NORTHWEST AIDS EDUCATION AND TRAINING CENTER

Primary HIV Infection

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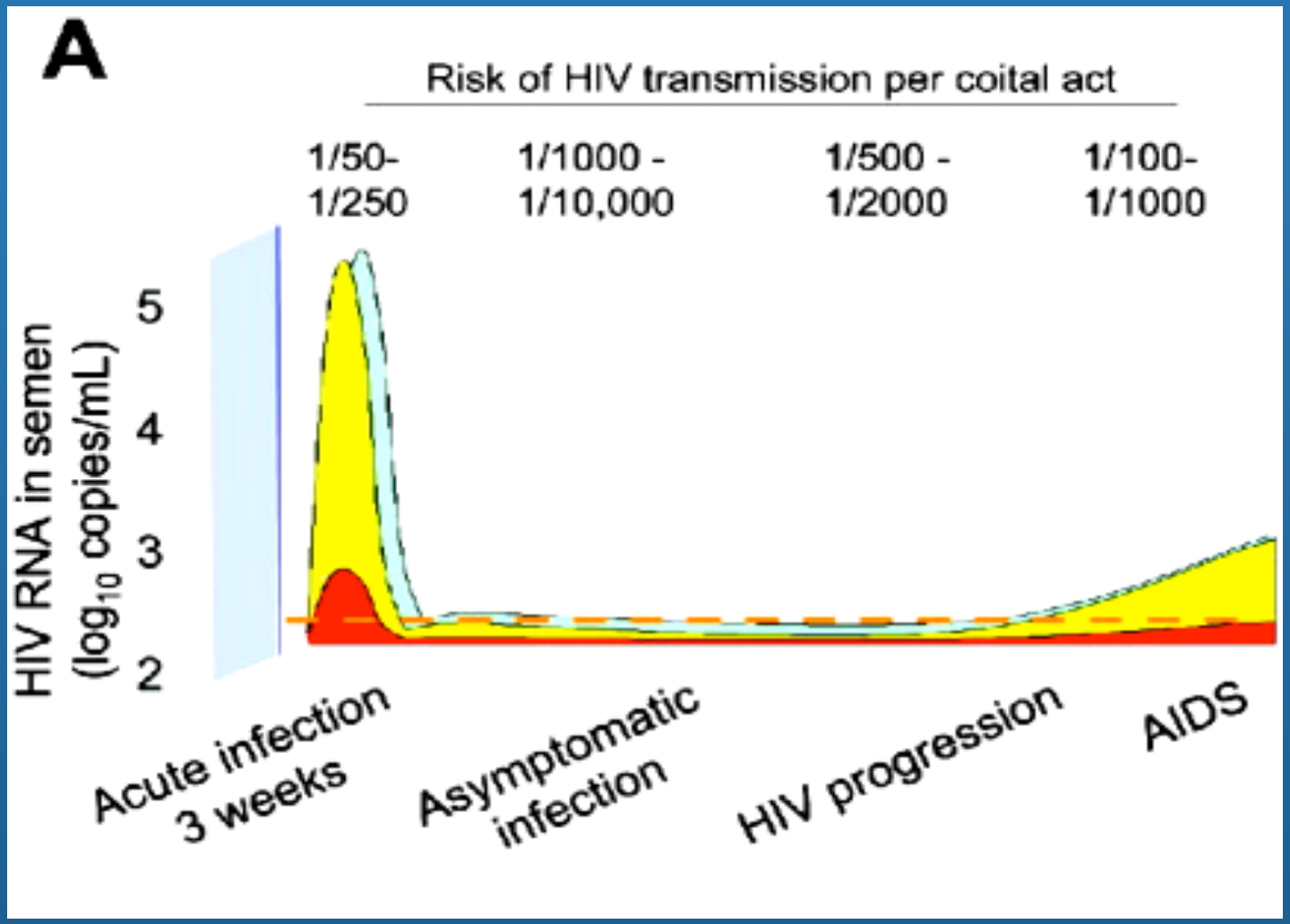
Learning Objectives

