TB-HIV Co-infection

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Medical Update Group/UOM

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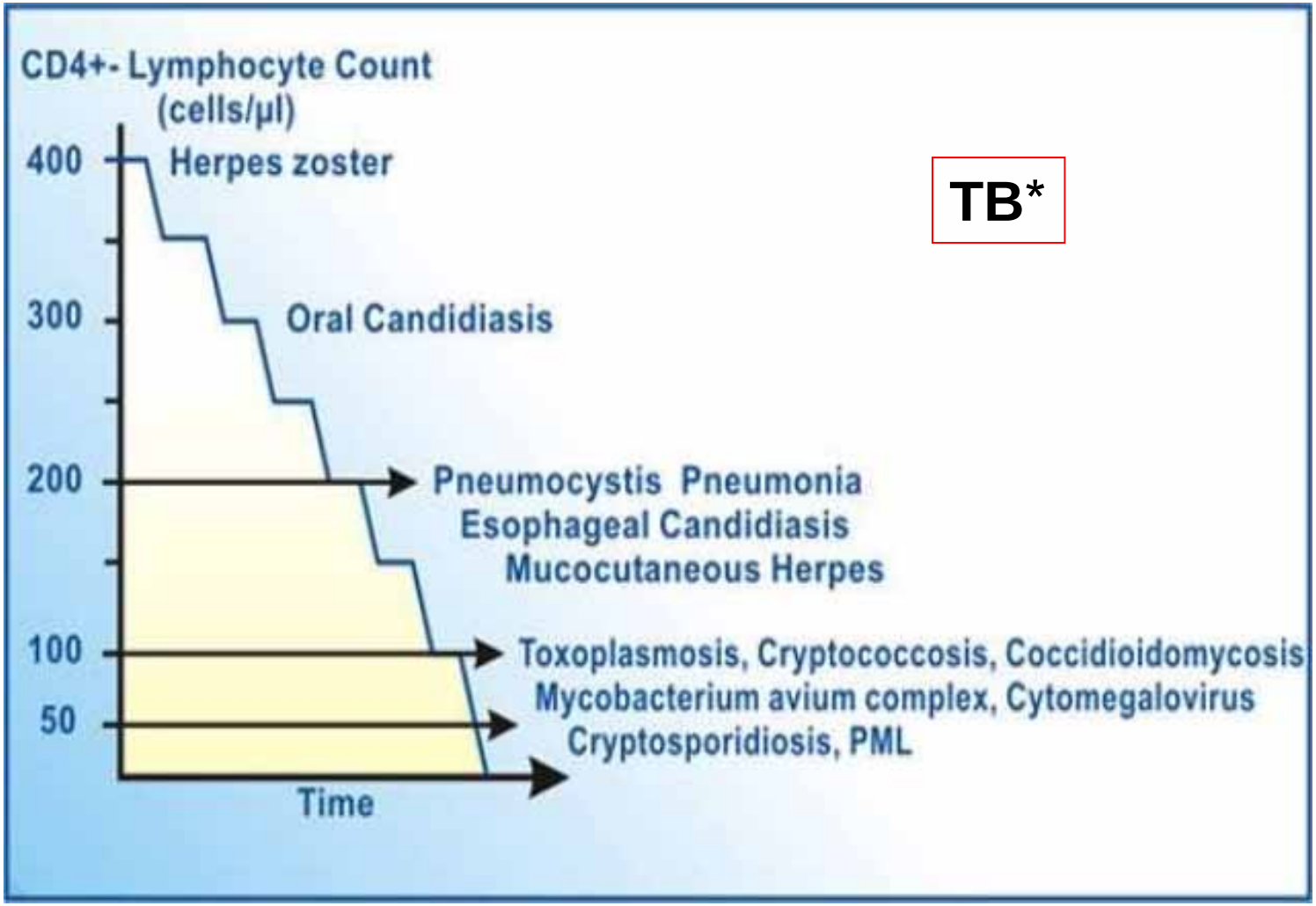
Opportunistic infection

- Opportunistic infn.: Infection by a microorganism or virus that **normally does not cause disease** but **becomes pathogenic when the body`s immune system is impaired**.
- Presence of one or more OIs with HIV: *AIDS-defining condition.*
- With HIV infection: depending on the level of immunosuppression, number of opportunistic infections occur.

Opportunistic Infections according to CD4 level



****Can occur at any CD4 level***

Why so much concern about TB-HIV?

- TB or HIV infection, if not treated, can kill
- When present together: each help the other in progressing
- HIV: One of the most important risk factors enabling progression of TB infection into TB disease
- TB: One of the most common OI and the most common cause of death in PLHIV

Burden of disease

Burden of TB, HIV

Global

2014[a]:

- Estimated incident cases of TB: 9.6 M
- HIV+: 12% of total TB(1.2 M)
- 0.4 M PLHIV died with TB (1/3 TB/HIV Pts died with TB)
- 1 in every 3 HIV deaths - due to TB (Total HIV deaths: 1.2 M)[b]

Mauritius

2015[c]:

