

HIV and TB Coinfection

Norman Bernstein, MD, FACP
Medical Director, Infectious Diseases
MWH



Introduction

- Definition of Terms
- Overview of HIV
 - Understanding immunology of HIV
 - CDC statistics
- Effect of TB on HIV
- Effect of HIV on TB
- TB treatment
- Unique issues in TB care of HIV patients
- Review aspects of HIV/TB Coinfection that are of importance to the caregiver



Definition of Terms

- HAART – Highly Active Anti-Retroviral Therapy
- ART – Anti-Retroviral Therapy
- CD4 lymphocyte count – T4 helper cells
- HIV quantitative RNA PCR – Viral Load
- Co-infection – 2 infections that influence the progression of each other
- Opportunistic infection – an infection that takes the opportunity in the (HIV) immuno-compromised state to present itself in an aggressive way



Overview of HIV

- Estimated 42 million people infected with HIV worldwide; >25% have active TB.
- Most patients live in countries with limited health care resources in Africa and Asia.
- Nevertheless, USA is affected by these health care results:
 - Immigrants
 - Refugees
 - Travelers
 - Tourists
 - Business
 - War
 - Diplomacy



Overview of HIV

- HIV infection is the strongest known risk factor for progression from latent to active TB.
- TB is the leading cause of death for people with HIV/AIDS worldwide
- CD4 lymphocyte count values reflect the immune response
 - >500 – normal
 - 200-500 – zoster, pulmonary TB
 - <200 – opportunistic infection Higher Frequency Extra Pulmonary TB



Understanding Immunology of HIV





Slow train =
low HIV
viral load

*Where is the
train on
the track?*

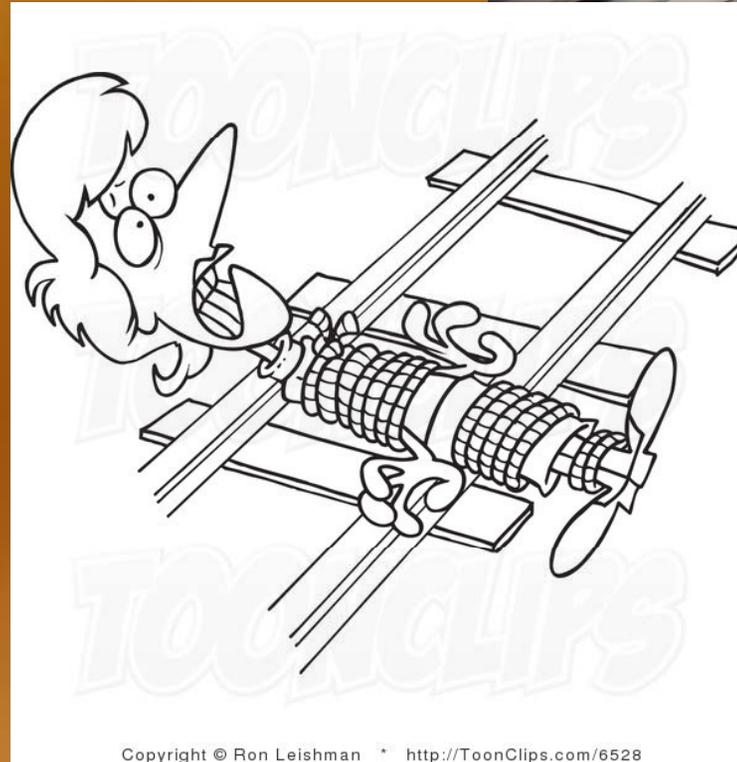
Fast train =
high HIV
viral load

*Where is
the train on
the track?*





High viral load +



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Low CD4 count

= *not in therapy*

Overview of HIV

- All HIV patients should be in care
- Options:
 - Inexperienced providers
 - Experienced providers
 - Ryan White Program providers
- What should you expect?