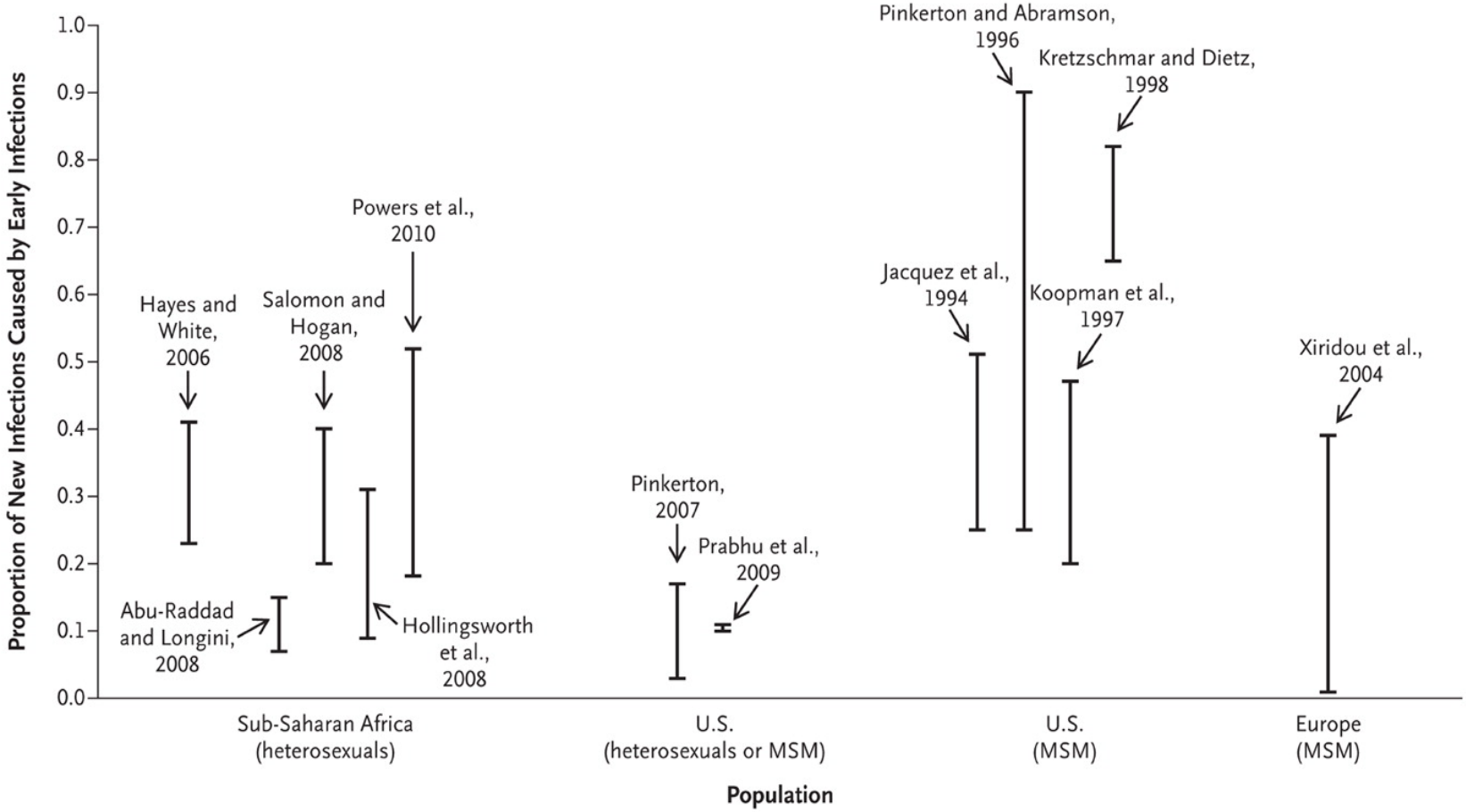
1. What is “primary HIV infection”?
2. Why primary HIV infection is important.
3. How to recognize and test for primary HIV infection.
4. Specific issues with treatment

