NORTHWEST AIDS EDUCATION AND TRAINING CENTER

Tuberculosis Overview

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TB & HIV: Reasons to Pay Attention

- TB is the leading immediate cause of death worldwide among HIV-infected patients
- HIV co-infection present in 10% of TB cases nationwide
- TB accelerates HIV-related immunosuppression
  - Up-regulation of target cells
  - Increased viral load
  - Decreased survival
- HIV increases risk and velocity of development of active TB after acquisition of TB infection
- HIV alters clinical presentation of active TB

Tuberculosis Morbidity-NWAETC Region, 2010

State	Rate/100K	Cases	Foreign Born	US Born	Unknown
Alaska	8.0	57	8	40	9
Idaho	1.0	15	9	6	--
Montana	0.6	6	--	6	--
Washington	3.5	239	167	67	5
United States	3.6	11,182	6,720	4,393	69

Centers for Disease Control and Prevention. Tuberculosis in the United States, 2010.

Clinical Presentation of TB in HIV by CD4 Count

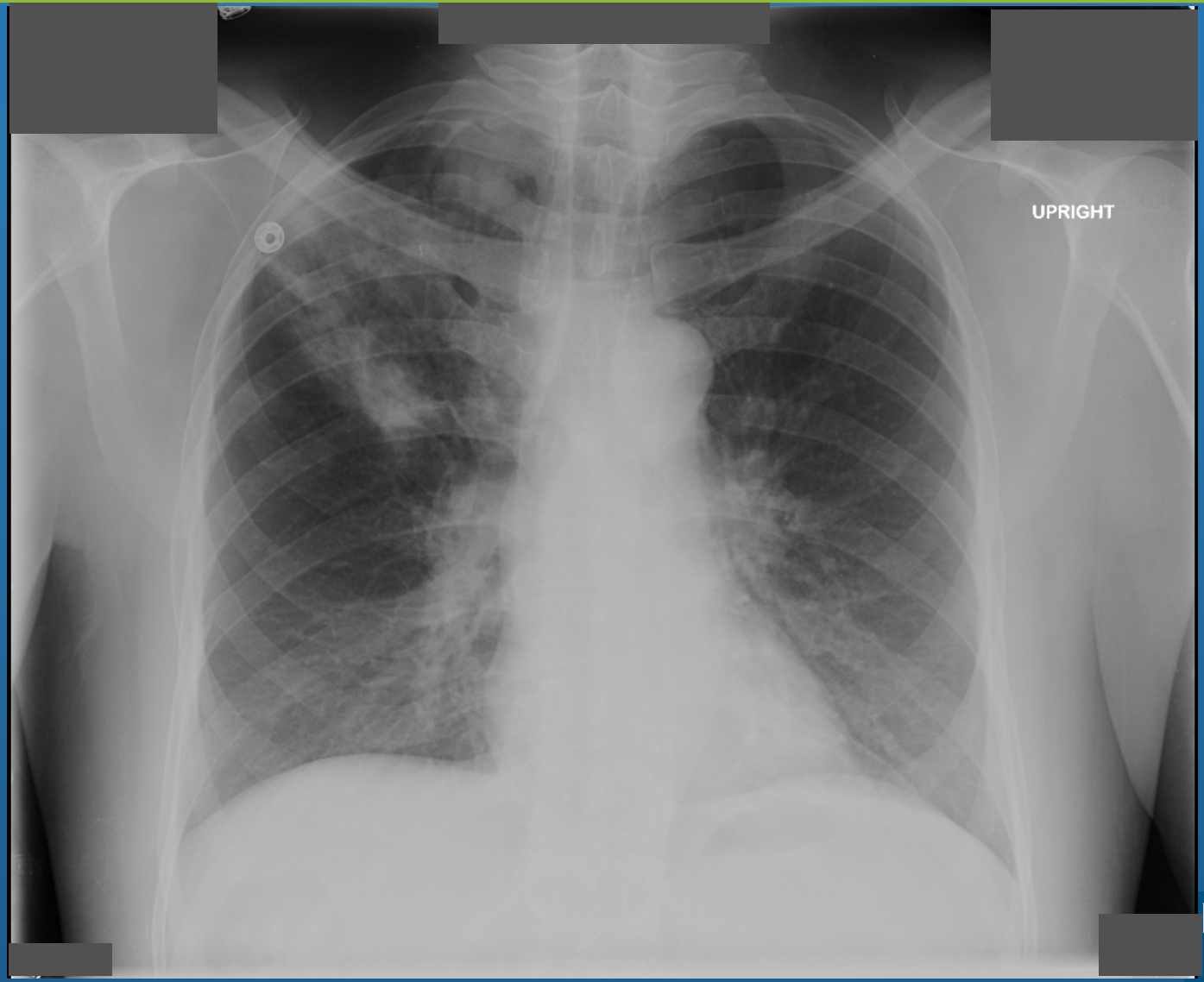
CD4 <200/ul

- Adenopathy
- Effusions
- Dissemination
- Extrapulmonary sites
- Smear-negative
- More IRIS