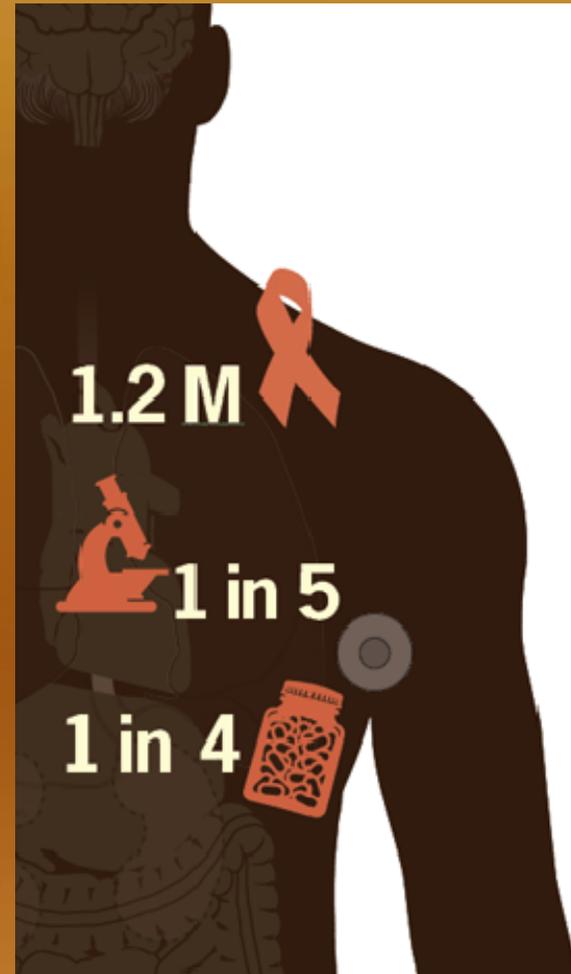


Overview of HIV

About **1.2 million people** in the US are living with HIV.

Nearly **1 in 5 people with HIV** don't know they are infected, don't get HIV medical care, and can pass the virus on to others without knowing it.

Only 28% of people with HIV are taking HIV medicine regularly and have their virus under control.



For every 100 people living with HIV

80 are aware of their infection

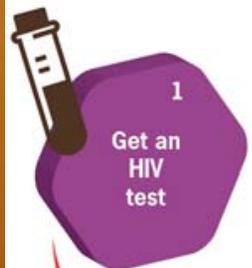
62 are linked to HIV care

41 stay in HIV care

36 get antiretroviral therapy

28 have a very low amount of virus in their body

Route to healthy living with HIV and preventing new infections



Lower amount of virus means

- Better health
- Longer life
- Fewer new infections
- Helping to stop HIV in the US

Overview of HIV

- Psychiatric morbidity
 - Major depression and substance disorders are frequent co-occurring psychiatric disorders in persons living with HIV/AIDS
- Psychosocial issues
 - Confidentiality
 - Stigma
 - Support system
 - Domestic abuse

Effect of TB on HIV

- TB increases HIV viral replication
- Immune activation
- Increased risk of progression to AIDS
- Overlapping toxicities, drug interactions and complications



Effects of TB on HIV

Other Examinations to Conduct When TB Treatment Is Initiated

- Counseling and testing for HIV infection (HIV antibody test)
- CD4+ T-lymphocyte count for HIV-positive persons
- Hepatitis B and C serologic tests, if risks present

