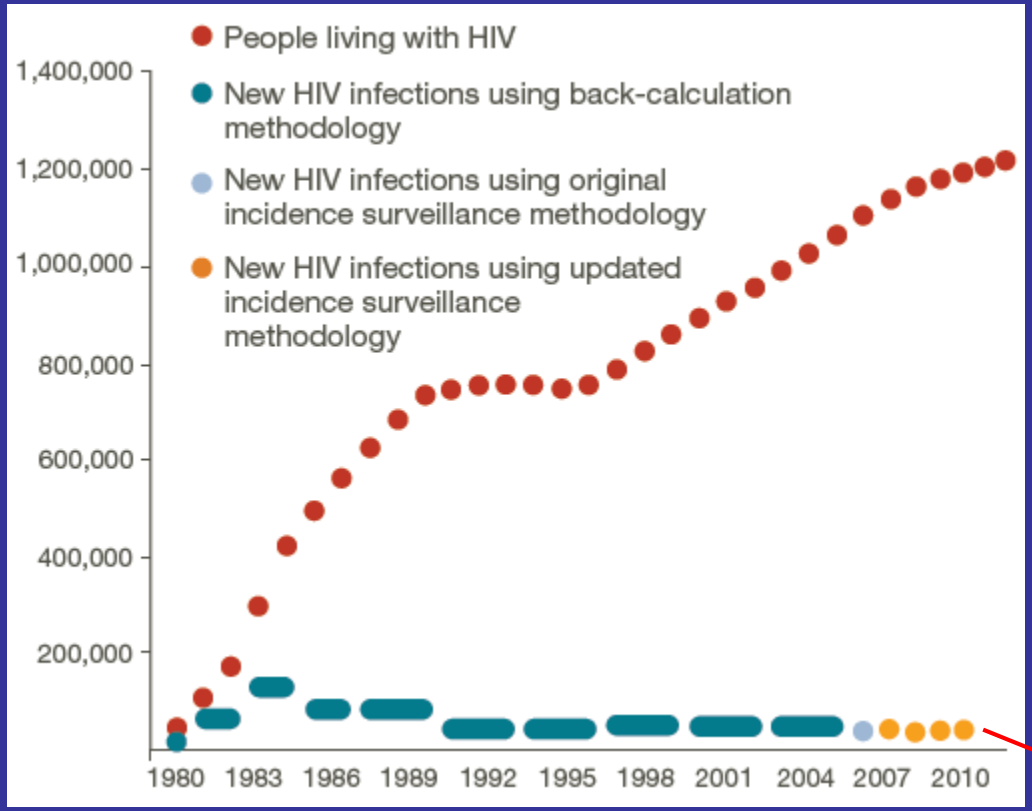
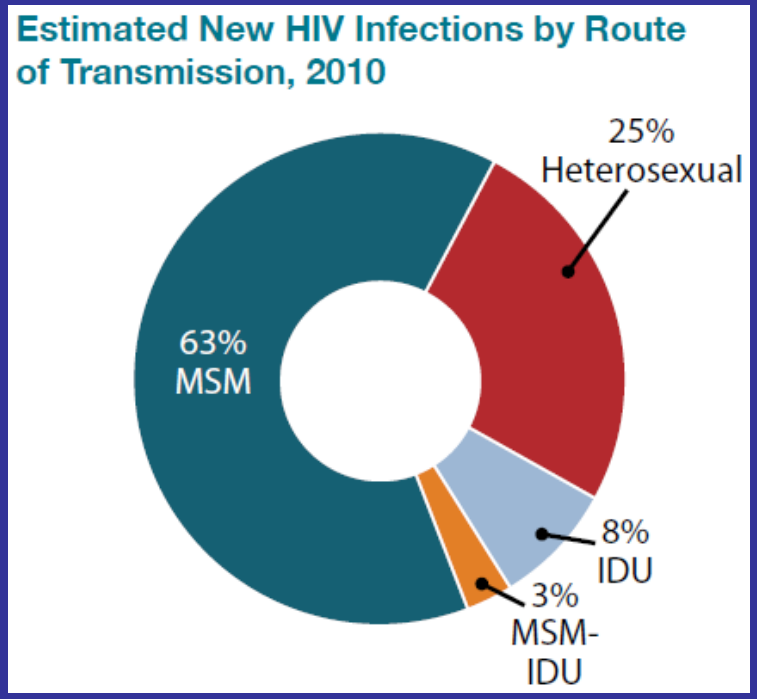
HIV / AIDS
&
Opportunistic Infections

www.hivma.org

Epidemiology





45,700 → 39,000
Annual new diagnoses
2008-2013

~85% know they are infected
~50% are virally suppressed

http://www.cdc.gov/nchhstp/newsroom/

22F presents for a follow-up appointment. She was just diagnosed with syphilis last week and treated with IM PCN. At that visit an HIV test was performed and returns with the result below.

HIV 1/2 Ag/Ab Screen (4th Gen)	HIV 1/2 Ag/Ab Screen (4th Gen) * A Auth (Verified)
HIV 1/2 Ag/Ab (4th Gen) Comment	See Comment * Auth (Verified)
HIV 1 Antibody	Positive A Auth (Verified)
HIV 2 Antibody	Negative * Auth (Verified)

What is her likely diagnosis?

