

HIV 101

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Case

- 25 year old man is admitted to the hospital with multiple injuries after a motor vehicle accident.
- He was previously healthy, has no past medical history and is not on any medications.

- Should you test him for HIV?

MNWR

MORBIDITY AND MORTALITY WEEKLY REPORT

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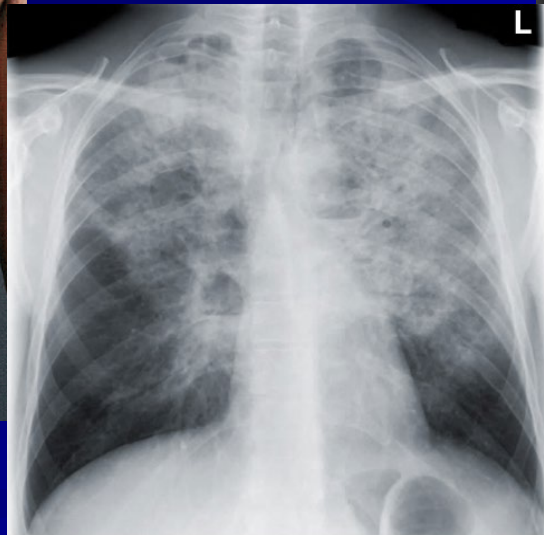
Epidemiologic Notes and Reports

Pneumocystis Pneumonia — Los Angeles

In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.

1981

Pneumocystis pneumonia and Kaposi's sarcoma reported in 26 men in NYC and California



MNWR

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MORBIDITY AND MORTALITY WEEKLY REPORT

Epidemiologic Notes and Reports

Kaposi's Sarcoma and *Pneumocystis* Pneumonia Among Homosexual Men — New York City and California

During the past 30 months, Kaposi's sarcoma (KS), an uncommonly reported malignancy in the United States, has been diagnosed in 26 homosexual men (20 in New York City [NYC]; 6 in California). The 26 patients range in age from 26-51 years (mean 39 years). Eight of these patients died (7 in NYC, 1 in California)—all 8 within 24 months after KS was diagnosed. The diagnoses in all 26 cases were based on histopathological examination of skin lesions, lymph nodes, or tumor in other organs. Twenty-five of the 26 patients were white, 1 was black. Presenting complaints from 20 of these patients are shown in Table 1.

Skin or mucous membrane lesions—often dark blue to violaceous plaques or nodules

Discovery of HIV-1

- 2 French researchers discovered HIV in 1983; both received the Nobel Prize in 2008

Discovery of HIV

100 nm



Luc Montagnier *
Pasteur Institute, France
HIV-1 1983; HIV-2 1986

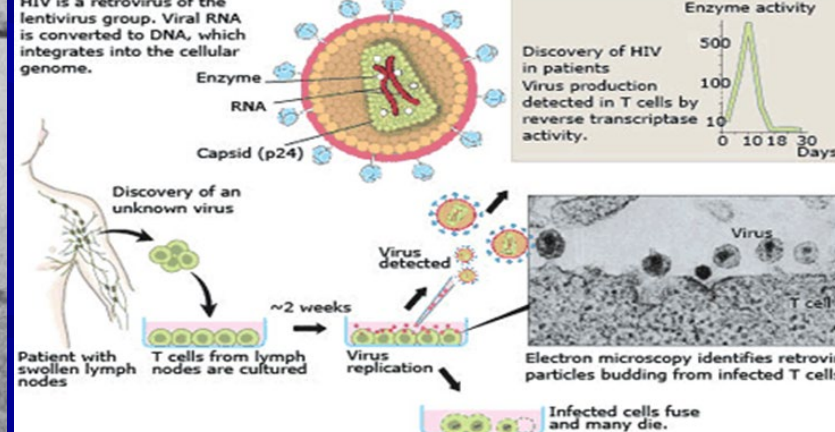


Françoise Barré-Sinoussi *

* 2008 Nobel Prize laureates

HIV – human immunodeficiency virus

HIV is a retrovirus of the lentivirus group. Viral RNA is converted to DNA, which integrates into the cellular genome.



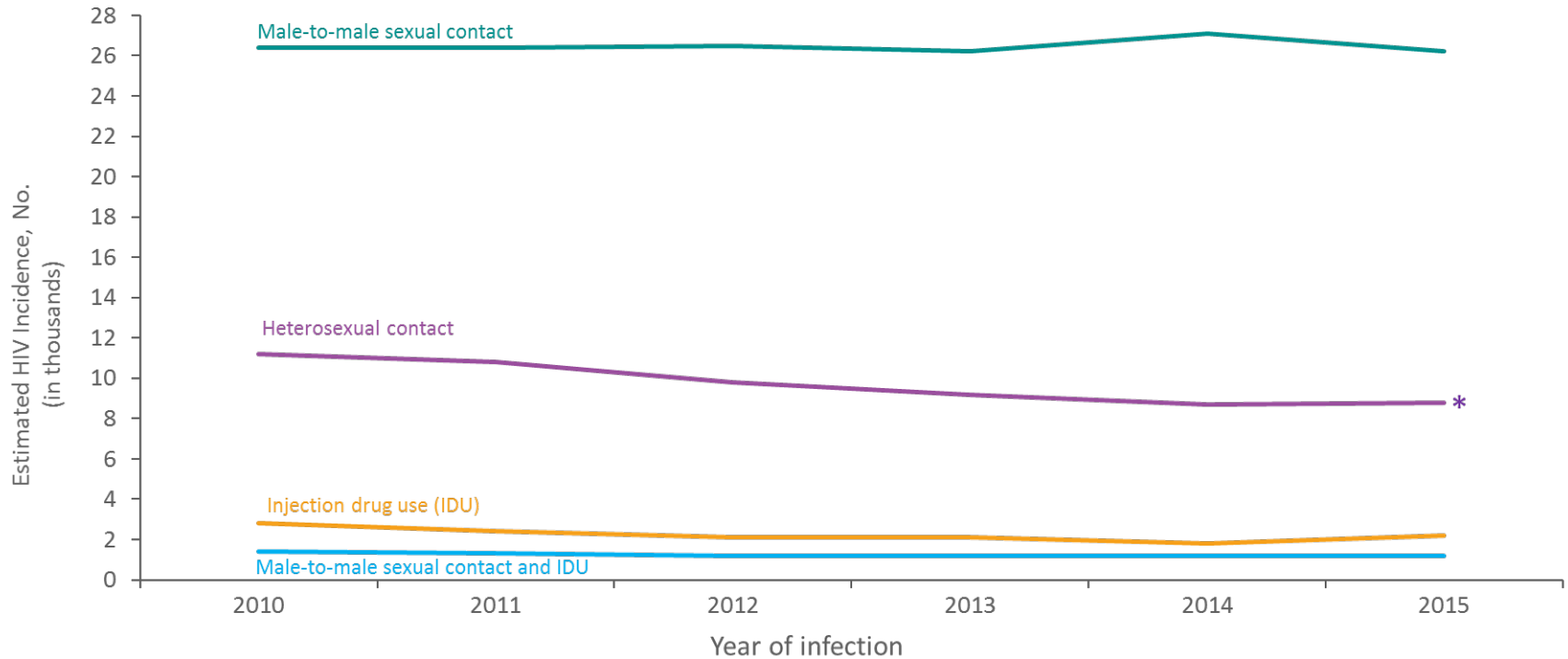
© The Nobel Committee for Physiology or Medicine 2008 Illustration: Annika Röhl

- What is the prevalence of HIV in the United States?
 - 1. 1 out of 300
 - 2. 1 out of 2500
 - 3. 1 out of 12000
 - 4. In out of 27000

■ What is the prevalence of HIV in the United States?