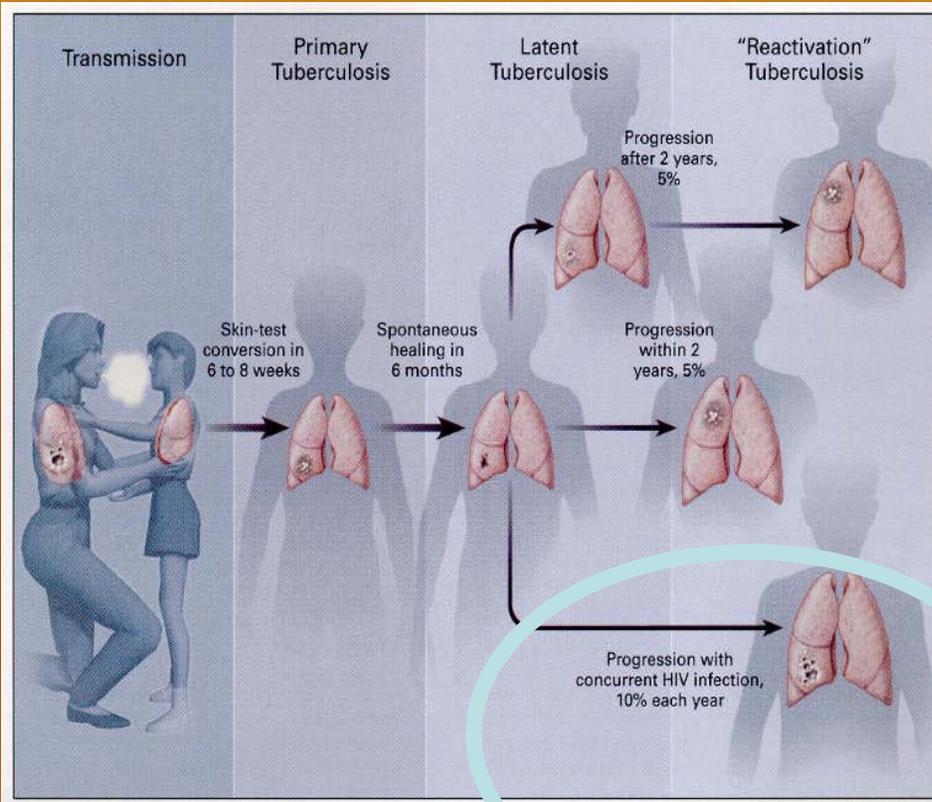


Effect of HIV on TB

- Most potent risk factor for development of TB
 - 100-fold
 - All forms of TB
- Yearly risk: 7-10%
 - vs. *lifetime* 5-15% in HIV negatives
- Increased risk of death
 - Regardless of CD4 count
- Hardest to diagnose
 - Smear negative disease, EPTB, cryptic/disseminated disease
- Risk of undiagnosed disease



HIV/TB: Profound Effect on Individuals



The annual risk of TB in HIV infected approximates the lifetime risk of HIV uninfected

Small and Fujiwara, N Eng J Med 343:189, 2001



Mary Washington Healthcare

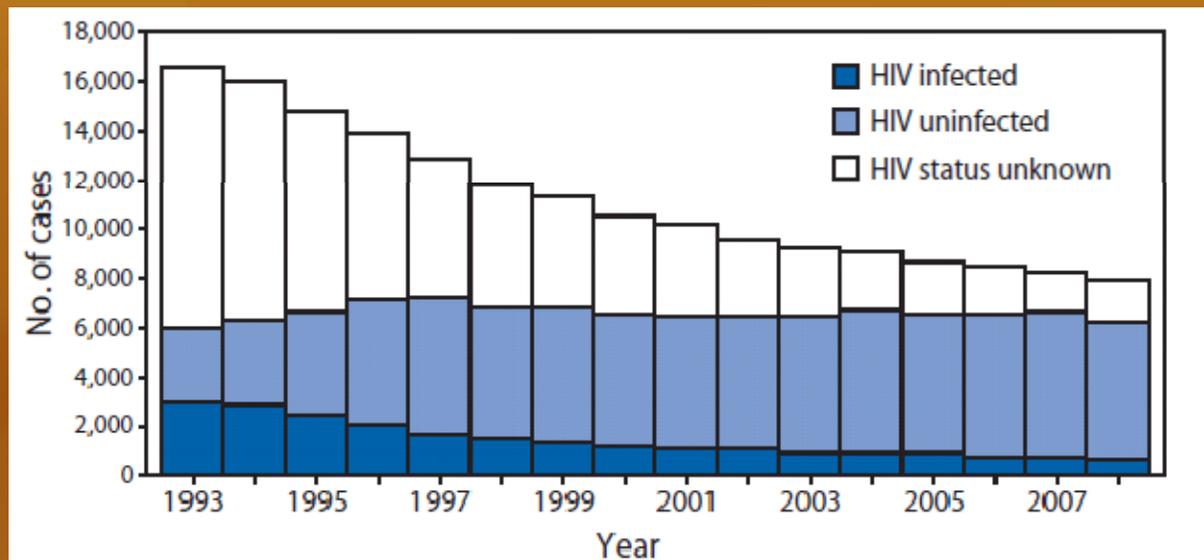
Effect of HIV on TB

- With falling CD4 counts, rates of anergy increase
- PPD ≥ 5 mm is considered positive
- No significant difference in outcomes in LTBI rx of non-anergic patients (no mortality impact)
- Repeating TST in patients with immune reconstitution
 - 11% of PPD negative patients with CD4 < 200 will be noted to be PPD+ when re-tested after CD4 > 200
- IGRAs Interferon gamma release assay
 - Might be better at screening
 - Quantiferon Gold or T-Spot



Effect of TB on HIV

Number of culture-confirmed tuberculosis patients with a recorded HIV test result, by HIV infection status --- United States,* 1993—2008