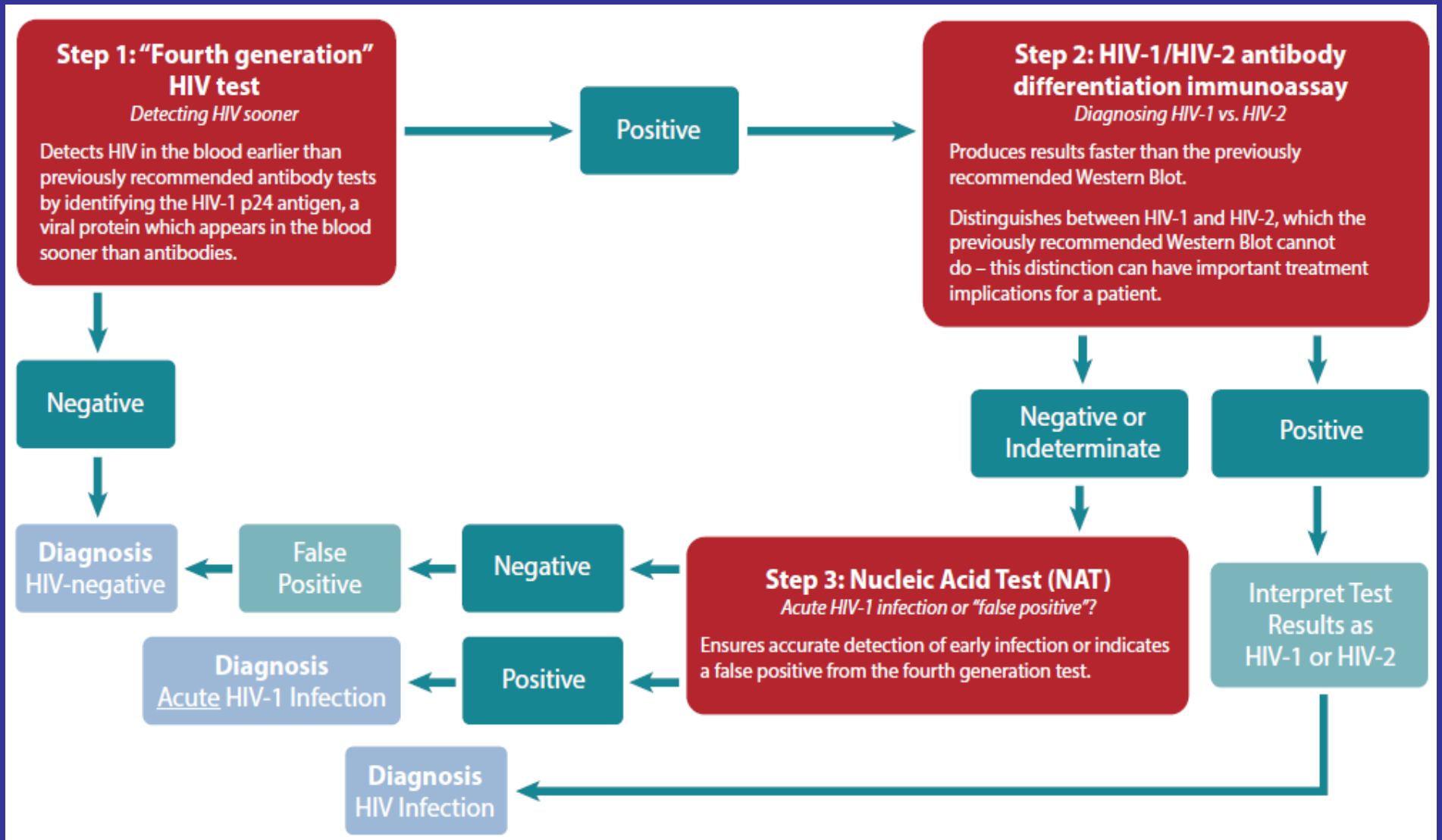
A. HIV-1 infection
B. HIV-2 infection
C. Suspected HIV-1, but need to wait for confirmatory test result

- Virtually all HIV in the U.S. = HIV-1
- Who should be tested?

Adolescents and Adults 15-65 Years Old	The USPSTF recommends that clinicians screen for HIV infection in adolescents and adults aged 15 to 65 years. Younger adolescents and older adults who are at increased risk should also be screened. Go to the Clinical Considerations for more information about screening intervals.	A
Pregnant Women	The USPSTF recommends that clinicians screen all pregnant women for HIV, including those who present in labor who are untested and whose HIV status is unknown.	A

- HIV testing:
  - HIV-1/2 Antigen and Antibodies, 4th Gen, with Reflexes
    - Reflex HIV-1/2 antibody differentiation test
    - Reflex PCR for indeterminate/negative results
    - CDC recommended screening test
    - Better sensitivity within window period, faster TAT
  - HIV-1/0/2 with Reflex HIV-1 WB

