

Clinical Presentation of TB in HIV

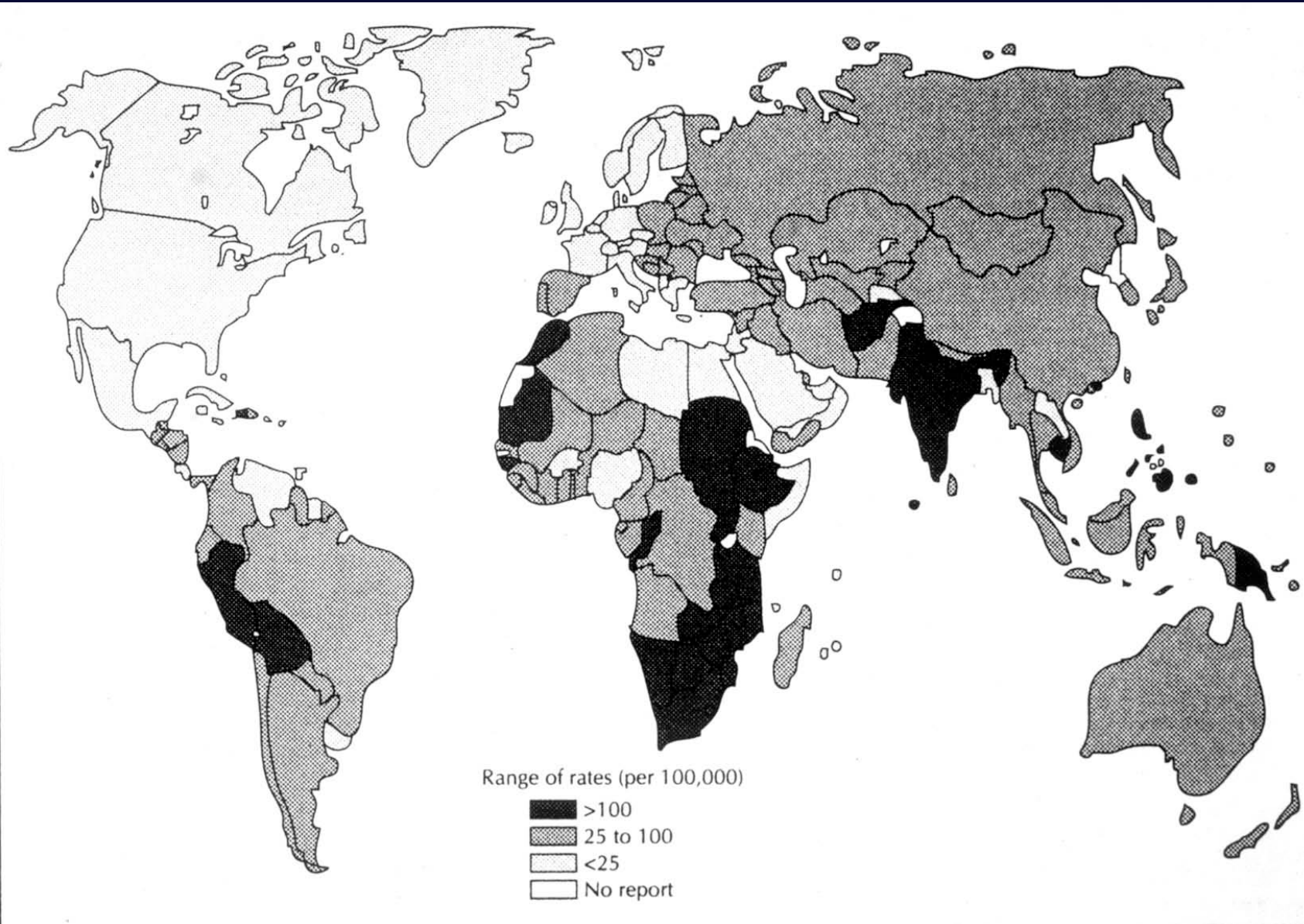
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