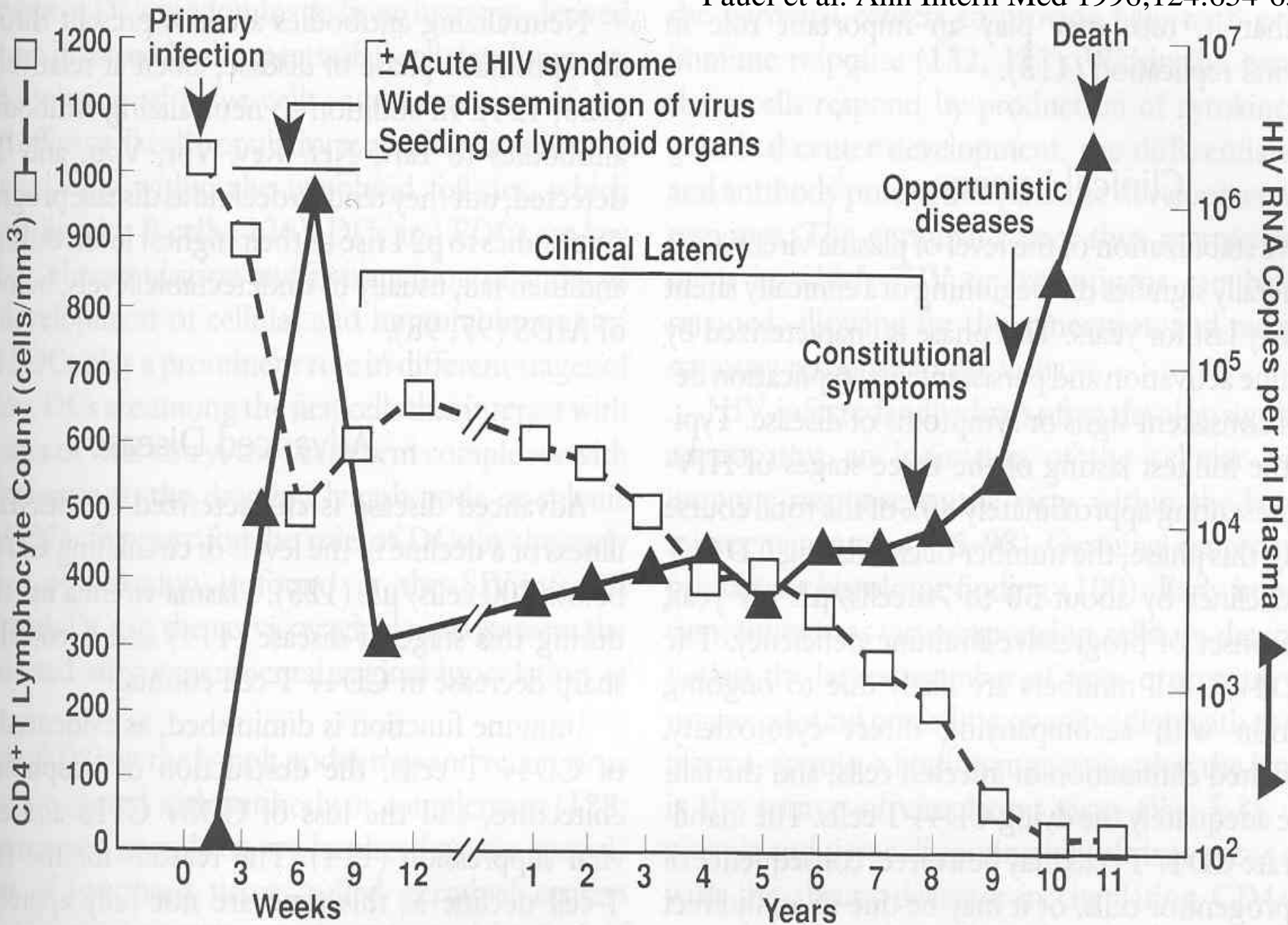


# Acute HIV Infection (AHI): An Opportunity for Prevention?

Robert Dubrow

- Features of AHI
- AHI as a potential target for prevention
- Diagnosis of AHI
- Study: Understanding the Social and Psychological Context of Acute HIV Infection
- Discussion



# Acute HIV Infection

- Earliest period of HIV infection (2-5 weeks) before anti-HIV antibodies can be detected (window period)
- Diagnosis
  - Positive HIV RNA viral load (or p24 antigen) test
  - Negative or indeterminate HIV antibody test (ELISA, rapid test, Western blot)