CDC Recommendations for HIV Testing in Laboratories

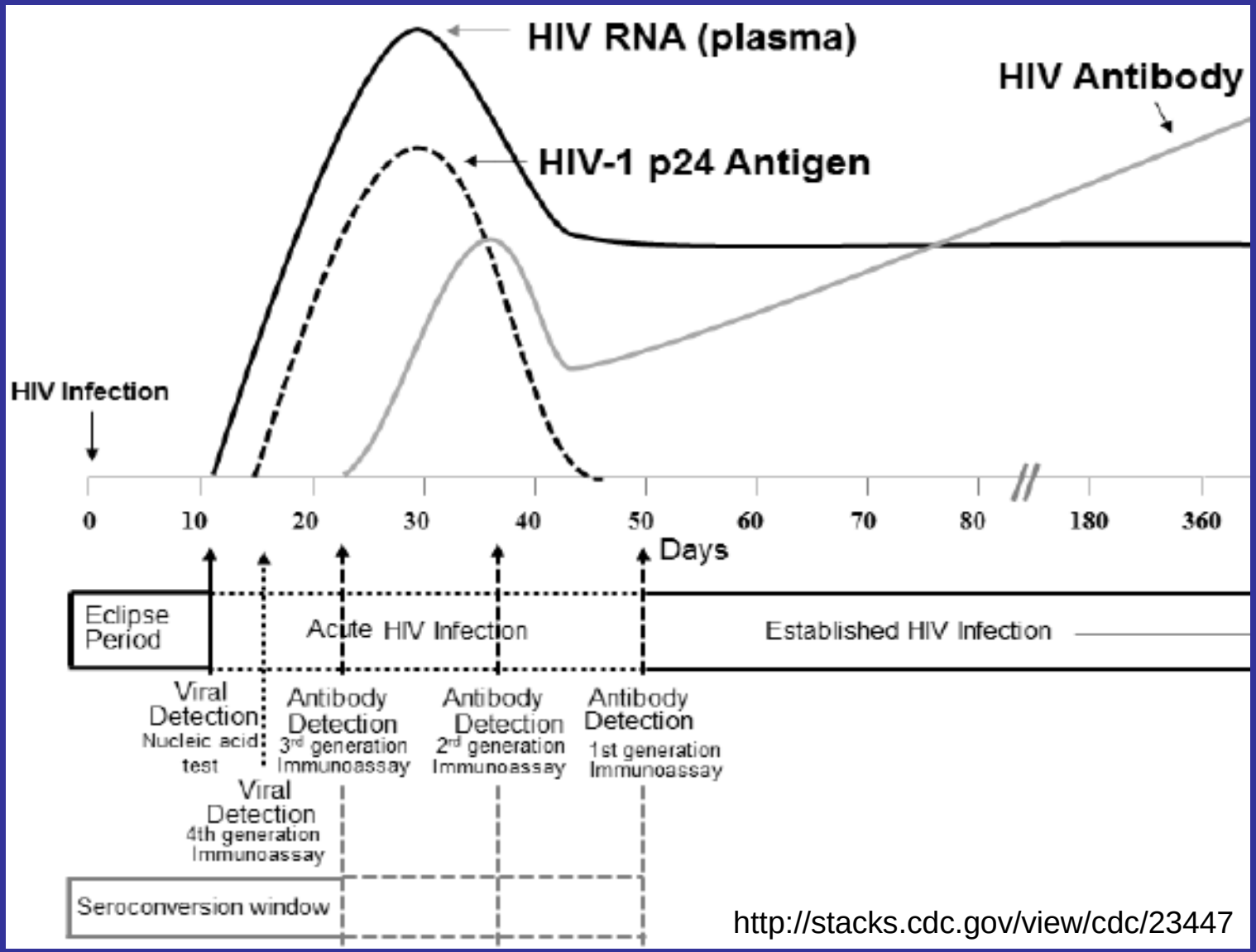


22F presents with fevers & sore throat for the past 3 days and now has developed diffuse macular rash starting today. Examination reveals T 39^0C, pharyngeal erythema without exudate, small erythematous macular lesions on her chest. She reports exchanging sex for drugs and has had multiple partners over the past month.

Which of the following test is optimal for diagnosis?

A. HIV-1/0/2 with reflex HIV-1 WB
B. HIV-1/2 antigen and antibodies, 4^{th} Gen, with reflexes
C. HIV p24 antigen assay
D. HIV quantitative RT-PCR
E. Monospot (for EBV)

Window Period



http://stacks.cdc.gov/view/cdc/23447

22F is here for follow-up with new diagnosis of HIV after routine STI screening. She is without any symptoms. Exam unremarkable other than anxious appearing individual and white plaques on her soft palate. Routine blood tests are sent including CD4 count, HIV quantitative RT-PCR, and HIV genotype resistance testing. A TST is placed.

Which of the following should be performed immediately?

A. Pneumococcal vaccination with PPV23
B. Start antiretroviral therapy
C. Start Trimethoprim/Sulfamethoxazole
D. Start Trimethoprim/Sulfamethoxazole and Azithromycin
E. Chest radiograph

Primary Care for HIV

HIV-disease tests

Serologic testing
CD4 count and percentage
Plasma HIV RNA (viral load)
HIV resistance testing (genotype)

Metabolic tests

Fasting lipid profile
Fasting glucose
Urinalysis

HIV-associated infections

Viral hepatitis (A,B,C)
STD screening
Syphilis
Gonorrhea/Chlamydia
Tuberculosis screening
HPV - cervical cancer screening

Vaccinations

PCV13 followed by PPV23 (>8 wks)
HBV - if seronegative
HAV - if MSM, IVDA
HPV - males to age 26, if MSM
MCV4

Adapted from Clin Infect Dis 2009; 49:651-81

22F is here for follow-up with new diagnosis of HIV after routine STI screening. She is without any symptoms. Exam unremarkable. Her CD4 count is 650 and VL 10,000 copies/mL. The remainder of her lab studies are normal including resistance testing. She is very interested in starting cART. She reports that she is in a heterosexual monogamous relationship.

When is the ideal time to start cART for this patient?