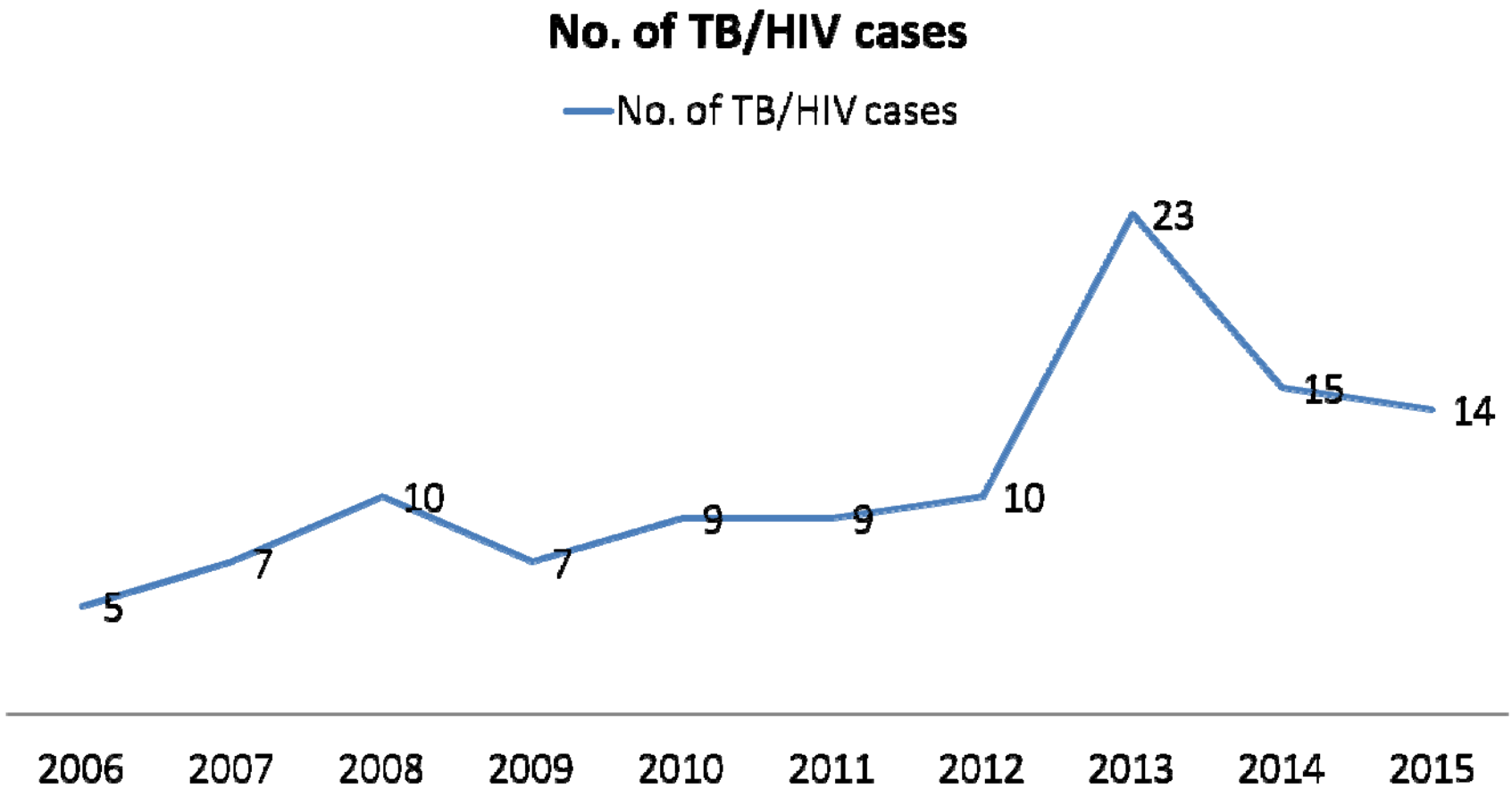
- Total No. of TB cases notified: 129
- Total No. of TB/HIV cases: 14
- Total No. of TB deaths: 8
- Total TB/HIV deaths: 3