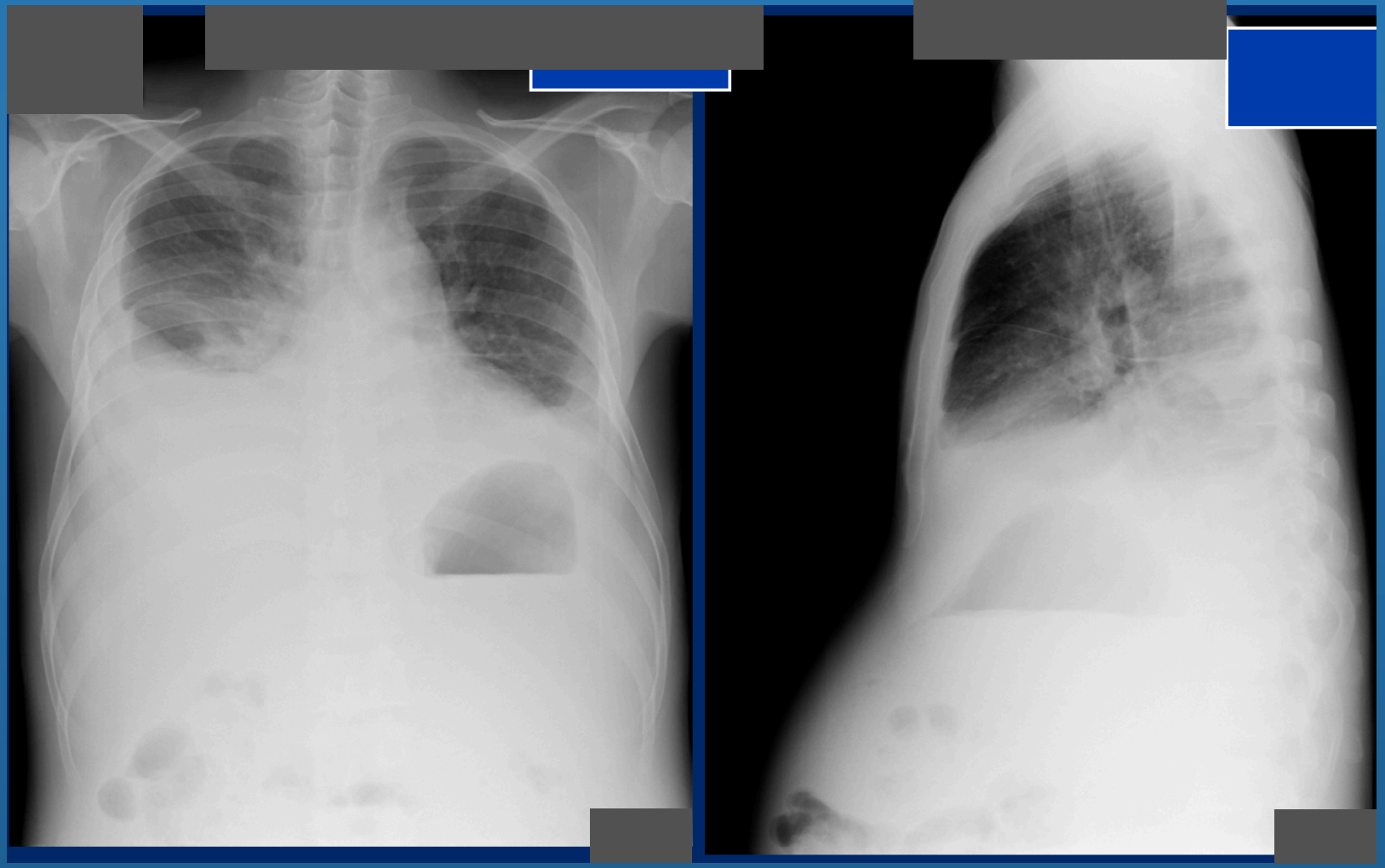
CD4 ≥200/ul

- Pulmonary
- Reactivation type
- Cavitation
- Less extrapulmonary
- Smear positive
- Less IRIS

