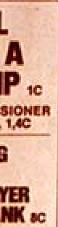
Diseases caused by acid-fast organisms, *Mycobacterium*, et al.

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

Tuberculosis, TB, major Eskimos, an example

- 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, immunocompromised (AIDS)

- 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!!



LAYOFF:

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BANK TRADER COULD FACE EXTRADITION TO SINGAPORE

CO-WORKERS CHEER ARREST; REPORTS SUGGEST BARINGS KNEW OF HUGE DEALS THAT RESULTED IN ITS FAILURE, 1B

GO! AHEAD, ROLL DICE IN 'OTHER VEGAS' 450

WEEKLY GUIDE TO FUN -



NICK LEESON: In custody in Frankfurt, 18

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 8½hour Chicago-to-Hawaii flight last May apparently infected four nearby passengers.

► A flight attendant with ac-

tive 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 TR," he says.

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

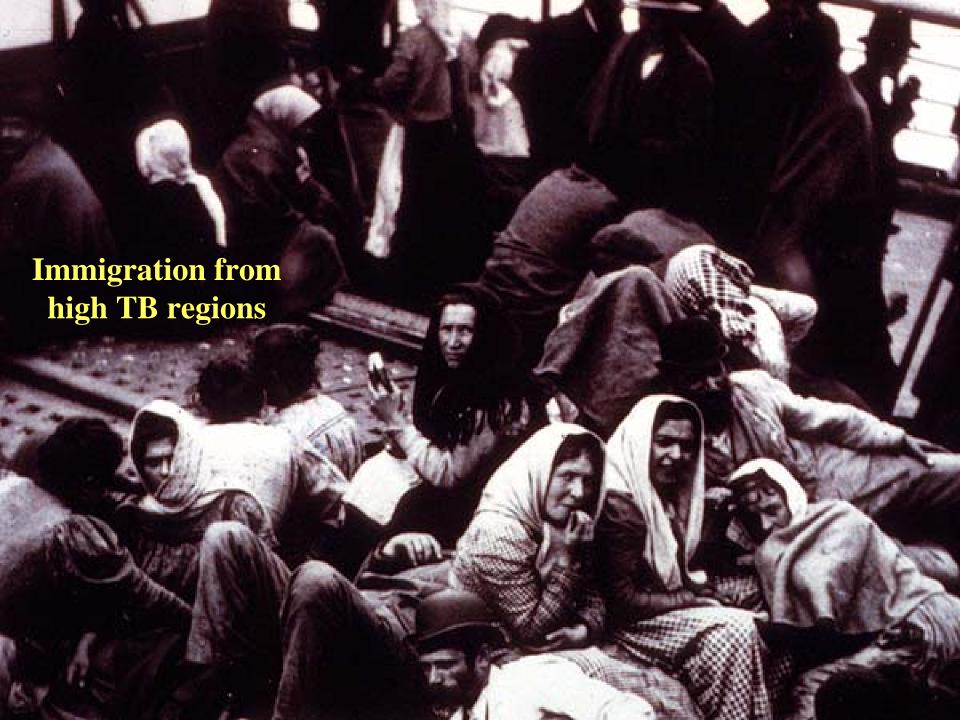
TB is spread by droplets in coughs, sneezes or breath.

Filers with airborne infectious diseases can be denied boarding, says Chris Chiames, 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.

Backing their plea: consumer groups who Thursday asked the government for fresh air standards for airliners.