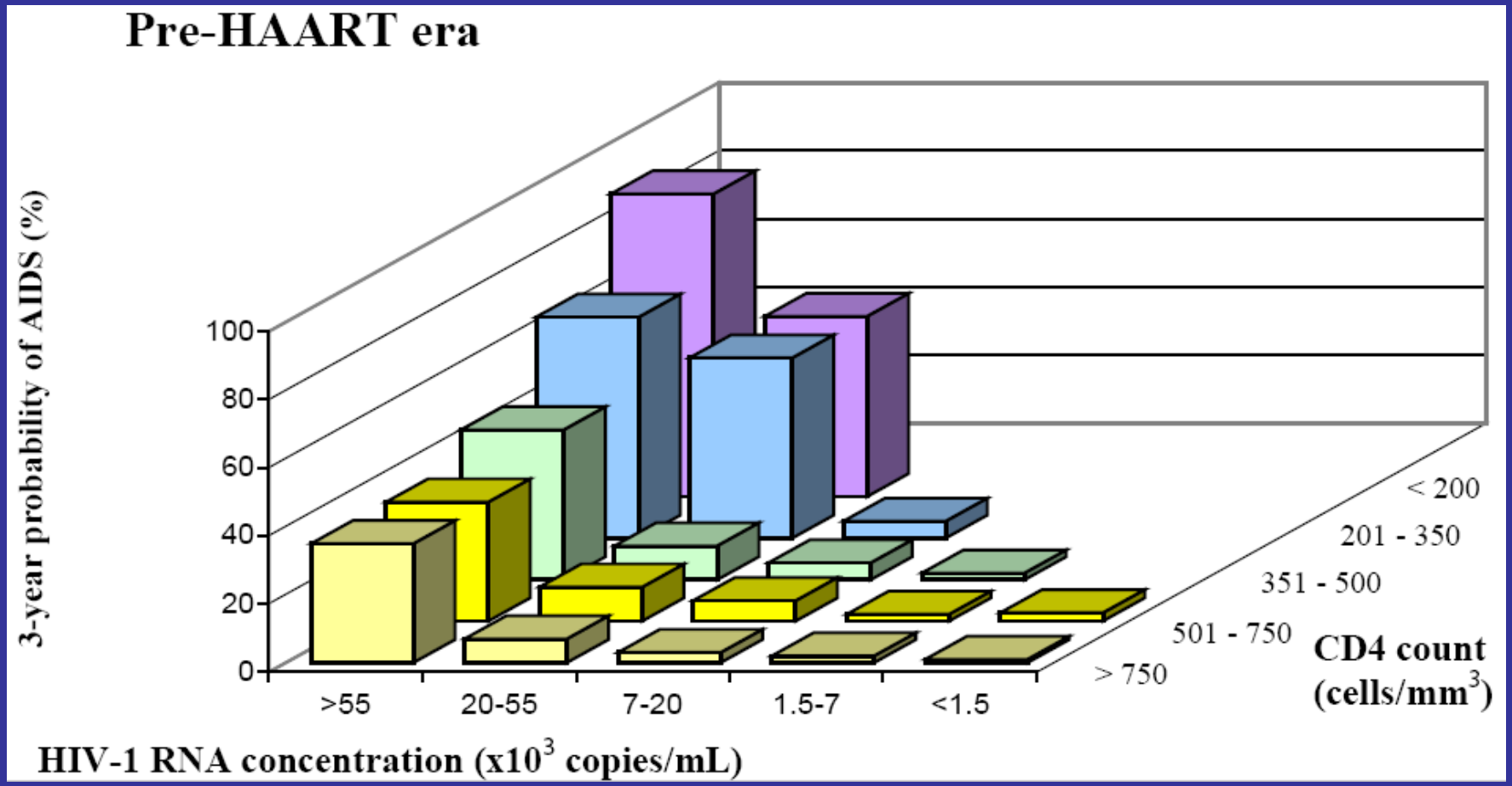
A. Start once CD4 count is < 200
B. Start once CD4 count is < 350
C. Start once CD4 count is < 500
D. Start now

When to Start

Panel's Recommendations
• Antiretroviral therapy (ART) is recommended for all HIV-infected individuals, regardless of CD4 T lymphocyte cell count, to reduce the morbidity and mortality associated with HIV infection (**AI**). • ART is also recommended for HIV-infected individuals to prevent HIV transmission (**AI**). • When initiating ART, it is important to educate patients regarding the benefits and considerations regarding ART, and to address strategies to optimize adherence. On a case-by-case basis, ART may be deferred because of clinical and/or psychosocial factors, but therapy should be initiated as soon as possible.
Rating of Recommendations: *A = Strong; B = Moderate; C = Optional* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

http://aidsinfo.nih.gov/guidelines

Prognosis



3-yr probability of AIDS = AIDS defining illness or death, not CD4<200

http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf

AIDS Defining Illnesses

- Candidiasis
  - Esophageal
  - Tracheal, bronchial
- Cervical Cancer, invasive
- Coccidioides – disseminated
- Chronic diarrhea (>1 month)
  - Cryptosporidia or Isospora
- Cryptococcus – extrapulmonary
- CMV
  - Retinitis
  - Other (not liver, spleen, LN)
- HSV
  - Chronic ulcer (>1 month)
  - Pulmonary, esophageal
- Histoplasma – disseminated
- HIV encephalopathy
- Kaposi's sarcoma
- Lymphoma (NHL)
  - Burkitt's
  - Immunoblastic
  - Primary CNS
- Mycobacterium
  - TB – any
  - Other – disseminated/extrapulmonary
- Pneumonia
  - Pneumocystis
  - Recurrent bacterial (within 1 yr)
- PML
- NT Salmonella septicemia, recurrent
- Toxoplasmic encephalitis
- Wasting syndrome - HIV