- 1. 1 out of 300
- 2. 1 out of 2500
- 3. 1 out of 12000
- 4. In out of 27000

Estimated HIV Incidence among Persons Aged ≥13 Years, by Transmission Category, 2010–2015—United States

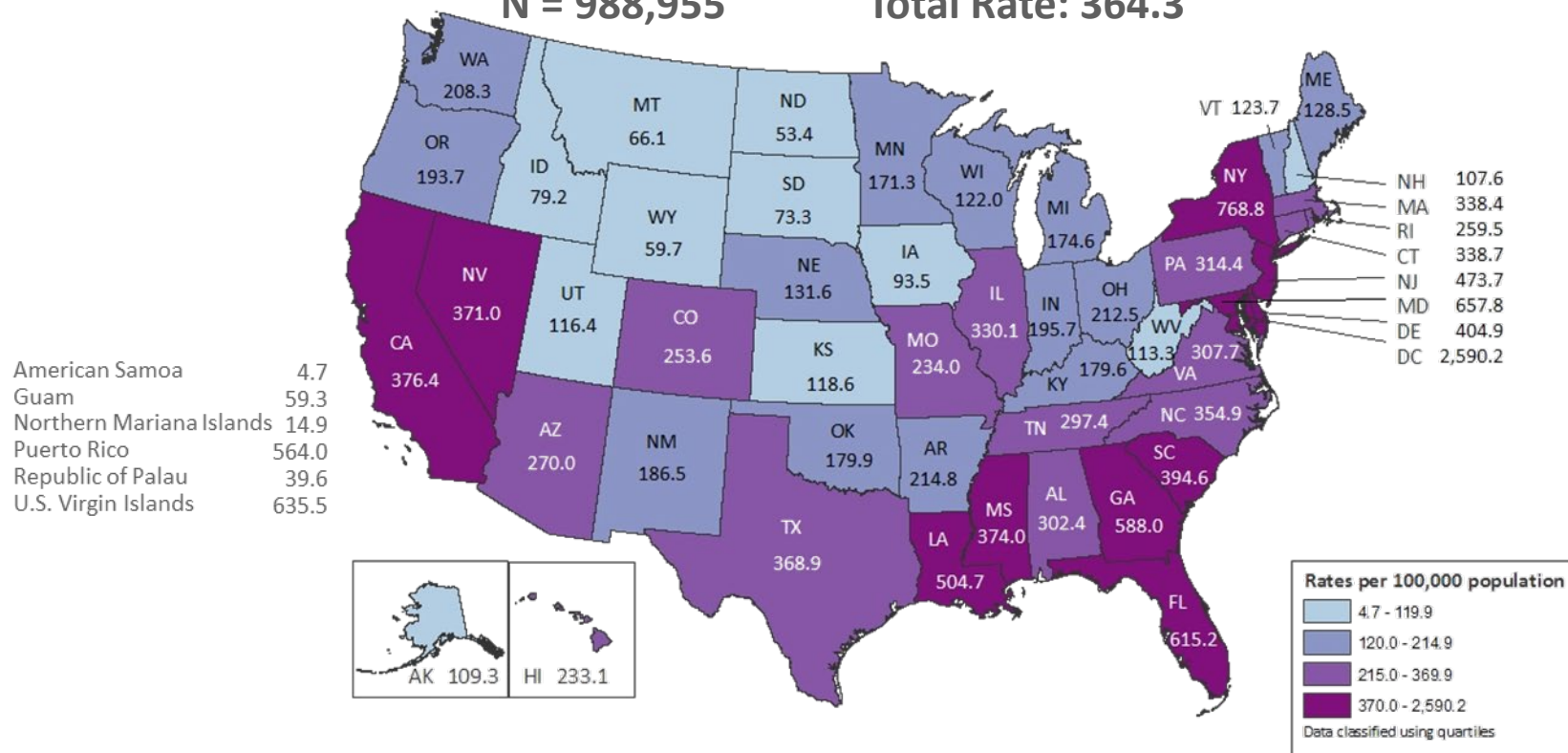


Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Data have been statistically adjusted to account for missing transmission category. Heterosexual contact is with a person known to have, or to be at high risk for, HIV infection.

* Difference from the 2010 estimate was deemed statistically significant ($P < .05$).

Rates of Adults and Adolescents Living with Diagnosed HIV Infection, by Area of Residence, Year-end 2015 — United States and 6 Dependent Areas

N = 988,955 Total Rate: 364.3



Note. Data are based on address of residence as of December 31, 2015 (i.e., most recent known address).





HIV Testing recommendations

- **CDC Recommendations: 2006**
- Routine, voluntary HIV screening for all persons 13-64 in health care settings, not based on risk
- A separate signed HIV consent is not recommended.
- Pretest and post-test HIV counseling not required
- **USPSTF: 2013 (currently being updated)**
- Grade A recommendation
 - Clinicians should screen all people age 15-65
 - Younger adolescent and older adults at increased risk
 - (Breast cancer screening is Grade B)

Case

- 19 year old male presents to the ED with fevers, chills and a sore throat
- Exam:
 - Pharyngitis
 - Lymphadenopathy



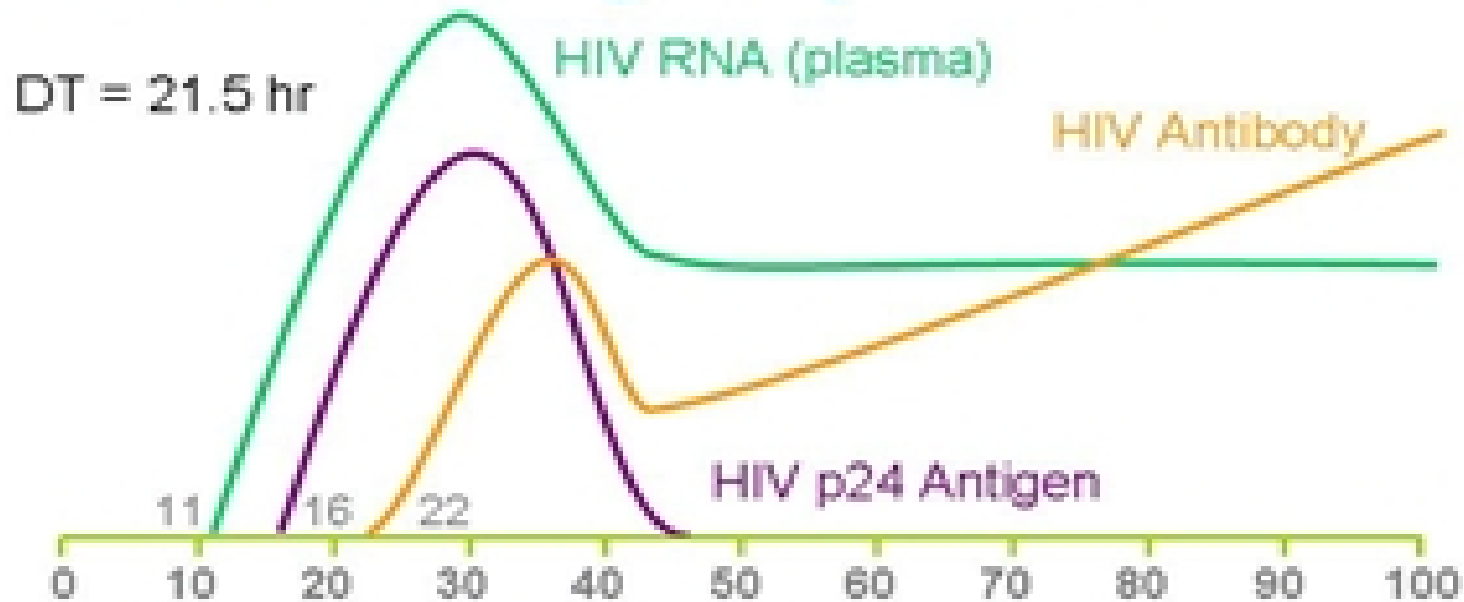
Acute Retroviral Syndrome:

■ Fever	96%
■ Lymphadenopathy	74%
■ Pharyngitis	70%
■ Rash	70%
■ Myalgia or arthralgia	54%
■ Diarrhea	32%