# Acute Retroviral Syndrome

- 50-75% of AHI cases are symptomatic
- Nonspecific symptoms
- Develops within days to weeks of transmission
- Duration usually < 2 weeks

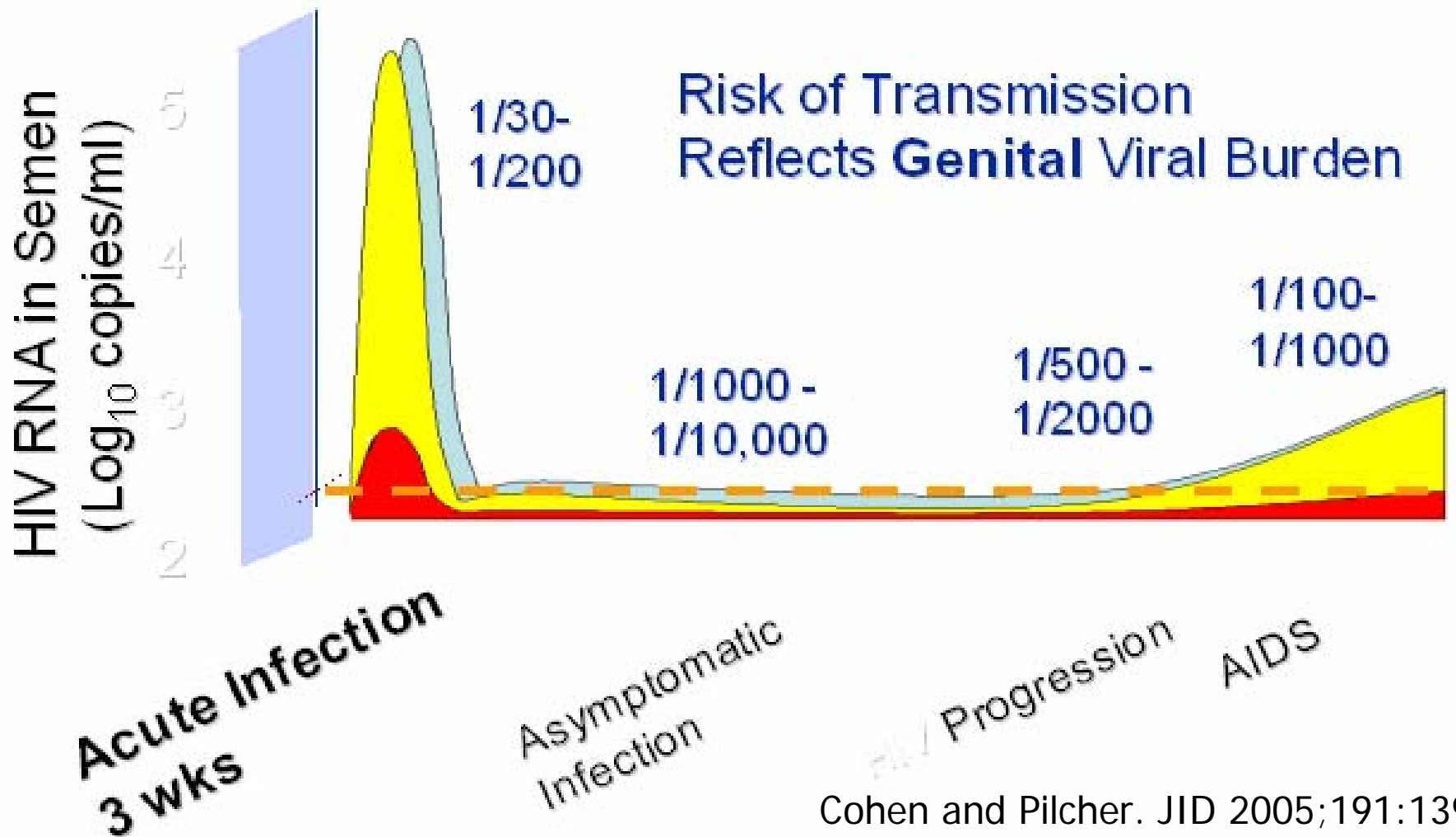
# Acute retroviral syndrome symptoms

- \*Fever
  - \*Fatigue/malaise
  - \*Rash
  - \*Lymphadenopathy
  - \*Headache
  - \*Pharyngitis
  - \*Arthralgia/myalgia
  - \*Night sweats
  - Nausea/vomiting
  - Diarrhea
  - Weight loss
  - Anorexia
  - Mucocutaneous ulcers
  - Oral candidiasis
  - Cough
  - Abdominal pain
  - Odynophagia
  - Stiff neck
  - Photophobia
  - Peripheral neuropathy
  - Guillian-Barre syndrome
  - Retro-orbital pain
- \*most common