Why is primary HIV infection important? Risk of HIV transmission



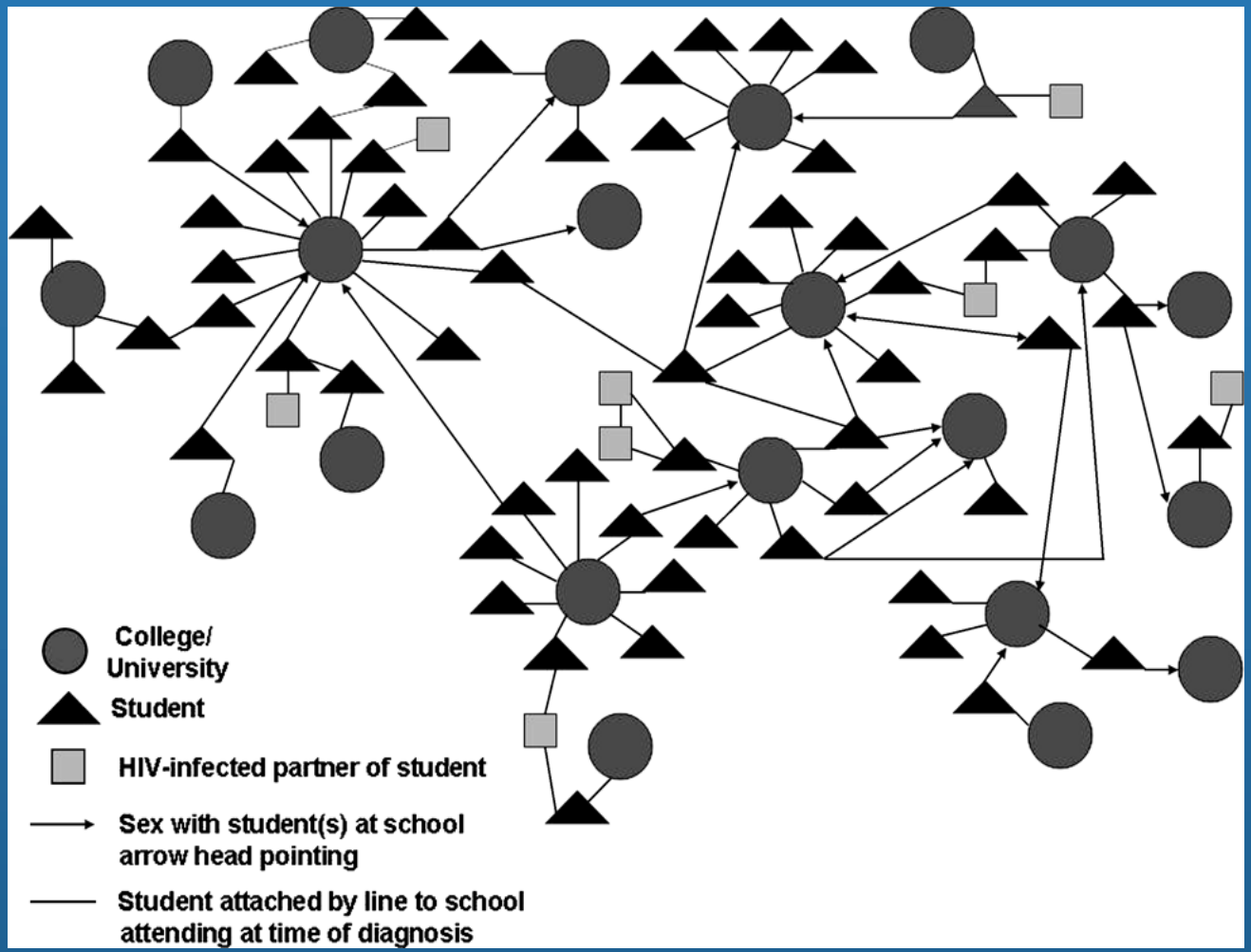
Cohen JID 2005; 191(9); 1391-1393

Why is primary HIV infection important? Contribution to HIV incidence



Cohen et al. NEJM, 2011; 364:1943-1954

Why is primary HIV infection important? Identification of transmission clusters