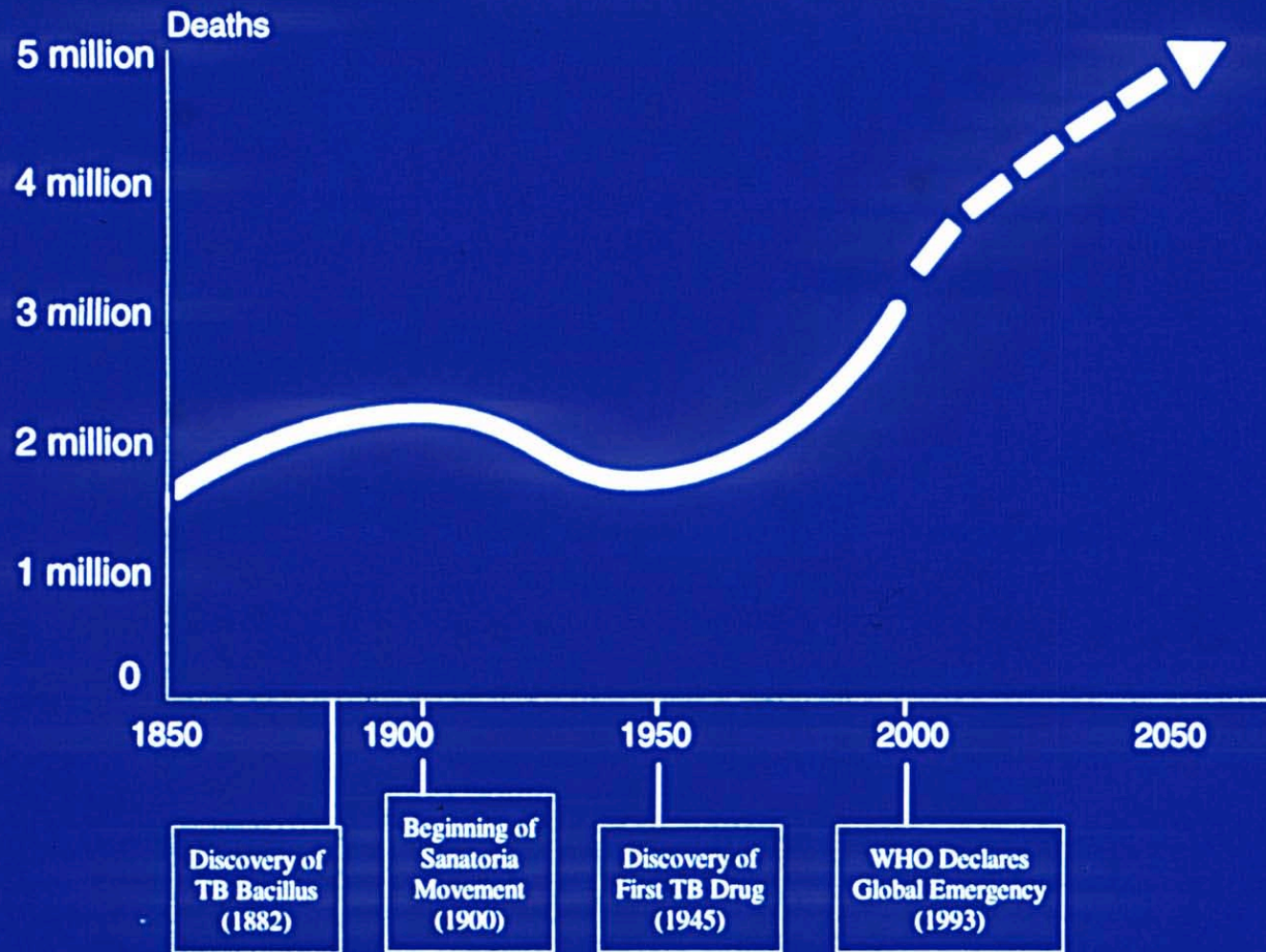
**Department of Internal Medicine, School of Medicine,
MUHAS**

