

# HIV PEARLS FOR INTERNISTS

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**Thomas Holland, MD**

Hilton Head, SC

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# Disclosures

- **Consulting:** The Medicines Company, Basilea Pharmaceutica
- **Scientific Advisory Board:** Motif Bio
- **Adjudication committee:** Achaogen
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- **Royalties:** UpToDate
- **Employment:** Duke University

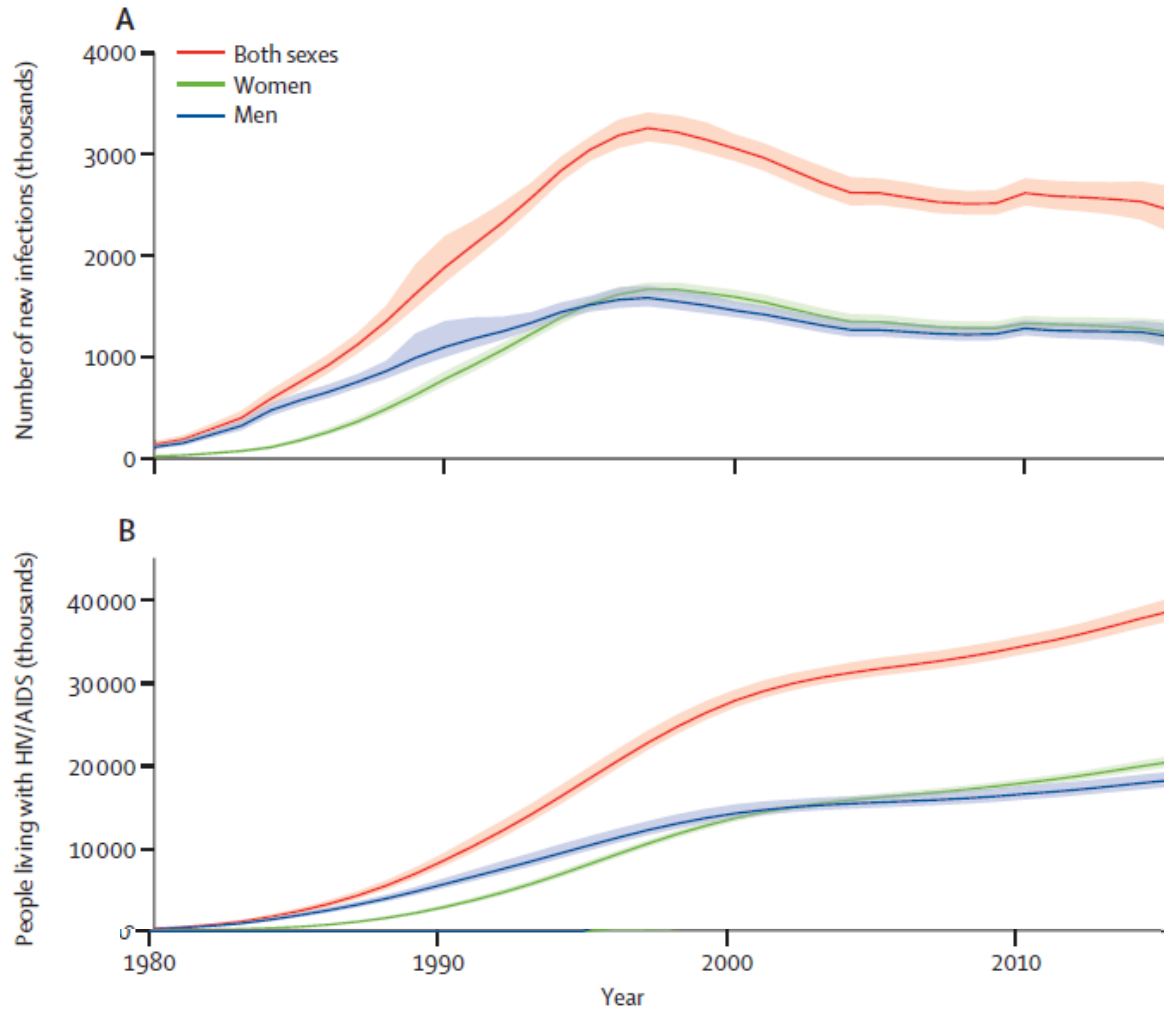
# Objectives

- Review some updated stats on the HIV epidemic, with an emphasis on the local picture
- Common urgent/emergent HIV presentations
- Think through three case presentations
- HIV Pearls
- Avoid conversation about specific antiretroviral agents

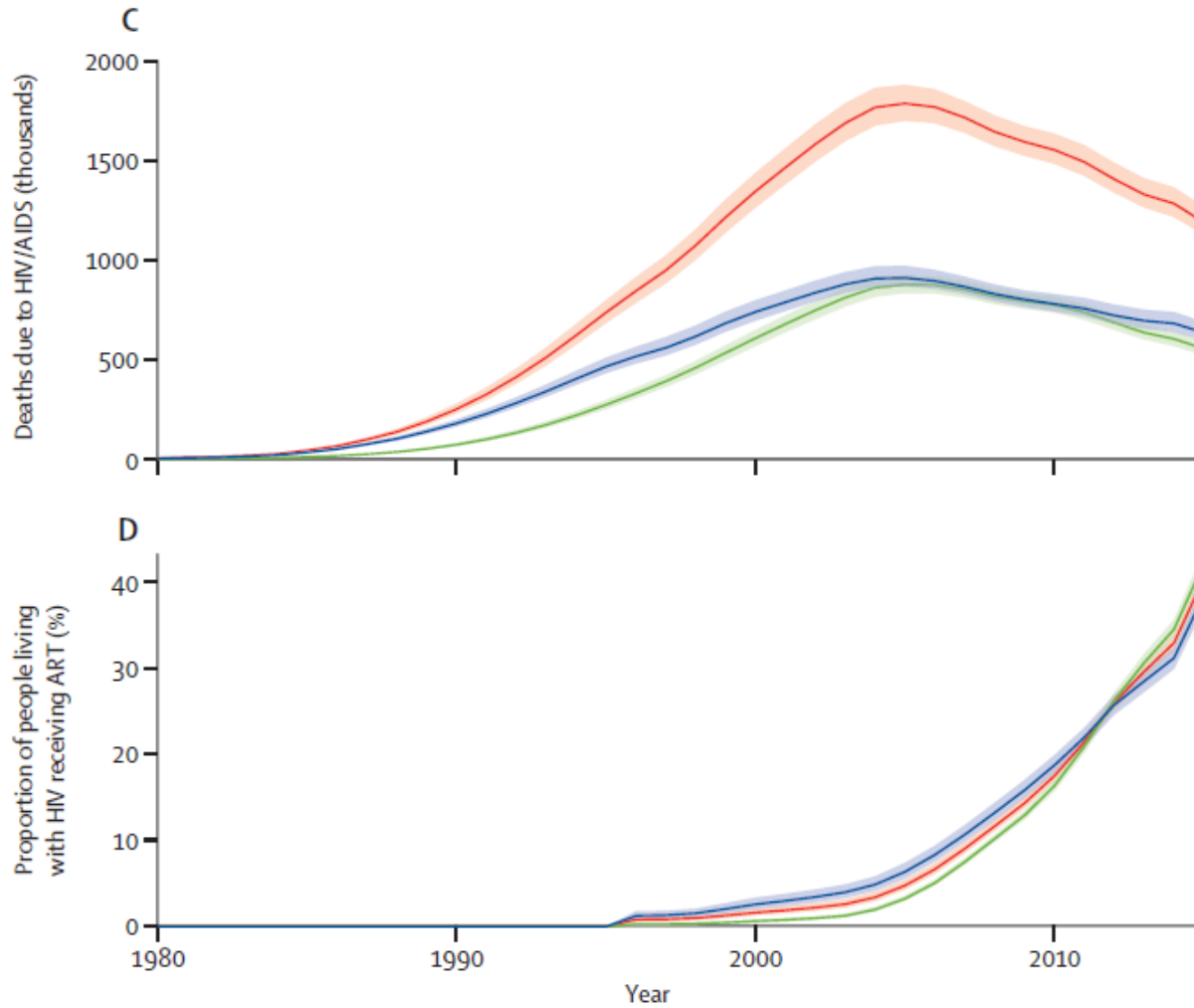
# Everybody likes True/False questions!