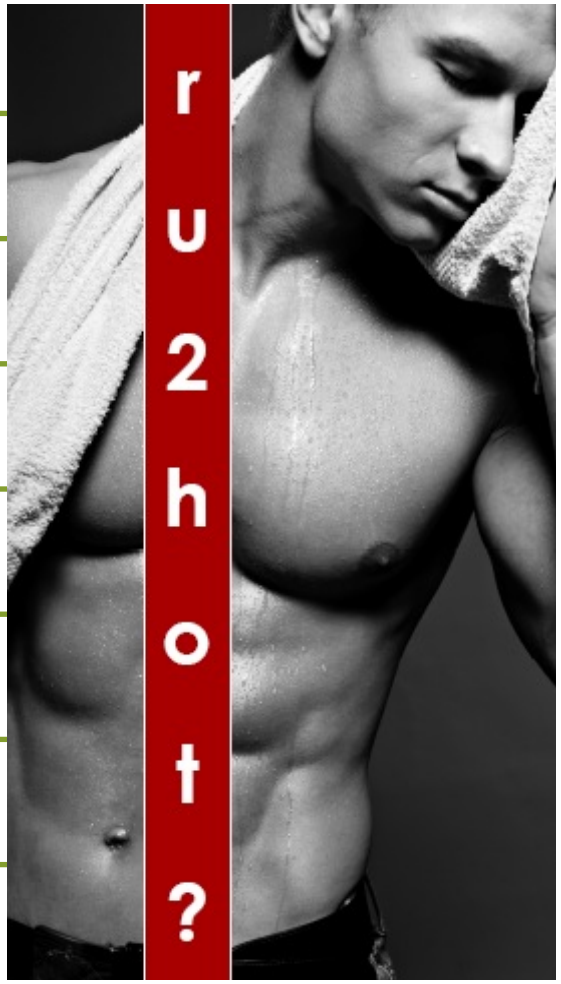


Hightow, JAIDS 2005; 38:531-7

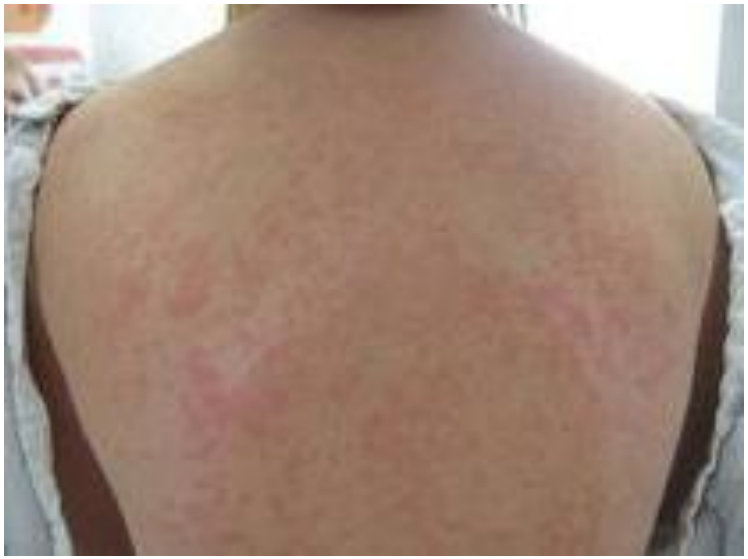
Why is primary HIV infection difficult to recognize? Non-specific symptoms

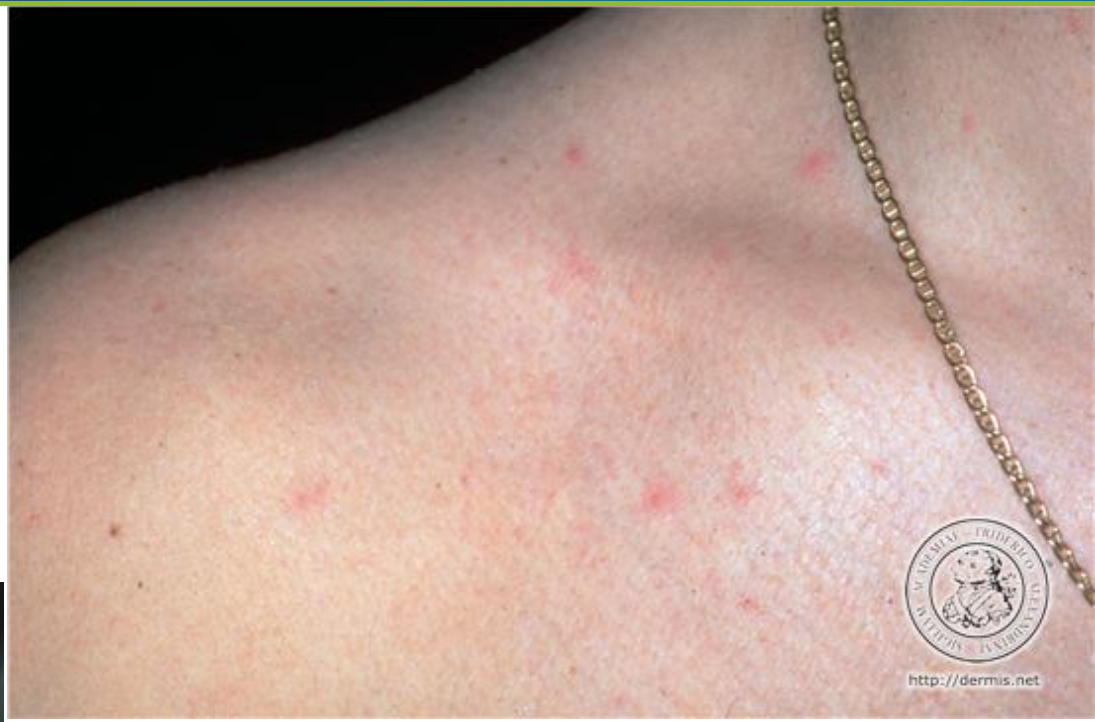
Approximately **50-90%** of individuals experience ≥1 symptom(s) ~2 weeks after infection