[a] *WHO Global Tuberculosis Report 2015*

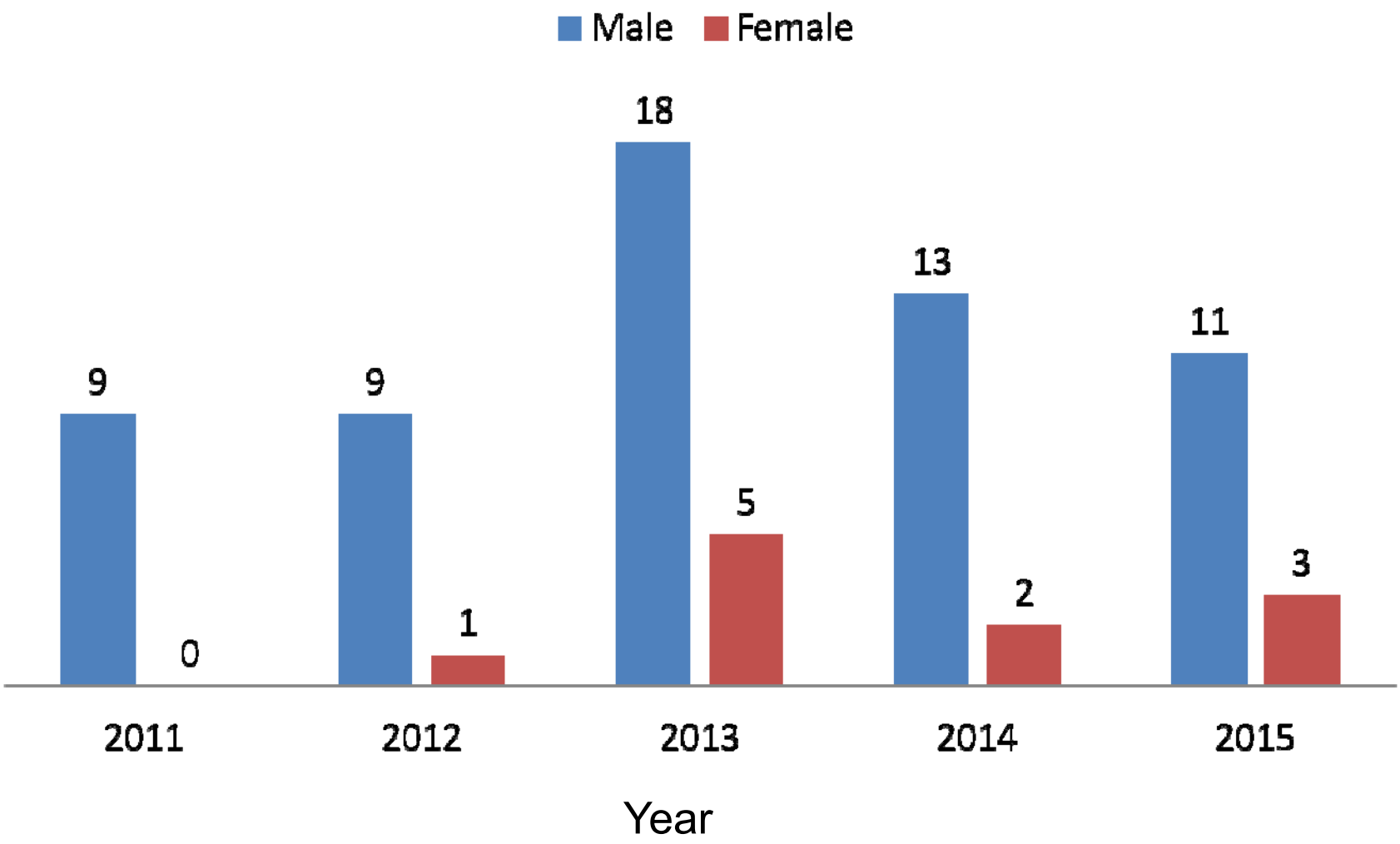
[b] *Factsheet 2015/UNAIDS*

[c] *Chest Clinic Port Louis*

Trend of TB/HIV cases in Mauritius (2006 -2015)



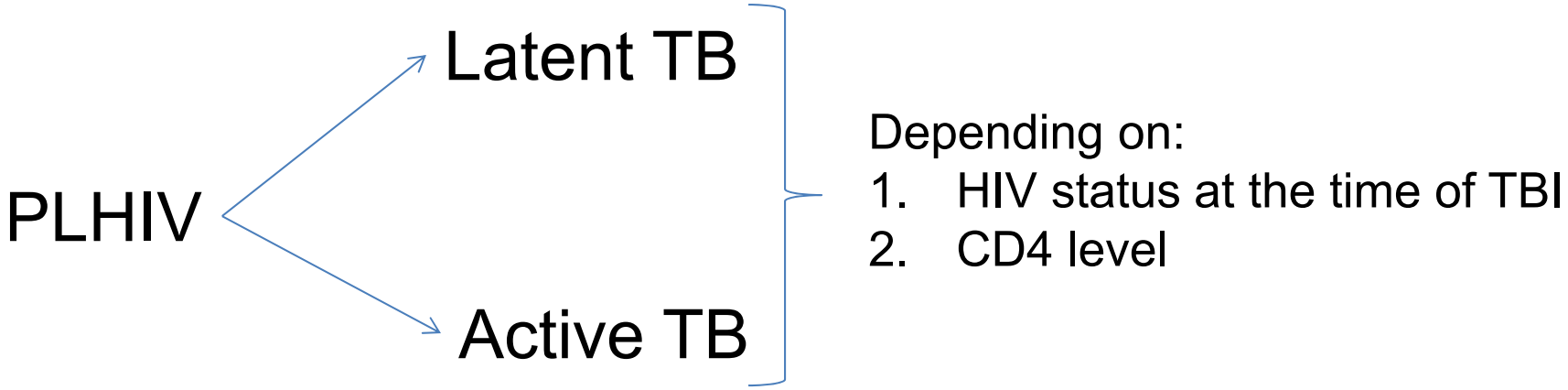
Sex distribution of TB/HIV cases (2011-2015)



Diagnosing TB in PLHIV

- A CHALLENGE

TB/HIV Co-infection



Latent TB Infection

- Defined as presence of immune responses to *M. tuberculosis* antigens **without clinical evidence of active TB;** Mantoux or IGRA test +ve
- No signs or symptoms of TB; not infectious.
- Lifetime risk of LTBI developing into TB dis in HIV –ve: 5-15% (occurring within 1st 5 yrs after infection)
- In PLHIV: 10% annually; 26 – 31 times greater

Active TB disease

- If CD4 > 400: Presentation as in immunocompetent host
- As immunosuppression progresses (CD4 <300): Presentation less typical:- extrapulmonary & disseminated disease in 40-80% cases
- TB can be:
  - Primary – developing as early as 60 – 100 days after exposure, or
  - Secondary, developing after a period of latency

Symptoms of PTB

- Cough > 2 weeks
- Fever
- Night sweats
- Loss of appetite
- Weight loss
- Fatigue
- SOB
- Chest pain
- Haemoptysis

Symptoms of TB

With progression of HIV disease – few symptoms

Advanced disease (CD4 <200) – Extrapulmonary TB :

- Symptoms depending on organ involved
- **Disseminated disease** – multiple organs involvement (bone marrow, bone, urinary and gastrointestinal tracts, CNS, liver, regional lymph nodes)