November, 2007 at Kempinski-Kilimanjaro Hotel,

Dar es Salaam



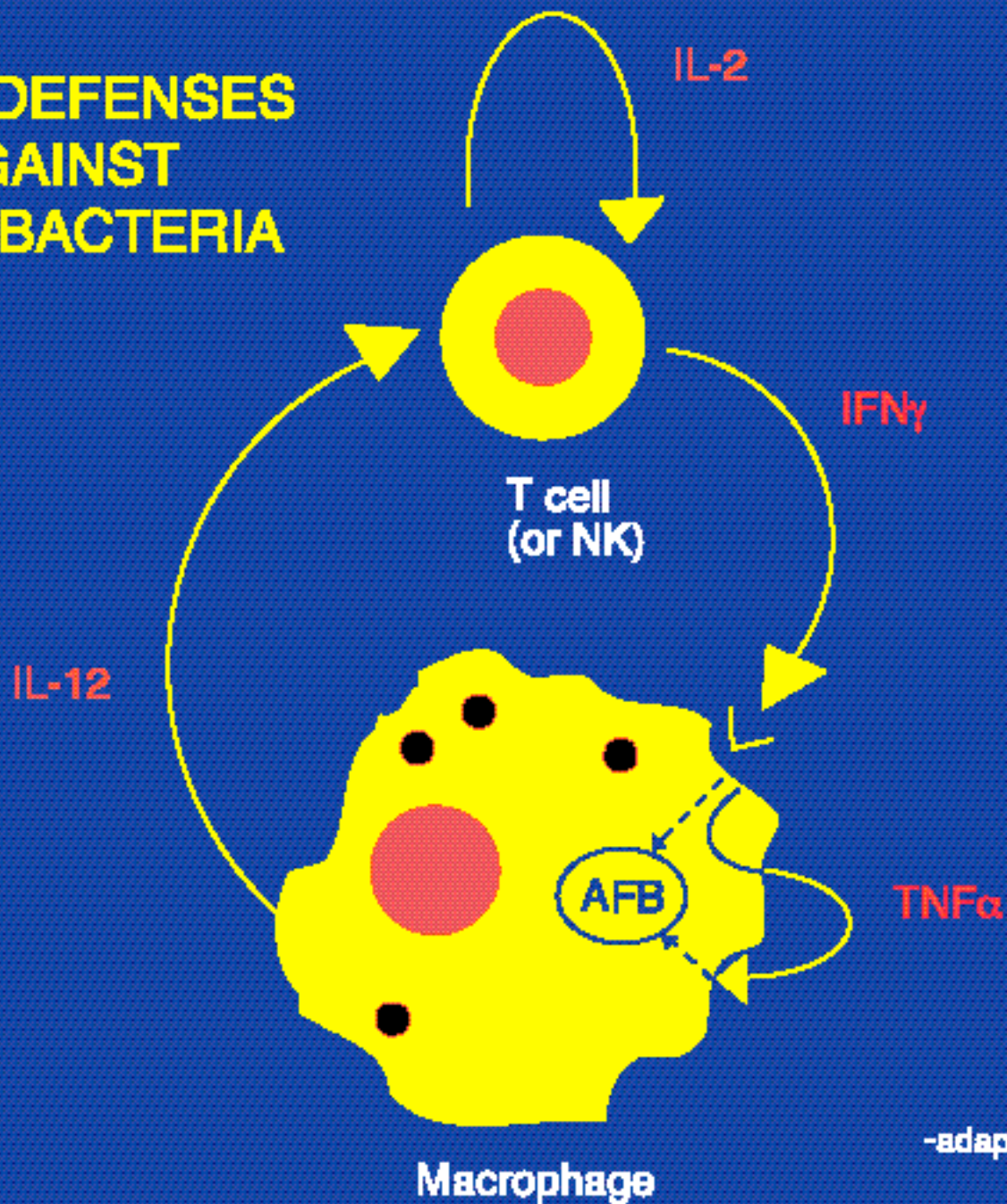
Annual TB Deaths



Estimated Global Trends of TB Deaths

Source: WHO Global Tuberculosis Programme Estimates

HOST DEFENSES AGAINST MYCOBACTERIA



-adapted from Holland

TB is the leading
cause of death
among HIV-infected
persons

Adults with Fever admitted in Muhimbili

- 145/517 (28%) had Blood Stream Infections (BSI)
- 118/145 (81%) were HIV-1 infected
- HIV +ves more likely than HIV-ve ones to have BSI (118/282 vs. 27/235; $P < .0001$).
- The 3 most frequently isolated pathogens:
 - ◆ *Mycobacterium tuberculosis* (60[39%]),
 - ◆ non-typhi *Salmonella* species (29 [19%]), and
 - ◆ *Staphylococcus aureus* (13[8.3%]).
- The incidence of malaria parasitemia was similar in study and control patients (9.5% vs. 8%).