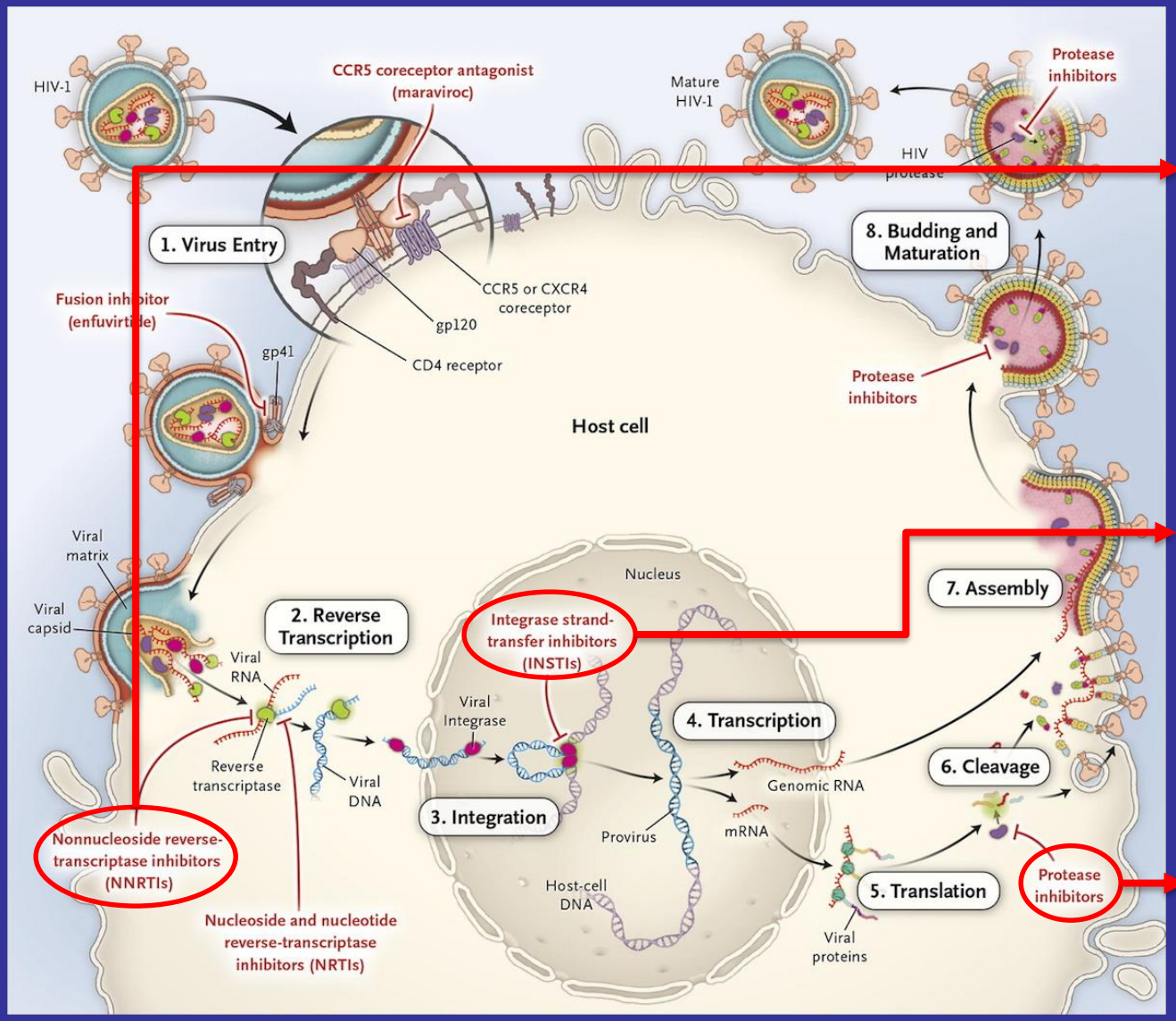
MMWR 1992; 41 (RR17)

40F with HIV presents with complaint of 15 lbs weight gain and fatigue for the past 3 months. She denies any change in her diet, and despite vigorous exercise continues to gain weight especially around her belly and face. PMH: Asthma, hx of syphilis 10 yrs ago (at time of HIV diagnosis). Meds: Symtuza (TAF/FTC/DRV/c), OCP, inhalers (albuterol, fluticasone). Labs: CD4 count 430 and VL<20. On exam: facial plethora, protuberant abdomen with striae.

What is the most likely cause of this patient's symptoms?

A. Drug-drug interaction
B. Cervical cancer
C. HIV associated lipodystrophy
D. Protease inhibitor associated diabetes

Antiretrovirals



ATRIPLA
(efavirenz + tenofovir disoproxil fumarate + emtricitabine)
One tablet once a day. Each tablet contains 600 mg efavirenz + 300 mg tenofovir disoproxil fumarate + 200 mg emtricitabine. Take on an empty stomach. Dose should be taken at bedtime to minimize dizziness, drowsiness and impaired concentration.

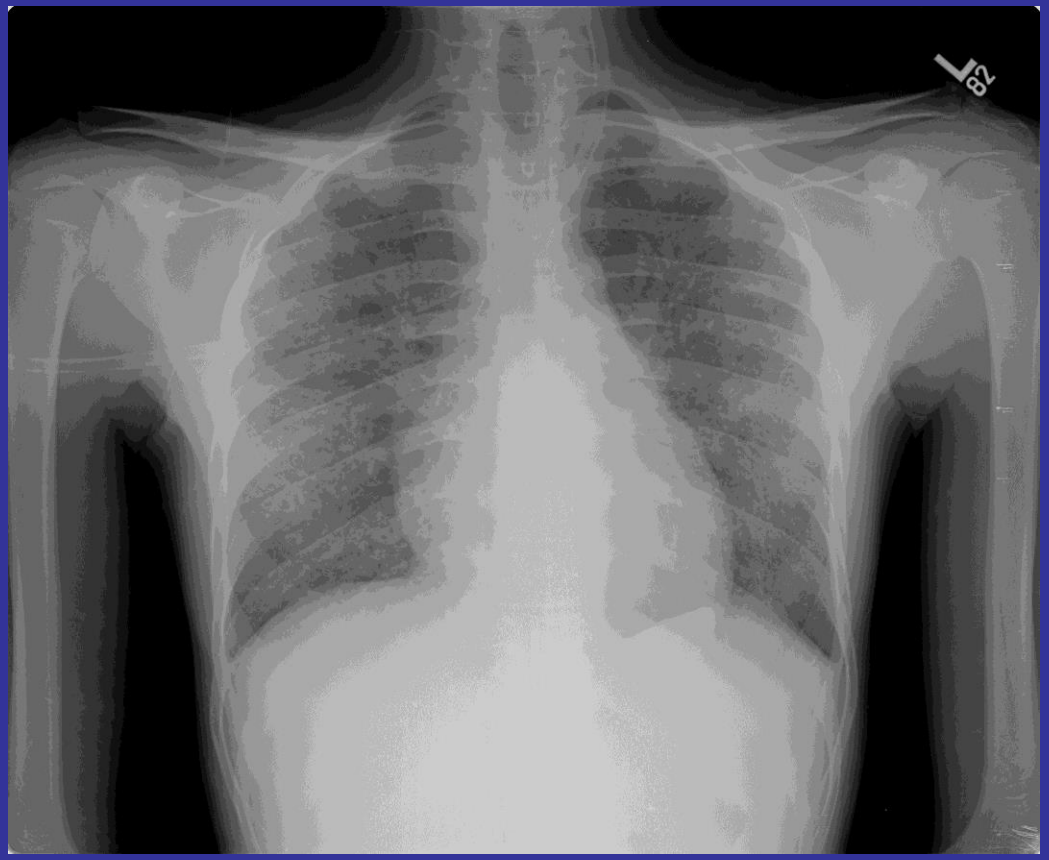
BIKTARVY
(bictegravir + tenofovir alafenamide + emtricitabine)
One tablet once a day. Each tablet contains 50 mg bictegravir + 25 mg tenofovir alafenamide + 200 mg emtricitabine. Take with or without food.