- 1) T/F: Incidence of HIV in the United States is declining.
- 2) T/F: The majority of new HIV infections in the US are in men who have sex with men
- 3) T/F: HIV cases associated with IVDU have declined by more than half in the last 15 years.

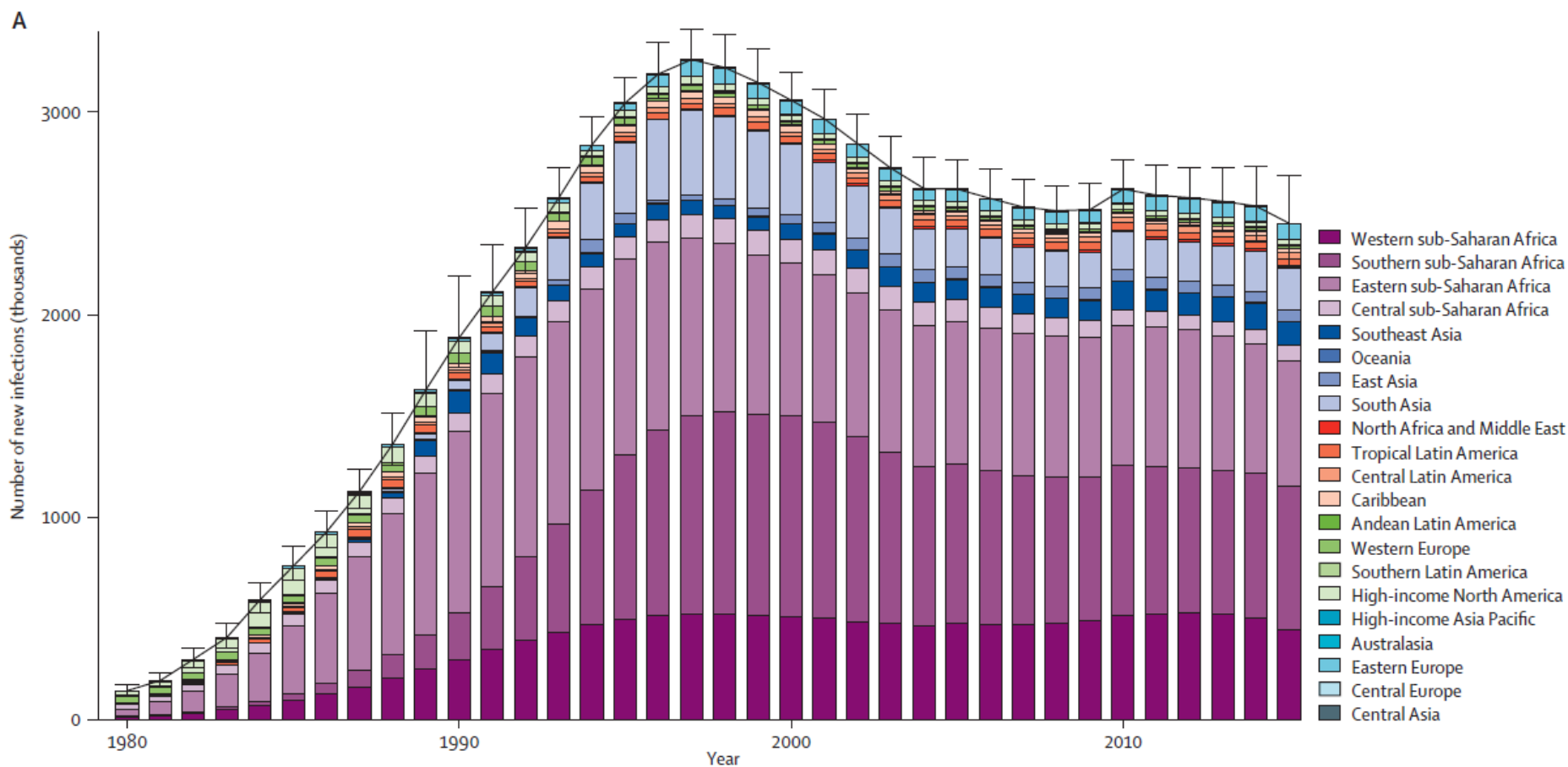
# Estimates of global, regional, and national incidence, prevalence, and mortality of HIV, 1980–2015: the Global Burden of Disease Study 2015