Reference: Archibald LK, den Dulk MO, Pallangyo KJ, Reller LB. Clin Infect Dis 1998 Feb;26(2):290-6

Tuberculosis as a cause of death in HIV + patients in Africa: autopsy

Autopsies on 108 HIV+ patients in Botswana (selected)

Cause of death:







Tuberculosis	37%
Pneumonia	14%
Pneumocystis	11%
Kaposi's sarcoma	7%
Cryptococcosis	6%
Other	25%

- Ansari (Int J Tuberc 2002)

Types of Tuberculosis

- **Pulmonary tuberculosis (PTB)**
 - ◆ Affects lungs
 - ◆ Commonest form of TB
 - ◆ Is the infectious form of TB
- **Extra-pulmonary tuberculosis (EPTB)**
 - ◆ Affects organs other than lungs
 - ◆ Commonly: pleura, lymph nodes, pericardium, brain, meninges, spine, joints, abdomen, genitourinary tract, skin.
- **Disseminated TB (dTB)**
 - ◆ Bacteremic TB (Mycobacteremia)

TB in HIV

-  Clinical Presentation depends on degree of immunodeficiency
-  High rate of reactivation disease
-  High rate of extrapulmonary disease, especially bacteremic or disseminated TB in developing countries
-  Same immediate response to Rx as in HIV negative but higher one year all cause mortality
-  TB is the leading cause of death in HIV infection
-  IRIS TB in those receiving ART

PTB in HIV

With mild immunosuppression:

- Typical chest x-ray (CXR) findings include:
 - ◆ upper lobe and or bilateral infiltrates
 - ◆ cavitation
 - ◆ pulmonary fibrosis
 - ◆ shrinkage
- Clinical picture often resembles post-primary pulmonary TB (PTB)
- Sputum smear is usually positive

PTB in HIV, Presentation

- Risk begins at CD4 count 300-500 (=early HIV infection)
- Symptoms:
 - ◆ Persistent cough for ≥ 3 weeks, unresponsive to antibiotics
 - ◆ Sputum production \pm haemoptysis
 - ◆ Chest pain; SOB
 - ◆ Systemic symptoms
 - ◆ Weight loss; Fevers (evening); Night sweats; fatigue
 - ◆ HIV risk
 - ◆ \pm other features of immunodeficiency: Past herpes zoster, Seborrheic dermatitis
- Signs:
 - ◆ Consolidation; cavity; fibrosis