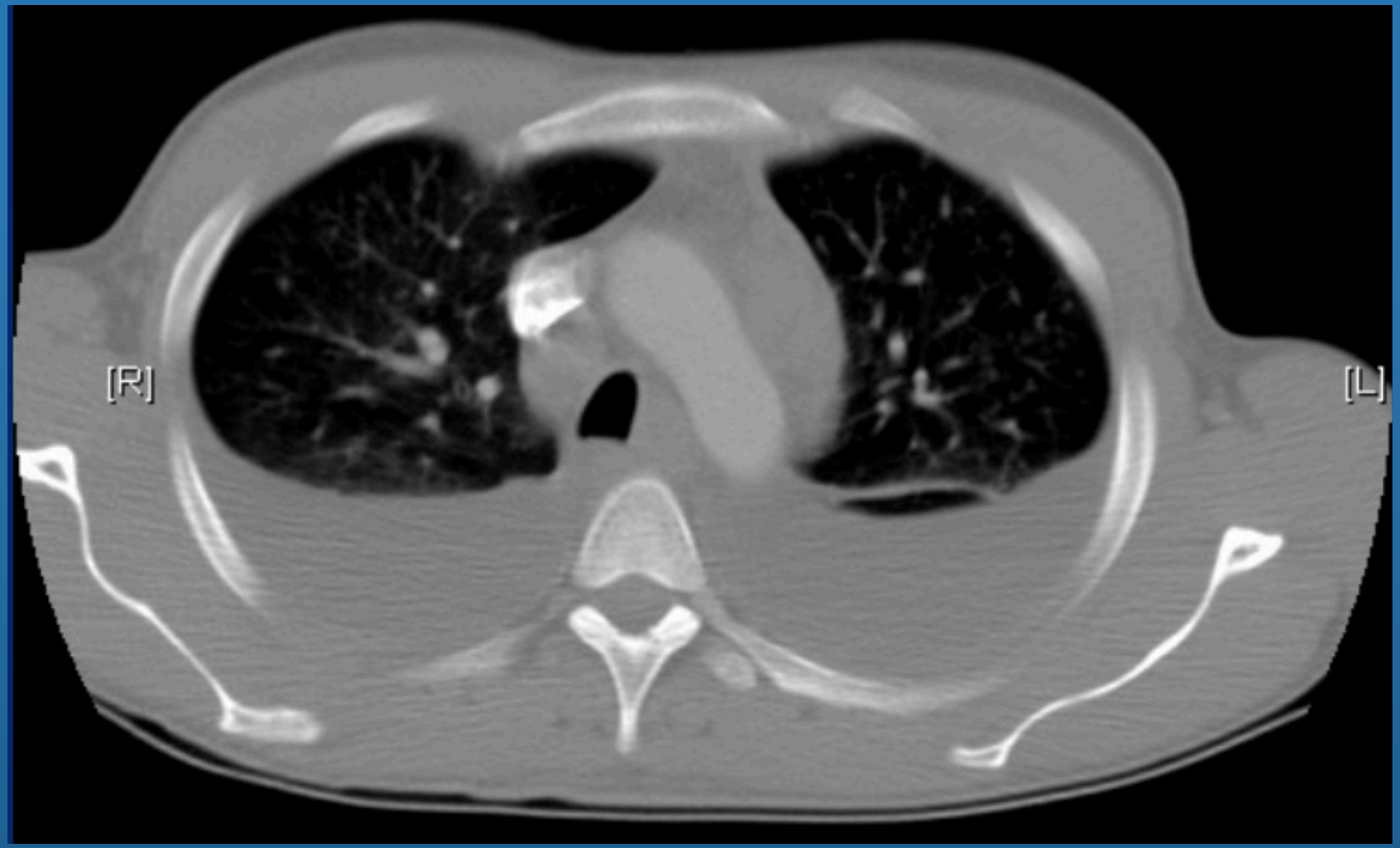
Common Radiographic Appearance of Chest TB CD4>200/ul