HIV Markers During Early Infection



Theoretical infectivity

HIV RNA

HIV p24 antigen

HIV antibody

Day 0

Day 11

Day 16

Day 22

5 days

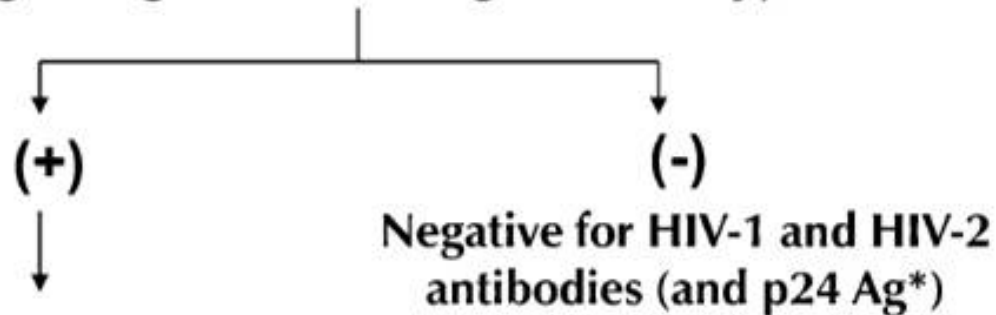
6 days

HIV Testing in 2009

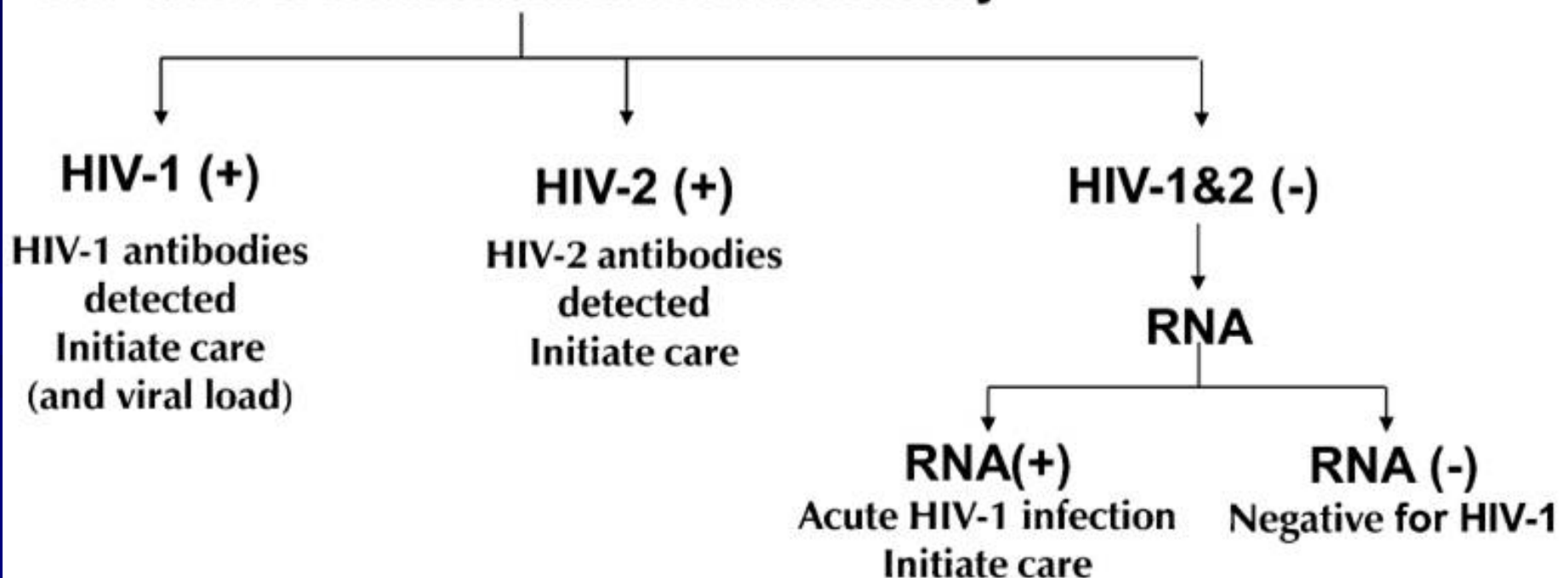
CPH17542-12

Sensitive HIV-1/2 Immunoassay

(eg, 4th generation Ag/Ab assay)



HIV-1/HIV-2 differentiation immunoassay



Window Period

- Time during which a recently infected person will have a negative HIV Antibody test
- Usually 3-4 weeks
- With newer test as short as 10 days
- Associated with very high HIV viral load
- Can be associated with symptoms
- Highly contagious

Rapid HIV Testing

- Several FDA approved rapid HIV test kits
 - Use oral fluid, whole blood, plasma, serum
 - Sensitivity: 99.6-100%
 - Specificity 99.8-99.9%
- First FDA approved rapid HIVab/ag test (4th generation test)
- Need follow-up confirmatory testing with conventional (non-rapid) test

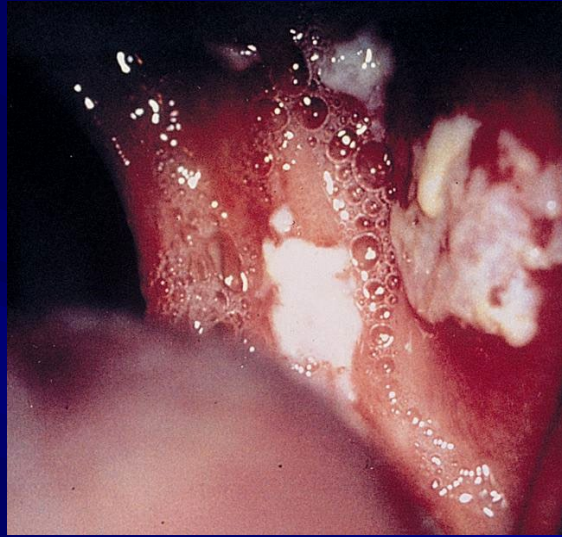


Obtain finger stick specimen

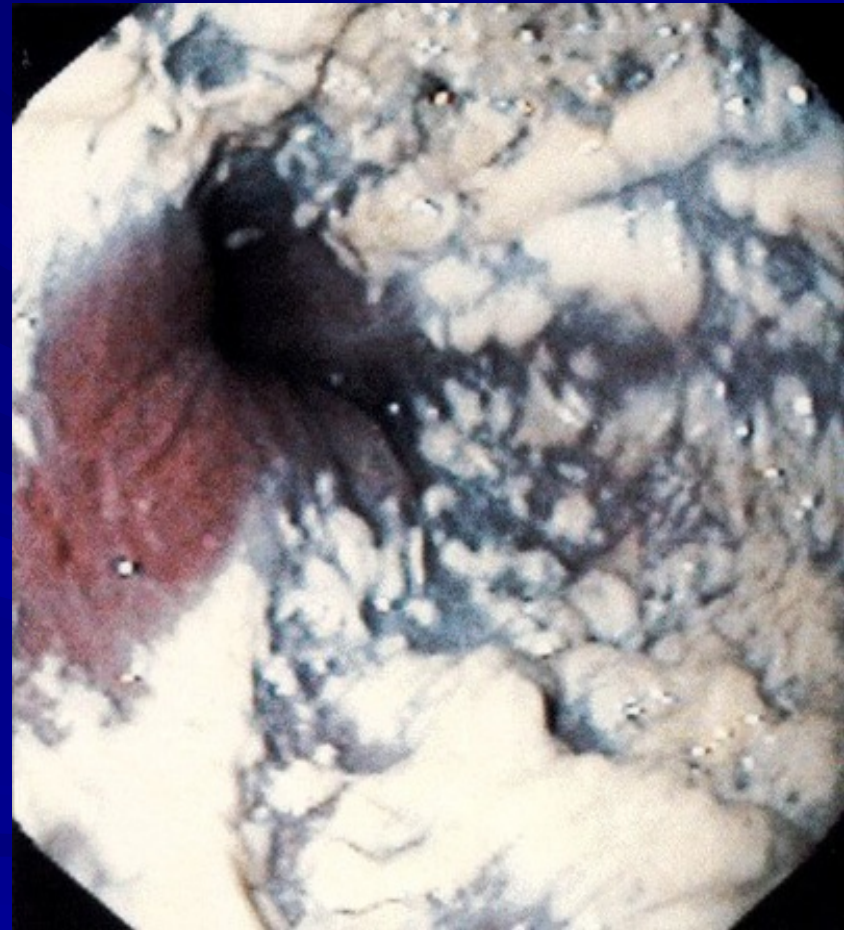
CD4+ Cells (T helper cells) and HIV Viral Load

- CD4- a T lymphocyte, measured by flow cytometry
 - HIV-1 infects CD4+ cells
 - In the absence of appropriate therapy leads to a profound CD4+ T cell lymphopenia.
 - Normal levels are 500 – 1500/ mm³
 - Absolute CD4 numbers can fluctuate
 - CD4% is a more steady marker and a CD4 of 200 is about 14%
- HIV Viral Load
 - Measures the amount of HIV virus RNA present in the *blood*
 - Monitored to look for response to therapy
 - Goal is Viral Load < 20

Oral Candidiasis



Candida Esophagitis



Oropharyngeal Candidiasis

- Thrush limited to oropharynx
- Esophagitis is more serious and seen with $CD4 < 100$
 - Odynophagia- painful swallowing
 - Chest pain
- Other causes of esophagitis
 - CMV (usually $CD4 < 50$)
 - HSV
 - Idiopathic ulceration ($CD4 < 50$)
 - Malignancy
 - Histoplasma