# AHI is a period of high HIV transmission

- High levels of virus in blood and semen
- Virus present during AHI is well adapted to transmission
- High-risk behaviors are likely to continue, particularly if infected person is unaware of infection
- High-risk sex or drug network (amplification effect)

# Viral Load and Sexual Transmission of HIV over Time



# AHI is a key target for prevention

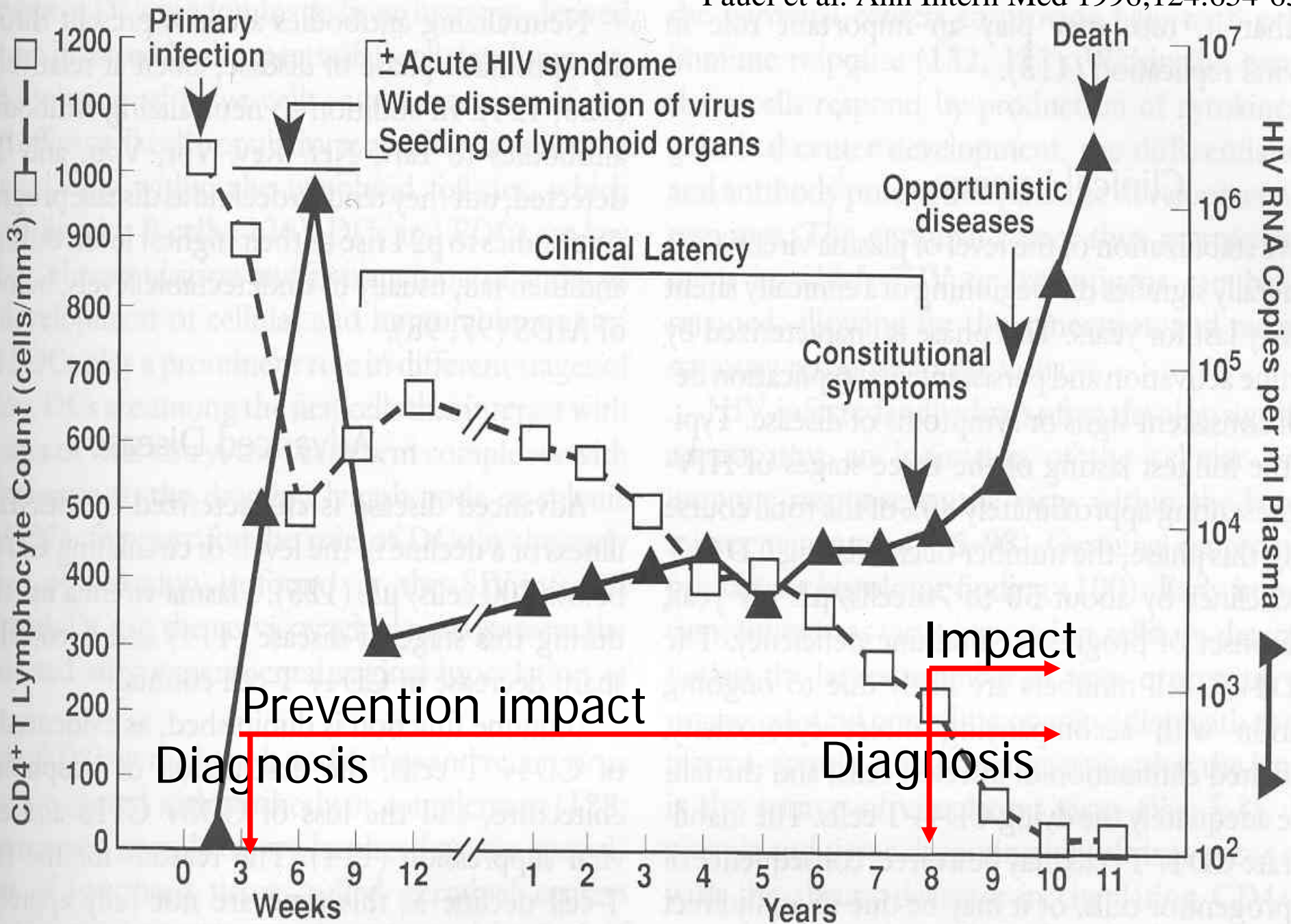
- Prevention among persons with AHI is an important special case of prevention among HIV-infected persons