Amendment loss stings GNF





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

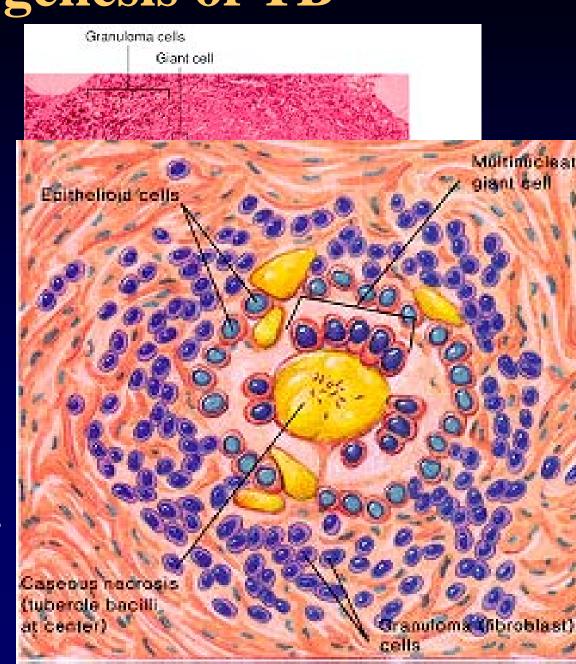
High Risk for TB

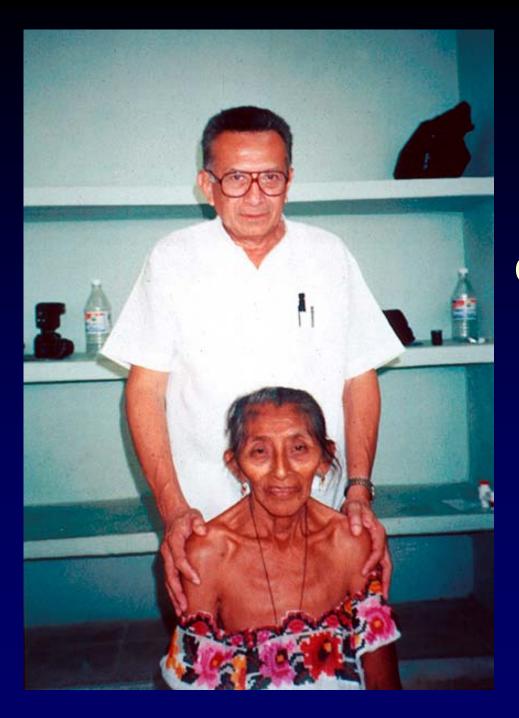
- HIV-positive patients
 - Close contact w/ TB cases
 - Medical conditions which predispose
 - Immigrants from high prevalence areas
 - Low-income populations
 - Alcohol and drug abuse
 - Residents in long-term facilities
 - --prisons
 - --mental institutions, etc.

Pathogenesis of TB
Macrophages present

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 macrophagesbecome 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

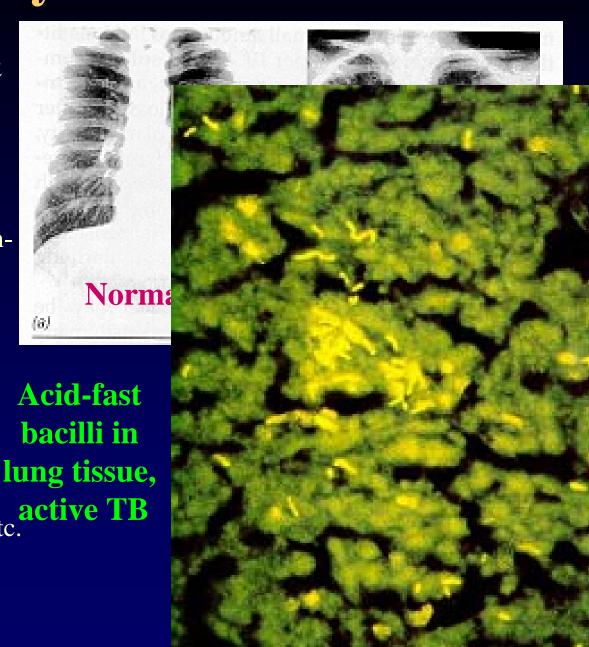
Initial proliferation

lungs, but also skin & bowel important

- bronchopneumonia
- Immunocompetent
 - necrosis-inflammationgranuloma formationfibrosis-healing with mineralization
- most infectionsprogress to latencywithout symptoms

• some malaise, fevers,, active TB pneumonia, wt loss, etc.