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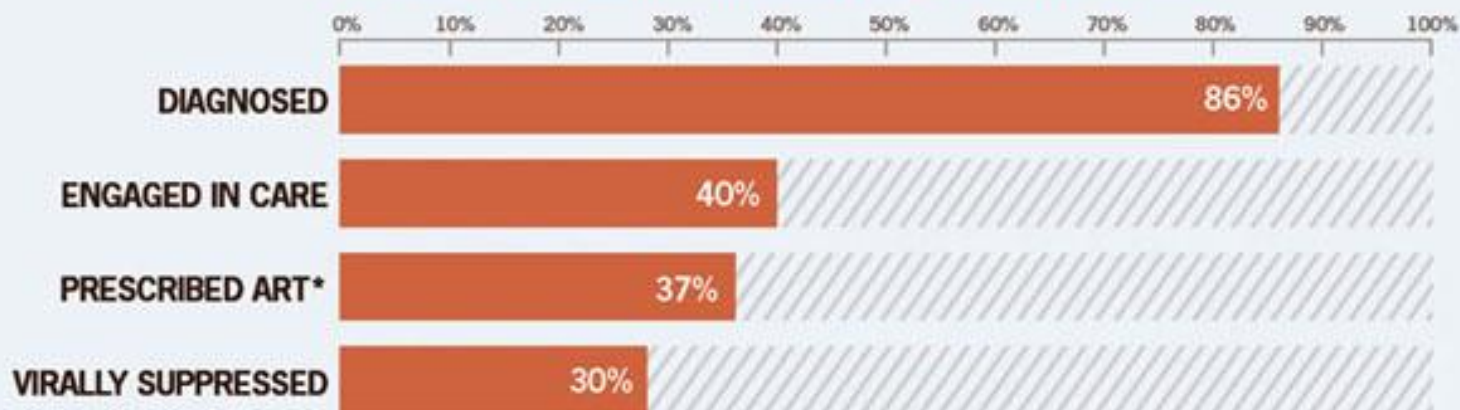
# Most new infections are still in Africa



# The Cascade of Care

## HIV Care Continuum Shows Where Improvements are Needed

In the US, 1.2 million people are living with HIV. Of those:



SOURCES: CDC National HIV Surveillance System and Medical Monitoring Project, 2011.