SYMTUZA
(darunavir + cobicistat + tenofovir alafenamide + emtricitabine)
One tablet once a day. Each tablet contains 800 mg darunavir + 150 mg cobicistat + 10 mg tenofovir alafenamide + 200 mg emtricitabine. Take with food.

31M with HIV presents with fevers and progressive DOE x 4 weeks. Diagnosed with HIV about 10 years ago when he developed shingles. He never followed-up and has never been on cART. ABG is performed and demonstrates an A-a gradient of 35 mm Hg. Induced sputum for PJP DFA +.

Which of the following is the best treatment for this patient?

A. TMP-SMX
B. TMP-SMX + prednisone
C. TMP-SMX + prednisone + cART within 2 weeks
D. TMP-SMX + acyclovir
E. TMP-SMX + Vanco + Zosyn



Pneumocystis jiroveci

Epidemiology

- 90% with CD4 < 200 or CD4% < 14%
- Thrush
- High risk for relapse

Clinical Manifestations

- Subacute. Fever, cough, dyspnea.
- Hypoxemia. O2 desat with exercise.
- CXR butterfly pattern. Early - negative.

Diagnosis

- Induced sputum 50-90%
- BAL 90-99%
- Direct immunofluorescent staining
- Non-specific: LDH, 1,3β-D-glucan

Treatment

- IV/PO TMP-SMX
- IV Pentamidine
- Clindamycin + primaquine
- Atovaquone
- Prednisone for A-a ≥ 35, pO_2<70
- Duration = 21 days

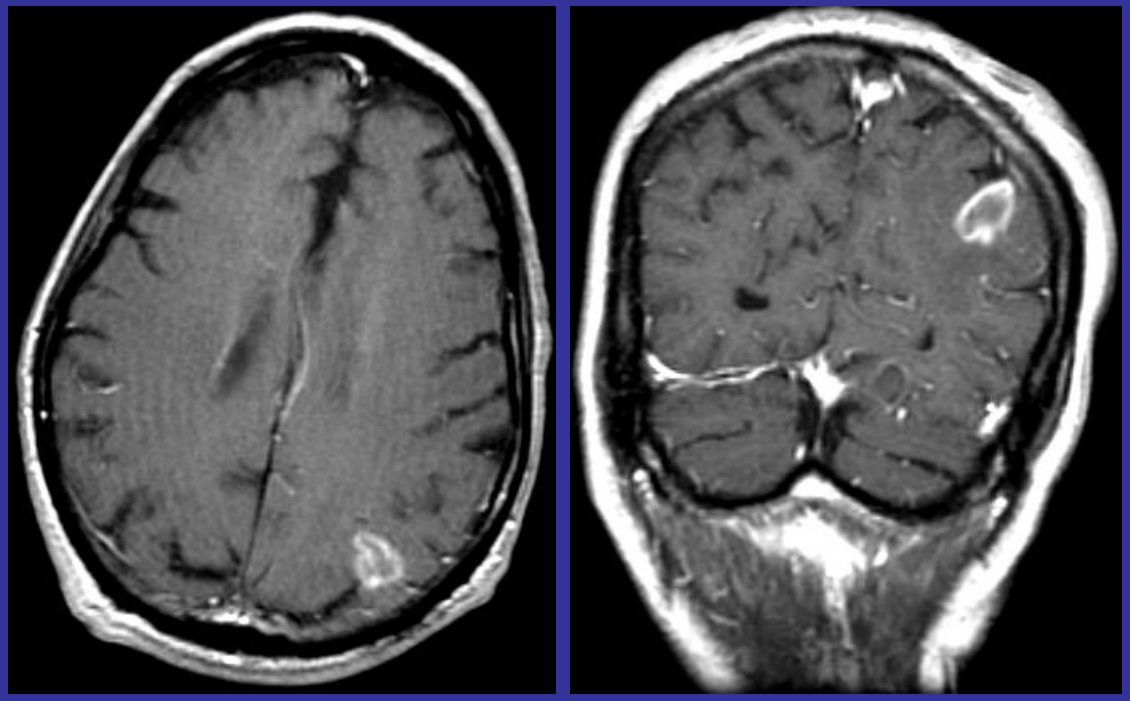
Prophylaxis

- Primary
  - CD4<200/14%, thrush, AIDS
  - TMP-SMX, dapsone, aerosolized pentamidine, atovaquone
- Secondary
- Stop when CD4 > 200 x 3 months

61M presents with unsteadiness and ataxia for the past 2 months. Frequently bumping into things. Progressive HA. MRI performed. Subsequent work-up HIV+, CD4 126. Serum Toxoplasma IgG +, IgM neg. LP: 20 WBCs (90%L), G normal, P120. CSF cytology neg. CSF Cryptococcal Ag and PCRs for EBV, JCV and Toxoplasma are negative.