Extra pulmonary TB

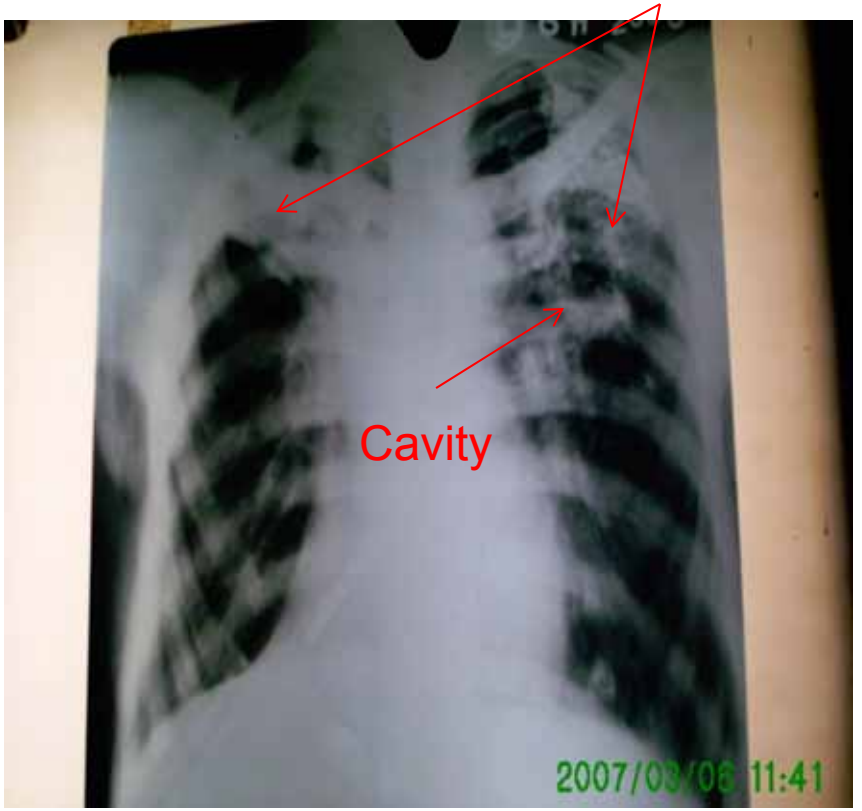
- Common presentations of extra-pulmonary TB
  - Lymphadenitis
  - Pleural effusion
  - Empyema
  - Skeletal – back pain
  - Peritoneal – abdominal pain
  - Miliary
  - Meningitis
  - Pericardial Effusion
- Diagnosis may be more challenging

Investigations

Chest X-ray – cornerstone of diagnosis of TB

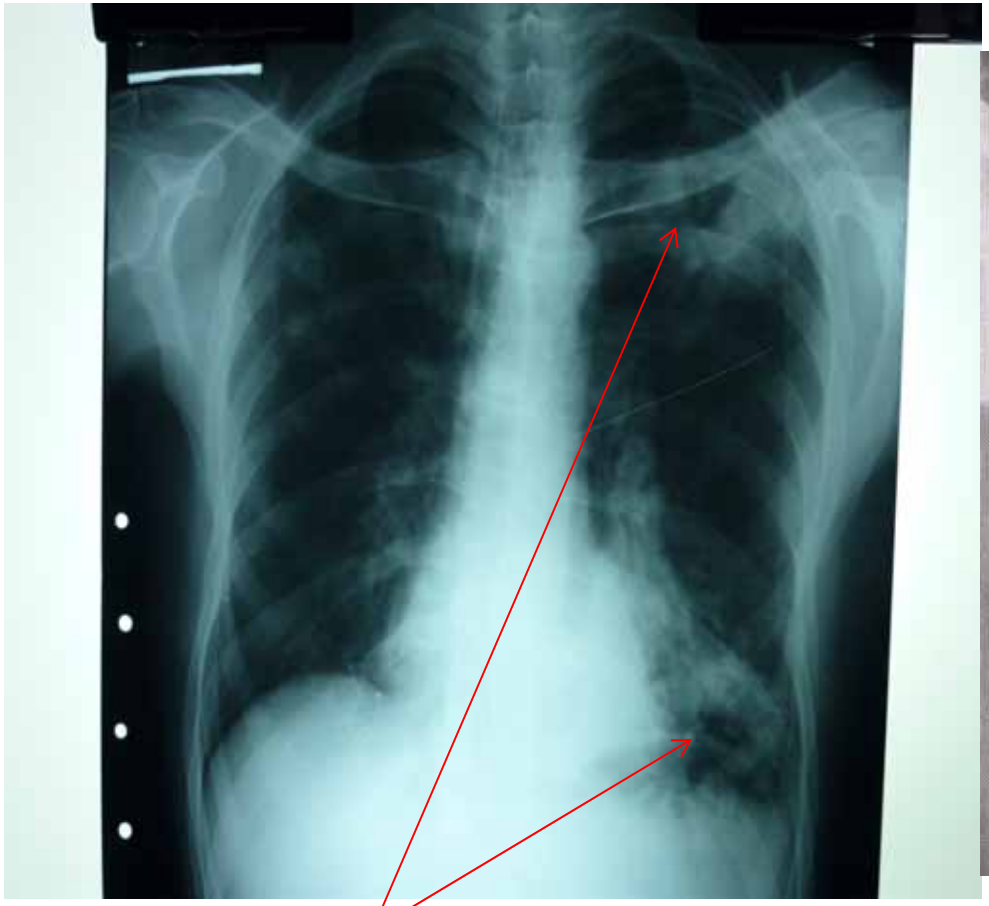
In early stage of HIV infection similar to immunocompetent host:

- ❑ Apical involvement
- ❑ Infiltrates
- ❑ Cavity

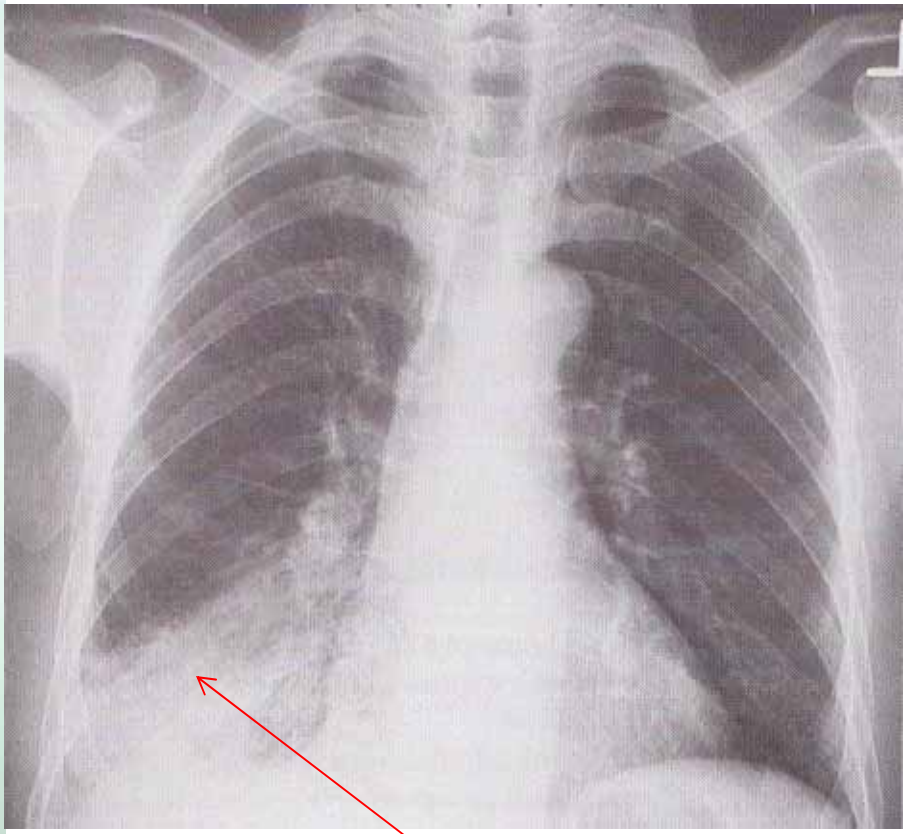


With progression of HIV infection

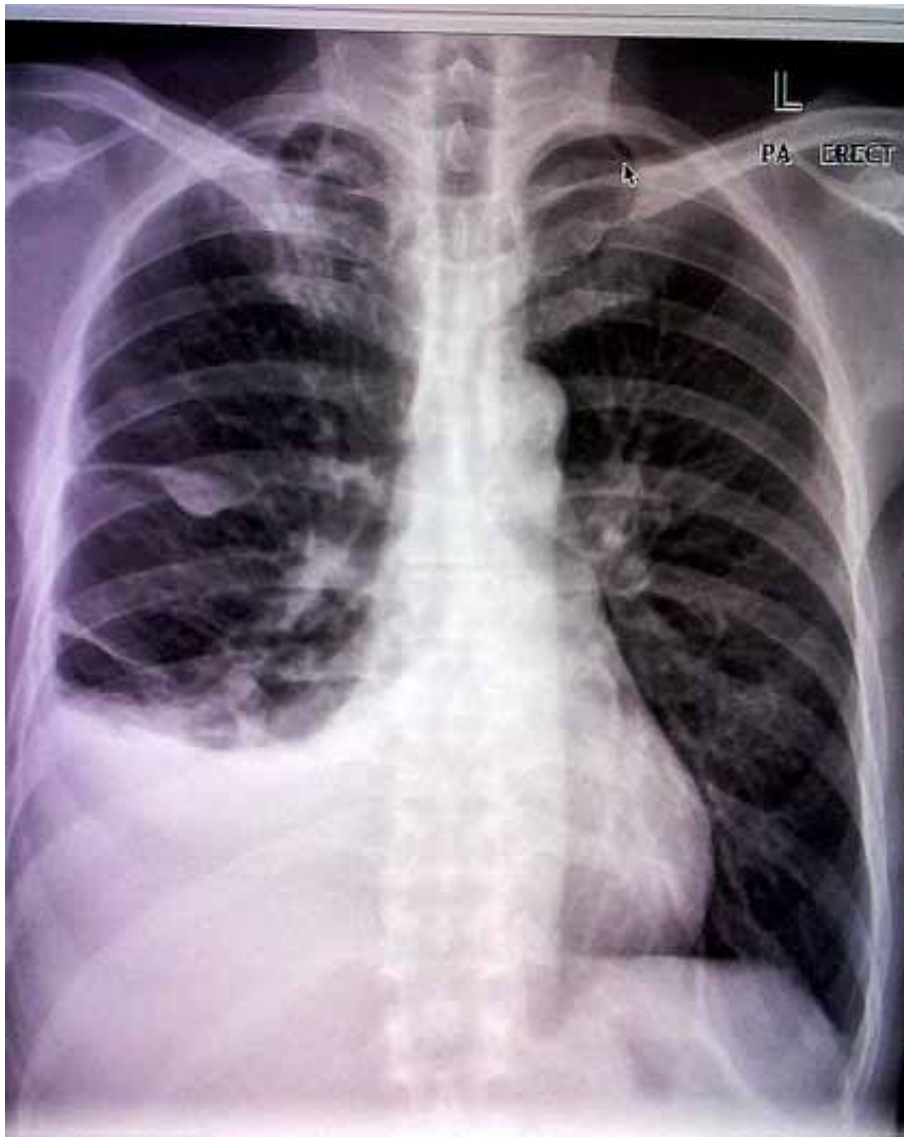
- CXR: findings less typical
- Apical infiltrates with cavitation replaced by infiltrates in lower zones (may be bilateral)
- Pleural effusion
- Perihilar or mediastinal lymphadenopathy without parenchymal involvement;
- Miliary shadows.
- 1/5 of patients have normal CXR



