

# **Implications of ART on TB and OI Management**

**Module A2 Session 3**

**Module B2 Session 1**



# Objectives

- Describe HIV-TB interaction, including:
  - Epidemiology
  - Prevention
  - Clinical features and diagnostics
  - Management
  - Implications of co-infection
- Describe the problems and management of ARVs in patients with other HIV-related infections and conditions such as OIs and hepatitis
- Describe the immune reconstitution syndrome and how to manage it



# HIV-TB Epidemiology

## Tuberculosis: HIV-TB interaction and co-infection

- Most common cause of death in people with HIV worldwide
- HIV infection increases the likelihood that new infection with *M. tuberculosis* (due to immune suppression) will progress rapidly to TB disease
- HIV is the most potent factor known to increase risk of progression from *M. tuberculosis* infection to disease



## HIV-TB Epidemiology, continued

- Among HIV-infected individuals, lifetime risk of developing active TB is 50%, compared to 5-10% in persons who are not HIV-infected
- In a person infected with HIV, the presence of other infections, including TB, allows HIV to multiply more quickly. This may result in more rapid progression of HIV infection
- HIV-related TB can present typical or atypical clinical and/or radiological features. Atypical features are usually found in HIV-infected individuals with severe immunosuppression



# Prevention

## TB Preventive Therapy

- Evidence shows it can be effective in HIV-infected people
- Can be given to people with HIV who:
  - have been screened to exclude active TB
  - have a high TB risk
  - Are motivated to adhere to therapy



## Prevention, continued

In a setting where it's not practical to do a PPD skin test, consider TB prophylaxis for the following individuals if they are HIV-infected:

- Individuals living in population with high prevalence for TB infection (>30%)
- Health care workers
- Household contacts of TB patients
- Prisoners
- Miners
- Other selected groups at high risk for acquisition or transmission of TB



## Clinical features

- Initial signs of TB disease may become apparent at any time during the evolution of HIV-infection
- Can come well before other manifestations of HIV infection or after patient has become symptomatic
- May be pulmonary or extra-pulmonary

Pulmonary TB is most common form—  
presentation depends on degree of  
immunosuppression



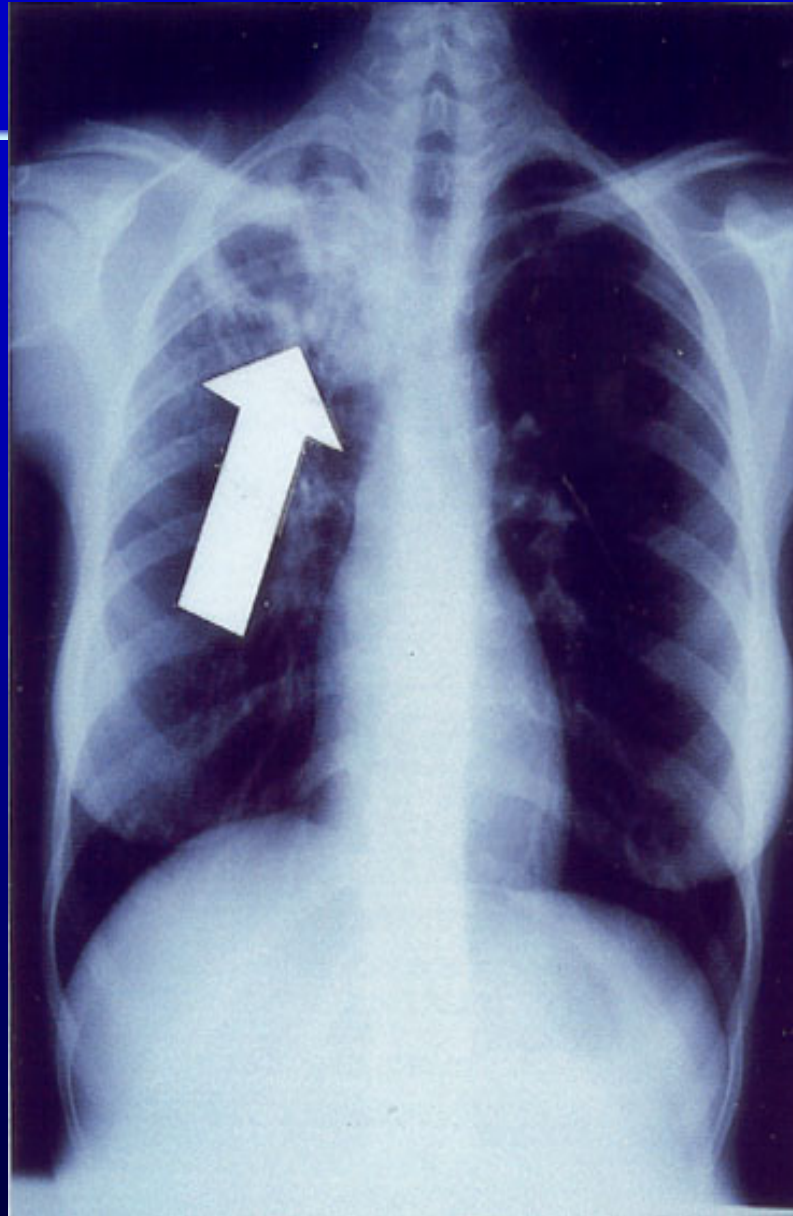
## Clinical features, continued

- Disseminated and extrapulmonary TB is more common in advanced HIV infection because the immune system is less able to prevent growth and local spread of *M.tuberculosis*.
- Unilateral or bilateral infiltrates in the lower lobes are seen more often than upper lesions and cavities
- Most common forms are lymphadenitis, pleural effusion, pericarditis, miliary disease, and meningitis