Granulomas prevent dissemination



Reactivation Tuberculosis

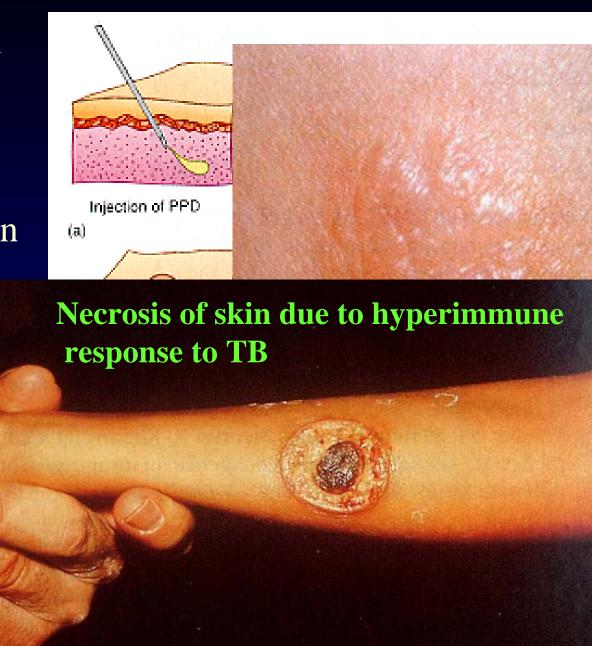
- When immunity wanes, granulomatous wall loses integrity:
 - bacilli proliferate and escape
 - (such as in AIDS, corticosteroid therapy, etc.)
 - infection spreads & becomes destructive
 - upper lobes of lungs mostly
 - cavitation with necrosis & release of large numbers of bacilli
 - hemoptysis is 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



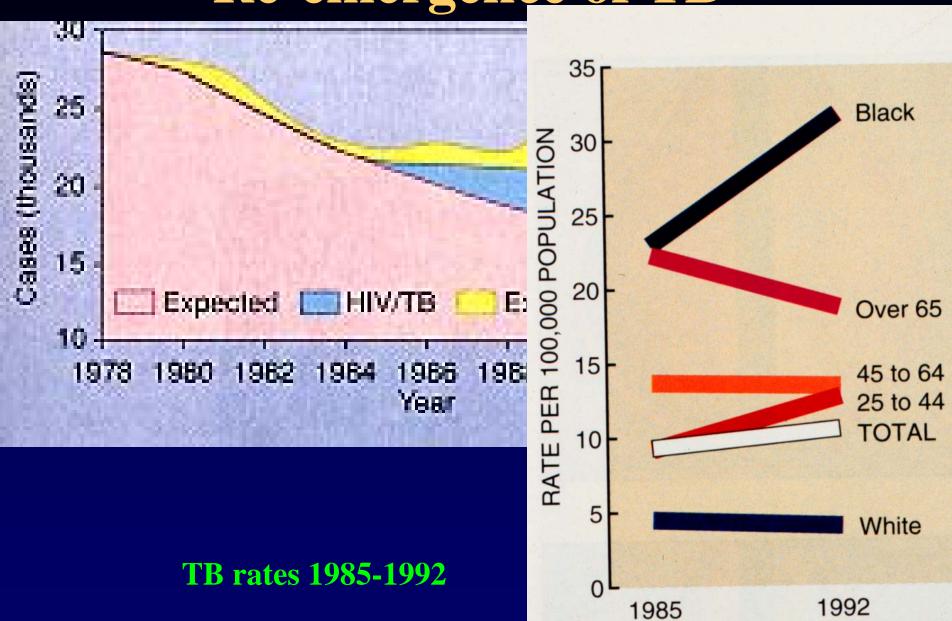
Treatment & Prevention of TB

- 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.



