Tuberculosis:
HIV-TB Interaction

Purpose

To learn about HIV and TB co-infection including

* clinical presentation
* recommended diagnostic tests/radiology and common findings
* management
* treatment

Objectives

- Understand the interaction between HIV and TB
- Describe the clinical presentation of TB and the most important signs and symptoms to look for
- List the recommended diagnostics and common findings

Objectives, continued

- Describe the treatment and management of HIV-positive patients with TB, including drug regimens and how to monitor during treatment
- Discuss treatment approaches and strategies including directly observed treatment strategies (DOTS)
- Discuss ART for individuals with TB co-infection

Overview

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

Overview, 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

Overview, continued

- 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

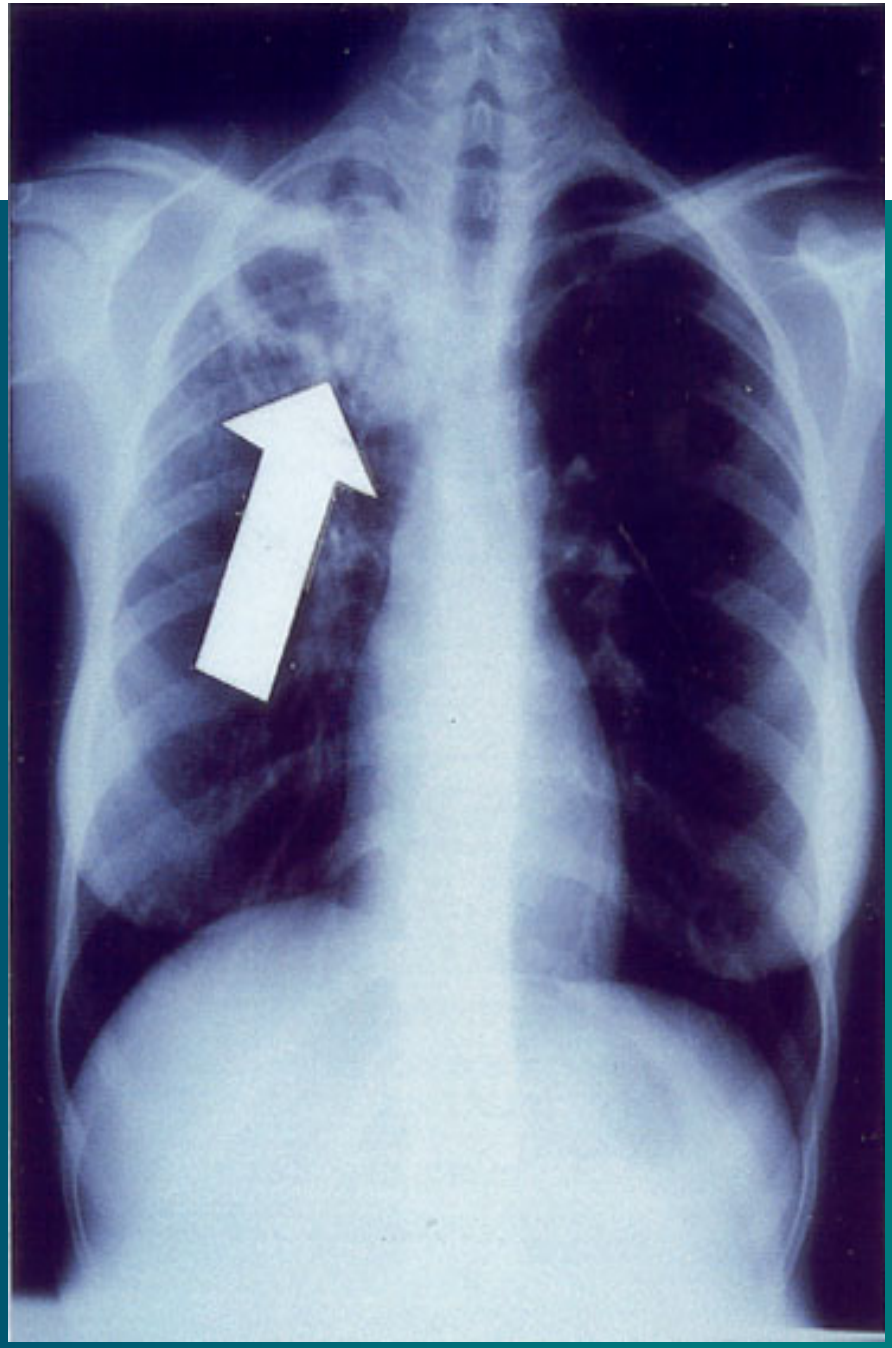
Pulmonary TB is most common form—presentation depends on degree of immunosuppression