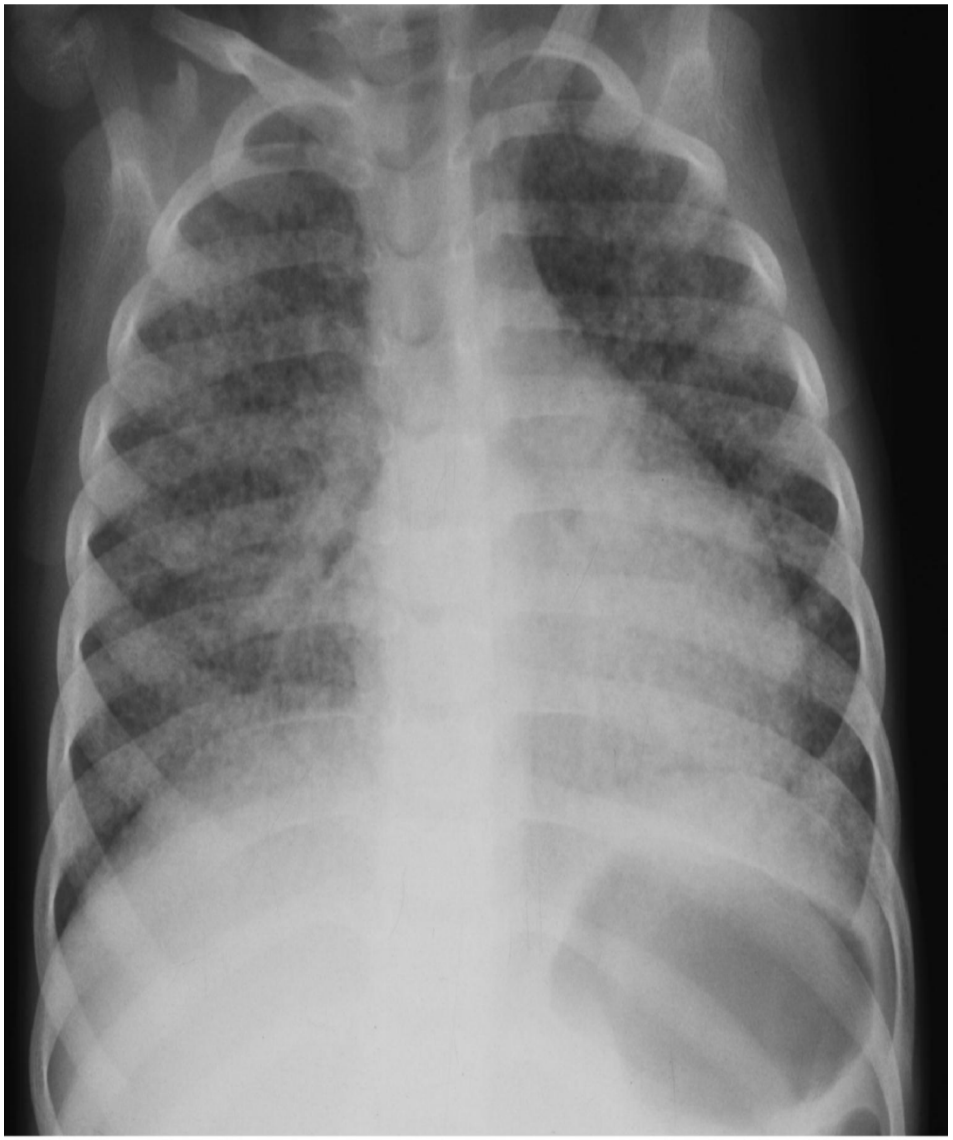
Cavities



Right Lower Zone Consolidation



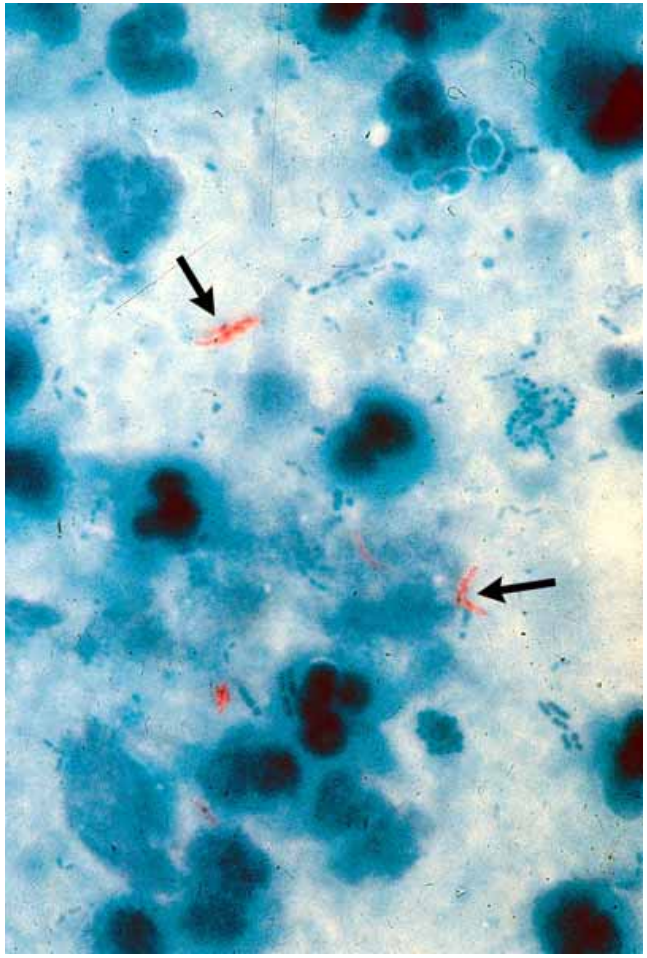
Right Pleural Effusion



Miliary TB

Sputum Smear microscopic examination

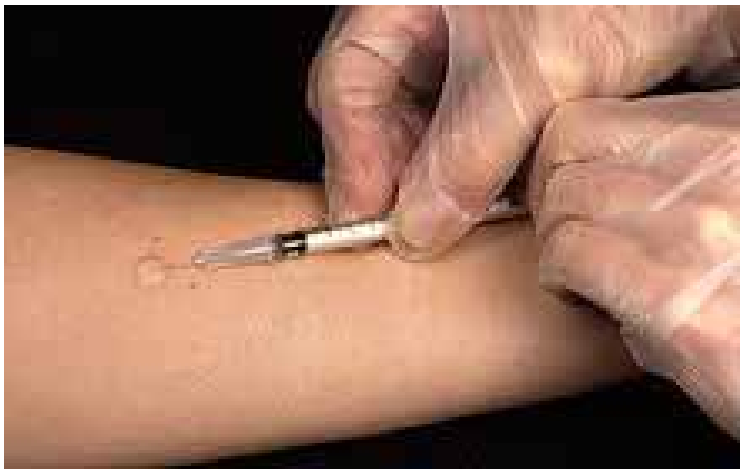
- Sensitivity in PLHIV reduced by 20 – 30% (Shed less bacilli)
- PTB: smear +ve in 50 - 70%; culture +ve in 90% (Disadv: 6-8 wks)
- Extra-PTB: SS often Neg