# Specificity of prevention among persons with AHI

- AHI diagnosis
  - Prerequisite for further intervention
  - Majority of people substantially reduce risky behaviors when they learn they are infected
- Time urgency to initiate risk reduction interventions
- Individual (not group) intervention
- Current high risk behavior
- Emphasis on network/partner notification interventions
- ARV treatment?

# The earlier the HIV diagnosis, the greater the potential prevention impact

- Ideal: diagnose every case of HIV during AHI
- Potential maximum benefit to individual
  - HIV care
  - Opportunity to protect others
- Potential maximum benefit to community
  - Opportunity for prevention
  - Transmission is 3.5 times higher by people who are unaware of their infection than by people who are aware of their infection



CD4+ T Lymphocyte Count (cells/mm<sup>3</sup>)

HIV RNA Copies per ml Plasma

Primary infection

± Acute HIV syndrome  
Wide dissemination of virus  
Seeding of lymphoid organs

Clinical Latency

Opportunistic diseases

Constitutional symptoms

Death

Diagnosis

Prevention impact

Impact

Diagnosis

Weeks

Years

# Current Reality in U.S.

- AHI is rarely diagnosed
- 39% of persons diagnosed with HIV infection progress to AIDS within 12 months
- 25% of HIV-infected persons are unaware they are infected

# Diagnosis of AHI

- Clinical suspicion prompts testing
- HIV RNA (or p24 antigen) test added to standard protocol at HIV C&T sites

# Clinical suspicion of AHI

- Acute retroviral syndrome symptoms
- Possible recent HIV exposure

# Acute retroviral syndrome symptoms

- \*Fever
  - \*Fatigue/malaise
  - \*Rash
  - \*Lymphadenopathy
  - \*Headache
  - \*Pharyngitis
  - \*Arthralgia/myalgia
  - \*Night sweats
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  - Photophobia
  - Peripheral neuropathy
  - Guillian-Barre syndrome
  - Retro-orbital pain
- \*most common

# Possible HIV exposure in past 2 months

- IDU who shared needles
- Sexually-transmitted infection
- Exchanged sex for money/drugs or vice versa
- Unprotected sex with an HIV-infected partner
- MSM who had unprotected anal sex
- Occupational exposure (e.g., needle stick)

# Differential diagnosis

- Primary CMV infection
- Mononucleosis
- Viral hepatitis
- Primary HSV infection
- Influenza
- Streptococcal pharyngitis
- Lyme disease
- Secondary syphilis
- Toxoplasmosis
- Rubella
- Brucellosis
- Malaria
- Rickettsial diseases
- Drug reaction
- Adult Still's disease
- Systemic lupus
- Systemic vasculitides
- Acute Crohn's disease
- AHI
- Most common diagnosis: viral illness not otherwise specified

# Importance of primary care clinicians in diagnosis of AHI

- Persons with acute retroviral syndrome (nonspecific symptoms) seek primary care
- High degree of clinical suspicion essential
- Clinician must elicit an accurate sex and drug use history

# AHI diagnosis by clinical suspicion

<b>Setting</b>	<b>N</b>	<b>Acute infection</b>	<b>Chronic infection</b>
Los Angeles referrals <sup>1</sup>	436	54 (12.4%)	79 (18.1%)
San Francisco referrals <sup>2</sup>	288	22 (7.6%)	57 (19.8%)
Boston urgent care center <sup>3</sup>	499	5 (1.0%)	6 (1.2%)