Common Radiographic Appearance of TB CD4<200/ul



Common Radiographic Appearance of Chest TB CD4<200/ul



Baseline Diagnostic Examinations for TB

- Imaging
- Sputum specimens
  - AFB smear, culture, and susceptibilities
  - nucleic acid amplification (NAAT)
- Extrapulmonary specimens
  - Chemistry, cell count and cytology on fluids
  - Routine pathology on tissues
  - AFB stain/smear and culture
  - NAAT on sputum, BAL, other fluids and unfixed tissues
  - ADA on pleural and peritoneal fluid
- Expedited molecular testing for drug resistance in special circumstances (rpoB, katG, inhA)
- TST and/or IGRA,CBC with differential, CMP, HIV, HBsAg, anti-HCV

Anti-TB Drugs

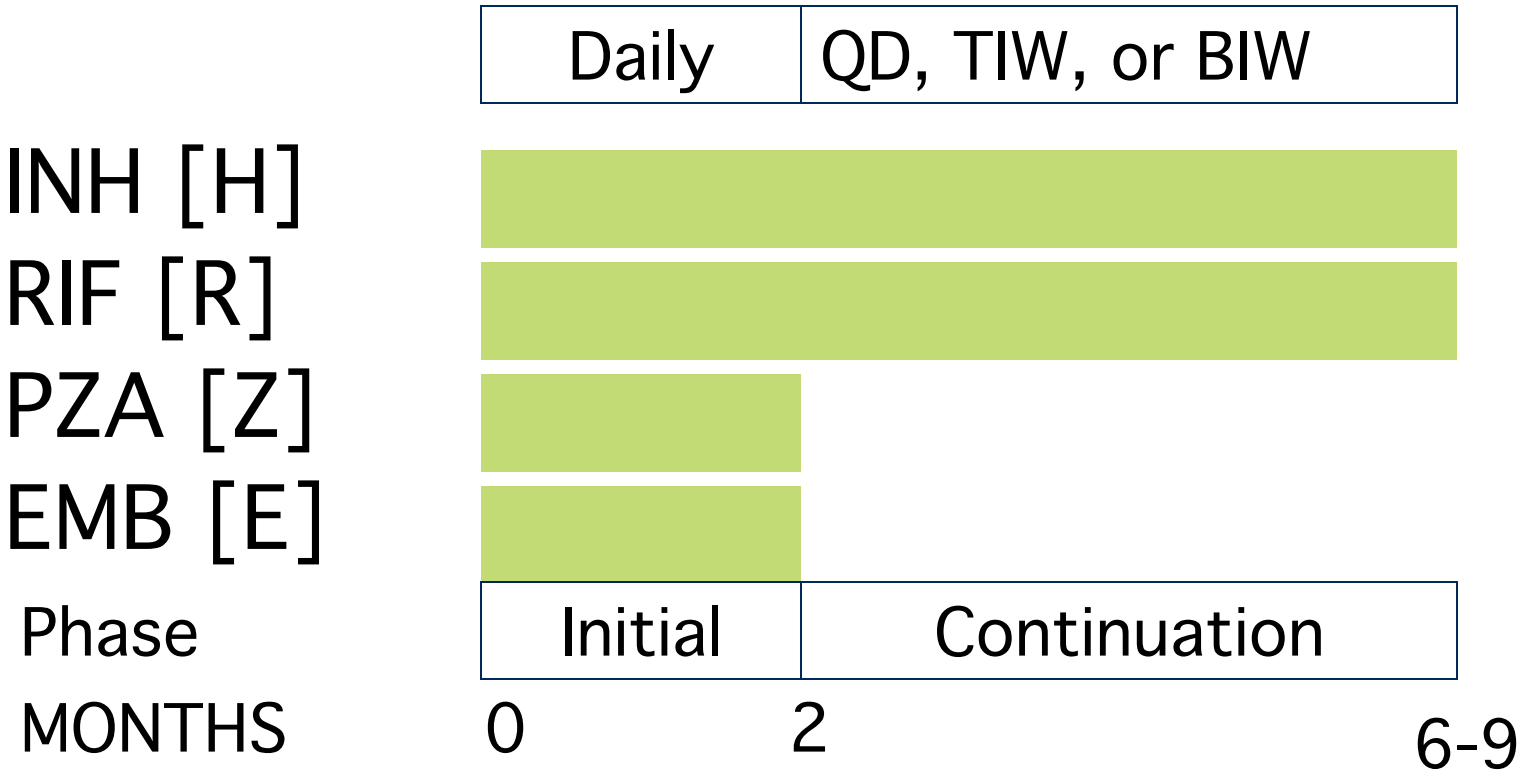
FIRST LINE

- Isoniazid (H)
- Rifampin (R)
- Pyrazinamide (Z)
- Ethambutol (E)
- Streptomycin (S)