- Other disadv of sputum examination:
  - Cannot distinguish b/w *M. tuberculosis* and other mycobacteria
  - No info about resistance profile of bacilli



AFB with ZN stain

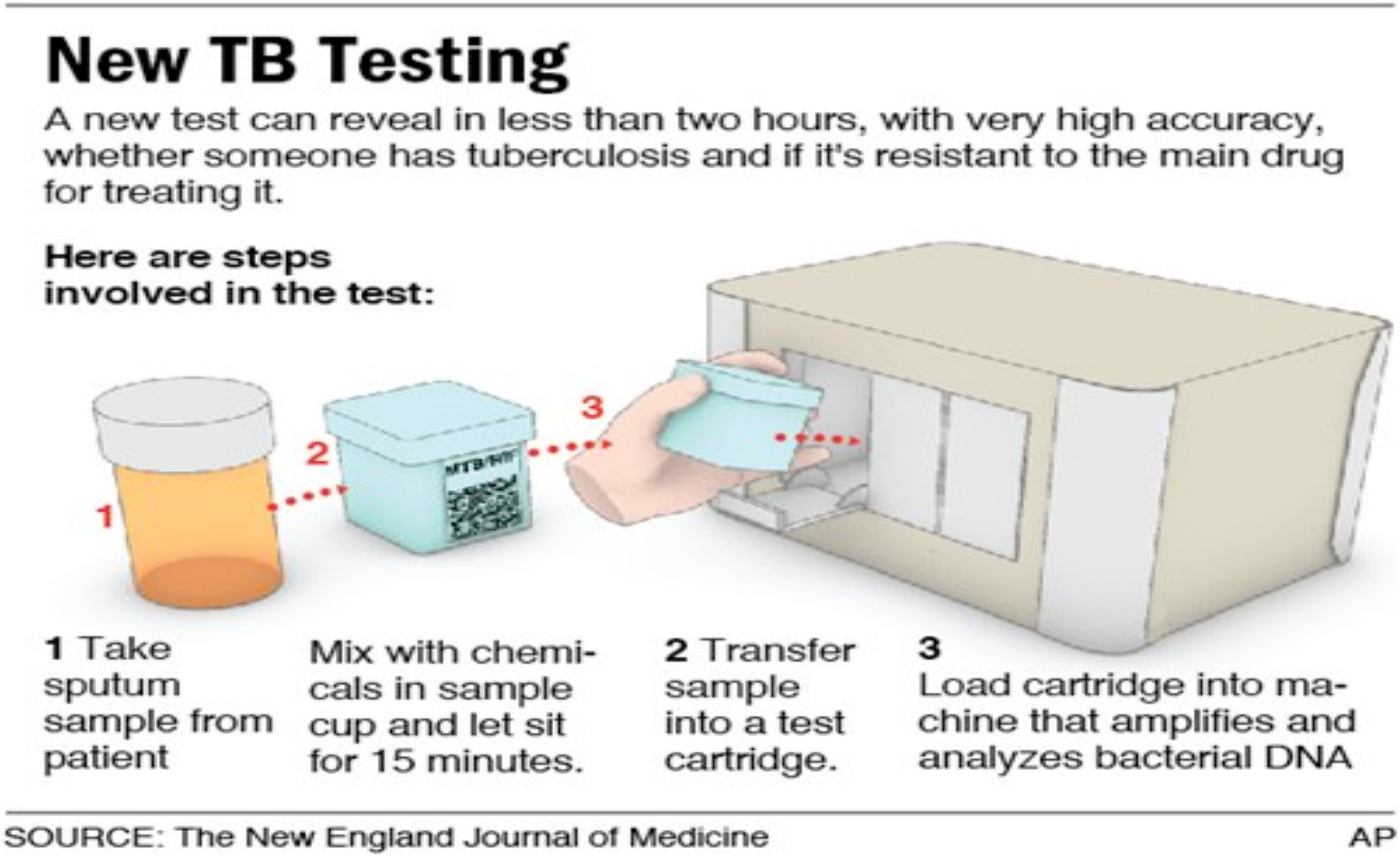
Mantoux Test

- Tuberculin Skin Test
  used to detect LTBI
- Poor sensitivity in HIV+ve people. Positive in only 30 -50% HIV patients (>5mm)
- A negative Mx does not exclude TB.