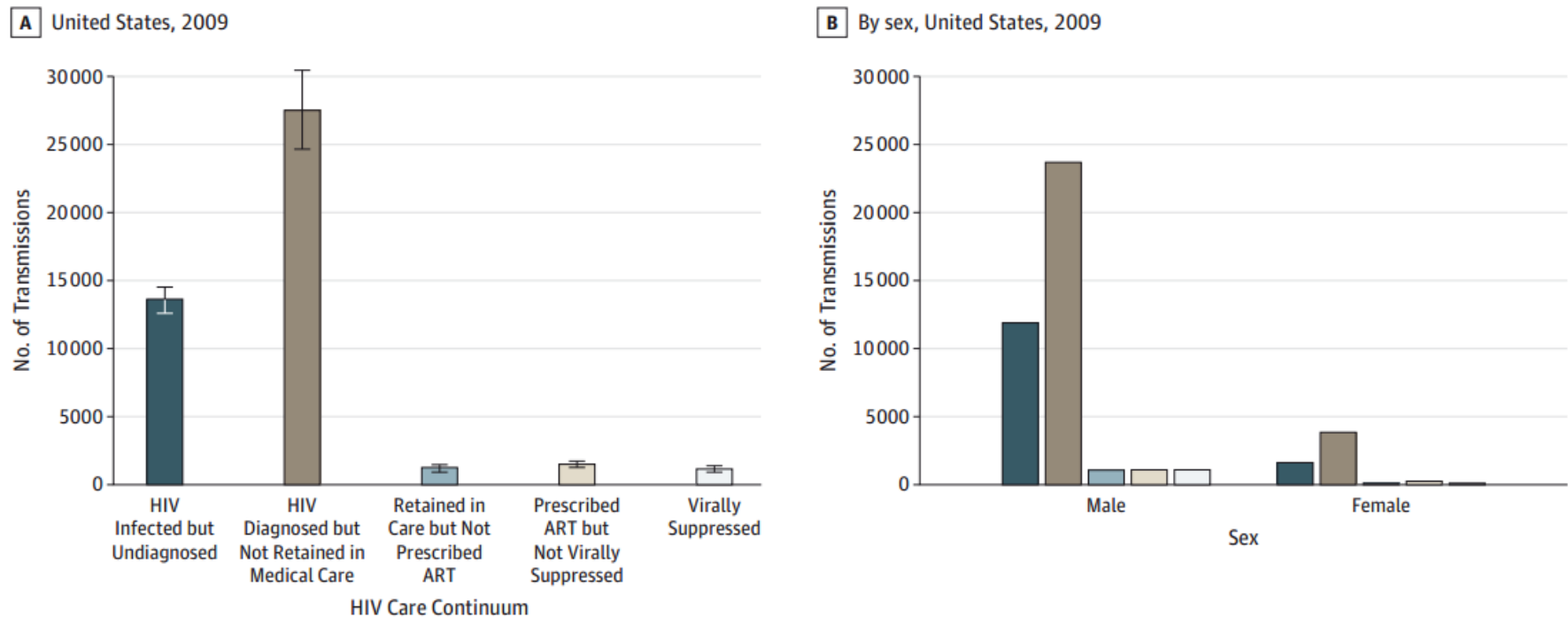
\*Antiretroviral therapy

<https://www.hiv.gov/federal-response/policies-issues/hiv-aids-care-continuum>

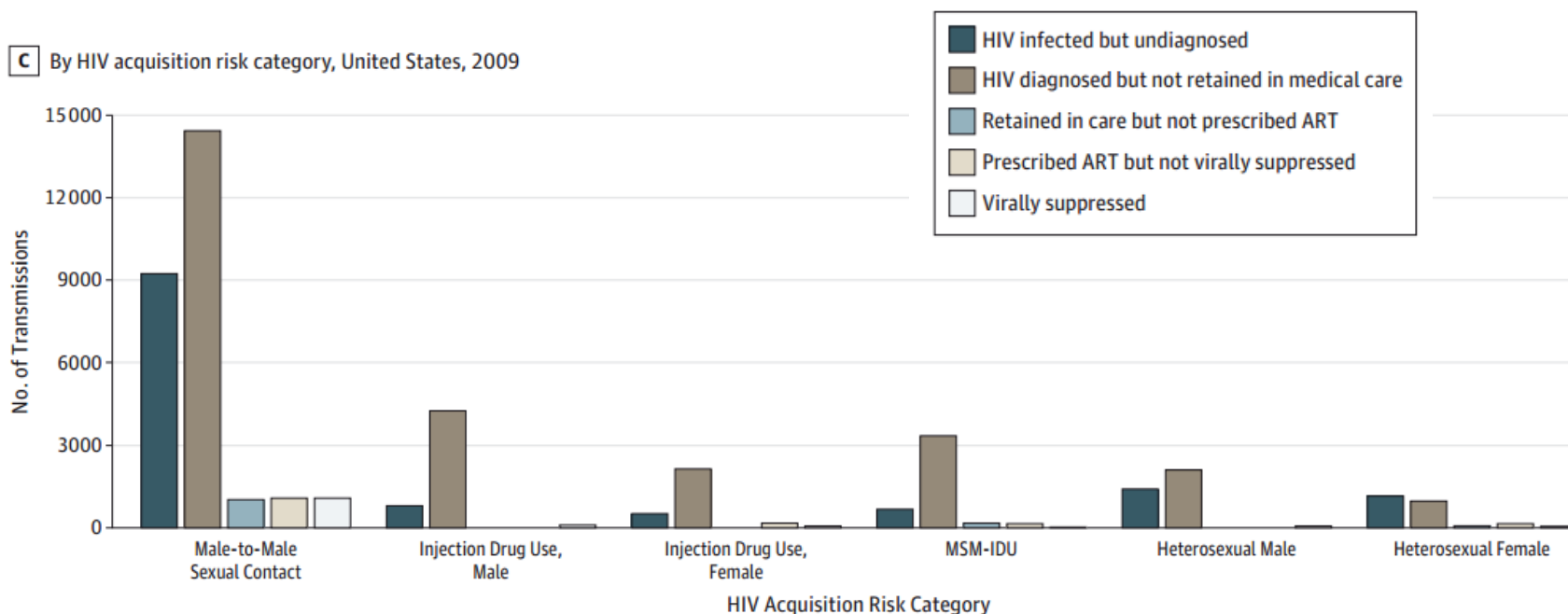


# >90% of HIV transmissions in the US are from those who are not retained in care

Figure 2. Estimated Number of Human Immunodeficiency Virus (HIV) Transmissions Along the HIV Care Continuum



# MSM constitute the highest risk group



From: Trends in Diagnoses of HIV Infection in the United States, 2002-2011

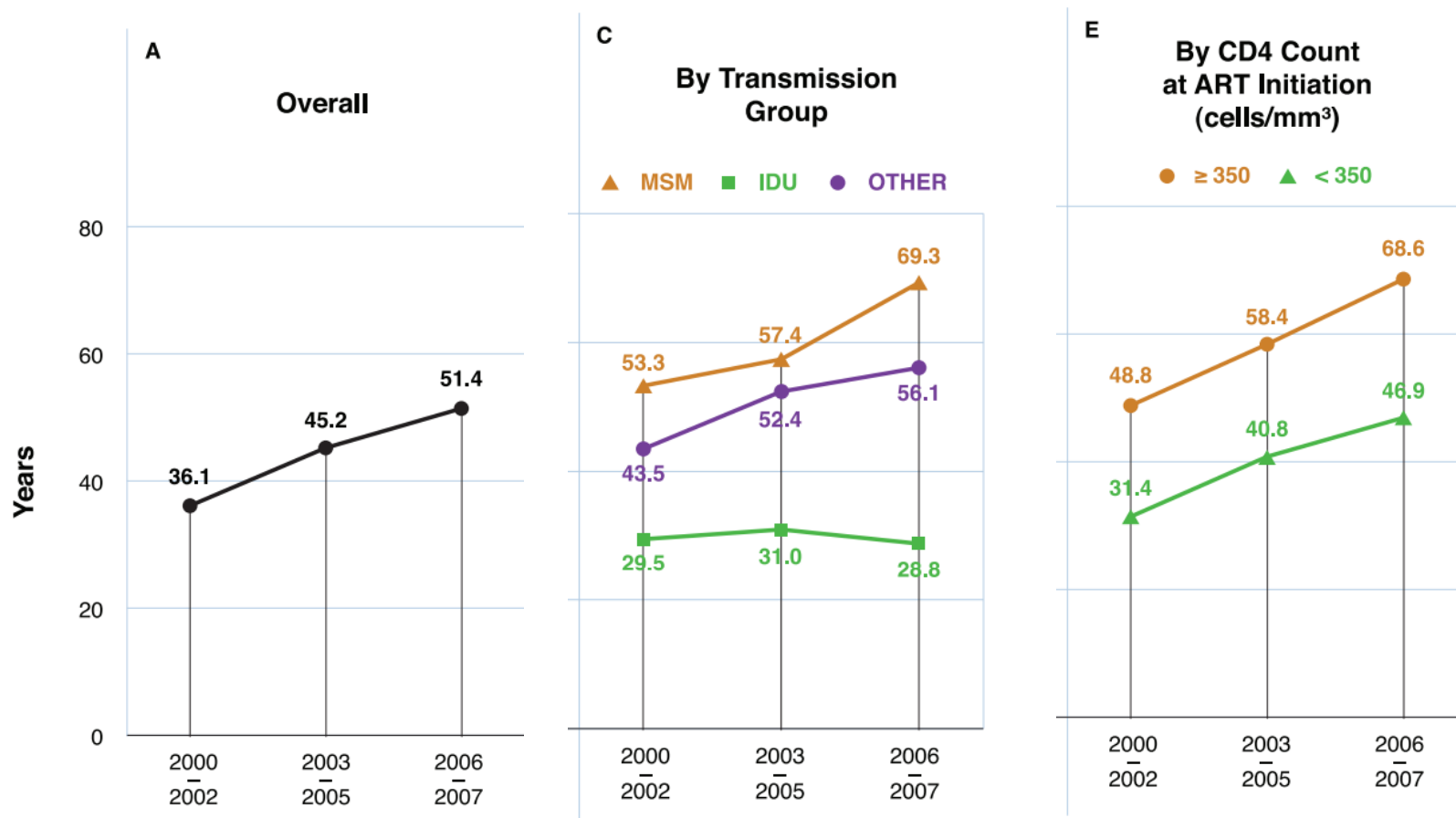
JAMA. 2014;312(4):432-434. doi:10.1001/jama.2014.8534

**Table 1. Human Immunodeficiency Virus (HIV) Diagnoses Among Persons Aged 13 Years or Older in the United States**

	HIV Diagnosis Rate/100 000 Population by Year of Diagnosis										% Change	EAPC (95% CI)
	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011		
<b>No. of HIV Diagnoses by Transmission Category and Year of Diagnosis<sup>c</sup></b>												
<b>Males</b>												
MTM sexual contact	26 021	25 251	26 240	25 838	26 313	27 614	27 466	26 685	26 035	26 033	0	0.3 (0.1 to 0.5)
Injection drug use	6004	5199	4592	4064	3860	3424	2937	2436	2102	1795	-70.1	-11.8 (-12.5 to -11.1)
Both of the above	2850	2587	2473	2320	2085	1956	1732	1513	1397	1211	-57.5	-8.6 (-9.4 to -7.8)
Heterosexual contact <sup>d</sup>	5980	5628	5546	5040	5187	5266	5043	4508	4123	3910	-34.6	-4.0 (-4.6 to -3.5)
Other <sup>e</sup>	155	118	107	83	79	52	60	39	37	31	-80.0	-16.3 (-23.0 to -9.0)
Subtotal	41 010	38 783	38 958	37 345	37 524	38 313	37 238	35 181	33 694	32 980	-27.1	-3.1 (-3.2 to -3.0)
<b>Females</b>												
Injection drug use	3892	3324	3060	2666	2443	2215	1981	1658	1358	1218	-68.7	-11.5 (-12.4 to -10.6)
Heterosexual contact <sup>d</sup>	11 695	10 896	10 651	10 094	10 169	10 262	9836	8755	8094	7507	-35.8	-4.1 (-4.4 to -3.8)
Other <sup>e</sup>	119	103	89	73	58	42	32	22	17	15	-87.4	-20.4 (-28.4 to -11.6)
Subtotal	15 705	14 323	13 800	12 834	12 670	12 519	11 850	10 435	9470	8740	-49.2	-6.6 (-6.8 to -6.4)
<b>Total</b>	<b>56 715</b>	<b>53 106</b>	<b>52 758</b>	<b>50 179</b>	<b>50 194</b>	<b>50 832</b>	<b>49 088</b>	<b>45 616</b>	<b>43 164</b>	<b>41 720</b>	<b>-33.2</b>	<b>-4.0 (-4.1 to 3.9)</b>