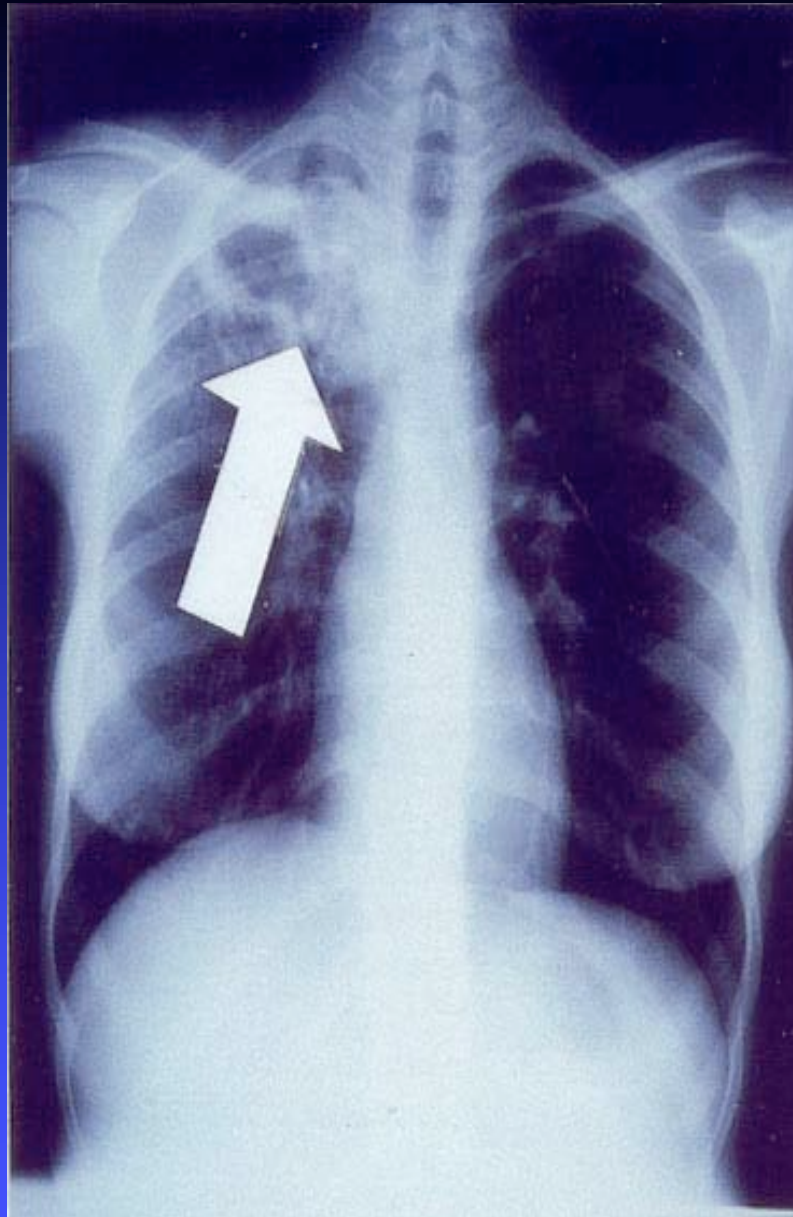
PTB in HIV, Diagnosis

- Sputum microscopy
 - ◆ To demonstrate AFB
 - ◆ X3: “spot, morning, spot”
 - ◆ Often negative!!
- Sputum culture
 - ◆ More sensitive than microscopy, “gold-standard”
 - ◆ Slow (2-8 weeks); and expensive
- CXR
 - ◆ Typical upper lobe involvement early on. (apical infiltrates)
 - ◆ mid and lower zones infiltrates, hilar opacities, pleural effusions later on

PTB in HIV, Diagnosis

- Tuberculin skin (mantoux) test
 - ◆ Demonstrates delayed type hypersensitivity
 - ◆ PPD from attenuated Mycobacteria
 - ◆ Millimeters of induration 48-72 hours after tuberculin injection
 - ◆ >5mm significant in HIV
- Erythrocyte Sedimentation Rate (ESR)
 - ◆ Non-specific
 - ◆ Often raised, but
 - ◆ Normal ESR does not exclude TB