Which is the next best step in management?

A. Pyrimethamine-sulfadiazine
B. TMP-SMX
C. Repeat LP for more studies
D. Brain biopsy
E. Lipid amphotericin



Toxoplasma Encephalitis

Epidemiology
- 80% have CD4 < 100
- 95+% Toxoplasma IgG+
- Undercooked meat, cat feces

Clinical Manifestations
- HA, confusion, lethargy, seziures
- 70% with focal signs on neuro exam
- ~30% single lesion

Diagnosis
- Ring enhancing hypodense 90%
- AIDS, Toxo IgG+, multiple lesions - 80% predictive value
- LP: cytology, EBV, JCV, Crypt Ag
- Toxo CSF PCR sensitivity 50%
- Definitive dx = brain bx

Differential
- PCNSL (EBV)
- PML (JCV)
- Brain abscess (bacterial, TB, Crypto)

Treatment
- Pyrimethamine/Sulfadiazine
- Pyrimethamine/Clindamycin
- 90% respond at 2 weeks

Prophylaxis
- Primary
  - CD4 < 100 & Toxo IgG +
  - TMP-SMX, Pyrimeth/Dapsone
- Secondary
- Stop when CD4 > 200 x 6 months

38F presents with fevers and progressive HA x 2 weeks, now with lethargy and slurred speech. Diagnosed with HIV 10 years ago but never followed-up. On examination: lethargic but arousable, slurred speech, right CN6 palsy, Head CT normal. LP is performed and OP 55cm H_2O.

Which of the following is the best treatment for this patient?

A. Fluconazole
B. Liposomal ampho
C. L ampho + flucystosine
D. Fluconazole + cART
E. L ampho + cART

LAB RESULTS

Serum
CD4 count 35

CSF

WBC	167	94%L
Gluc	31	
Protein	67	

India ink + encapsulated yeast

Cryptococcal Meningitis

Epidemiology

- Disseminated CD4 < 100
- Meningitis CD4 < 50
- Endemic, soil + bird guano

Clinical Manifestations

- Disseminated disease: pulmonary, blood, skin
- Acute/subacute meningoencephalitis
- Altered mental status, memory loss
- Elevated ICP > 75%

Diagnosis

- Cryptococcal antigen 90+% sensitive (serum & CSF)
- India ink 60-80% sensitive

Treatment

- Lipid amphotericin + flucytosine until CSF sterilization
- Follow with fluconazole maintenance
- Minimum duration of therapy = 1 year.
- Repeat LP for elevated ICP
  - Major cause of morbidity and mortality first 10 weeks.

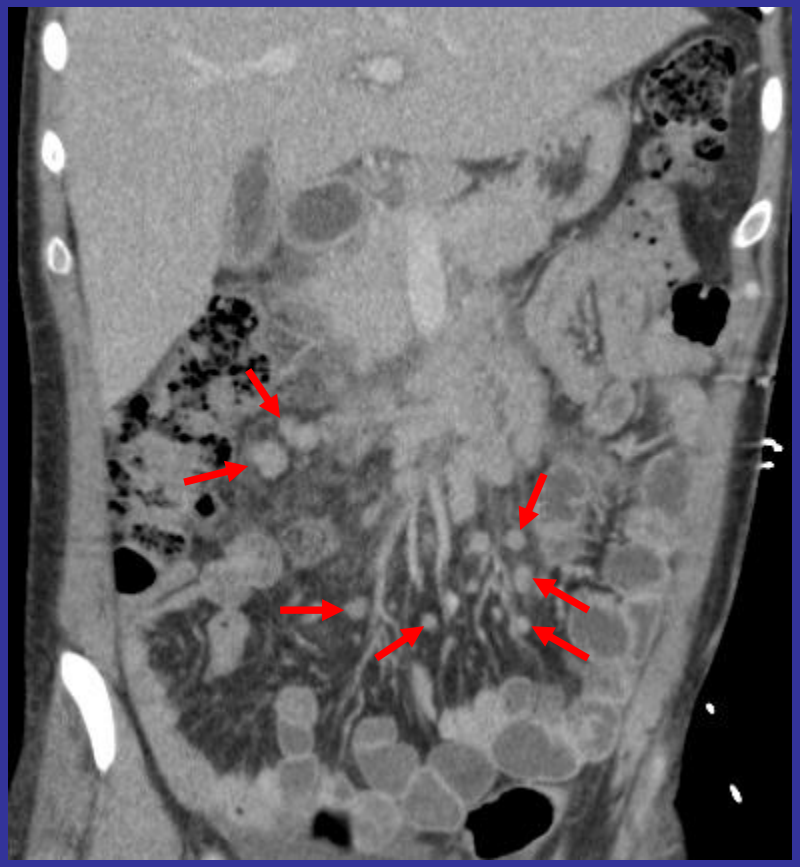
Prophylaxis

- Primary
  - NONE
- Secondary
  - Fluconazole
  - Minimum 1 year therapy
  - Stop when CD4 > 100 x 3 months

34M presents with fevers, night sweats, watery diarrhea, diffuse abdominal pain and 20 lbs weight loss x 2 months. Diagnosed with HIV 10 years ago but never followed-up. Labs: CD4 18, WBC 2.1, Hb 7.5, Ferritin 3200. CT AP performed - diffuse LAN. AFB blood cultures reveal MAC.