**Figure 2. Mid-point life expectancy estimates at age 20 years\* in three calendar periods, overall and by sociodemographic characteristics, 2000–2007.**

\*Among patients on ART



# For patients who are in care, what are common causes of death?

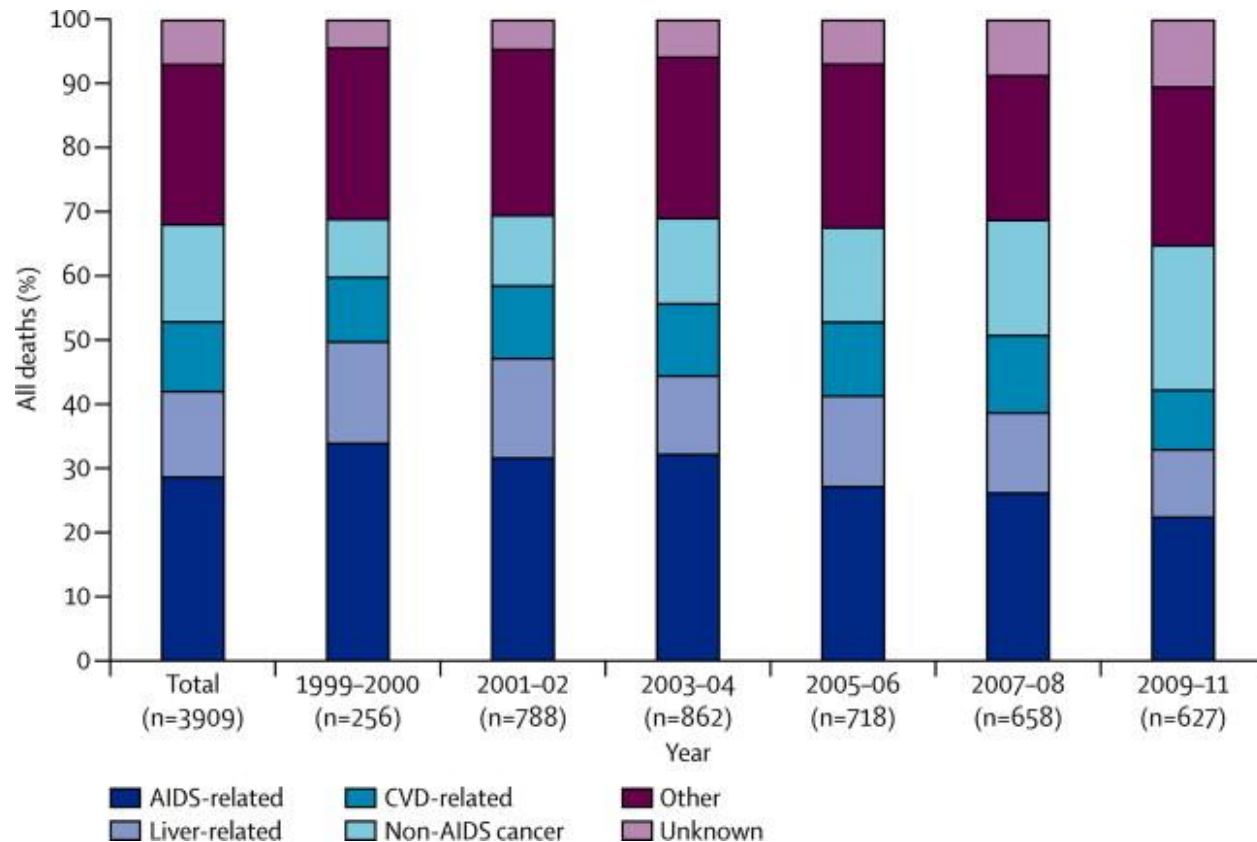


Figure 1 Most common causes of death in people with HIV

Trends in underlying causes of death in people with HIV from 1999 to 2011 (D:A:D): a multicohort collaboration