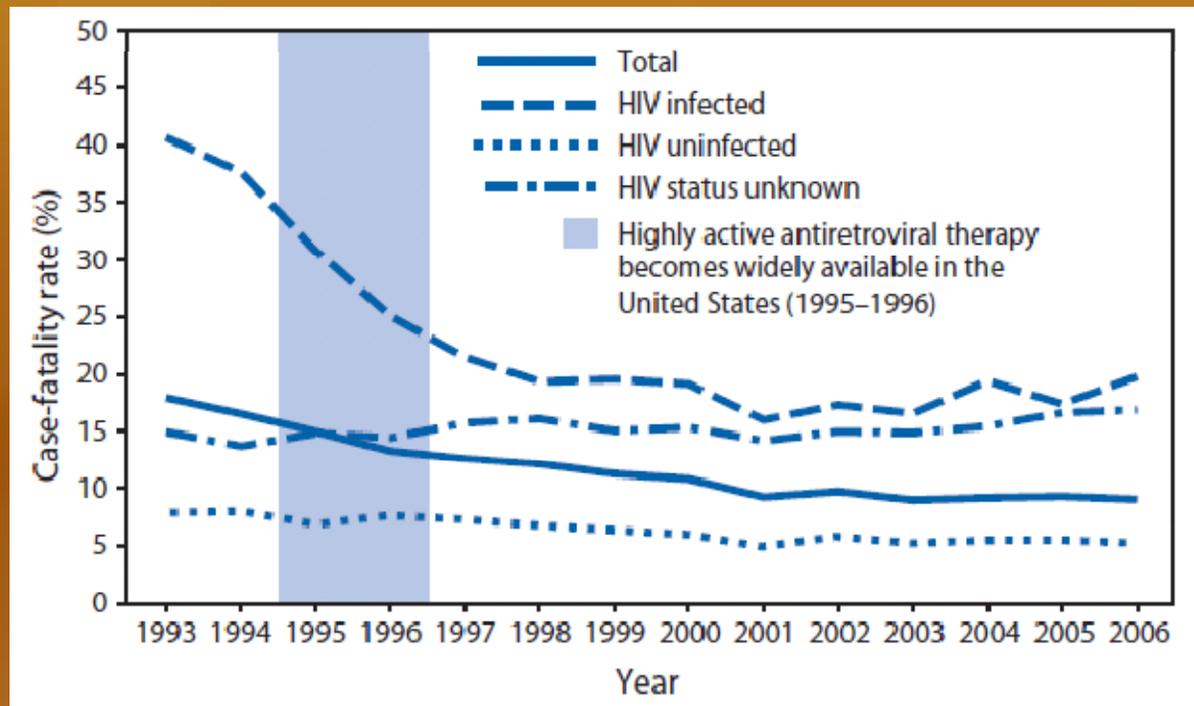


* Excludes California data because of lack of HIV data on patients with tuberculosis without AIDS.

Alternate Text: The figure above shows the number of culture-confirmed tuberculosis patients with a recorded HIV test result, by HIV infection status, in the United States during 1993-2008. The proportion of patients with TB who had documented HIV test results increased substantially, from 6,015 of 16,507 (36%) in 1993 to 6,234 of 7,872 (79%) in 2008.

Effect of TB on HIV

Case-fatality rates among culture-confirmed tuberculosis patients who were alive at diagnosis and whose treatment outcomes were known, by HIV infection status --- United States,* 1993--2006



* Excludes California data because of lack of HIV data on patients with tuberculosis without AIDS.

Alternate Text: The figure above shows case-fatality rates among culture-confirmed tuberculosis patients who were alive at diagnosis and whose treatment outcomes were known, by HIV infection status, in the United States during 1993-2006. The proportion of patients with TB who had a known outcome and were alive at diagnosis but died during TB treatment decreased from 2,445 of 13,629 (18%) in 1993 to 682 of 7,578 (9%) in 2006.