Gene Xpert MTB/RIF test

- Recommended as **Primary test** in PLHIV with S&S of TB(WHO)



Urine Lateral Flow Lipoarabinomannan (LF-LAM) Assay

- New test recommended by WHO for detection of TB in PLHIV
- LAM antigen – a lipopolysaccharide present in mycobacterial cell walls, released from metabolically active or degenerating bacteria, present in people with active TB
- Detection of LAM in urine better among PLHIV, & improves with lower CD4 counts

WHO recommendations on LF-LAM Assay*

LF-LAM:

1. **Should not** be used for the diagnosis of TB, except in persons with HIV with low CD4 counts or who are seriously ill
2. **May be used to assist** in the diagnosis of TB in:
   i. HIV+ve adult inpatients with S&S of TB (PTB &/or extrapul) with CD4 count ≤l 100 cells/µL), or
   ii. HIV+ve patients who are seriously ill regardless of CD4 count or with unknown CD4 count
3. **Should not be used** as a screening test for TB.

* *WHO Global Tuberculosis Report 2015*

Other Investigations

- **Bronchoscopy**
  - BAL fluid – smear for AFB & culture for mycobacteria
- **Biopsy**
  - Smear + culture

Treatment

Treatment of LTBI

- Important to prevent progression into active TB
- Recommended for:
  - PLHIV
  - Adults & Children < 5 years who are close contacts of a TB case
  - Pts with Silicosis
  - Pts initiating TNF treatment
  - Pts on dialysis
  - Transplant patients

Treatment Options

Drugs	Duration	Dose	Frequency
Isoniazid (INH)	**6 mo**	**Adult: 5mg/kg** **Child: 10 mg/kg** **Max: 300 mg**	**Daily**
		Adult: 15mg/kg Child: 10 mg/kg Max: 900 mg	Twice weekly
	9 mo	Adult: 5 mg/kg Child: 10-20 mg/kg Max: 300mg	Daily
		Adult: 15 mg/kg Child: 20-40 mg/kg Max: 900 mg	Twice weekly
Isoniazid + Rifapentine	3 mo	Adult, Children 12 y and over: INH: 15 mg/kg; max: 900 mg RPT: 10.0 – 14.0 kg 300 mg 14.1 – 25.0 kg 450 mg 25.1 – 32.0 kg 600 mg 32.1 – 49.9 kg 750 mg ≥ 50 kg 900 mg	Once weekly
Rifampicin + Isoniazid	3-4 mo	Adult: R 10 mg/kg Max 600 mg H 5 mg/kg Max 300 mg	Daily
Rifampicin	3-4 mo	Adult: 10 mg/kg Max 600 mg	Daily

Active TB: WHO DOTS Protocol

- New TB/HIV case:
  - 6-mo regimen: 2(HRZE) + 4(HR)
  - In case of cavitary disease: 9-mo treatment 2(HRZE) + 7(HR)
- If Pt already on ART: Replace Rifampicin by Rifabutin (R stimulates CP450 liver enzyme system → ↑metabolism of PIs and NNRTIs; also, PIs and NNRTIs can enhance or inhibit CP450 → alter R level. Results in ineffectiveness of ARV drugs or R, or drug toxicity)

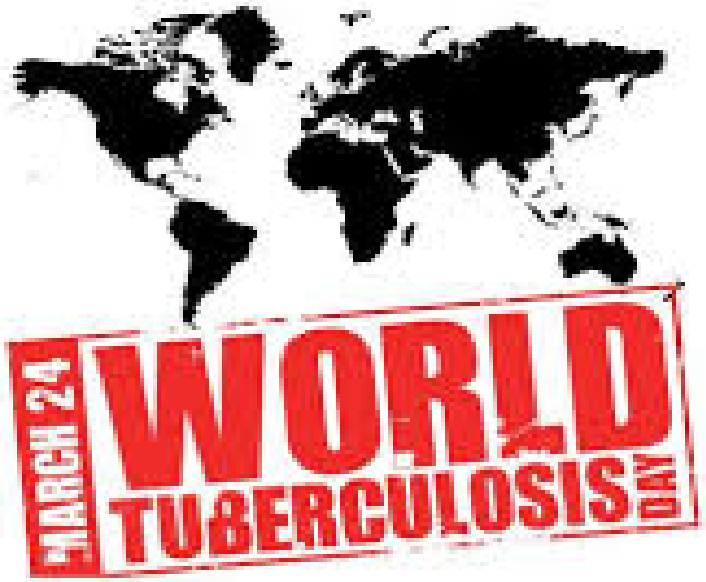
ART

- WHO recommends early initiation of ART soon after starting TB Tt (within 1st 2-8 wks)
- No need to wait for completion of anti-TB treatment.
- Survival benefit higher in patients with low CD4 counts (<50 cells/mm³) when ART started within 2 wks*
- Risk of Immune reconstitution inflammatory syndrome (IRIS) higher –requires careful monitoring and management

* *JW AIDS Clin Care Jun 20 2011*

TB – HIV collaborative activities

- Aim to ↓ morbidity and mortality from TB in PLHIV.
- Include the Three I`s for TB/HIV:
  - Intensified TB-case finding
  - Initiation of Isoniazid Preventive Therapy among PLHIV,
  - Infection control for TB
- Result: Reduction in the burden of TB



UNITE TO END TB

Thank you