SECOND LINE

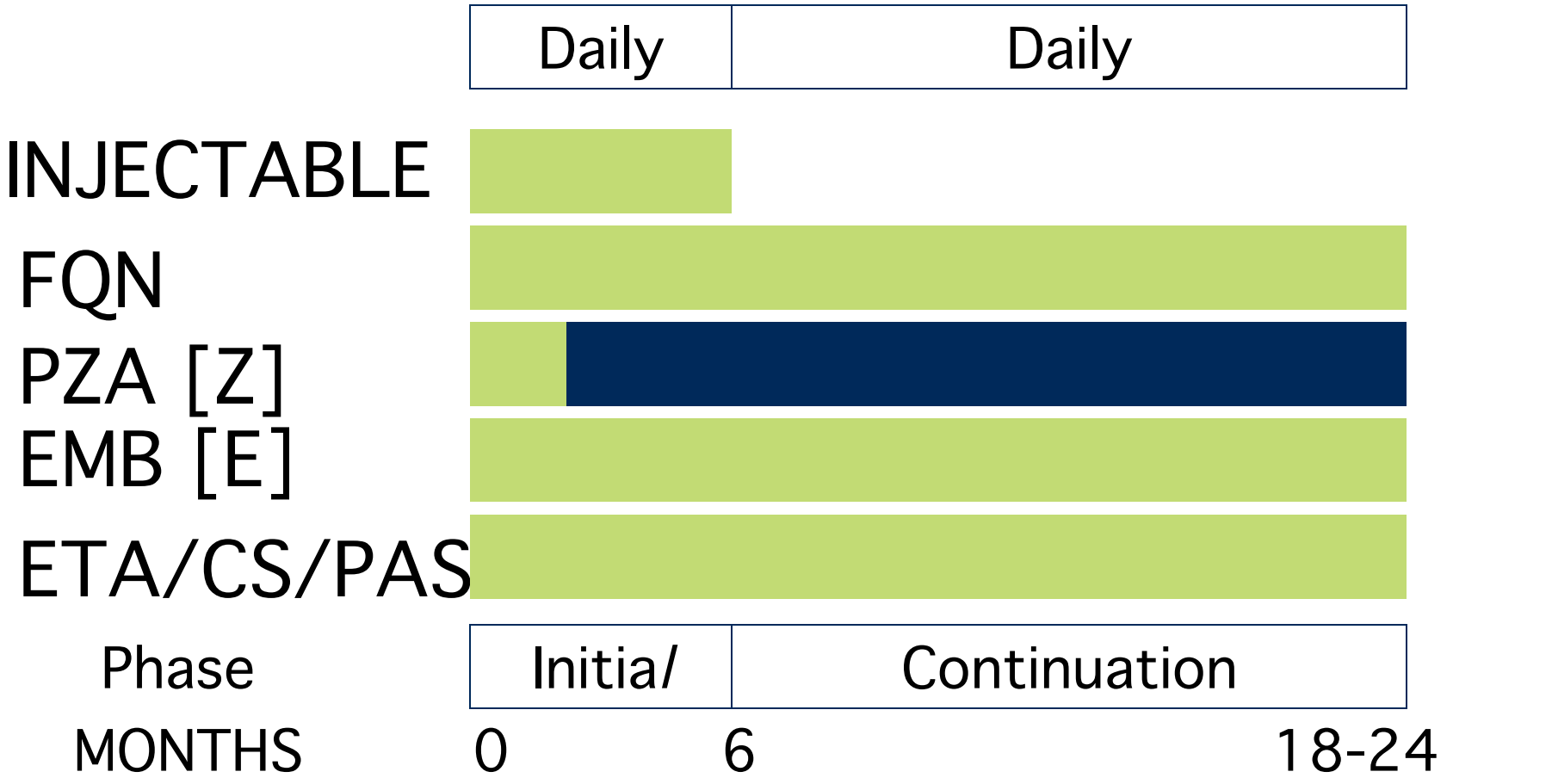
- Injectables (amikacin, kanamycin, capreomycin)
- Fluoroquinolones (moxifloxacin, levofloxacin)
- PAS, ethionamide, cycloserine

Standard Therapy for Active TB



American Thoracic Society. Treatment of Tuberculosis. AJRCCM 2003.