A Typical TB Sanatorium

Re-emergence of TB



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
 - Scrofula (ulcerating, draining cervical lymph nodes
- *Mycobacterium leprae* (later)
 - (in all these, acid-fast characteristics vary with species)



Swimming pool M. marinum

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 nonnecrotizing 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)

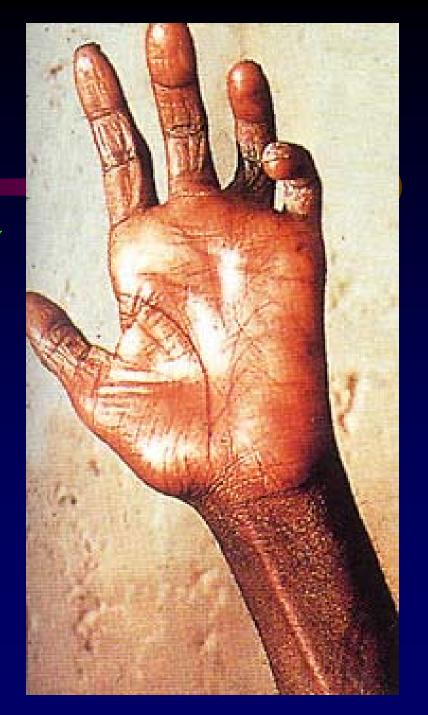
- Two forms of leprosy:
 - called "polar forms"
 - "T_H -1" & "T_H -2"
 - tuberculoid: vigorous
 CMI, T_H-1; low antibody
 - limited-self healing-few lesions-few organismstreatment stops on healing
 - lepromatous:minimal
 CMI:T_H-2; high antibody
 - progressive-fatal-nodulardiffuse-histocytes-massive # bacteria-treatment lifelong
 - Many infections between polar extreme