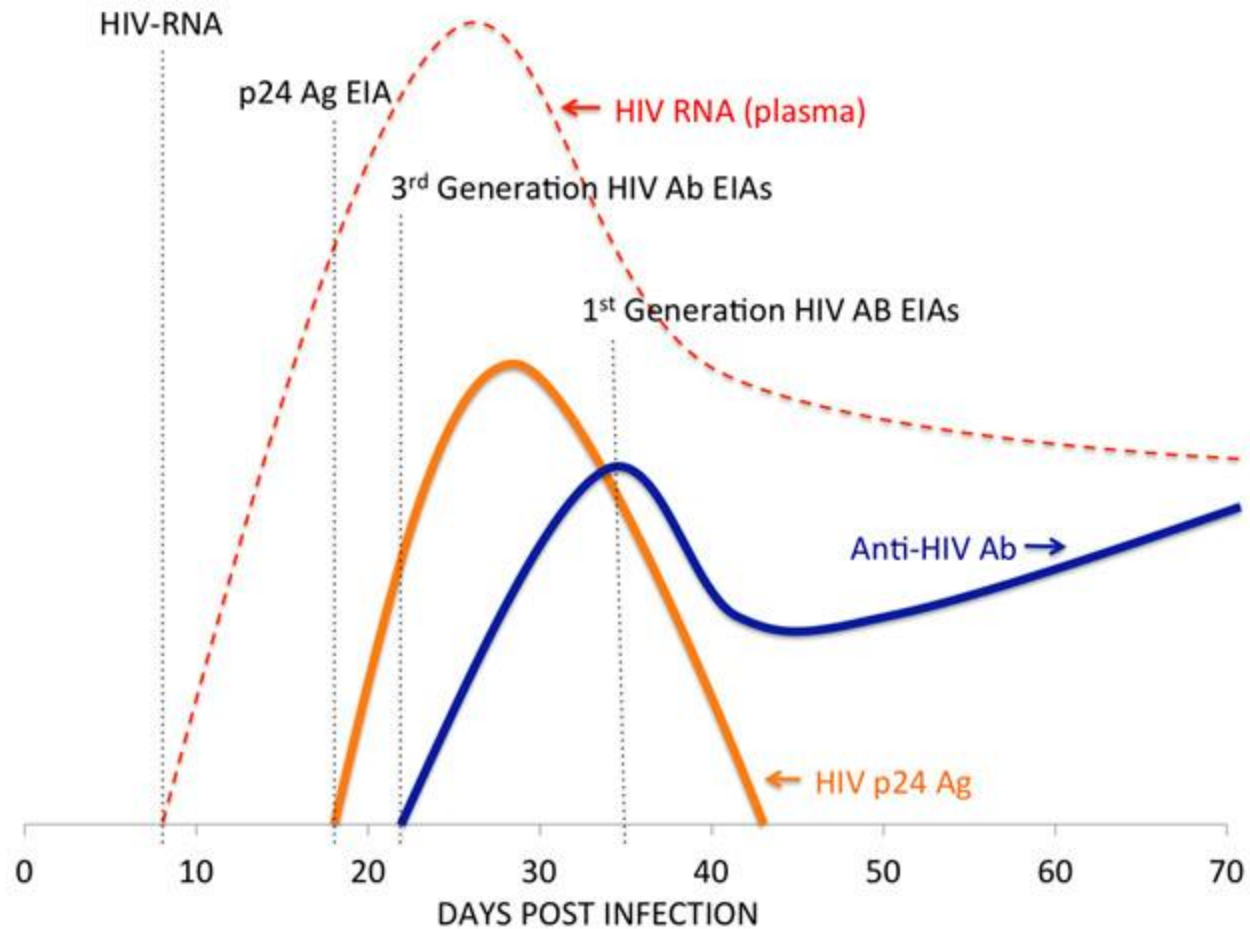
# HIV Epidemiology Key Points

- HIV incidence is falling, but prevalence increasing as people live longer with HIV
- MSM are the highest risk group in the US
- Most new infections are from people not retained in care
- Life expectancy is impacted by cd4 count at the time of diagnosis and comorbid conditions
  - Under ideal circumstances (high cd4 at diagnosis, engaged in care) it approaches the life expectancy of the general population

# Case Presentation #1

- 43yo female with Hb S-beta thal, chronic pain syndrome, p/w chest pain and back pain
- Usually has sickle cell pain in legs/arms
- +fever/chills at home, cough x4-5 days, sore throat, headache
- Has a new partner, tested 3 weeks ago for “STDs”, was negative
- On exam has thrush, anterior cervical adenopathy
- This all adds up to concern for acute HIV – what testing should you send?

# How does testing work



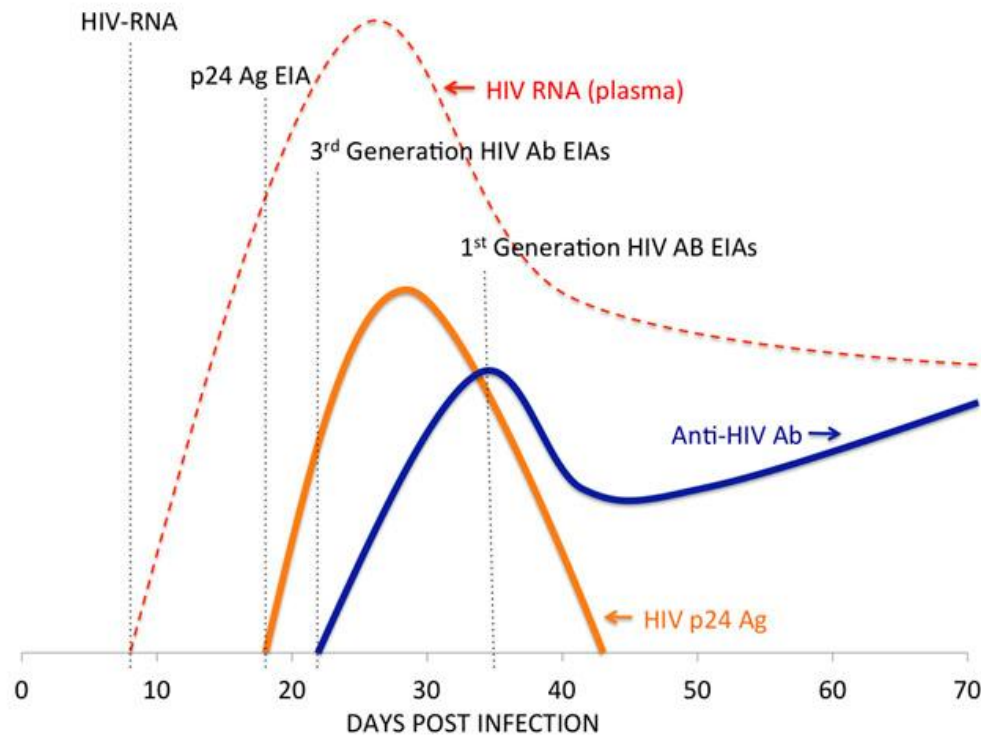


# Acute HIV clinical presentation

- Usual time course from exposure to symptoms is 2-4 weeks
- Think of a mono-like illness: fever, lymphadenopathy, sore throat, rash, myalgia, headache
- May present as aseptic meningitis
- Mucocutaneous ulcers, if present, are suggestive of HIV
- Opportunistic infections uncommon but thrush can be seen

# Testing for acute HIV

- Current recommendation is to send both HIV Ab/Ag testing and HIV viral load



# In our patient

- HIV Ab/Ag test was indeterminate (strongly suspicious for early seroconversion)
- HIV VL ~3.5 million, cd4 409
- She was enrolled in a study of acute HIV therapy
- After some fits and starts, became engaged in care, VL suppressed and cd4>1000
- She unfortunately passed away from complications of sickle cell disease in 2016

# You will never be faulted for testing for HIV

2006 CDC guidelines for HIV testing in health-care settings:

- *HIV screening is recommended for patients in all health-care settings after the patient is notified that testing will be performed unless the patient declines (opt-out screening).*
- *Persons at high risk for HIV infection should be screened for HIV at least annually.*
- *Separate written consent for HIV testing should not be required; general consent for medical care should be considered sufficient to encompass consent for HIV testing.*
- *Prevention counseling should not be required with HIV diagnostic testing or as part of HIV screening programs in health-care settings.*