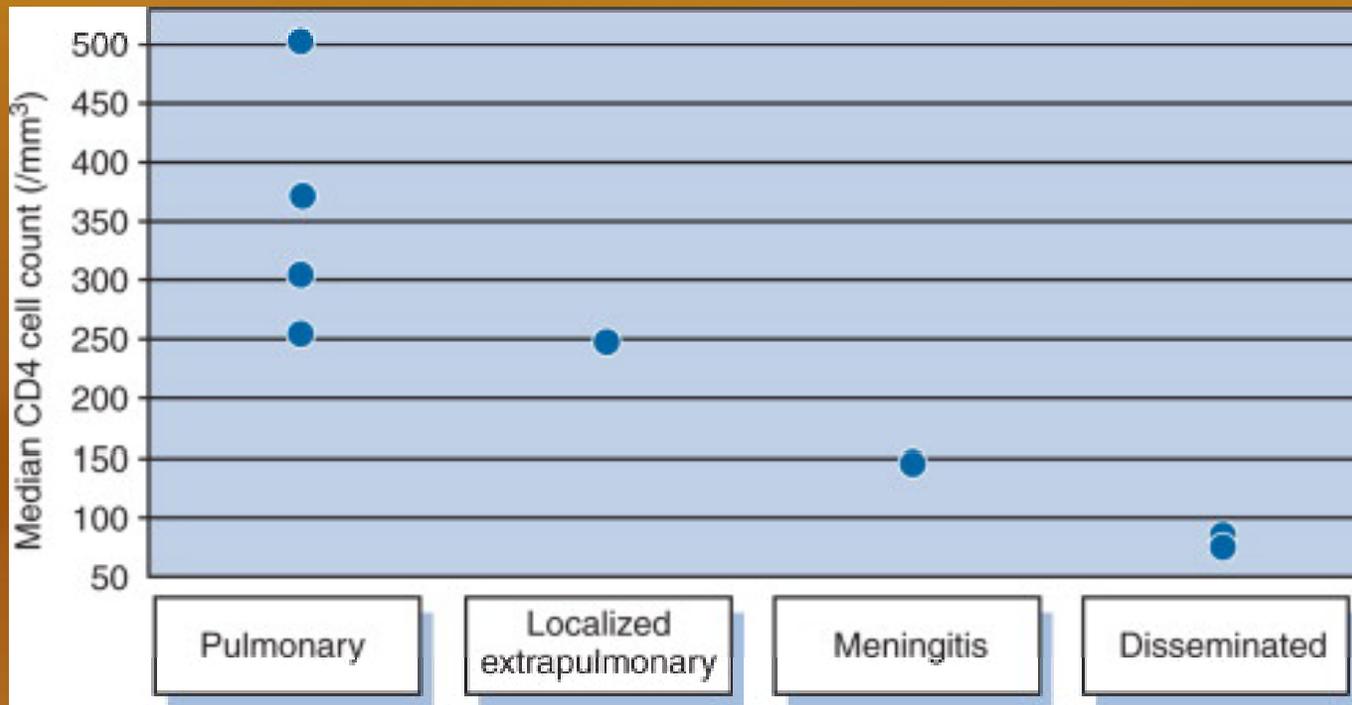
Effect of HIV on TB



Extensive bilateral pulmonary tuberculosis with upper zone predominance and lack of cavitation in a patient with advanced HIV infection (CD4 < 50).

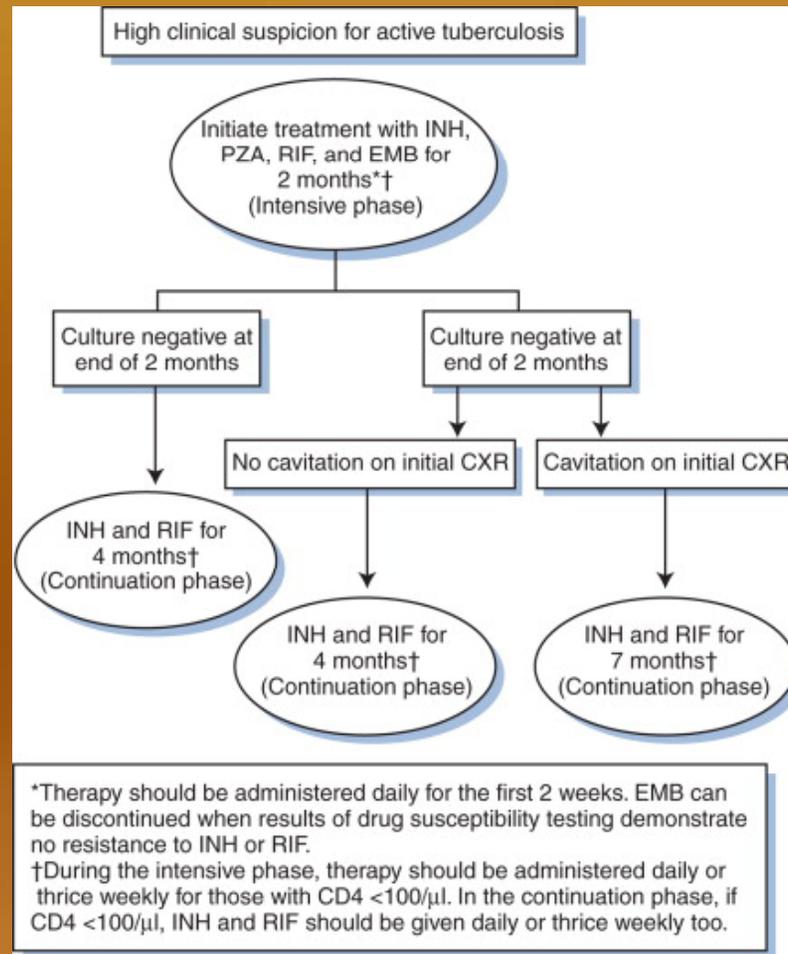


Effect of HIV on TB



Median CD4 counts (per mm³) in different groups of human immunodeficiency virus-positive patients with tuberculosis.
Adapted from De Cock KM, Soro B, Coulibaly IM, et al. Tuberculosis and HIV infection in sub-Saharan Africa. JAMA 268:1581-7, 1992.