Presentation of Kaposi's sarcoma

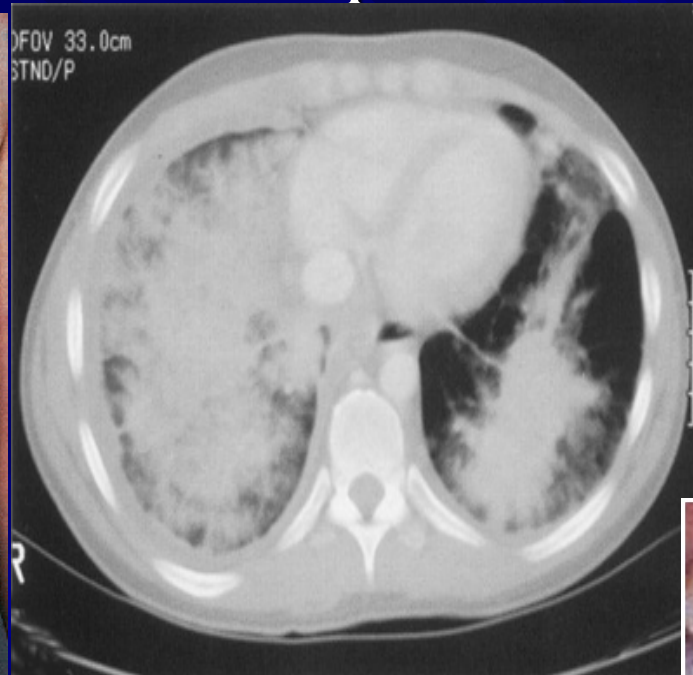


Photo Credit: Boston University

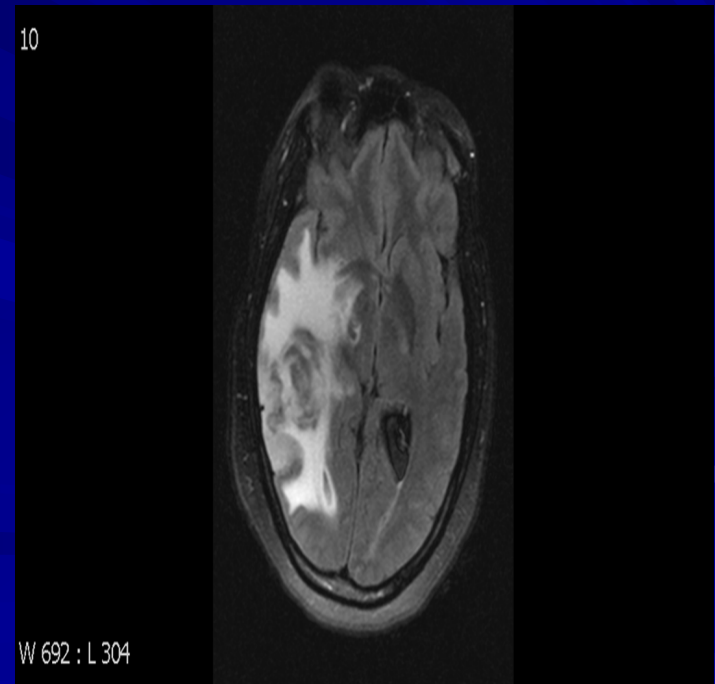
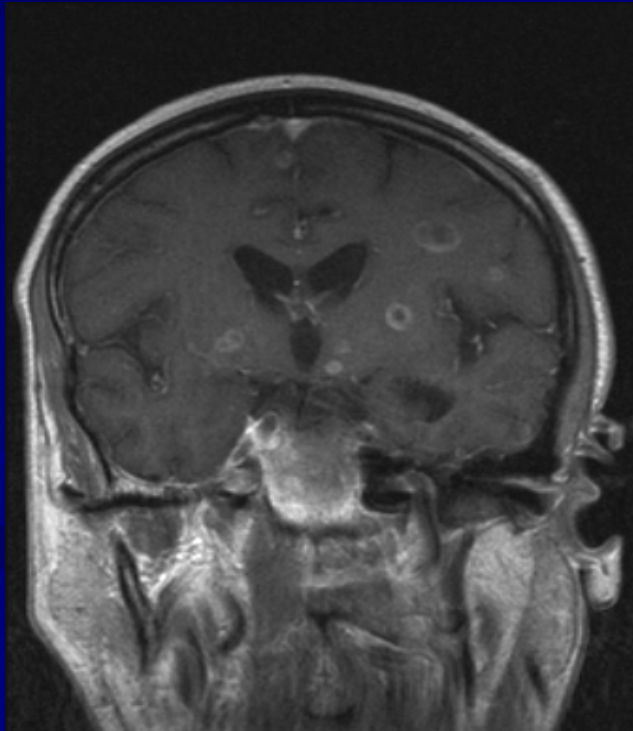
Differential for brain masses or ring enhancing lesions in an AIDS patient:

1. Cryptococcus

2. Cerebral toxoplasmosis : This is usually a reactivation infection that was previously acquired from cat litter, uncooked meats

3. Lymphoma

4. Less likely TB or Brain abscess or neurocysticercosis



C. neoformans meningoencephalitis

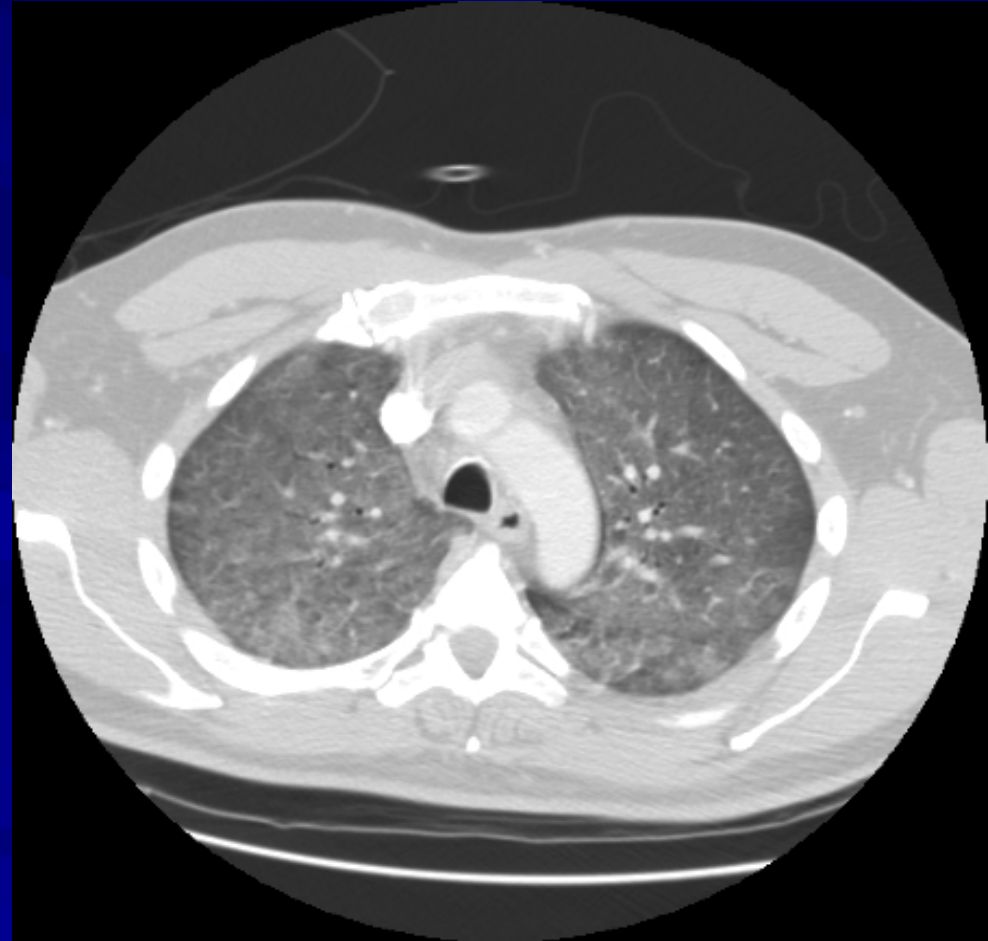
- Subacute presentation over several days or weeks
- Clinical features
 - Fever
 - Headache
 - Nausea
 - Altered mental status
- CSF
 - Raised opening pressure
 - Minimally raised protein and WBC
 - Positive cryptococcal Ag (98%)
- Blood
 - Positive cultures
 - Positive cryptococcal Ag (98%)
- Treatment
 - Reduce opening pressures with repeat LPs
 - Liposomal Amphotericin and Flucytosine
 - Followed by PO Fluconazole

- PML manifests as focal neurological deficits
 - Cognitive impairment, focal deficits, ataxia
 - Subacute- weeks to months
- JCV DNA
 - The assay is positive in approximately 70% to 90% of patients not taking ART
- The lesions are
 - typically involve white matter rather than gray matter
 - non-contrast enhancing and produce no mass effect



Case

- 57 year Caucasian male
- Cough , dyspnea, diarrhea for weeks
- ABG-pO₂ -90 on 100% NRB
 - Creatinine 1.8
 - WBC: 12