MMWR, Sept 22, 2006

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm>

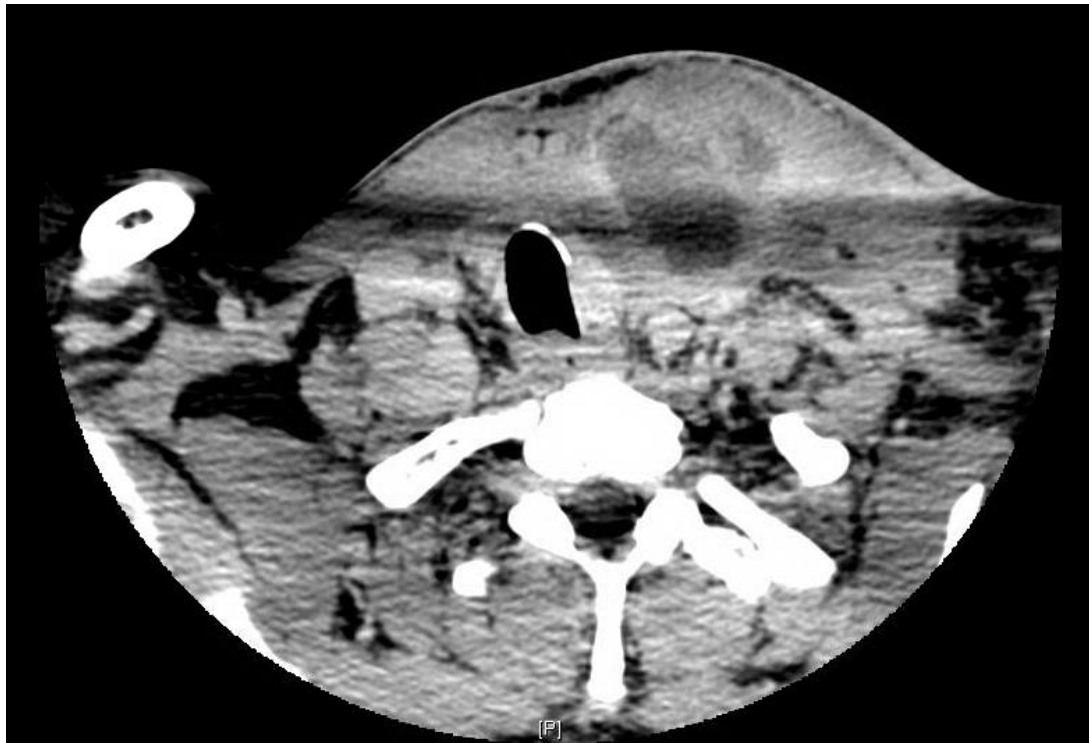
# HIV testing take-home points

- You can justify testing just about anybody for HIV, with an HIV Ab/Ag test
- To diagnose acute HIV requires that you think about it
  - Mono-like illness in a sexually active patient or patient with history of injection drug use

# Case presentation #2

- 7/1994: 26yo man p/w hydrocarbon inhalation
- 9/1994: p/w scalp contusion, closed head injury after assaulted with muffler pipe, was inebriated
- 5/1996: 23-hr obs after MVA, cannot remember event
- 6/1996: p/w deltoid injury – stabbed with steak knife by girlfriend
- 5/1999: p/w blow to head by baseball bat or bottle
- 6/1999: p/w arm pain after bee sting, consumed alcohol and cocaine to control pain
- 12/2000: p/w scalp lac, LOC after fight with brother
- 7/2001: p/w forearm lac, cut with box cutter
- 8/2005: now 37yo, p/w syncope, known HIV+ at that time (dx 2003 at another facility). First cd4 count at Duke was 14

- I met him in 2012 when he presented with unilateral neck pain and swelling, cd4 14.



- 3/2013: presents with dyspnea and syncope, L-sided chest pain
- Has non-productive cough
- T 38.0, sats 97% RA(?)
- What tests do you want?







- Cd4 = 2
- LDH 447
- pO<sub>2</sub> 102 on ABG, 2L NC
- A-a grad 69
- Empiric therapy?
- Should he be in isolation?

- What if I told you he is sulfa-allergic (rash)?

- Extended RVP neg
- Strep/legionella urine Ag neg
- PCP DNA positive

# PCP Pneumonia

- You can call it PJP if you want, but that won't make you any cooler
- Main risk factor is cd4 <200
- Most present with dyspnea with subacute presentation over days to weeks
- Fever and tachypnea are common
- Oral thrush a common co-infection
- CXR may be normal (~25%), most common abnormalities are diffuse bilateral interstitial infiltrates

# PCP treatment

- TMP/SMX DS 2 tabs q8h x21 days
  - Note that this regimen is prone to adverse effects: hyperkalemia, AKI, rash, GI intolerance, hepatitis
- Alternatives:
  - TMP/dapsone
  - Clindamycin/primaquine
  - Atovaquone (for mild disease only, \$\$\$\$)
- Steroids:
  - For  $\text{PaO}_2 \leq 70$ , A-a gradient  $\geq 35$ , resting hypoxemia on room air, worsening on therapy
  - Prednisone 40mg q12h x5d, then 40mg daily x5d, then 20mg daily x11d

# Clinical story, continued

- He was treated with trimethoprim/dapsone with initial improvement, then developed somnolence and found to have methemoglobinemia 7.8%
- Switched to clinda/primaquine, recovered, discharged
- Readmitted 6/2013, 8/2013, 3/2014, 4/2014, 5/2014 for PCP



- In the middle of this course, he presents to the ED with headache. He says he has been to the clinic at the health department and has started taking his antiretrovirals within the last few weeks
- His neuro exam is nonfocal
- What are you worried about?
- PCP, cryptococcus, toxoplasmosis, syphilis, PML, CNS lymphoma, drug side effect, IRIS

- What testing do you want for the patient with a low cd4 count and headache?
- Contrasted head CT
- LP – opening pressure, cell count, glucose, protein, cryptococcal Ag, VDRL
  - Depending on other studies: HSV PCR, VZV PCR, JC virus