Effect of HIV on TB



Treatment algorithm for pulmonary tuberculosis among those with HIV infection.
Adapted from American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America. *Treatment of tuberculosis. Am J Respir Crit Care Med* 167:603–62, 2003.

INH, rifampin, PZA, and ethambutol
(4 drugs, 10 pills once a day)



Burman WJ. CFAR Symposium 2005, Boston



Mary Washington Healthcare

Challenges to concurrent HIV and TB therapy

© Cartoon



"I've thrown in some prescription drugs that don't interact well."

- Pill burden
- Overlapping drug toxicities
- Pharmacokinetic drug-drug interactions
- Increased risk of immune restoration inflammatory syndrome
- *Keep checking the med list!*



INH, rifampin, PZA, ethambutol,
cotrimoxazole, AZT, 3TC, efavirenz (8 drugs,
14-16 pills, 2-3 doses per day)



“Are you sure that I won’t, like, blow up
if I take all of these pills?”



TB and HIV Coinfection: ART Recommendations (2)

- What antiretroviral regimens can be used concurrently with TB therapy?
- Toxicities
- Concerns
- How should patient be managed?



TB treatment

Rifamycins

- **Rifampin**

- **Rifabutin:**

- For patients receiving medications having unacceptable interactions with rifampin (e.g., persons with HIV/AIDS)

- **Rifapentine:**

- Used in once-weekly continuation phase for HIV-negative adults with drug-susceptible noncavitary TB and negative AFB smears at completion of initial phase of treatment



TB treatment

Treatment regimen observations

- **Rifampin \leq 2 months** - \uparrow treatment failure rate (worse with HIV)
- **CD4 $<$ 100** - \uparrow risk of rifamycin resistance if administered 1-2 times per week
- **Advanced HIV** – Rx rifamycin based regimen daily (5-7 days/week) for at least first 2 months