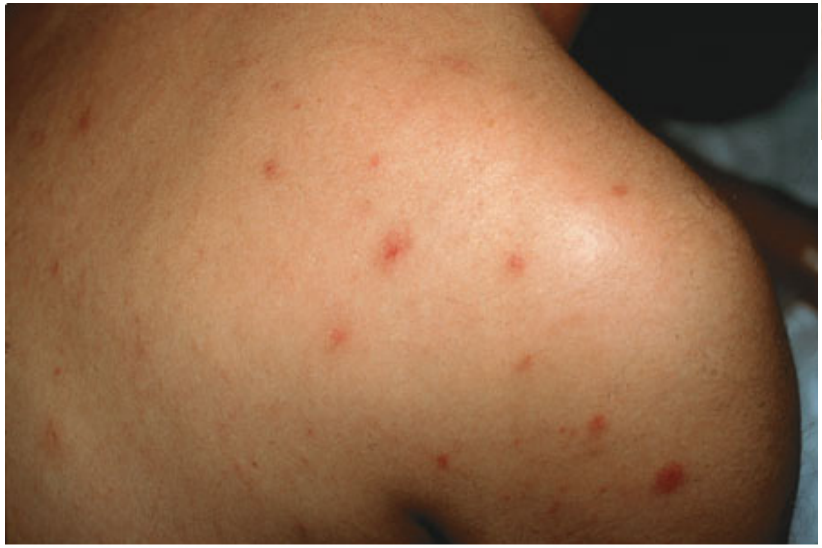
- Fever
- Fatigue
- Sore throat
- Muscle & joint aches
- Night sweats
- Headaches
- Diarrhea
- Rash

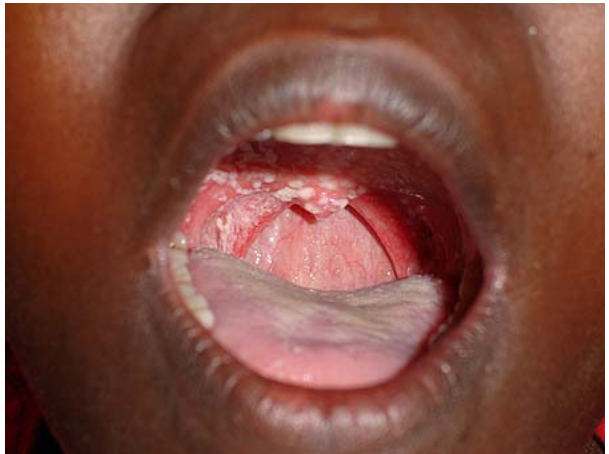


Acute Retroviral Syndrome









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Why is primary HIV infection difficult to recognize?

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A 21-year-old sexually active woman is evaluated because of a three-week history of fever, fatigue, headache, and a mild sore throat. On physical examination the patient is alert and oriented. Temperature is 38.0 C (100.4 F). A maculopapular rash is present over the trunk and face, and a few ulcers are seen on the soft palate. Her cervical lymph nodes are slightly enlarged, and her neck is stiff. Pelvic examination shows mild cervicitis.

Leukocyte count is 4600/cu mm with 10% atypical lymphocytes. Antistreptolysin O titer is normal. Infectious mononucleosis spot (Monospot) test and rapid plasma reagin (RPR) test are negative. A cervical swab is positive for *Neisseria gonorrhoeae* by DNA probe.

Lumbar puncture:

Cell count	60 WBCs/cu mm; 95% lymphocytes, 5% monocytes
Protein	73 mg/dL
Glucose	63 mg/dL (simultaneous plasma glucose 100 mg/dL)
CSF cultures	No growth

Which of the following is the most likely diagnosis?

