimos, an example
- Re-emerging in USA
  - declined until 1984
  - 6% in USA are +
  - role of AIDS
  - role of immigration
  - role of homelessness
- Global picture
  - 1/3 infected
  - Africa highest
  - 10 million active with 3.5 million deaths per annum
- Drug resistance!!
Spread of TB aboard airliners confirmed

By Anita Manning
USA TODAY

Passengers and flight crew on commercial airlines in the USA have been infected by tuberculosis bacteria, federal health officials say.

And though they stress the risk of catching TB on a plane is low, they advise people with active TB to take private transportation or postpone travel till they are no longer infectious.

The Centers for Disease Control and Prevention Thursday reported that:

- A sick woman on an 8½-hour Chicago-to-Hawaii flight last May apparently infected four nearby passengers.
- A flight attendant with active TB apparently infected two other crew members.
- Four other long-distance flights carrying a passenger with infectious TB were investigated. Others on those flights later tested positive for TB.

None of those exposed on an airplane developed active disease, says CDC’s Alan Hinman. “They developed a positive skin test, and if they don’t receive preventive treatment, they have a 5% to 10% lifetime risk of developing TB,” he says.

They were urged to begin a 6-month drug treatment that “eliminates the risk,” he says.

TB is spread by droplets in coughs, sneezes or breath.

Fliers with airborne infectious diseases can be denied boarding, says Chris Chalmer, Air Transport Association, but they’re “not always evident.”

The flight attendants union wants airlines to increase the amount of fresh air in cabins to reduce contaminants.

Back in their plea: consumer groups who Thursday asked the government for fresh air standards for airliners.
Immigration from high TB regions
Homelessness
Transmission of TB

• Aerosolization person to person
  – droplets pass down bronchial tree to alveoli
  – trapped, not swept out of lungs
    • Crowding, malnutrition, etc. play role
    • 10 organisms or less can establish infection
  – primary infection of lungs
    • Initially attached by PMNs & macrophages but these fail to kill, but in turn are killed by microorganisms
    • Macrophages become infected by TB bacilli
    • If contained, patient becomes latent carrier
    • If not contained, Tuberculosis results
High Risk for TB

- HIV-positive patients
- Close contact w/ TB cases
- Medical conditions which predispose
- Immigrants from high prevalence areas
- Low-income populations
- Alcohol and drug abuse
- Residents in long-term facilities
  -- prisons
  -- mental institutions, etc.
Pathogenesis of TB

- Macrophages present TB antigens to T-cells
- TB active T-cells induce cytokine cascade:
  - monocytosis
  - activated macrophages
  - granuloma formation
  - infection contained by CMI, O₂ bursts, etc.
  - Some macrophages become Langhans cells (giant cells)
- Caseation Necrosis:
- Wasting disease
Wasting in TB is due to excessive production of TNF-A
Anergy versus hypersensitivity

• Before macrophages are activated the bacilli multiply rapidly & the infection advances

• Early macrophages incubate & spread TB
  – this is the anergic state, which may continue as active TB until patient dies
  – AIDS patients remain anergic (HIV-infected, but not yet AIDS impacts TB status)

• Cytokine-activated macrophages kill bacilli
  – cannot clear infection, but allow it to become latent (but may be reactivated later)
    • skin-test positive, but X-ray negative
    • the hypersensitive state
Miliary Tuberculosis

• If enter blood, widely disseminated in body
  – small white lesions of active TB
  – looks like millet seed
  – any tissue (lung, liver, kidney, spleen, bone marrow, etc.)