Tuberculosis

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

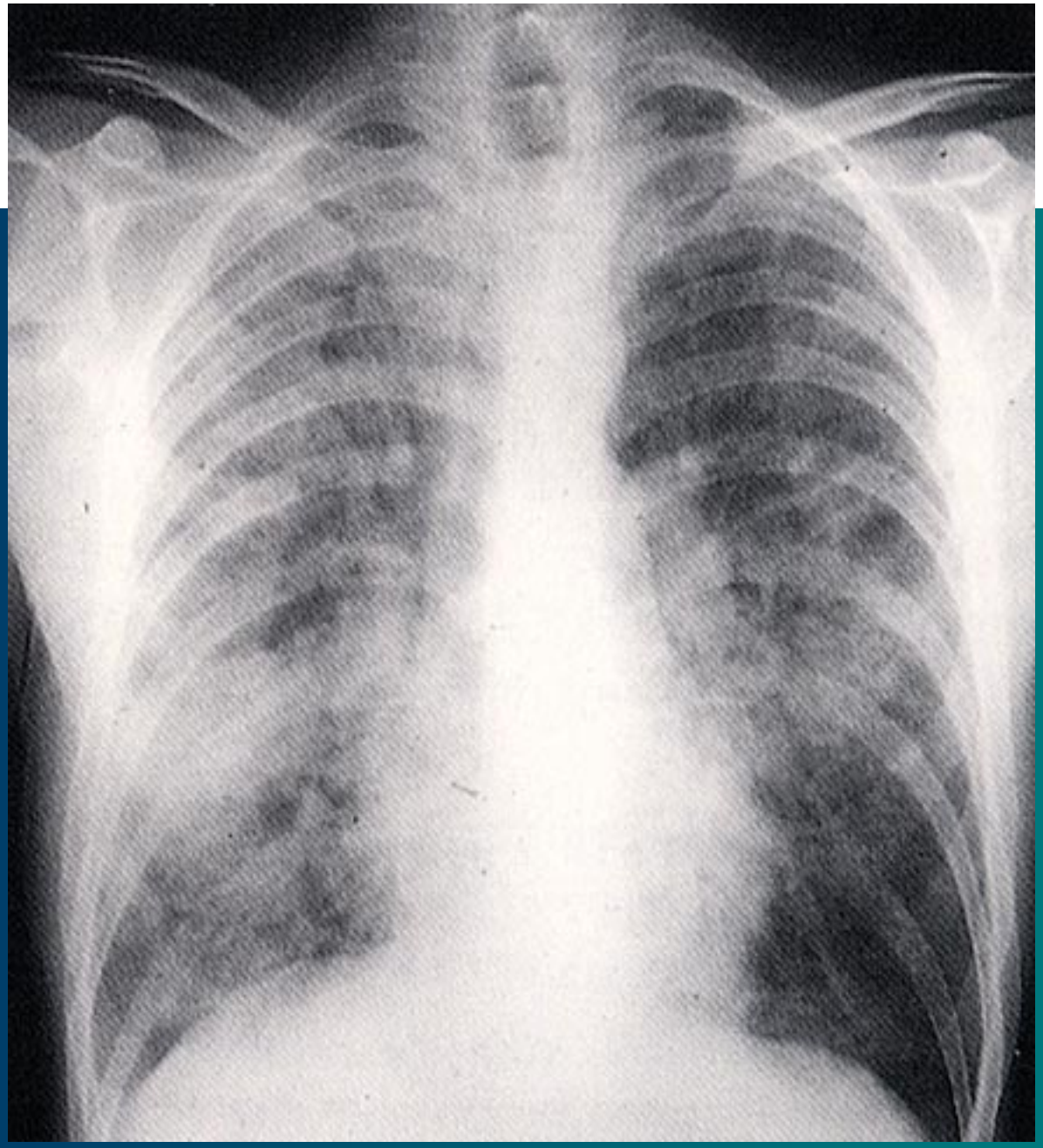
Arrow points to cavity in patient's right upper lobe --typical finding in patient with TB