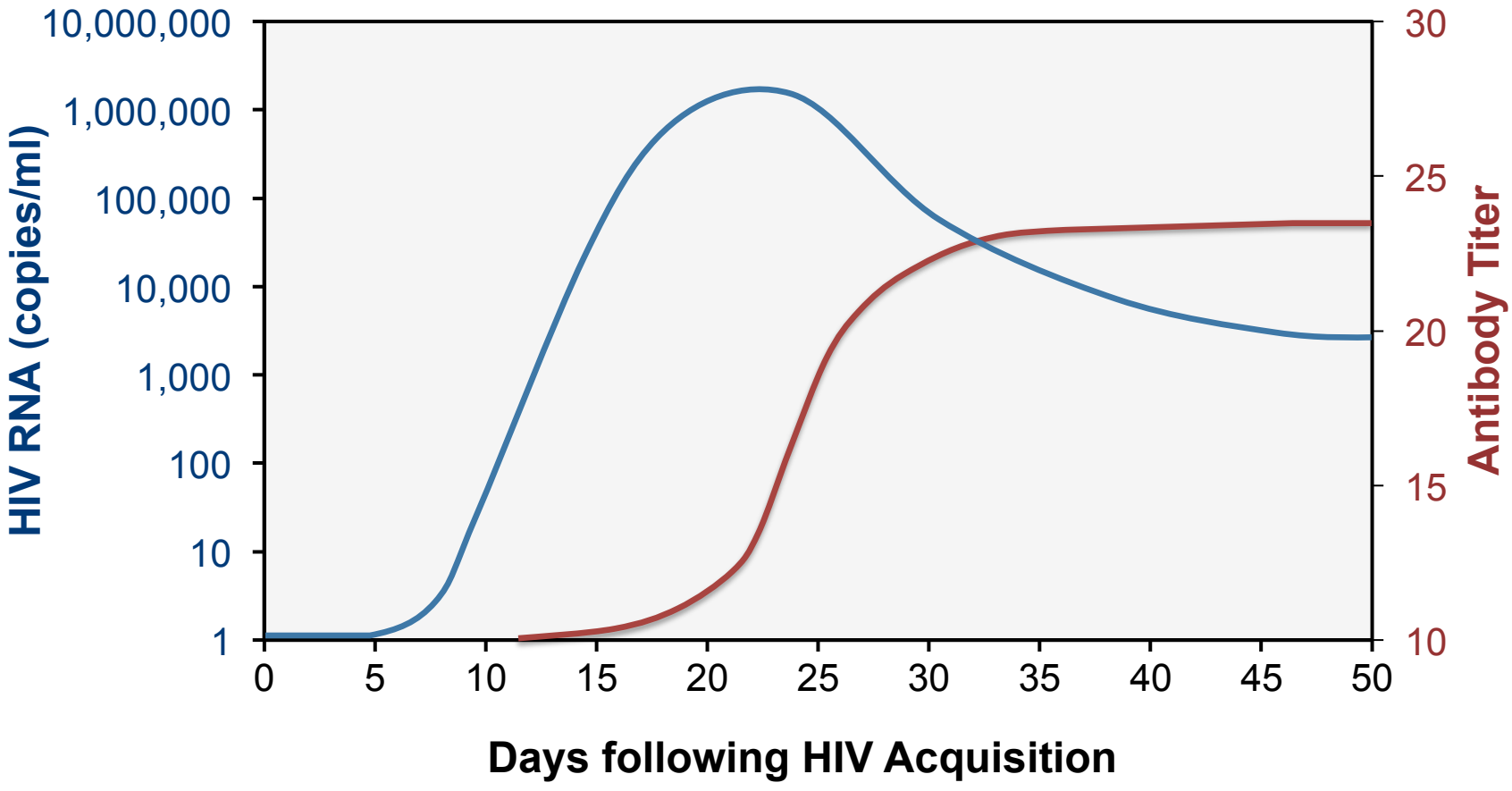
(A) Primary HIV infection
(B) Cytomegalovirus mononucleosis
(C) Primary herpes simplex virus infection
(D) Disseminated gonorrhea
(E) Secondary syphilis

Why is primary HIV infection difficult to recognize? Non-specific symptoms

Differential diagnosis:

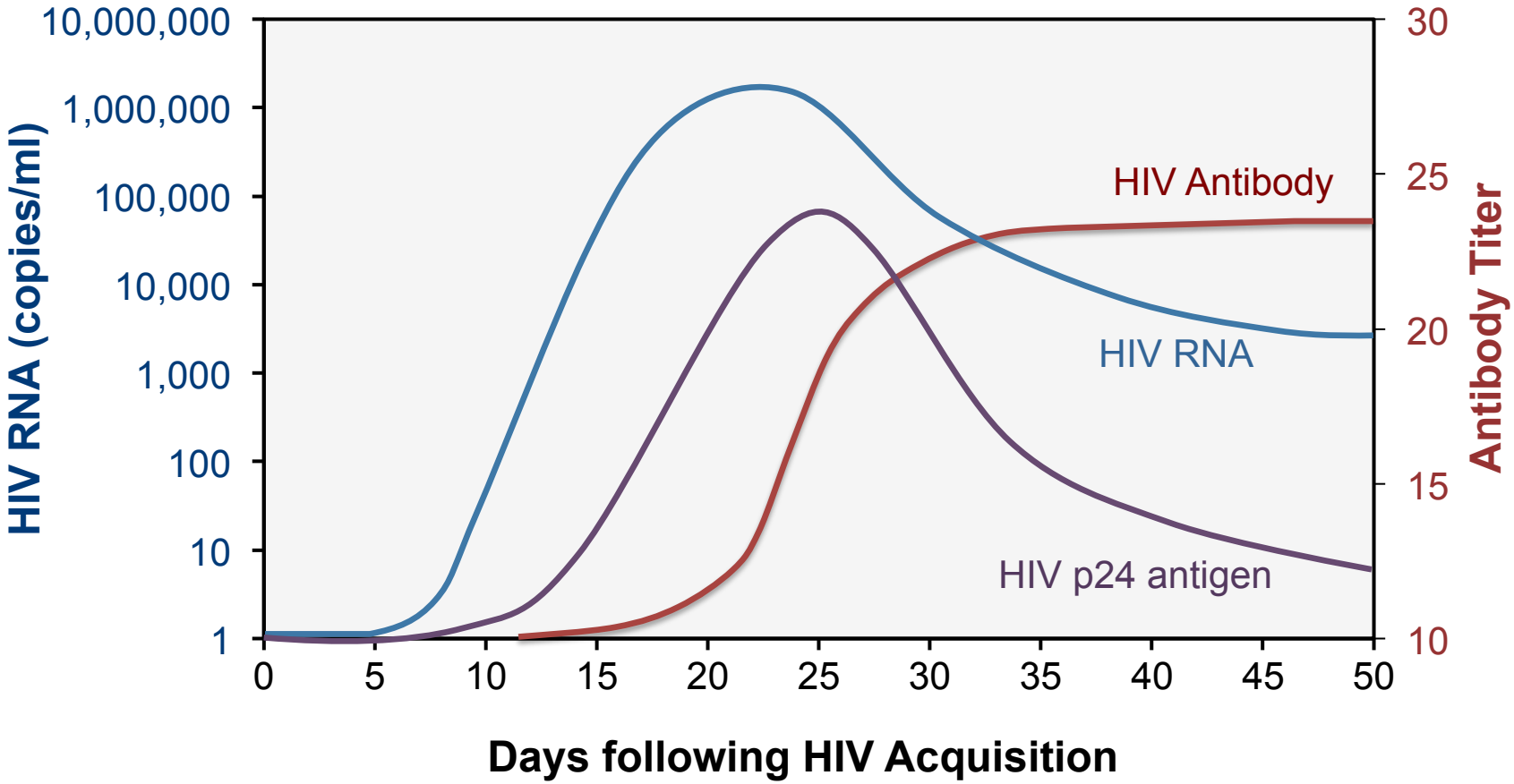
- acute (primary) HIV infection
- influenza
- mononucleosis (EBV, CMV)
- secondary syphilis
- streptococcal pharyngitis
- enteroviral infection
- acute hepatitis B virus
- acute toxoplasmosis
- other “viral illness”

How to test for primary HIV infection? HIV RNA testing and the "window period"



HIV RNA Precedes HIV Antibody

How to test for primary HIV infection?
p24 antigen testing



Timing of HIV RNA, HIV p24 antigen, and HIV Antibody

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How to test for primary HIV infection? HIV tests

HIV test	Method	Window
1st gen EIA (Ab)	viral lysate	~ 4-6 wks
2nd gen EIA (Ab)	purified HIV-1/2 Ag or recombinant	~ 3-4 wks
3rd gen EIA (Ab)	synthetic peptide, "antigen sandwich" detects IgM	~ 2-3 wks
4th gen assay (Ab plus p24 Ag)	detects either antibody or p24 Ag	~ 2 wks
Pooled HIV RNA (HIV NAAT)		<1-2 wks

Adapted from Stekler CID 2007

Initial Labs Following Positive Test

- If positive based on HIV RNA test, repeat HIV antibody test in 4-6 weeks to confirm seroconversion
- Screening for other STDs and infections: chlamydia, gonorrhea, syphilis, HBV, HCV and TB
- CD4 cell count and HIV viral load
- Baseline HIV genotype
  - Identify antiretroviral resistance early

Benefits of treating primary HIV infection

Known benefits

- ↓ severity of acute disease
- ↓ risk of transmission
- ↓ size of "latent pool"

Possible benefits

- ↓ viral "set point"
- ↓ rate of viral mutation
- Preserve immune function
- Maintain viral control after treatment interruption
- Improve long-term clinical outcomes