<sup>1</sup>Daar et al. Ann Intern Med 2001;134:25-9

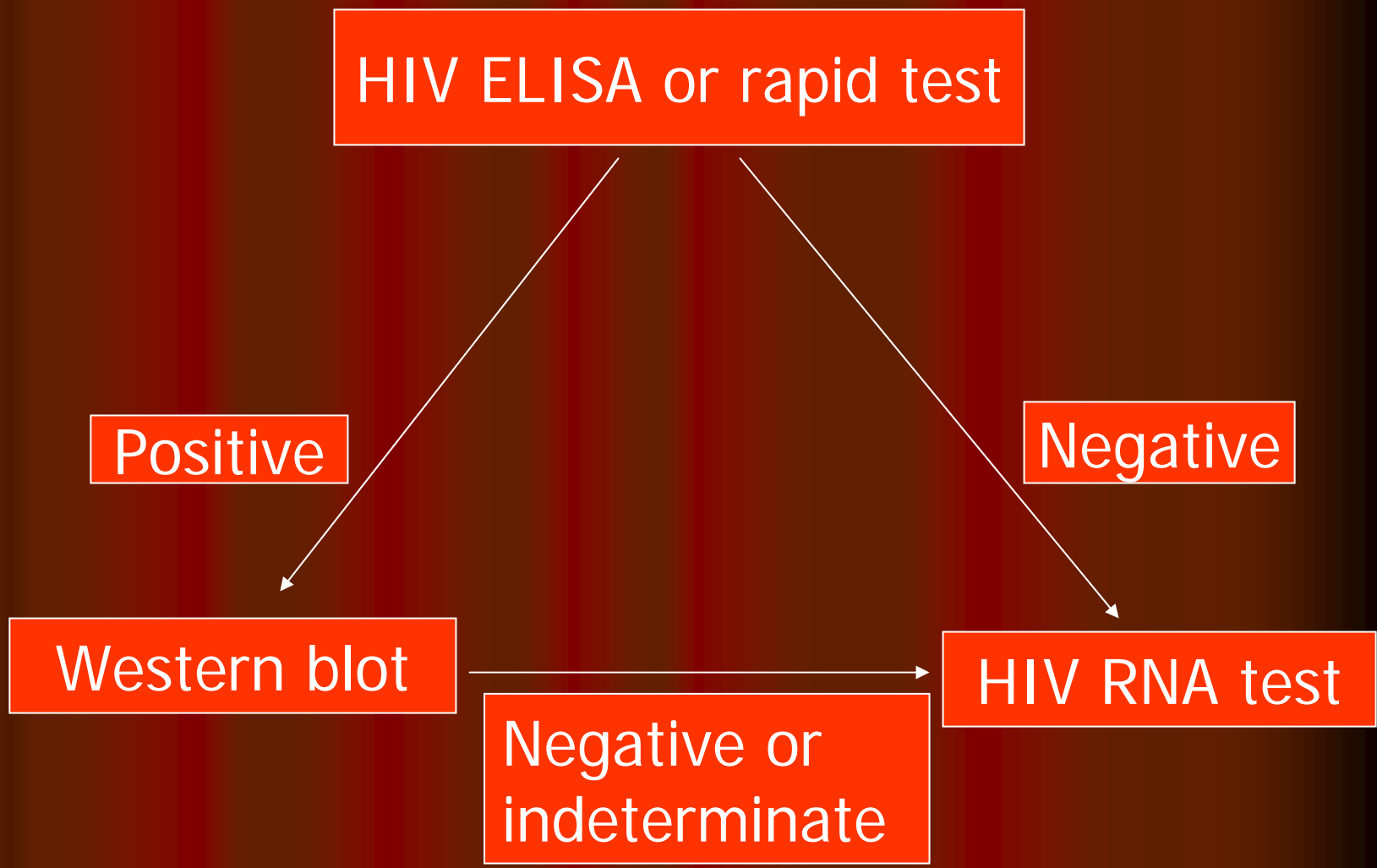
<sup>2</sup>Hecht et al. AIDS 2002;16:1119-29

<sup>3</sup>Pincus et al. Clin Infect Dis 2003;37:1699-1704

# Diagnosis of AHI

- Clinical suspicion prompts testing
- HIV RNA test added to standard protocol at counseling and testing sites

# HIV RNA test added to standard protocol at counseling and testing sites



# Screening for AHI

<b>Setting</b>	<b>N</b>	<b>Acute infection</b>	<b>Chronic infection</b>
North Carolina C&T sites <sup>1</sup>	109,250	23 (0.02%)	583 (0.5%)
San Francisco STD Clinic <sup>2</sup>	3,789	11 (0.3%)	125 (3.3%)
San Francisco City Clinic <sup>3</sup>	3,075	11 (0.4%)	105 (3.4%)
Los Angeles STD Clinics (males) <sup>3</sup>	1,712	1 (0.06%)	14 (0.8%)
Atlanta C&T sites <sup>4</sup>	2,202	4 (0.2%)	66 (3.0%)
Seattle C&T sites (MSM) <sup>5</sup>	3,525	7 (0.2%)	81 (2.3%)

# Citations for previous slide

<sup>1</sup>Pilcher et al. N Engl J Med 2005;352:1873-83

<sup>2</sup>Truong et al. AIDS 2006;20:2193-7.