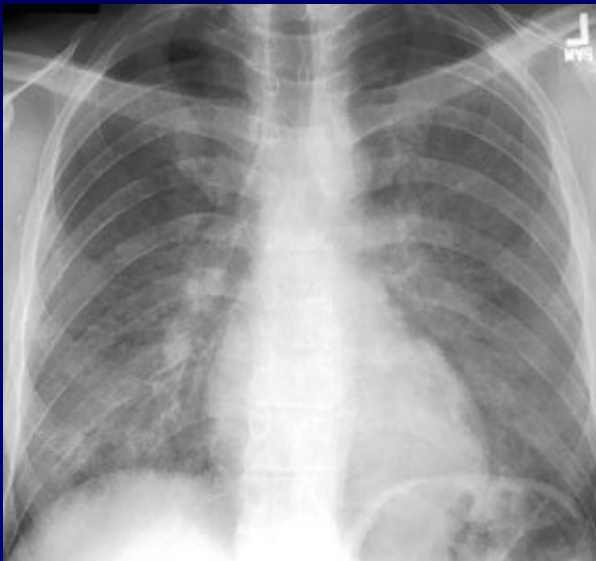
Pneumonia in HIV

- When in doubt, Respiratory isolation for Tb
 - *Streptococcus pneumoniae* is increased > 100 fold
 - PCP
 - Tuberculosis
 - Other atypical pathogens
 - Cryptococcus
 - Histoplasma

PCP

- PCP is a Subacute pneumonia caused by *Pneumocystis jirovecii*
- In one study 83% of infants had Pneumocystis antibody titers > 1:16 by 7 months
- Risk factors
 - CD4 < 200
 - Not on prophylaxis
 - High Viral load
 - Previous PCP
- S/S: Dyspnea, dry cough, chest discomfort, fever
- A normal CT chest makes PCP unlikely

PCP: Diagnosis (Imaging)



Chest x ray: PCP pneumonia with bilateral, diffuse granular opacities.

Credit: L, Huang, MD, HIV InSite

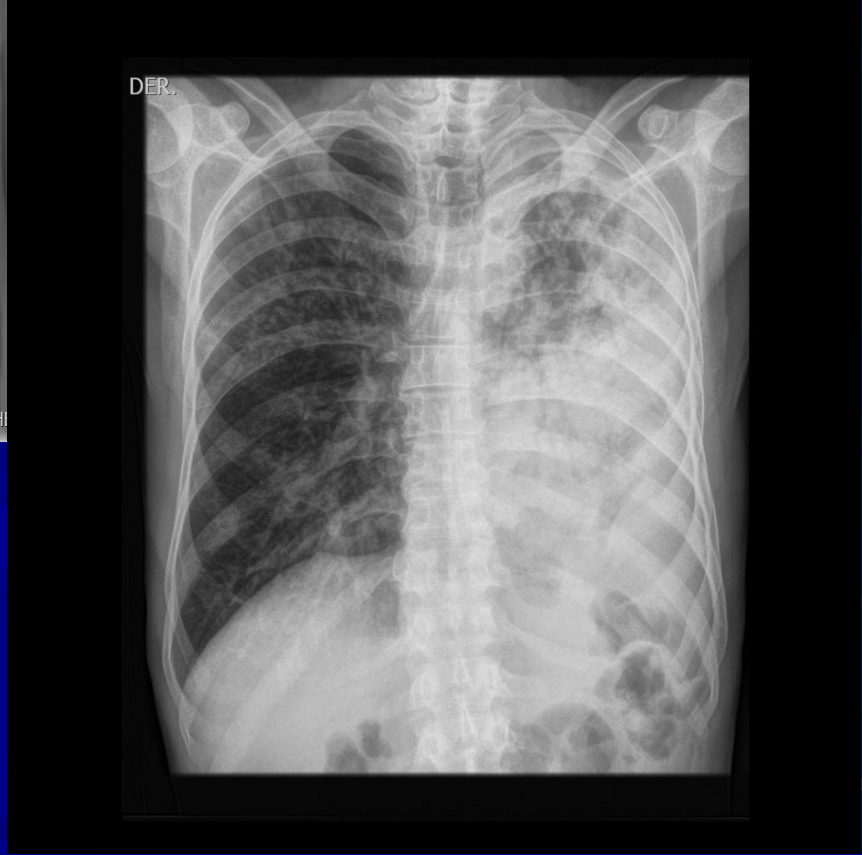
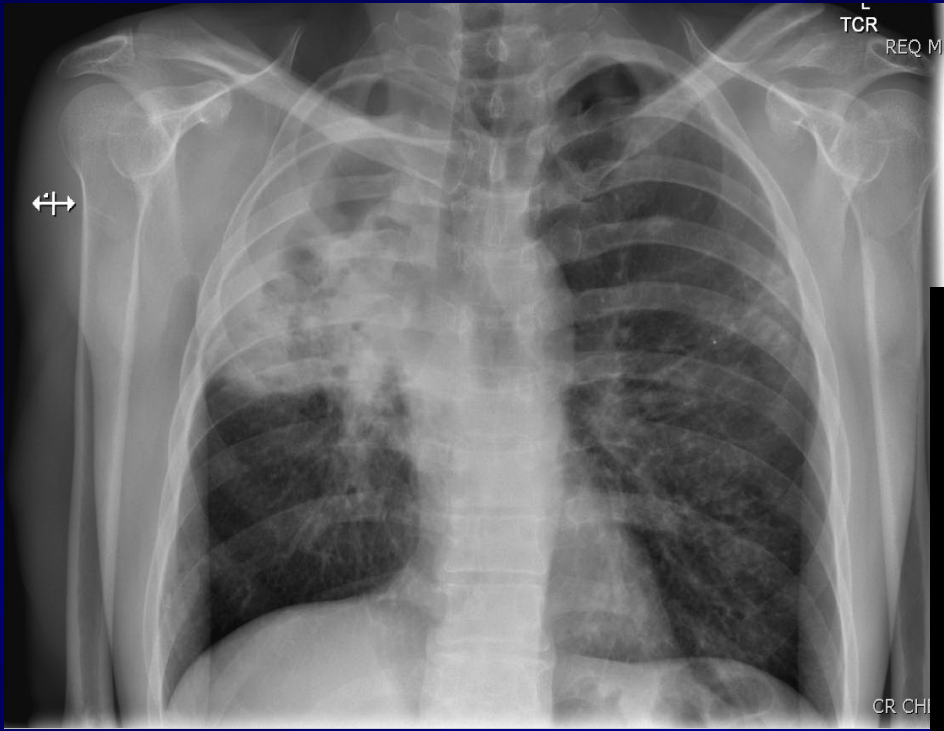


Chest x ray: PCP pneumonia with bilateral perihilar opacities, interstitial prominence, hyperlucent cystic lesions.

Credit: HIV Web Study, www.hivwebstudy.org, © 2006 University of Washington

TB/HIV Co-Infection

- Reactivation of latent TB
 - More likely in HIV-infected patients
 - 7-10% annual risk in HIV-infected patients with positive tuberculin skin test (TST)
 - In HIV uninfected, 5-10% lifetime risk
- The treatment of TB in patients with HIV infection should follow similar principles as for non HIV
- Directly observed therapy is strongly recommended



Case

PORTABLE X-RAY CHEST PA OR AP VIEW

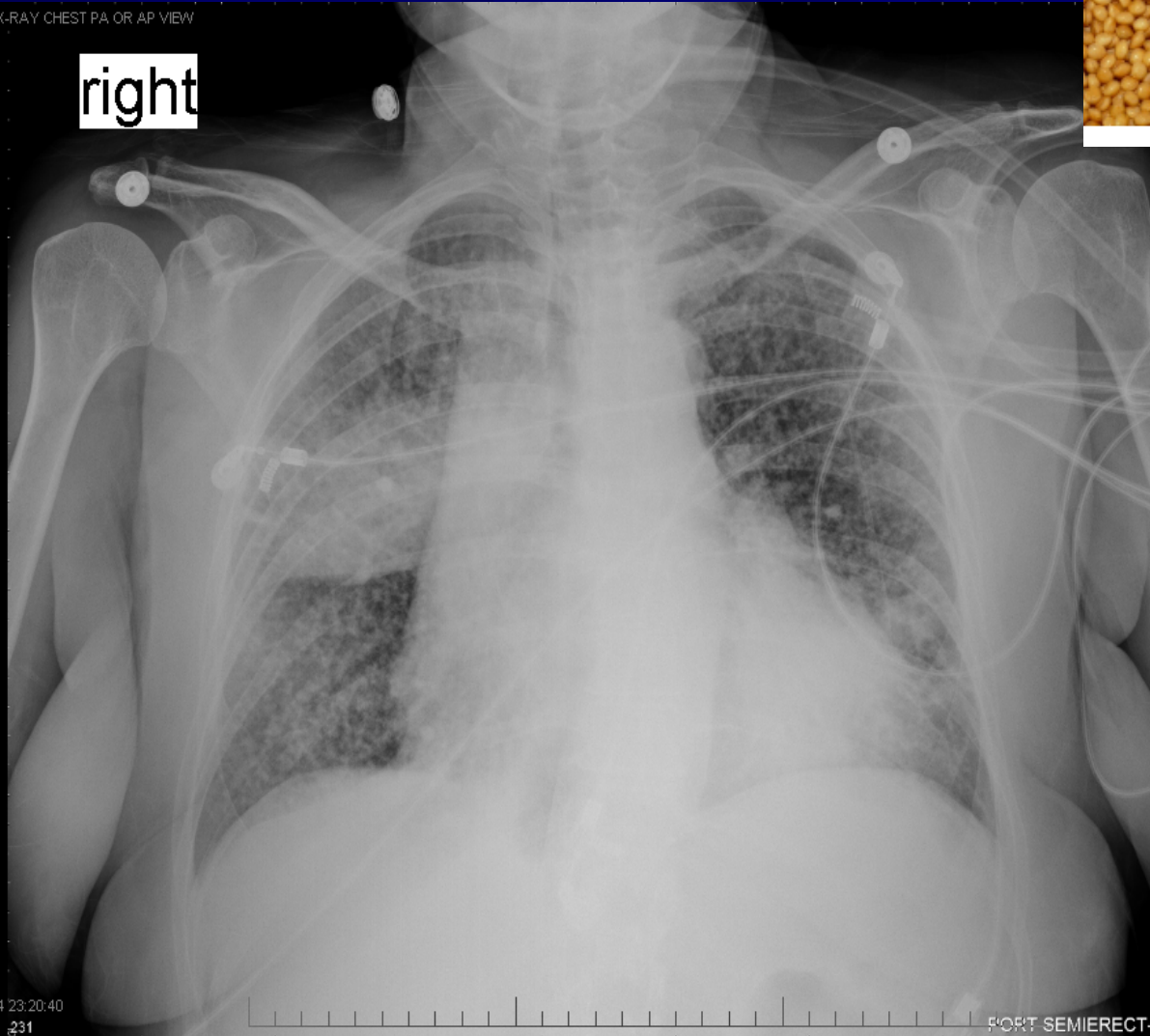
Series
Series #1
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Dec 28, 2004 23:20:40
XPCH1V 31
Key