***Arrow points to cavity
in
patient's right upper
lobe
--typical finding in
patient with TB***



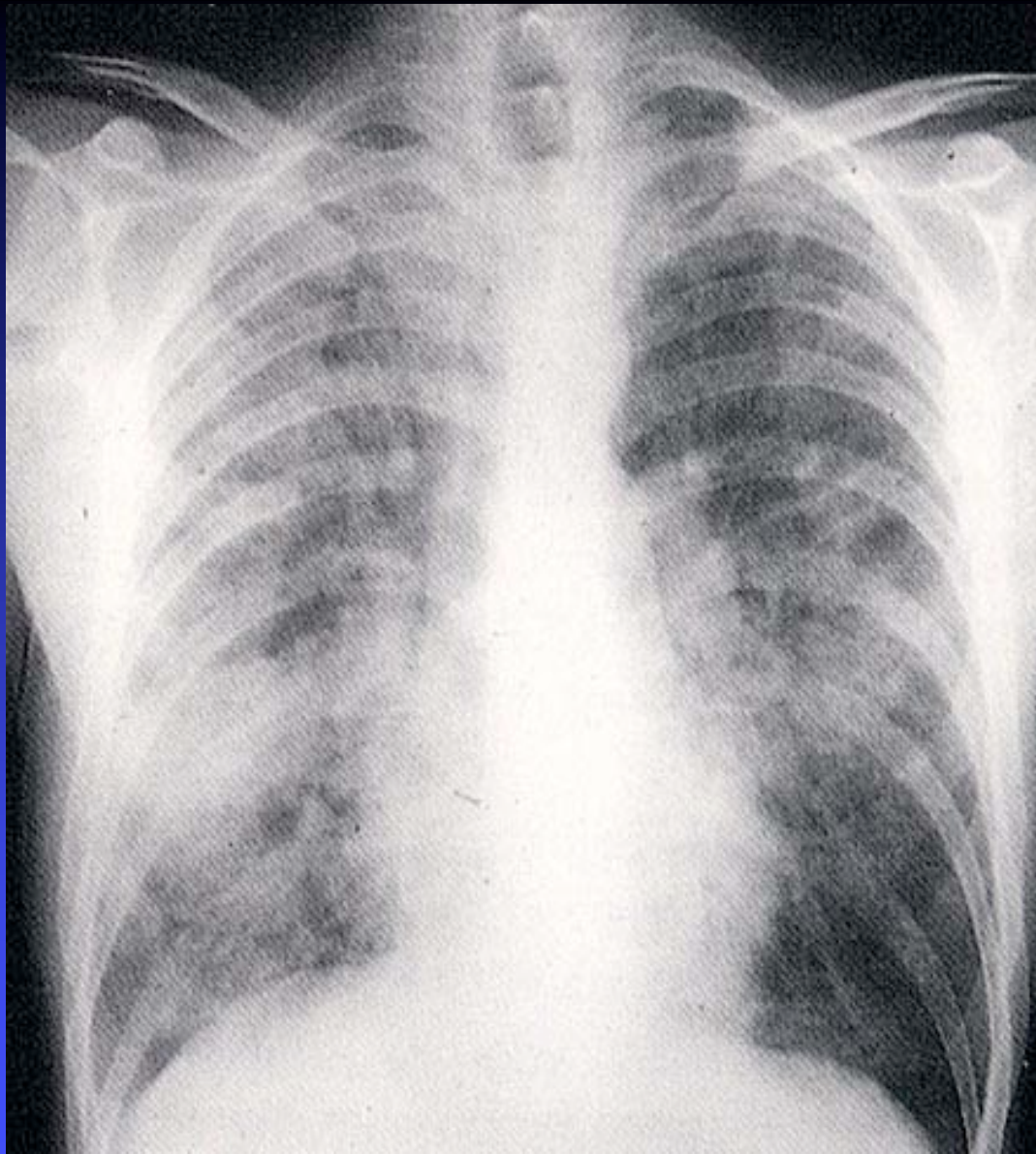
PTB in HIV

In severely immunosuppressed patient, the features are atypical, resembling that of primary PTB:

sputum smear often negative

CXR shows interstitial infiltrates especially in lower zones with no features of cavitation and fibrosis

CXR may look exactly like that in bacterial pneumonia



X-ray in a TB patient may look like this one of a patient with confirmed PCP

EPTB in HIV

■ Lymph nodes

- ◆ Painless cervical lymphadenopathy; initially discrete, later may be matted and may suppurate. Other lymph node regions, especially para-tracheal and abdominal lymph nodes, may also be involved

■ Bones and joints

- ◆ Thoraco-lumbar vertebrae most commonly involved (Pott's disease) -- wedge collapse of multiple vertebral bodies, which may result in paraplegia. Para-vertebral (cold) abscesses may also occur

■ Genitourinary system

- ◆ May be asymptomatic; sterile pyuria; haematuria; painless unilateral scrotal swelling; may lead to destruction of the kidneys and chronic renal failure

EPTB in HIV

■ Abdomen

- ◆ Depends on organ involved -- peritoneal involvement results in ascites; intestinal involvement -- masses, malabsorption syndrome; peri-anal lesions -- abscess, fistulae and fissures

■ Pericardium

- ◆ Pericardial effusion -- usually sero-sanguineous; constrictive pericarditis; occasionally cardiac tamponade

■ Central nervous system

- ◆ Severe disease -- insidious onset headache, altered sensorium, neck stiffness, progressing to coma. May present with cranial nerve palsy, especially affecting the 6th, 7th and 8th cranial nerves