Issues with treating primary HIV infection
Treatment initiation guidelines

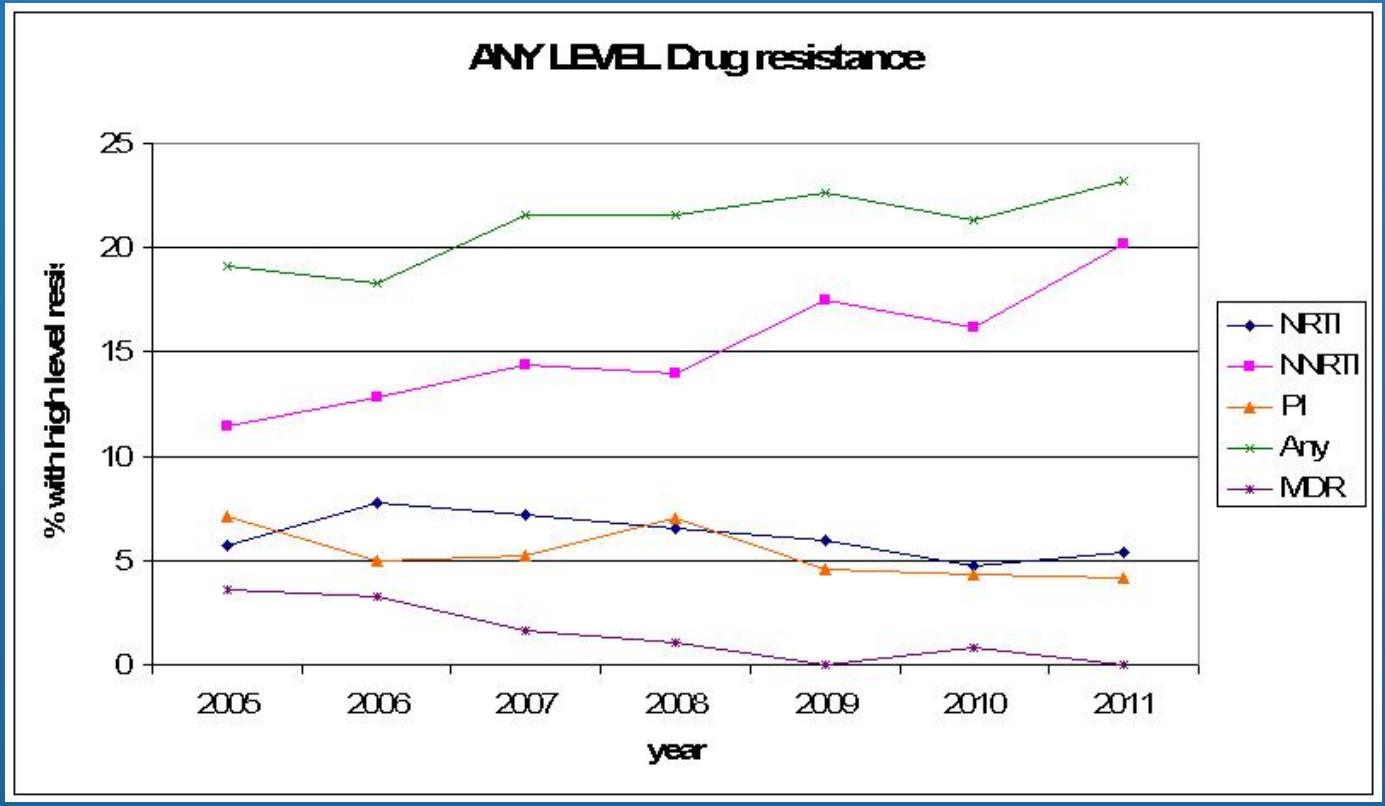
CD4 Cell Count	Recommendation for Antiretroviral Therapy
<350 cells/mm^3	Strongly Recommended Initiating Therapy (**AI**)
350-500 cells/mm^3	Recommended Initiating Therapy (**A/B-II**): - 55% of panel voted for strong recommendation (**A**) - 45% of panel voted for moderate recommendation (**B**)
>500 cells/mm^3	Recommended Initiating Therapy (**B/C-III**): - 50% of panel favor starting antiretroviral therapy (**B**) - 50% of panel view treatment is optional (**C**)
Initiating Antiretroviral Therapy Regardless of CD4 Cell Count	
• History of AIDS-defining illness (**AI**) • Pregnancy (**AI**) • HIV associated nephropathy (**AII**) • Hepatitis B virus (HBV) co-infection when treatment of HBV is indicated (**AIII**)	

Treatment of acute HIV infection
DHHS guidelines (Jan 10, 2011)

- It is unknown if treatment of acute HIV infection results in long-term virologic, immunologic, or clinical benefit; treatment should be considered optional (CIII).

- Because clinically significant resistance to PIs is less common than NNRTIs, a ritonavir-boosted regimen should be used if therapy is initiated before drug resistance test results are available (AIII).

What ARVs to start (or avoid)? Transmitted drug resistance in King County



Summary

- Primary HIV is a crucial time for HIV transmission as people are highly infectious and unaware of their status.
- Primary HIV manifests as non-specific symptoms. Be aware, and think about it.
- HIV RNA tests and p24 antigen tests can detect HIV during the “window period.”
- There may not be specific reason to start ARVs during primary infection, but, if you do, avoid using NNRTIs.

UW PRIMARY INFECTION CLINIC

- Since 1992 (20 years)
- More than 350 participants
- Thousands of study visits
- Helping to understand early HIV

Cabrini Medical Tower
901 Boren, suite 1300
206-667-2300
www.primaryhiv.org

Questions?