Typical MDR Regimen



WHO Recommendations for HIV/TB Co-infection Management

- Start ART in all HIV-infected individuals with active TB, irrespective of the CD4 cell count (strong recommendation, low quality of evidence)
- Start TB treatment first, followed by ART as soon as possible afterwards and within the first eight weeks (strong recommendation, moderate quality of evidence).
- Use efavirenz (EFV) as the preferred NNRTI in patients starting ART while on TB treatment (strong recommendation, high quality of evidence)

Source: ***Antiretroviral therapy for HIV infection in adults and adolescents: recommendations for a public health approach*** **— 2010 revision. Geneva: World Health Organization, 2010.**

Timing of ART Initiation in Newly Diagnosed HIV/TB

CD4 COUNT (cells/ul)	DURATION OF TB THERAPY @ ART INITIATION		
	<2 weeks	2-7 weeks	8-12 weeks
<50	A-I Conditional	A-I Strong	CNS TB A-I Strong
50-199		A-I Conditional	A-I Strong
200-349			A-I Strong
350-499			A-I Strong
≥500			B-I Conditional
CNS TB & ANY CD4			A-I Strong

Supporting references: see next slide

Timing of ART Initiation in Newly Diagnosed HIV/TB

- Blanc F-X, et. al. Early versus late initiation of antiretroviral therapy HIV-infected adults with tuberculosis. N Engl J Med 2011; 365:147
- Havlir DV, et. al. The timing of anti-retroviral therapy for HIV-1 infec and tuberculosis. N Engl J Med 2011; 365:1482-91.
- Abdool Karim SS, et. al. Integration of antiretroviral therapy with tuberculosis treatment. N Engl J Med 2011;365:1492-501.
- Torok ME, et. al. Timing of antiretroviral therapy in human immunodeficience virus (HIV)-associated tuberculous meningitis. C Infect Dis 2011;52(11):1374-1383.
- Nanteza MW, et. al. A Randomized Trial of Punctuated Antiretrovira Therapy in Ugandan HIV-Seropositive Adults With Pulmonary Tuberculosis and CD-4+ T-Cell Counts of ≥350 cells/uL. J Infect Dis 2011;204:884–92.
- Abdool Karim SS, et. al. Timing of Initiation of Antiretroviral Drugs d Tuberculosis Therapy. N Engl J Med 2010;362:697-706.

TST or IGRA for LTBI Diagnosis in HIV?

- Systematic review of 37 studies including 5736 participants
- **Questions**
  1) are IGRAs better than TST at predicting which HIV-infected individuals are at highest risk of progression to active TB?
  2) are IGRAs more sensitive than TST for diagnosis of MTB infection, particularly in HIV-infected individuals with advanced immunosuppression?
- **Answer**: insufficient evidence to favor one over the other
- **Observation**: IGRAs (T-SPOT in particular) may be less prone to perturbation by immunosuppression
- **Implications**:
  - No evidence based argument for promoting one methodology over another.
  - Consider dual testing w/ acceptance of any positive result as evidence of infection
  - Practice should be driven by local guidelines and logistics

Cattamanchi A, et. al. JAIDS 2011;56(3):230-238.

Regimen Options for Latent TB

Isoniazid	Daily or twice-weekly
Rifampin	Daily
Isoniazid + Rifapentine	q7d

WEEKS	0	12	18	39

http://www.cdc.gov/tb/topic/treatment/ltbi.htm

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Caveats to LTBI Regimen Selection

- Baseline health
- Active TB excluded with clinical evaluation, radiography, and (if indicated) sputum examination
- Isoniazid
  - Highest risk of liver injury
  - Also the strongest evidence base for efficacy
  - Usually accompanied by pyridoxine
- Once- and twice-weekly regimens should be closely supervised (CDC says “DOT”)
- Beware rifamycin drug interactions with cytochrome P oxidase system substrates
- Communication about adverse effects and what to do

TB/HIV Co-infection: Key Points

- TB presents with more lymphatic, other extrapulmonary, and disseminated involvement among severely immunosuppressed patients (e.g.,CD4 <200/ul).
- Standard initial regimen for active TB in previously untreated patients is isoniazid, rifampin, pyrazinamide, and ethambutol (plus pyridoxine)—involve the local TB control program from the outset for DOT, case management, and contact investigation. Avoid (or anticipate) rifamycin-ART drug-drug interactions.
- Get expert consultation if drug resistance suspected or drug intolerance emerges.
- Test and treat for latent TB in patients with epidemiologic risk factors. There is no evidence to support using one LTBI testing modality over another. Many experts use both in HIV infecion.
- Isoniazid is the preferred agent for treatment of LTBI among HIV infected patients who do not have active liver disease.