Tuberculous Meningitis with a tuberculoma



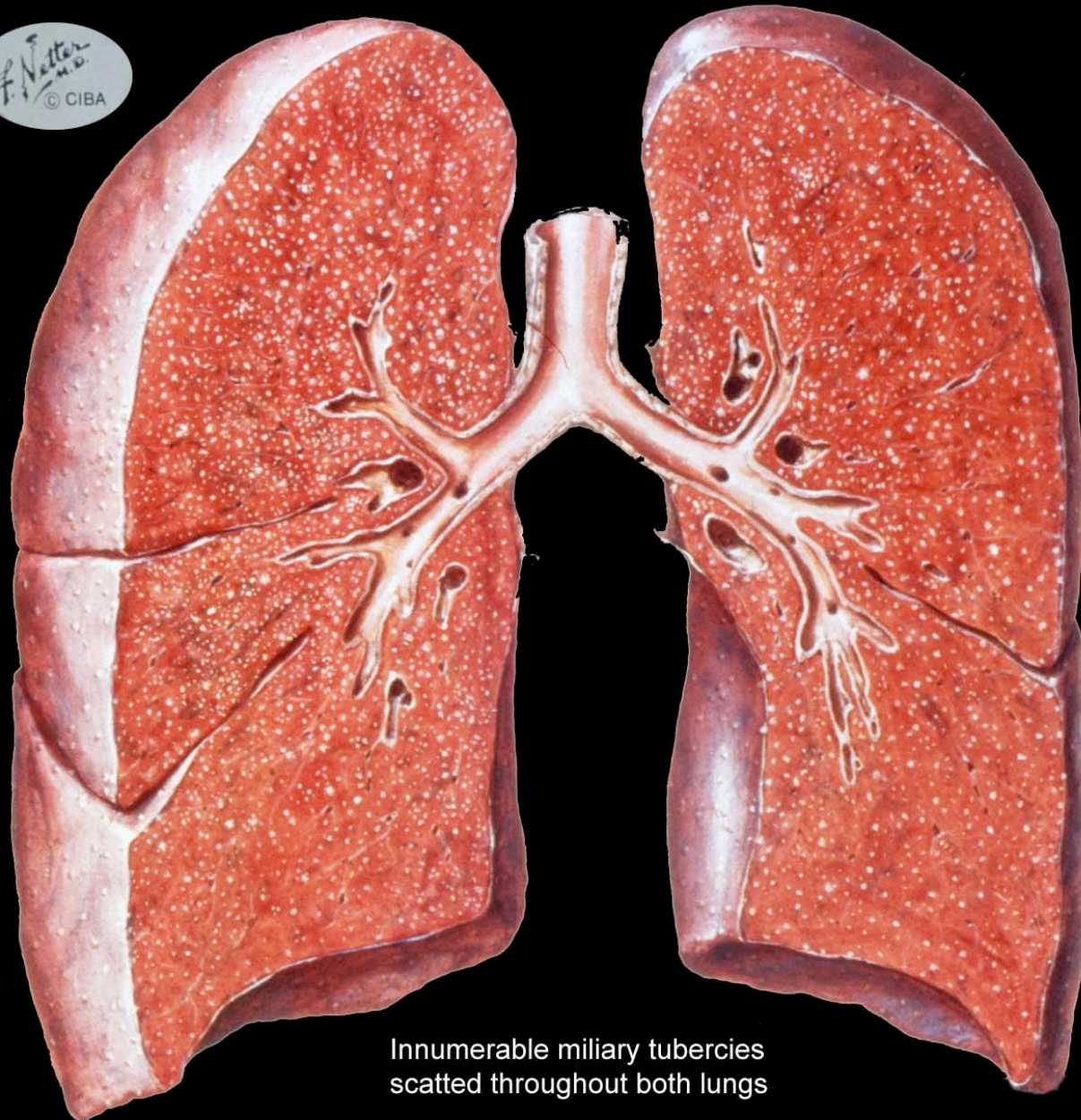
Disseminated (bacteremic) tuberculosis

- ❑ Bacteremia described in both primary and miliary tuberculosis
- ❑ bacteremia reported in patients with advanced AIDS in US and developing countries
- ❑ Diagnosis using mycobacterial blood culture (lysis-centrifugation, BACTEC, MB/BacT)
- ❑ is this reactivation of latent infection, relapse of previously treated disease, or new infection (disseminated \pm pulmonary) in patients with no prior mycobacterial experience?