PORT SEMIERECT-



Case

- 33 year female
- CD4 12, noncompliant with treatment
- 1 month of wt loss, night sweats, fever
- Cachexia, lymphadenopathy, palpable liver
- WBC-2.4, Alk PO4-1291, AST-245, ALT-257
- Abdominal Ultrasound-Normal, Chest X Ray-normal

Diagnosis?

- A. Lymphoma
- B. Tuberculosis
- C. Disseminated MAC

Disseminated Mycobacterium avium intracellulare

- Usually a disseminated multi organ infection
 - fever, night sweats, weight loss, diarrhea, abdominal pain
 - lymphadenitis (cervical or mesenteric),
 - hepatomegaly, splenomegaly
 - anemia, elevated liver alkaline phosphatase

Treatment:

Azithromycin + Rifabutin + Ethambutol

Antiretrovirals



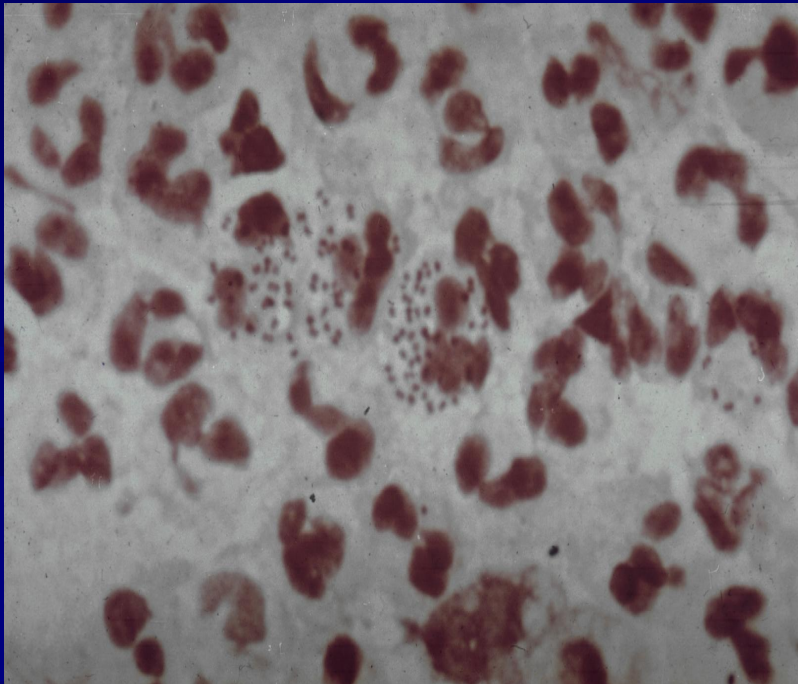
Case

- 28 year HIV positive male with CD4 of 250
- Fever, malaise and a rash
- Penile ulcer



Case

- 24 year male, sexually active
- Presents with 4 day history of dysuria and penile discharge



OI Prophylaxis

Primary Prophylaxis

- *Pneumocystis jiroveci* pneumonia (PCP)- TMP/SMX if CD4 <200
- Tuberculosis- PPD/IGRA
- Toxoplasmosis- TMP/SMX if CD4 < 100
- *Mycobacterium avium* complex (MAC) – Macrolide if CD4 < 50
- *S pneumoniae* infections
- Hepatitis A and B
- HPV
- Influenza
- HPV

Case : 25 yr-Old Newly Diagnosed

- 25-yr-old black woman who went for her biannual women's health visit
 - Diagnosed with HIV infection based on a routine HIV test
- CD4+ cell count: 748 cells/mm³
- HIV-1 RNA: 32,250 copies/mL
- Physical exam normal; no other significant past medical history



Based on current US guidelines, what would you recommend?

- A. She can wait until her HIV-1 RNA is higher
- B. She can wait until her CD4+ cell count is lower
- C. ART decision to be made at next visit in 2 months
- D. She should start ART now

Recommendations for Initiating ART

- “ART is recommended for all HIV-infected individuals to reduce the risk of disease progression.”
 - ART is recommended as soon as possible and moving towards starting the same day as the diagnosis

Treatment Goals

- Reduce morbidity and mortality
- Improve quality of life
- Restore/preserve immune function
- Suppress viral load
- Decrease **risk of transmission**

Treatment as Prevention

■ HPTN-052: (NEJM, 2011)

- Immediate ART -883 couples
- Delayed ART-877 couples (when CD4 <250)
- HIV Transmission reduced by 96%

■ Opposites Attract Study

- MSM with undetectable viral load do not transmit HIV in spite of thousands of condom-less acts

■ PARTNER

- 1,110 HIV serodiscordant couples in Europe
 - 2/3rd heterosexual and 1/3rd MSM
- The HIV-infected partner had VL <200
- No documented HIV transmission

Potential Benefits of Early Therapy

- Potential decrease in risk of many complications, including:
 - HIV-associated nephropathy
 - Liver disease progression from hepatitis B or C
 - Cardiovascular disease
 - Malignancies (AIDS defining and non-AIDS defining)
 - Neurocognitive decline
 - Blunted immunological response owing to ART initiation at older age
 - Persistent T-cell activation and inflammation

Table 2. Demographic and Clinical Characteristics of Treated Human Immunodeficiency Virus (HIV)-Infected Patients Versus HIV-Negative Controls, by Healthcare Coverage Payer: 2003–2013

Characteristic/Comorbidity	Commercial			Medicaid			Medicare		
	HIV Infected (n = 20 519)	Controls (n = 46 763)	P	HIV Infected (n = 16 020)	Controls (n = 36 791)	P	HIV Infected (n = 461)	Controls (n = 1184)	P
Age, y									
Mean ± SD	46.2 ± 9.4	46.2 ± 9.2	1.000	44.8 ± 9.4	44.7 ± 9.7	.272	66.8 ± 8.9	66.9 ± 8.9	.838
≥50	13.1	13.0	.753	18.4	17.8	<.001	89.8	89.4	.829
Male sex	84.3	84.3	.934	53.5	53.8	.512	84.2	84.1	.983
Cardiovascular events									
Any	6.7	4.0	<.001	10.4	7.6	<.001	26.9	26.7	.932
Myocardial infarction	1.7	1.0	<.001	3.2	1.7	<.001	8.2	6.7	.266
Peripheral vascular diseases	1.6	1.2	<.001	2.9	3.3	.039	11.3	12.4	.526
Deep vein thrombosis	2.6	1.1	<.001	3.8	1.9	<.001	9.1	5.8	.017
Cardiovascular and renal risk factors									
Essential hypertension	31.2	30.2	.005	37.3	33.8	<.001	65.7	69.8	.106
Diabetes mellitus	10.1	10.2	.704	16.0	18.1	<.001	29.5	33.9	.089
Obesity/overweight	5.6	6.7	<.001	7.6	9.9	<.001	3.5	8.1	<.001
Hyperlipidemia	31.1	30.4	.076	22.4	24.0	<.001	47.9	55.9	.004
Hepatitis C	5.4	0.5	<.001	22.9	3.7	<.001	8.2	1.5	<.001
Renal impairment	8.8	2.8	<.001	15.2	5.9	<.001	31.0	18.2	<.001
Fracture or osteoporosis	7.6	6.4	<.001	13.0	10.0	<.001	18.2	16.4	.372
Other conditions									
Endocrine disease (including diabetes)	20.9	18.1	<.001	26.3	24.5	<.001	43.4	45.4	.452
Thyroid disease	4.7	5.9	<.001	5.5	7.7	<.001	9.3	14.9	.003
Cancer	8.0	4.1	<.001	9.8	4.2	<.001	26.5	20.8	.013
Liver disease	6.2	2.4	<.001	11.3	4.5	<.001	8.9	20.8	.012
Rheumatoid arthritis	0.4	0.6	.001	1.2	1.8	<.001	0.7	3.5	.002
Alcoholism	3.1	1.6	<.001	12.2	5.9	<.001	2.8	2.6	.820

Data are percentage of patients, unless otherwise indicated.