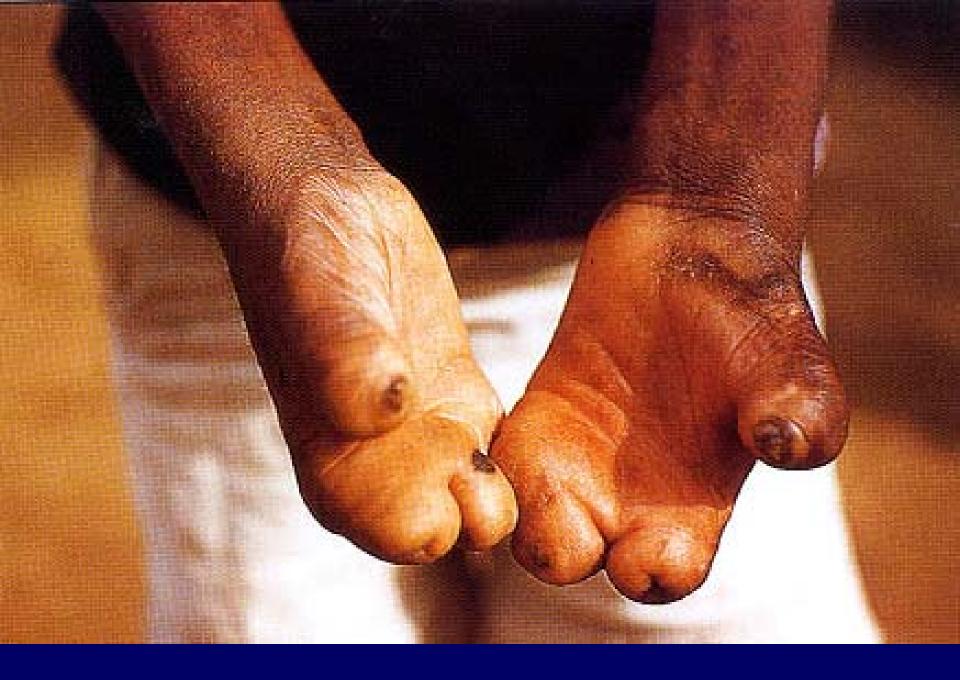
Clinical features

- 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

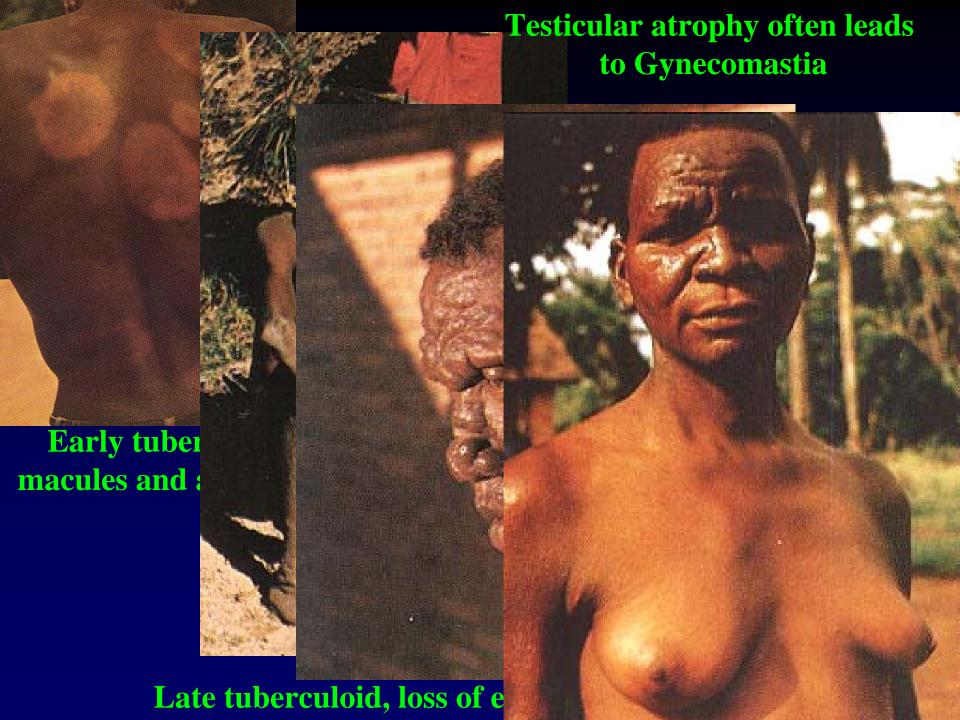


Damage to the ulnar nerve in Tuberculoid leprosy leads to weakness and wasting, followed by complete paralysis and atrophy of the innervated hand muscles.



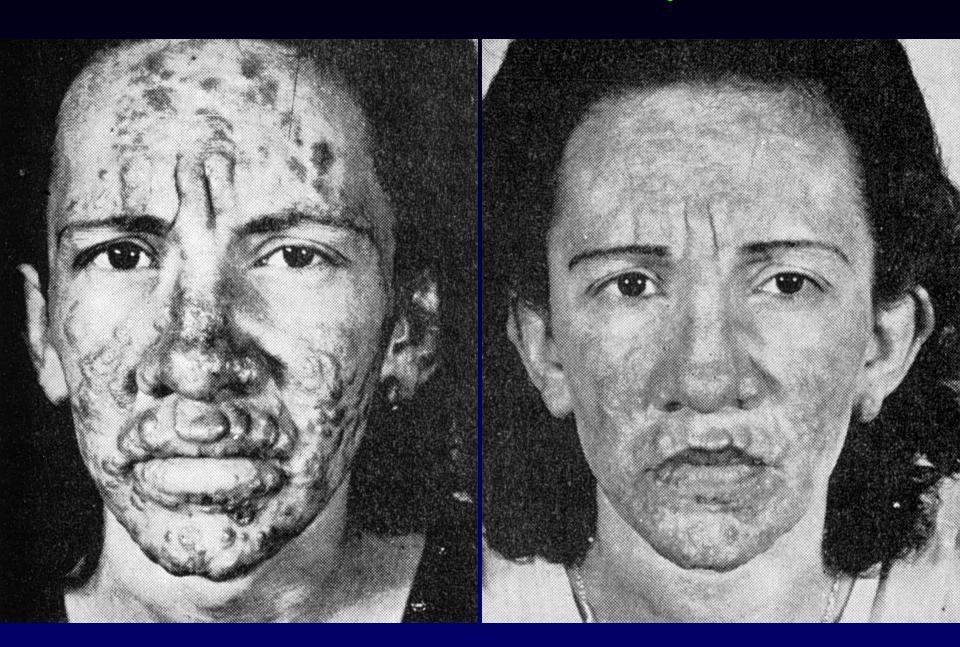


Loss of extremities in late tuberculoid leprosy



Leprosy before Treatment

After one year of 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.