Which of the following is the best treatment for this patient?

A. INH + RIF + PZA + EMB
B. Clarithro + EMB
C. Clarithro + EMB + rifabutin
D. Azithro + 4 drug TB therapy
E. Clarithro + EMB + cART



Disseminated MAC

Epidemiology

- CD4 < 50 (usually less than 25)
- Ubiquitous in environment, water

Clinical Manifestations

- Fevers, NS, weight loss, anemia
- Abd pain, diarrhea, intra-abd LAN, HSM, elevated alk phos
- Disseminated disease: spleen, LN, liver, intestines, and bone marrow. Lung involvement rare (< 10%).

Diagnosis

- AFB blood culture 90-95%
- BM, LN, GI tract biopsy
- Can take up to 6 weeks to grow

Treatment

- Clarithromycin + Ethambutol
- High mortality within 6 months
- cART essential for cure
- Add rifamycin if no plan for cART
- Minimum duration = 1 year

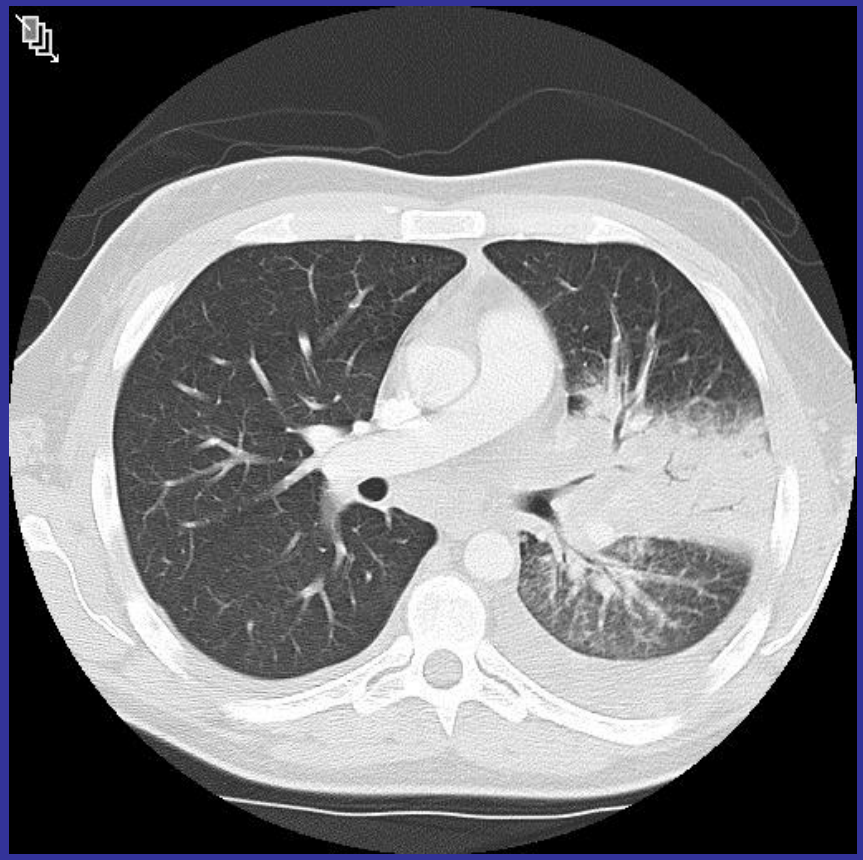
Prophylaxis

- Primary
  - CD4 < 50 ***if not starting cART***
  - Azithromycin Qweek
  - Clarithromycin BID
  - Stop once cART initiated
- Secondary
  - Same as trmt, stop CD4>100 x6m

29M diagnosed with AIDS (CD4 26) two months ago - asymptomatic. He was started on prophylaxis and cART. Now presents with fever, cough, pleurisy. CD4 146. CT chest - consolidation and hilar LAN. BAL negative bacterial, fungal, AFB cxs. Hilar LN biopsy - granulomas. Cx - MAC.

Which of the following is the best treatment for this patient?

A. Continue cART. Start Claritho/EMB.
B. Stop cART. Start Clarithro/EMB.
C. Continue cART. Start Clarithro/EMB and prednisone.
D. Continue cART, no need to treat MAC
E. Continue cART. Start HRZE.



Immune Reconstitution Inflammatory Syndrome

Paradoxical

Worsening of clinical or lab parameters despite ↑ CD4 counts and ↓ viral loads.

Unmasking

Inflammatory reaction to a subclinical (unrecognized) infection.

Occurs in 10-25% of those initiating cART (weeks to months).

Diagnosis:

Low pretreatment CD4 count (< 100)

Positive response to cART

No evidence of OI treatment failure

Temporal association with cART

Pathogen	Manifestation
Mycobacterium avium complex	Skin, focal lymphadenitis, pulmonary infiltrates, mediastinitis, liver granuloma, osteomyelitis, cerebritis
Mycobacterium tuberculosis	Pneumonitis, adult respiratory distress syndrome, lymphadenitis, hepatitis, CNS tuberculosis, gut perforation, renal failure, epididymitis
Mycobacterium leprae	Cutaneous lesions
Cryptococcus species	Meningitis, palsy, hearing loss, abscess, mediastinitis, lymphadenitis
Pneumocystis jirovecii	Pneumonitis
Histoplasma species	Lymph node granuloma
Hepatitis B and C viruses	Hepatitis
JC virus	Contrast-enhanced CNS lesions, inflammatory infiltrates on biopsy
BK virus	Hemorrhagic cystitis
Herpes simplex virus	Chronic erosive ulcera, encephalomyelits
Varicella-zoster virus	Zoster flares, sine herpete flares
Cytomegalovirus	Vitritis, cystoid macular edema, uveitis, vitreomacular traction

CID 2004; 38:1159-66