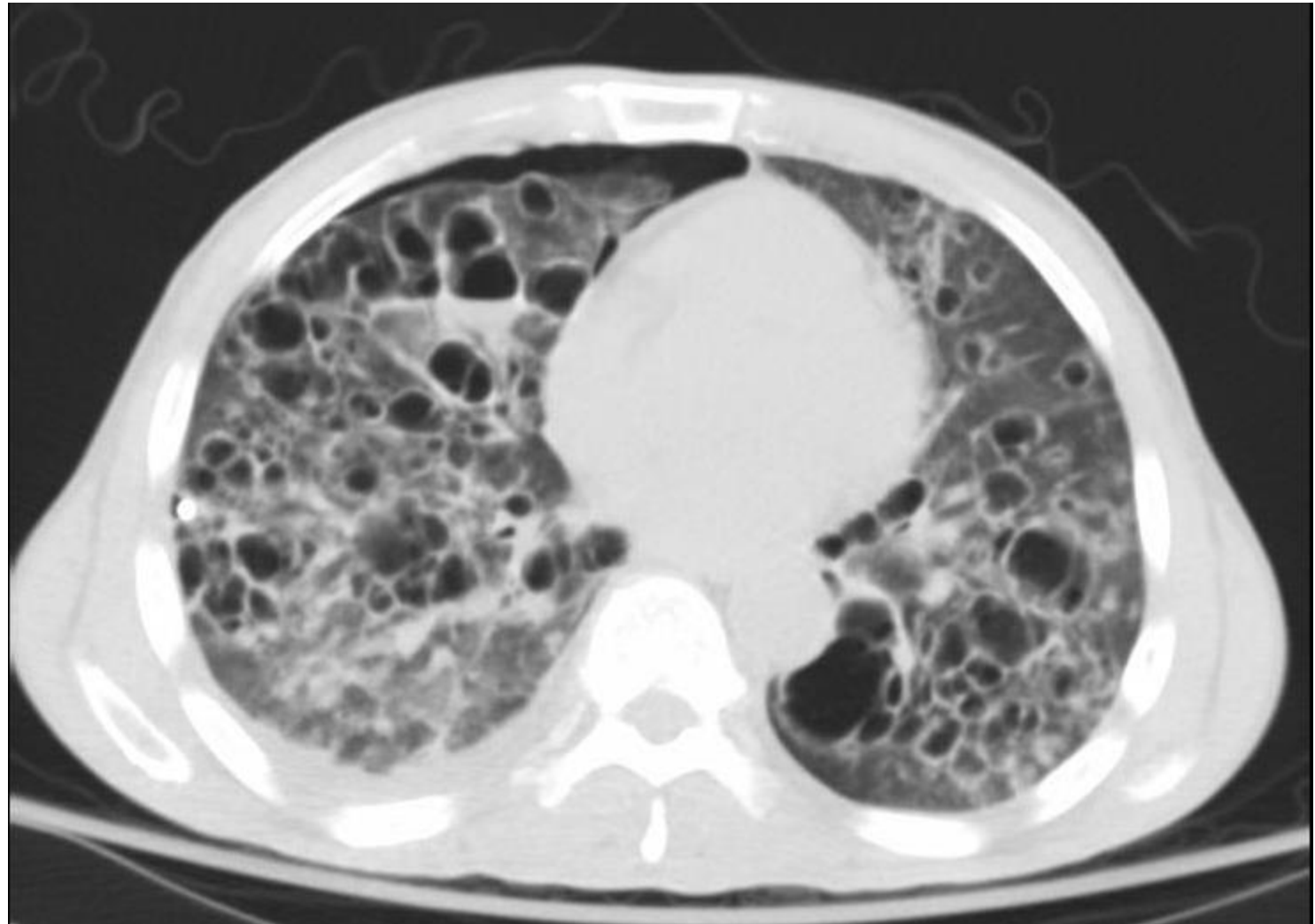
# Cryptococcal meningitis

- Uniformly fatal if untreated
- Induction therapy with 2 weeks of amphotericin B 0.7 mg/kg/day + flucytosine 100mg/kg/day in 4 divided doses
- Therapeutic LP – decrease opening pressure to  $<20$ , or by half if  $>40$
- Consolidation with fluconazole 400mg/day x8 weeks
- Then maintenance with lower dose fluconazole for at least a year, discontinue if patient has CD4 recovery to  $>100$

# Continued...

- Our patient did not have a new diagnosis made at the time he presented with headache
- Presented again in 11/2014 with chest pain after a fall





- Placed back on therapy for PCP, chest tube in place, palliative care involved and he transitioned to hospice

# Case presentation #3

- 35yo female with ~15yr hx of HIV infection, in and out of care and never able to take ARVs in sustained fashion, is directed to the ED for lab finding of K<sup>+</sup> 2.1. She is 5'7" and weighs 73 lbs on presentation (BMI 11.4). Last known cd4 count = 4, three months prior to presentation.
- Labs otherwise notable for WBC 0.3, Hb 8.4, plt 247, alk phos 124, AST 16, ALT 22
- Aside from AIDS wasting syndrome, what other infection(s) are of concern based on these labs?



# Disseminated MAC

- Terminology note: MAC = Mycobacterium avium complex
  - With the advent of molecular testing methods, now at least 11 distinct species in this group. Let's just stick with calling it MAC for now
- Cd4<50 is the primary risk factor
- Incidence ~20-40% in the absence of ART or prophylaxis
- Incidence has fallen >10-fold since the introduction of effective ART
- Presenting symptoms of disseminated disease include fever, night sweats, diarrhea, weight loss, abdominal pain
- Signs include anemia, elevated alkaline phosphatase

# Case (continued)

- Goals of care conversations, including with family and her outpatient provider, lead to placement of a G-tube and initiation of tube feeds as well as ARVs
- AFB blood culture returns positive and she is initiated on MAC therapy with azithro/ethambutol
- Also treated with fluconazole for esophageal candidiasis and TMP/SMX for PCP prophylaxis
- Hospital course also complicated by enterobacter bacteremia, refeeding syndrome, and ongoing depressed mood

# Case (continued)

- 2 weeks into therapy, she develops worsening abdominal pain and has new transaminitis
- The ddx is broad but this is the right timing for MAC-IRIS or for a drug side effect
- Her medication regimen is simplified (stop fluconazole, TMP/SMX, cefepime, dose-reduce azithro) and treatment for HIV and MAC is continued
- Transaminitis improves
  - If it hadn't → would have added steroids

# Case resolution

- Pending...

# OI risk at different cd4 counts

- PCP:  $cd4 < 200$ , prophylaxis with TMP/SMX
- Toxoplasmosis: 33% annual incidence if  $cd4 < 100$  AND seropositive, presents as cerebral abscesses or meningoencephalitis
- MAC: 20-40% prevalence in patients with  $cd4 < 50$ , prophylaxis with a macrolide (azithro preferred)
- Cryptococcus: majority of cases with  $cd4 < 50$
- CMV:  $cd4 < 50$ , retinitis, encephalitis, esophagitis, colitis, hepatitis
- Coccidioidomycosis, histoplasmosis – uncommon in NC

# Miscellany

- Who needs a cd4 count checked in the hospital?
  - Maybe nobody... but reasonable to send one in an HIV+ patient being admitted and who does not have one within the last year
- Who should be on antiretroviral therapy?
  - All patients with HIV should be offered ARVs
  - Data for mortality and morbidity benefit is stronger the lower the cd4 count goes
- In what setting should you hold antiretrovirals?
  - Only if you think they are part of the problem (e.g. abacavir hypersensitivity syndrome, renal failure on tenofovir, NNRTI rash)
  - Conversely, missing a single day of ARVs is not going to break anybody

# Summary

- HIV incidence is falling but our HIV-infection patient population continues to increase as life expectancy improves
- Test anybody you like for HIV
- Think about acute HIV
- OI risk correlates (inversely) with cd4 count, and the ddx widens as cd4 count falls