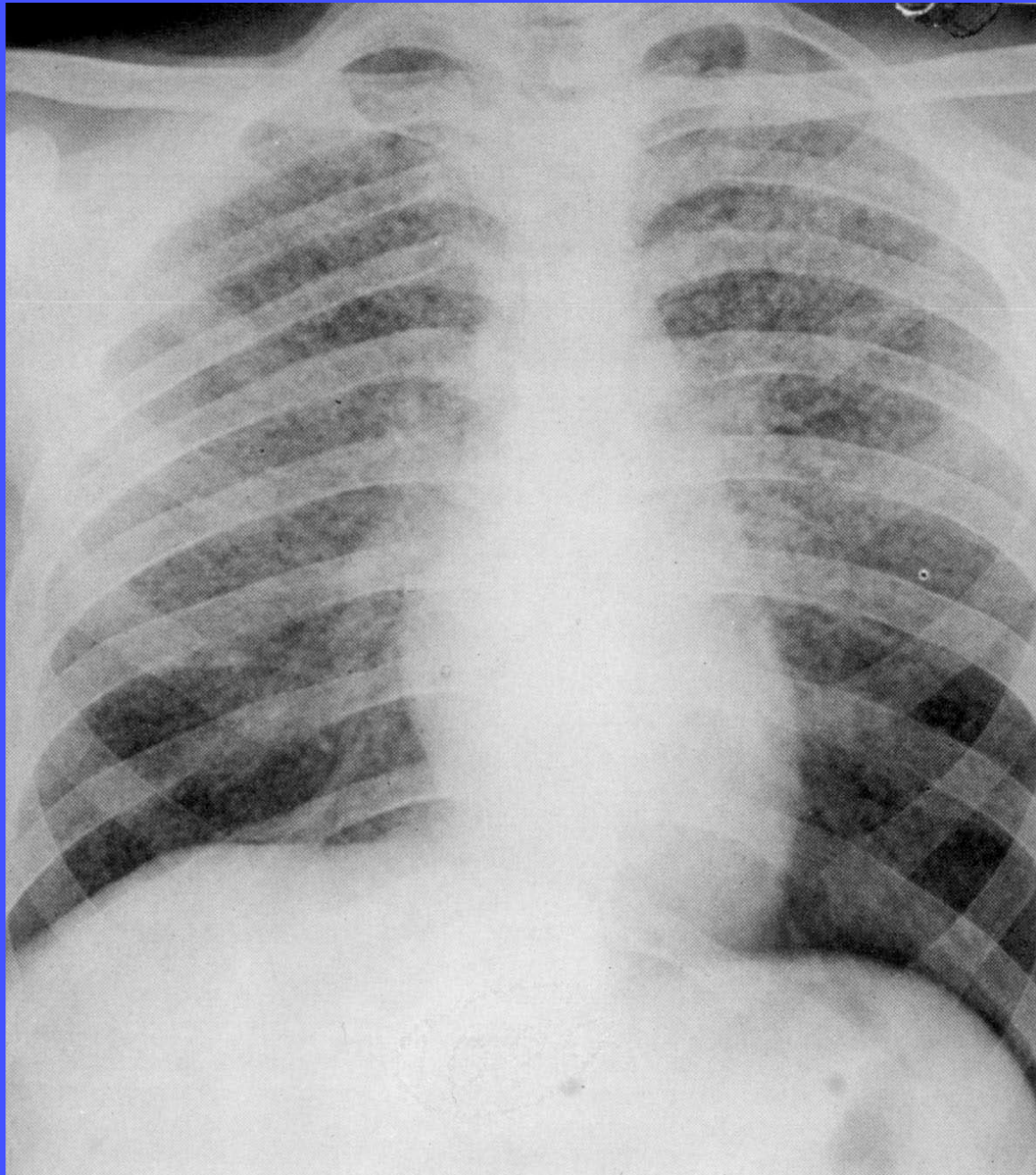
Disseminated TB

- Proliferation of M tb and dissemination throughout the body.
- Can have “miliary” pattern on CXR
- Features
 - ◆ generally non-specific; dominated by systemic effects, particularly fever, weight
 - ◆ loss, night-sweats, anorexia, and weakness.
 - ◆ Cough could be there
 - ◆ Headache and mental status changes are less frequent
- O/E:
 - ◆ Fever, wasting, hepatomegaly, pulmonary findings, lymphadenopathy, and splenomegaly occur in descending order of frequency.
 - ◆ Choroidal tubercle, strongly suggestive.

Miliary Tuberculosis



Innumerable miliary tubercles
scattered throughout both lungs



Diagnosis of EPTB in HIV

- **CD4 count often <200 (AIDS defining)**
- **TB adenitis (axillary, cervical) (Lymph node aspiration/Bx)**
- **Thoracic, abdominal, retroperitoneal lymphadenitis (CXR, Abdo US, paracentesis)**
- **Pleural Effusion (CXR, Fluid aspiration and testing)**
- **Pericardial Effusion (CXR, ECHO)**
- **CNS disease (meningitis, tuberculomas) in 5-10% (LP, CT scan)**
- **Rare forms:**
 - **Cutaneous disease**
 - **Renal disease**

Diagnosis, newer approaches

- Newer culture and sensitivity systems, eg Bactec
- Recognition of bacilli
 - ◆ Mycobacterial antigen detection, using Abs to PPD and BCG
 - ◆ PCR for Mycobacterial DNA/RNA
- Recognition of host response
 - ◆ mycobacterial serology, ELISA or monoclonal antibodies
 - ◆ adenosine deaminase levels (from lymphocytes and macrophages activated to TB)
 - ◆ interferon gamma levels (from T-

Conclusion

- TB in HIV
 - ◆ Leading cause of death
 - ◆ Important cause of illness and suffering
- Hence:
 - ◆ Prompt and effective diagnosis can be a challenge,
 - ◆ **Low threshold for diagnosis??**
 - ◆ Prevention is very important, **Being addressed in the DARDAR Health Study**