Joel Gallant et al, Comorbidities Among US Patients with Prevalent HIV Infection—A Trend Analysis, *The Journal of Infectious Diseases*, Volume 216, Issue 12, 19 December 2017,

HIV: Causes of Death

■ ART-CC

- 13 cohorts from Europe and NA
- 1876 deaths among 39,272 patients starting ART between 1996-2006
- AIDS-related causes - 43% of the deaths
- Non-AIDS deaths accounted for greater proportion of death than AIDS causes
 - malignancy, infections, violence, LD, CVD

Cancer risk in HIV

- Cohort of HIV-infected people identified in HIV registries in Colorado, Connecticut, Georgia, Maryland, Michigan, New Jersey, New York, Puerto Rico, Texas; 1996 - 2012
- Calculated standardized incidence ratios (SIRs) to measure cancer risk in HIV vs general population
 - 448 258 people with HIV
 - 21 294 incident cancers, risk was elevated ($p < 0.0001$)
 - Overall SIR 1.69, 95% CI 1.67–1.72
 - SIR high for KS, NHL , cervix, anus, Hodgkins, liver and lung

Cancer risk in HIV-infected people in the USA from 1996 to 2012: a population-based, registry-linkage study. The lancet. HIV, ISSN: 2352-3018, Vol: 4, Issue: 11, Page: e495-e504 : 2017

DHHS Guidelines: Recommended Regimens for First-line ART

Class	Regimen
INSTI	<ul style="list-style-type: none">▪ BIC/TAF/FTC (Biktarvy®)▪ DTG/ABC/3TC (Triumeq®)▪ DTG + (TAF or TDF)/FTC (Tivicay® + Descovy® or Truvada®)▪ RAL + (TAF or TDF)/FTC (Isentress® + Descovy® or Truvada®)

Elvitegravir/**COBI**/tenofovir/emtricitabine: Moved to alternative

This change was made because these combinations include cobicistat, EVG also has a lower barrier to resistance than DTG and BIC.

DHHS Guidelines. 2018.

HIV:Single Tablet Regimens



Atripla



Genvoya



Complera



Juluca



Triumeq

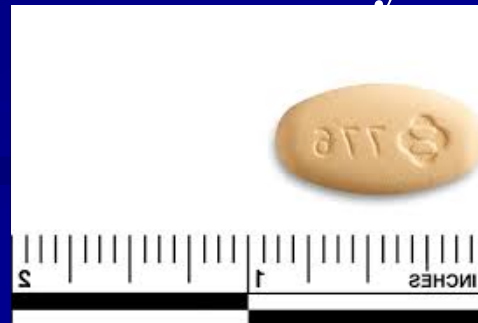


Odefsey



Biktarvy

Stribild



Delstrigo

Fixed Dose Daily Combinations

Drugs	Brand Name	Admin	Notes
BIC/TAF/FTC	Biktarvy®	+/- food	False SCr elevation/cations
DRV/COBI/TAF/FTC	Symtuza®	With food	COBI, TAF
DTG/ABC/3TC	Triumeq®	+/- food	HLAB*5701 testing
EVG/c/FTC/TDF	Stribild®	Take with food	Monitor CrCl, false elevation in SCr (Cobicistat), SE: GI
EVG/c/FTC/TAF	Genvoya®	Take with food	Monitor CrCl, false elevation in SCr (Cobicistat), SE: GI
RPV/FTC/TDF	Complera®	Take with food	Caution with acid reducing agents, SE: mood/rash
RPV/FTC/TAF	Odefsey®	Take with food	Caution with acid reducing agents, SE: mood/rash
EFV/FTC/TDF	Atripla®	Take on an empty stomach (preferably at night)	Pregnancy category X in 1 st trimester, SE: CNS toxicity
DOR/TDF/3TC	Delstrigo®	+/- food	DOR available alone

Ibalizumab :Monoclonal Antibody

- Ibalizumab (Trogarzo)
 - Human monoclonal antibody that binds the CD4 receptor
 - Post-attachment HIV-1 inhibitor
 - Active against all clades and CCR5 and CXCR4 tropic virus
 - No cross resistance with existing ARV
 - Long acting (bi-weekly IV injection)
 - Given in combination with other antiretrovirals
 - Indicated for heavily treatment-experienced adults with multidrug resistant HIV-1 infection failing their current antiretroviral regimen.

AIDS Drug Assistance Programs (ADAPs)

**Provides HIV-related prescription drugs
to low-income people with HIV/AIDS
who have limited or no prescription
drug coverage**

HIV and Pregnancy

When does transmission occur?

- Intrapartum ~80%
- Breastfeeding ~14%
- Antenatal ~20%

- Use ART per DHHS guidelines
- Goal: To get the viral load < 20 ASAP

Immune Reconstitution Inflammatory Syndrome

- **Characterized by fever, worsening clinical signs of the OI; symptoms of new OI**
- **Occurs in the first weeks after starting ART**
- **Associated with a rise in CD4 and/or a fall in viral load**
- **Usually occurs within first few weeks of ART but may occur up to several months later**

90-90-90

- An ambitious treatment target to help end the AIDS epidemic by 2020



diagnosed



on treatment

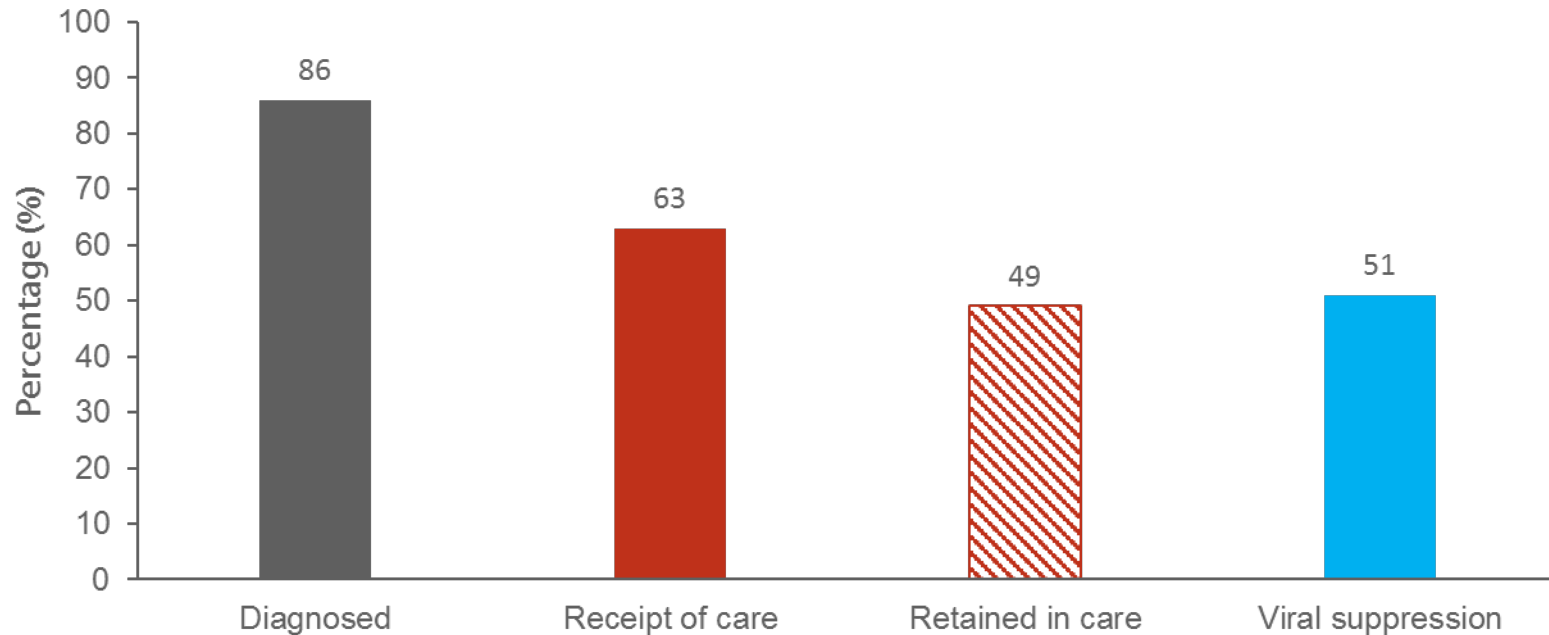


virally suppressed



Persons Living with Diagnosed or Undiagnosed HIV Infection

HIV Care Continuum Outcomes, 2015—United States



Note. Receipt of medical care was defined as ≥ 1 test (CD4 or VL) in 2015. Retained in continuous medical care was defined as ≥ 2 tests (CD4 or VL) ≥ 3 months apart in 2015. Viral suppression was defined as < 200 copies/mL on the most recent VL test in 2015.