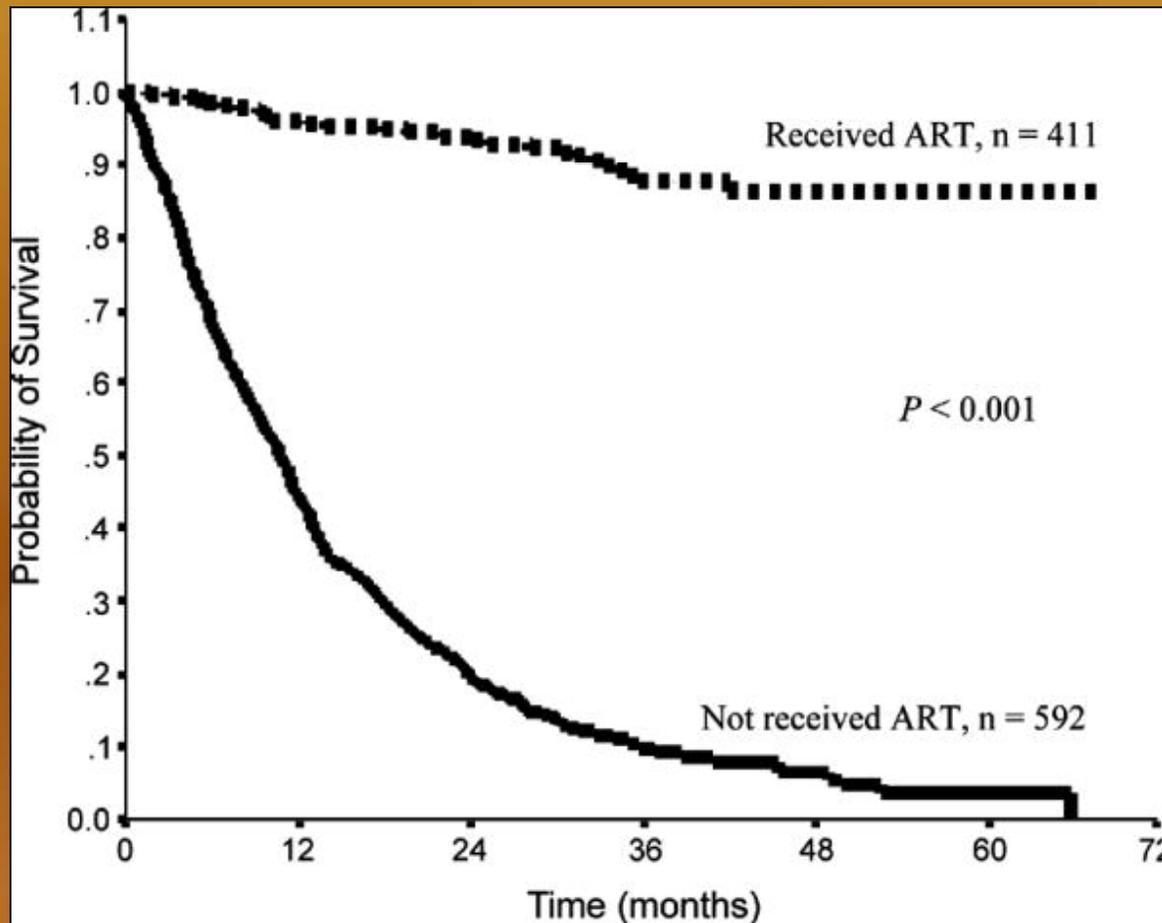
TB treatment

Adherence

- **Rifabutin Rx with HIV and pt on a PI**
Rifabutin dose decreased with PI
- **DOT for both TB and PI meds**



Effect of ART on survival



Concomitant HAART markedly improves survival in HIV-infected patients with HIV/TB co-infection. Manosuthi, W et al. JAIDS. 43(1):42-46



TB treatment

TB and HIV Coinfection: ART Recommendations (1)

- Patients not on ART:
 - Immediately initiate TB treatment
 - If CD4 count <50 cells/ μL : start ART within 2 weeks of starting TB treatment
 - If CD4 count ≥ 50 cells/ μL and clinical disease is severe: start ART within 2-4 weeks of starting TB treatment

March 2012

www.aidsetc.org



TB treatment

TB and HIV Coinfection: ART Recommendations ⁽¹⁾

- Patients not on ART (Continued):
 - If CD4 count ≥ 50 cells/ μ L and clinical disease is not severe: ART can be delayed beyond 2-4 weeks of starting TB treatment but should be started within 8-12 weeks
 - If CD4 > 500 cells/ μ L: above recommendations are softer (BIII)

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TB and HIV Coinfection: ART Recommendations (2)

- Pregnant women:
 - Start ART as early as feasible
 - In some cases, augmented immune or inflammatory response may be present (eg, with meningitis, pericarditis, or respiratory failure); if severe/life-threatening, delay in ART initiation may be appropriate
 - Consult with experts
- Documented MDR or XDR TB
 - Start ART within 2-4 weeks of TB drug resistance report and initiation of second-line TB therapy



Pregnant women and children

- Efavirenz is contraindicated during at least the first trimester of pregnancy
- Higher risk of hepatotoxicity in women with CD4 >250 cell/ μ L with nevirapine
- Efavirenz should not be used in children < 3 years old
- No drug-drug interaction studies in pregnant women
- Limited drug-drug interactions studies in children
- Triple nucleoside therapy may be used when options are severely limited



Unique issues in TB care for HIV patients

- Tuberculosis–associated Immune Reconstitution Inflammatory Syndrome (IRIS) and Unmasking of Tuberculosis by Antiretroviral Therapy
- Pregnancy and HIV
- Children and HIV