• Miliary TB is highly fatal
Primary Tuberculosis

- Initial proliferation
  - lungs, but also skin & bowel important
  - bronchopneumonia
- Immunocompetent
  - necrosis-inflammation-granuloma formation-fibrosis-healing with mineralization
  - most infections progress to latency without symptoms
    - some malaise, fevers, pneumonia, wt loss, etc.
- Granulomas prevent dissemination

Acid-fast bacilli in lung tissue, active TB
Reactivation Tuberculosis

• When immunity wanes, granulomatous wall loses integrity:
  – bacilli proliferate and escape
  – (such as in AIDS, corticosteroid therapy, etc.)
  – infection spreads & becomes destructive
  – upper lobes of lungs mostly
  – cavitation with necrosis & release of large numbers of bacilli
  – hemoptysis is common (what is this??)
  – spreading to other tissues common
Generally, upper lobes are site of reactivated TB
The Mantoux Test

- Latent infections leak TB antigens, maintaining T-cell immunity
- Subcutaneous injection of PPD elicits a type IV hypersensitivity
  - T-cells produce cytokines
  - Activate macrophages
  - Delayed induration
  - Sometimes severe

Necrosis of skin due to hyperimmune response to TB
Treatment & Prevention of TB

- Role of pasteurization
- Old days- Quarantine
- Today: Directly observed therapy (DOT) why?
  - *Rifater* = INH + rifampin + pyrazinamide.
  - Vaccine = Bacille Calmet-Guerin (BCG) strain of *M. bovis*.
    BCG about 80% effective in kids, only 20-50% effective in adults.
Re-emergence of TB

TB rates 1985-1992
*Mycobacterium spp Other Than M. tuberculosis (MOTT)*

- *Mycobacterium avium* complex (MAC)
  - Secondary infections in AIDS patients
- *Mycobacterium kansasii*
  - TB-like disease (milder)
- *Mycobacterium fortuitum*
  - Post-surgical skin infections
- *Mycobacterium marinum*
  - Localized skin infections
- *Mycobacterium scrofulaceum* (Swimming pool *M. marinum*)
  - Scrofula (ulcerating, draining cervical lymph nodes)
- *Mycobacterium leprae* (later)
  - (in all these, acid-fast characteristics vary with species)
Hansen’s Disease

• AKA leprosy
  – Biblical leprosy was probably a variety of diseases
  – Hansen’s disease is a systemic infection of *M. leprae*
  – Common in tropics, where it is widely spread
    • Global incidence is 10-12 million cases
  – Difficult to treat or control
**Mycobacterium leprae**

- Cannot be cultivated
  - foot-pads armadillos
- Provokes broad non-necrotizing CMI
- Invades & destroys nerves
- Invades tissues below body temperature
  - skin, testes, ear lobes, nasal mucosae
- Long incubation, 2-5 yrs (40 yrs has been documented)

- Two forms of leprosy:
  - called “polar forms”
  - “TH -1” & “TH -2”
  - tuberculoid: vigorous CMI, TH -1; low antibody
    - limited-self healing-few lesions-few organisms-treatment stops on healing
  - lepromatous:minimal CMI:TH -2; high antibody
    - progressive-fatal-nodular-diffuse-histocytes-massive # bacteria-treatment life-long
    - Many infections between polar extreme
Clinical features

- Invades & destroys nerves
  - loss of nerve functions
    - debilitation with anesthesia leads to ulcers & tissue destruction
    - Contraction deformities
  - Tuberculoid lesions:
    - localized skin lesions
    - hyperesthesia or anesthesia
    - granulomas around infected nerves
  - Lepromatous lesions:
    - massive skin lesions
    - foamy histiocytes

“claw-hand” contraction
Ulcers lead to loss of feet and hands
Damage to the ulnar nerve in Tuberculoid leprosy leads to weakness and wasting, followed by complete paralysis and atrophy of the innervated hand muscles.
Loss of extremities in late tuberculoid leprosy
Early tuberculoid, macules and anesthesia

Late tuberculoid, loss of extremities,

Lepromatous skin lesions

Testicular atrophy often leads to Gynecomastia
Leprosy before Treatment

After one year of treatment
After treatment
**Mycobacterium ulcerans**

- **Buruli ulcer**
  - painless necrotizing ulcer
  - skin & dermal layers then to muscle, bone
  - no fevers or malaise
  - secondary infections are very rare
  - due to necrotic exotoxin

- **Contact with water**
  - reservoir unknown
  - Africa, Australia, China, etc.
Nearly healed ulcer

Badly necrotic leg

Several months later
Surgical Repair is Treatment of choice