Early Initiation of ART: Evidence for Early Start?

- **Start Study**

- ART naïve patients
- CD4 >500 cell/mm³
- Study outcome: AIDS events, Non-AIDS event, Death
- Early treatment 57% reduction in a serious event
- Immediate ART reduced both AIDS-event and non-AIDS related events

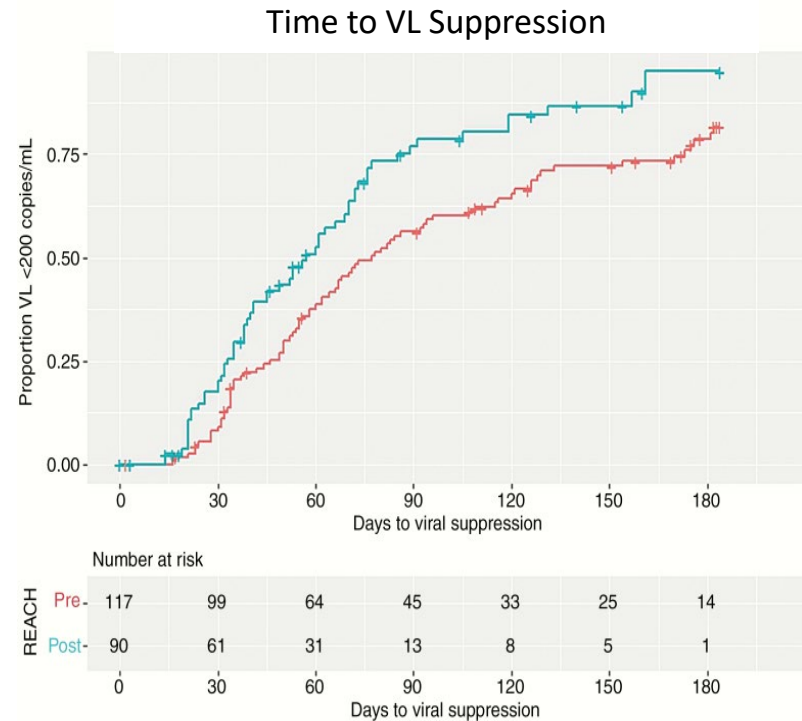


Rapid Initiation- Data to support this practice.

When to Start: Immediately after HIV
Diagnosis

A Rapid Entry Program- Atlanta

- Rapid Entry and ART Clinic for HIV (REACH) program
- Goal: 1st appointment and ART offered within 72 hours
- Pre and post REACH
- Days to 1st appt: 14 vs. 4 days
- Days to ART: 22 vs 4 days



<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6022569>

/

Rapid Initiation- Guideline

When to Start: Immediately after HIV Diagnosis

- 2017 WHO Guidelines: endorse immediate ART (within 7 days of diagnosis) for all
- 2018: IAS Guidelines endorse immediate ART
- 2018: DHHS guidelines pending a decision on immediate ART

<http://apps.who.int/iris/bitstream/handle/10665/255884/9789241550062-eng.pdf;jsessionid=2A0EAAFA754A0B62E2F0C73BF42A48D0?sequence=1>



PrEP: Who Needs It?

US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES – 2017 UPDATE

A CLINICAL PRACTICE GUIDELINE

MSM	Heterosexual Men and Women	Injection Drug Users
<ul style="list-style-type: none">• Commercial sex workers• HIV positive partner• Recent STI• Multiple partners• Inconsistent/No condom use	<ul style="list-style-type: none">• Commercial sex workers• HIV positive partner• Recent STI• Multiple partners• Inconsistent/No condom use• High prevalence area	<ul style="list-style-type: none">• HIV positive injecting partner• Sharing needles/injection equipment

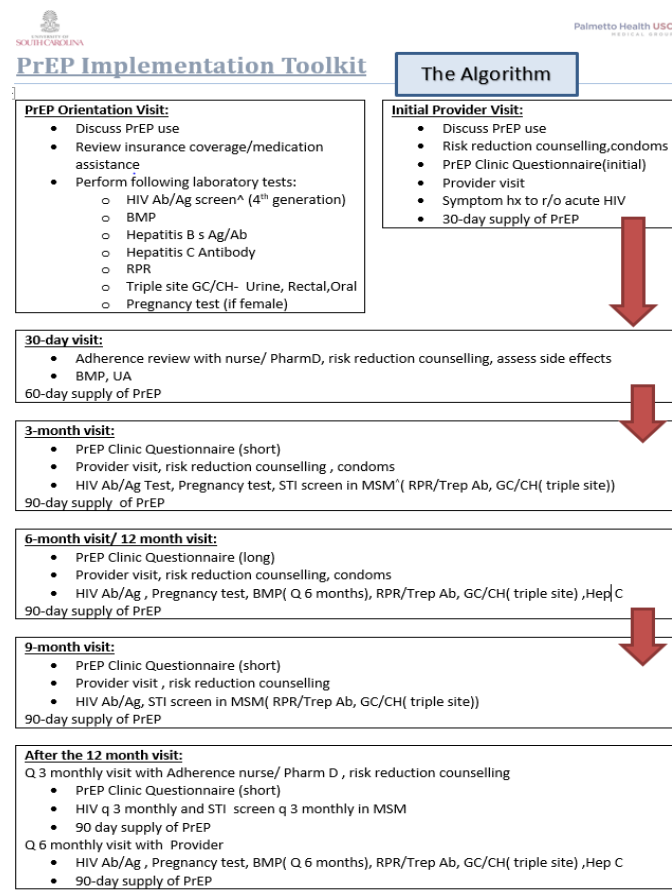
<https://www.cdc.gov/hiv/risk/prep/index.html> (2017 guidelines)

Don't forget about your LGBTQ+ patients!

PrEP- Implementation

Highlights:

- **HIV Ab/Ag screen** baseline and q 3 months
- Hep B/Hep C testing before starting PrEP
- Renal function q 3 months
- No labs, no PrEP refill
- STI (gonorrhea, chlamydia, syphilis) q 3-6 months
 - MSM q3 months, triple site for GC/Chl
- Risk reduction counseling- sex and drugs
- Assessing adherence every visit
- Provide **condoms**



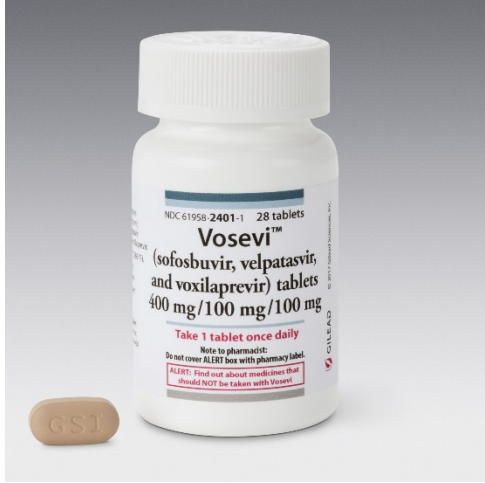
HIV/HCV- 10-30 % co-infection rate

- All patients with HIV should be screened for HCV infection
 - At-risk patients should undergo repeat testing annually(MSM).
- Patients with HCV/HIV coinfection:
 - Counsel to avoid alcohol and to use appropriate precautions
 - Should be screened for active and prior hepatitis B virus by testing
 - Hepatitis B surface antigen (HBsAg)
 - Hepatitis B surface (HBsAb)
 - HBcAb; total or IgG
- Active HBV infection : ART that includes TAF/TDF
- HCV treatment in HIV infected patients follows similar principles as mono-infected patients
 - Look for drug interaction

Available co-formulated DAAs



Tablet may not be shown at actual size. For illustration purposes only.



Sources For Further Information

- <http://AIDSinfo.nih.gov>

- www.cdc.gov

- South East AETC