TB

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**



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

TB

- 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

Clinical Presentation
Signs and Symptoms

Most important symptoms

- Cough lasting more than 3 weeks and not responding to usual antibiotic treatment
- Production of purulent, sometimes blood-stained sputum
- Evening fevers
- Night sweats
- Weight loss

Diagnostic Tests

Microscopic examination of specimen of sputum that has been stained by the Ziehl-Neelsen (ZN) method

A PTB suspect should submit three sputum samples for microscopy:

- ***Sample 1*:** On first visit, the patient should provide an on-the-spot sputum sample
- ***Sample 2***: Give the patient a sputum container to take home for an early morning sample on the following day (day 2)
- ***Sample 3:*** On day 2, when the patient brings sample 2 in, he/she provides another on-the-spot sample.

Diagnostic tests, continued

- An inpatient can provide 3 early morning sputum samples

- False negative reports:

  A PTB suspect with 3 negative ZN sputum smears may actually have TB due to sample being inadequate or faulty smear preparation/interpretation

Diagnostic tests, continued

Radiology

- If TB is still suspected despite negative smears, a chest x-ray should be done. Classical pattern is upper lobe infiltrates with cavitation
- However, no chest x-ray is absolutely typical of PTB patients with HIV infection

  In severe immunosuppression, the appearance is often atypical, as described above

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

Treatment, continued

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

Treatment, continued

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

Treatment, continued

Monitoring during treatment

- Bacterial monitoring is only possible for patients with smear positive PTB
- Sputum smear exam should be done as follows
  - At the time of diagnosis
  - At the end of initial phase
  - During the continuation phase—at the end of month 5
  - On completion of treatment—month 6 or 8
- Using chest x-ray as a monitoring tool is unnecessary and wasteful

Treatment, continued

Treatment approaches and strategies

- Directly observed treatment, short course (DOT)
  - It is difficult to adhere to anti-TB treatment for 6-8 months or more
  - It is also difficult to predict which patients will adhere to self-administered treatment
  - One certain way to ensure patient adherence is through DOT where a trained supervisor watches the patient swallow the drugs

Basic principles of DOT, continued

- For patients who need admission, DOT should be started right away and supervised by the nursing staff
- For patients requiring no admission or for discharged patients, DOT may be supervised by staff of a nearby health facility, a trained community health worker, or a trained family member

DOT, cont'd

- Directly Observed Treatment Strategy (DOTS)

  DOTS is a strategy for TB control which aims to detect 70 percent of active TB cases and to successfully treat 85 percent of them. The essential features of DOTS include:

  - Government commitment to sustained TB control activities
  - Case detection by sputum smear microscopy among symptomatic patients self-reporting to health services
  - Directly observed, standardized treatment regimen of six to eight months

Directly Observed Treatment Strategy (DOTS), continued

- Efficient information systems for monitoring and reporting treatment outcomes
- A regular, uninterrupted supply of all essential anti-TB drugs

Table . WHO Recommended TB treatment regimen for each treatment category:

Treatment Category	Patients	Alternative TB Treatment Regimens	
		Initial Phase (Daily or 3 x/wk)	Continuation Phase
I	New smear-positive PTB; new smear-negative PTB with extensive parenchymal involvement; new cases of severe forms of extra-pulmonary TB	2 EHRZ (SHRZ)[a] 2 EHRZ (SHRZ) 2 EHRZ (SHRZ)	6 HE 4 HR 4 H_3R_3[b]
II	Previously treated smear-positive PTB: relapse; treatment failure; treatment after interruption	2 SHRZE/1 HRZE 2 SHRZE/1 HRZE	5 $H_3R_3E_3$ 5 HRE
III	New smear-negative PTB (other than category I); new less severe forms of extra-pulmonary TB	2 HRZ 2 HRZ 2 HRZ	6 HE 4 HR 4 H_3R_3
IV	Chronic case (still sputum positive after supervised re-treatment)	NOT APPLICABLE: refer to WHO guidelines for use of second-line drugs in specialized cntrs	

WHO Recommended TB treatment regimen, continued

N.B. Some authorities recommend 7 month continuation phase with daily isoniazid and rifampicin (7HR) for Category 1 patients with various forms of disease: TB meningitis, military TB, spinal TB with neurological signs.

Examples:

a. **2 HRZE / 6 HE**: This is a common regimen. The *initial phase* is **2 HRZE**. The duration of the phase is 2 months. Drug treatment is daily (no subscript number, e.g., $_3$, after the letters), with isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E). Alternatively, streptomycin (S), isoniazid (H), rifampicin (R), pyrazinamide (Z).

The *continuation phase* is **6 HE**. The duration of the phase is 6 months. Drug treatment is daily, with isoniazid (H) and ethambutol (E).

WHO Recommended TB treatment regimen, continued

b. 4 H_3R_3: In some countries, resources are available to provide rifampicin in the continuation phase as well as in the initial phase.

The *initial phase* is **2 $H_3R_3Z_3E_3$.** The duration of the phase is 2 months. Drug treatment is 3 times per week (subscript number $_3$ after the letters). The *continuation phase* is **4 H_3R_3**. The duration is 4 months, with izoniazid and rifampicin three times per week (subscript number $_3$ after the letters).

WHO 1997

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 (i.e., a CD4 count <200/mm^3 or the presence of disseminated TB).

Antiretroviral Therapy for Individuals with Tuberculosis Co-infection, continued

- In cases where a person needs TB and HIV treatment concurrently, first line treatment options include ZDV/3TC or d4T/3TC plus either an NNRTI or ABC.
- Except for SQV/r, PIs are **not** recommended during TB treatment with rifampicin due to its interactions with the latter drug

Table X. Antiretroviral Therapy for Individuals with Tuberculosis Coinfection

Situation	Recommendation
Pulmonary TB and CD4 count < 50/mm^3 or extrapulmonary TB	Start TB therapy. Start one of the non-PI regimens listed below concurrently with TB therapy • ZDV/3TC/ABC[a] • ZDV/3TC/EFV • ZDV/3TC/SQV/r[b] • ZDV/3TC/NVP
Pulmonary TB and CD4 50-200/mm^3 or total lymphocyte count <1200/mm^3	Start TB therapy with one of these regimens after 2 months of TB therapy: • ZDV/3TC/ABC[a] • ZDV/3TC/EFV • ZDV/3TC/SQV/r[b] • ZDV/3TC/NVP
Pulmonary TB and CD4 >200/mm^3 or total lymphocyte count 1200/mm^3	Treat TB. Monitor CD4 counts if available. Start ART as indicated in Table A4, 2.1 in Part One/Module 4/Session 2:

[a] NOTE: Subsequent research does not support this regimen. [b] NOTE: According to current research, the option of 2 NRTIs and a ritonavir-enhanced PI or nelfinavir should not be used as a first choice. Such a regimen should only be used if a NNRTI regimen is not indicated, e.g., in the case of an HIV-2 infection or if a patient presents with side effects to EFV or NVP. From WHO 1997

Prevention

TB Preventive Therapy

- **Evidence shows it is effective in HIV-infected people**
- **Can be given to people with HIV who:**
  - have been screened to exclude active TB
  - are PPD positive (Mantoux test ≥5mm)
  - have not been BCG vaccinated
  - have a high TB risk

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