TB IRS



Unique issues in TB care for HIV patients

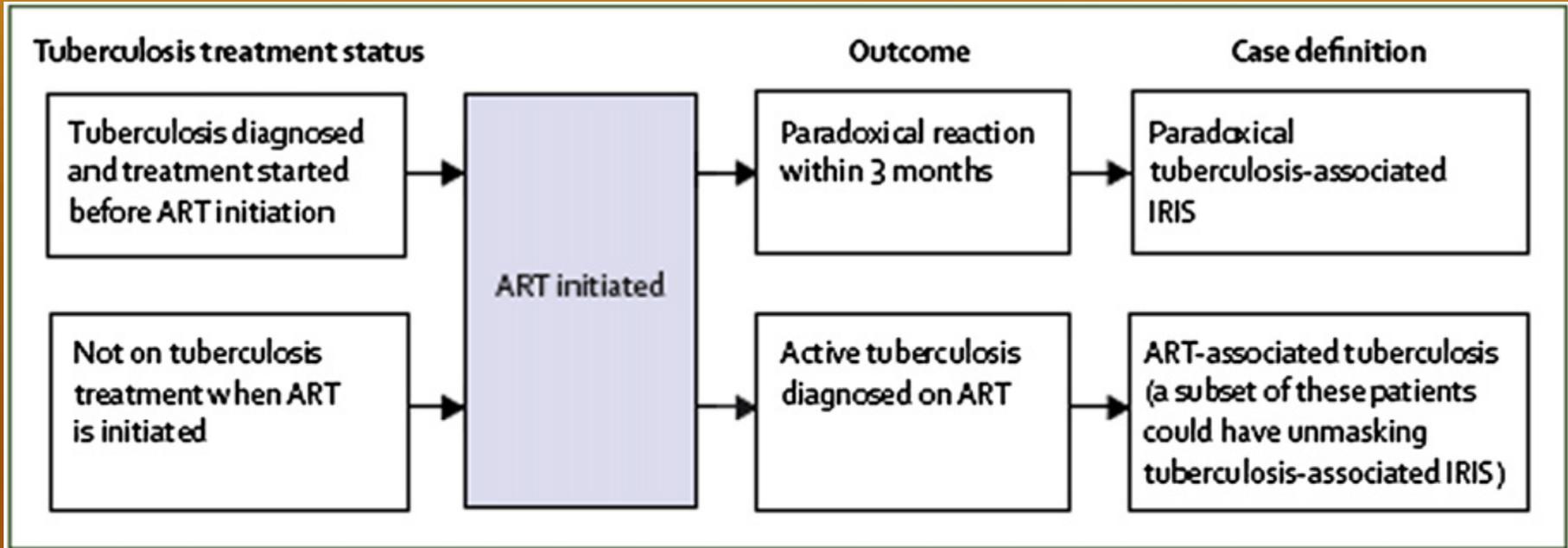


Fig.1. Different forms of TB-IRIS and ART-associated TB. (From Meintjes G, Lawn SD, Scano F, et al. Tuberculosis associated immune reconstitution inflammatory syndrome: case definitions for use in resource-limited settings. *Lancet Infect Dis* 2008;8(8):516–23; with permission.)

Unique issues in TB care for HIV patients



Fig. 2 TB abdominal lymphadenitis. A 21-year-old woman infected with HIV-1, with a CD4 count of 77 cells/mL, was diagnosed with pulmonary TB (*Mycobacterium tuberculosis* isolated from sputum, susceptible to rifampicin and isoniazid). She commenced ART.

Unique issues in TB care for HIV patients

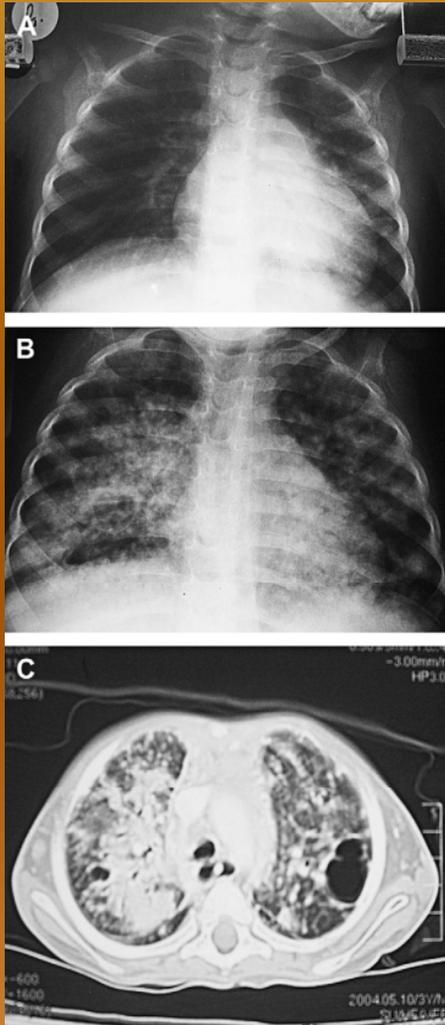


Fig. 3. Pediatric paradoxical TB-IRIS. A 3-year-old child infected with HIV-1, with severe immunosuppression, was diagnosed with drug-susceptible pulmonary TB and started on rifampicin, isoniazid, ethambutol, and pyrazinamide. Two weeks later the child started ART. Ten days after initiation of ART the child developed fever, respiratory failure, and exacerbation of pulmonary infiltrate with formation of multiple cavities

Immune restoration inflammatory syndrome (IRIS)

- Paradoxical worsening of TB symptoms on TB plus HIV therapy
- Incident TB (unmasked TB) within 4 months of starting ART in HIV-infected patients
- Risk factors include CD4 count < 50 , brisk response to HAART and extrapulmonary TB
- Immunopathological response to treatment
- Continue or initiate concurrent therapy
- Symptomatic therapy with NSAIDs or steroids may be necessary



Review/Summary

HIV-Related Tuberculosis

- Know your patient
- Know the med list
- Know the provider

Be cognizant of unusual symptoms and signs – such as IRIS

DOT may mean adherence to both TB and HIV meds

Be prepared for more than twice a week DOT

- The HIV-TB co-infection is associated with higher mortality
- The timing of concurrent ART should be individualized; in general it should be started as soon as TB therapy is tolerated – follow guidelines
- Efavirenz is preferred in setting of rifampin-containing TB therapy
- Both protease inhibitor or non-nucleoside reverse transcriptase inhibitors can be used with rifabutin