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

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





## Diagnostic features, continued

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
- **In the setting of an HIV epidemic, it is not possible to look at a CXR and say that it is or is not TB**



# Treatment

HIV infected patients should be treated according to national guidelines and in cooperation with local authorities such as the district medical officer (DMO) and the district TB supervisor.

## Aims of treatment

- To cure the patient of TB
- To prevent death from active TB or its late effects
- To prevent TB relapse
- To decrease TB transmission to others

### Drug regimens

- Initial phase—first 2-3 months
  - During the initial phase, there is rapid killing of TB bacilli
  - Three or more drugs are used in combination
  - Infectious patients become non-infectious within about 2 weeks and symptoms usually improve

- Continuation phase-additional 4-6 months
  - Fewer drugs are necessary (usually 2), but longer time
  - These drugs eliminate the remaining bacilli



# Antiretroviral Therapy for Individuals with Tuberculosis Co infection

## WHO Recommendations for ARV Therapy

- WHO recommends that people with TB/HIV **complete their TB therapy prior to beginning ARV treatment** unless there is high risk of HIV disease progression and death during the period of TB treatment:
  - CD4 count  $<200/\text{mm}^3$
  - disseminated TB.

## TB and HIV Co-infection, continued

CD4 cell count	Recommended regimen	Comments
<200/mm <sup>3</sup>	Start TB treatment. Start ART as soon as TB treatment is tolerated (between 2 weeks and 2 months)	Recommend ART. EFV is contraindicated in pregnant women (or in women of childbearing potential without effective contraception)
200-350/mm <sup>3</sup>	Start TB treatment. Start ART after intensive phase	Consider ART
>350	Start TB treatment	Defer ART



## TB and HIV Co-infection: ART regimen

- If treatment of HIV and TB needs to be simultaneous, choose:
  - d4T or AZT plus
  - 3TC plus
  - \*EFV (but increase dose to 800 mg/day)
  
- \*Alternatives:
  - ABC
  - SQV/r
  - NVP (higher potential for hepatotoxicity than EFV with rifampicin; give if rifampicin not used)



# HIV and TB: Treatment Implications

- Drug – drug interactions common
  - Can affect the levels of either anti-TB meds or antiretrovirals
    - Can lead to resistance or increased toxicity
  - CRITICAL to look up interactions of meds and adjust doses where necessary
  
- Sometimes cause similar side-effects
  - Difficult to determine which med caused the side effect
    - Example: Isoniazid can also cause peripheral neuropathy
  
- Adherence problem: pill burden
  - Taking 3-4 drugs for TB plus 3 antiretrovirals plus taking any recommended prophylactic medication



## Other OIs

- Patients who develop other OIs should be treated with ARVs unless there are major interactions
- In contrast to the situation with TB, drug interactions with standard ARV regimens do not pose a significant problem
  - Ketoconazole may boost PI levels
  - Co-trimoxazole may exacerbate anemia from AZT
- Prompt initiation of ART should be considered when
  - OIs occur for which treatment is not available or for which it is suboptimal
    - Improvement of the immune system may enhance recovery
    - Ex: chronic diarrhea with cryptosporidium



# Hepatitis


- Patients coinfectd with hepatitis B or C can safely be treated with several ARV regimens
- Avoid regimens which have ARVs that can cause additive hepatotoxicity
- 3TC and TDF are both active against hepatitis B and may even have a protective effect against new infections.
  - Patients receiving 3TC or TDF who are known to have hepatitis B and experience ARV regimen failure may wish to continue these medications when the ARV regimen is switched.



## ART and Antimicrobial Prophylaxis

- ART very effective at decreasing risk of OIs by boosting immune system
- However, patients who still have severe immune suppression should take OI prophylaxis (namely co-trimoxazole)
- Based on observations in developing countries, patients responding to ART with sustained elevation in CD4 cell counts above 200 cells/mm for 3-6 months may be able to discontinue prophylaxis for some OIs

# Immune Reconstitution Syndrome

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- **Mechanism:**
  - For many OIs, including TB, there can be a transient worsening of infection 2-3 weeks after initiation of ART.
  - This is called immune reconstitution syndrome. Initiation of ART can unmask previously undiagnosed infections by augmenting the inflammatory response



## Immune reconstitution syndrome, continued

- Clinical presentation:
  - fevers
  - lymphadenopathy
  - worsening pulmonary lesions
  - expanding lesions of the central nervous system
  
- Management:
  - Reactions are self-limiting although they may require a brief course of corticosteroids to reduce inflammation of CNS or severe respiratory symptoms
  
  - ART should not be interrupted if immune reconstitution syndrome occurs