<sup>3</sup>Patel et al. JAIDS 2006;42:75-9.

<sup>4</sup>Priddy et al. JAIDS 2007;44:196-202.

<sup>5</sup>Stekler et al. AIDS 2005;19:1323-5

# Screening for AHI: STD clinics in international settings

<b>Setting</b>	<b>N</b>	<b>Acute infection</b>	<b>Chronic infection</b>
Malawi <sup>1</sup>	928	23 (2.5%)	434 (46.8%)
Malawi <sup>2</sup>	1,450	21 (1.4%)	588 (40.6%)
India <sup>3</sup>	6,495	58 (0.9%)	1,462 (22.5%)

<sup>1</sup>Pilcher et al. AIDS 2004;18:517-24.

<sup>2</sup>Fiscus et al. JID 2007;195:416-24.

<sup>3</sup>Bollinger et al. JAMA 1997;278:2085-9.

# Understanding the Social and Psychological Context of Acute HIV Infection

- Multi-center pilot study funded by National Institute of Mental Health
- Formative research to develop AHI prevention intervention

# Participating Centers

- Yale Center for Interdisciplinary Research on AIDS (CIRA)
- UCSF Center for AIDS Prevention Studies
- UCLA Center for HIV Identification, Prevention, and Treatment
- UCSD HIV Neurobehavioral Research Center
- Columbia University HIV Center for Clinical and Behavioral Studies
- Medical College of Wisconsin Center for AIDS Intervention Research
- Brown University Center for AIDS Research

# Yale Team

## Investigators

- Robert Dubrow, M.D., Ph.D.
- Michael Merson, M.D.
- Kathleen Sikkema, Ph.D.
- R. Douglas Bruce, M.D.
- Aaron Roome, Ph.D.
- Dana Dunne, M.D.

## Key Personnel

- Pamela Julian, M.P.H.
- Alexandra Boeving, Ph.D.

# Yale Institutional Collaborators

- Hill Health Center HIV/AIDS Division (Thomas Kidder, Director)
- South Central Rehabilitation Center (R. Douglas Bruce, Medical Director)
- New Haven Health Dept. STD Clinic (Fred Gager, Director)
- CT Dept. of Public Health STD Control Program (Heidi Jenkins, Program Director)
- CT Dept. of Public Health HIV/AIDS Surveillance Program (Aaron Roome, Director)
- Yale-New Haven Hospital Emergency Dept. (Linda Degutis, Research Director)

# Specific Aims

- To determine the feasibility of detecting and recruiting individuals with AHI for prevention research
  - Sample size goal: 50 cases
- To better understand the social and psychological context of recent HIV transmission
  - In-depth interviews
- To assess sexual behavior, substance use and psychological state of individuals with AHI
  - Structured interviews

# Yale case identification

- HIV RNA test added to standard protocol at C&T sites
- Referral of suspected AHI cases based on clinical suspicion: Yale-New Haven Hospital Emergency Dept. (YNHH ED)
- Referral of known AHI cases by clinicians and social service providers

# Yale case identification: HIV RNA test added to standard protocol at C&T sites

- Hill Health Center HIV/AIDS Division
  - South Central Rehabilitation Center (SCRC): acute drug and alcohol detoxification facility
  - Grant Street Partnership (GSP): substance abuse program
- New Haven Health Department STD Clinic

# Referral based on clinical suspicion from YNHH ED

- Primary site of routine medical care for high risk groups in New Haven
- Estimate that 10 AHI cases/year come through YNHH ED
- AHI had never been diagnosed in YNHH ED

# Results

- CIRA center
  - Completed data collection in January 2007
  - 2 AHI cases identified and recruited
- All centers
  - Will complete data collection by May 2007
  - 26 AHI cases identified and recruited through March 2007

# Yale screening for AHI

<b>Site</b>	<b>N</b>	<b>Acute infection</b>	<b>Chronic infection</b>	<b>Total HIV infections</b>
SCRC	394	1 (0.3%)	4 (1.0%)	5 (1.3%)
GSP	30	0	0	0
STD Clinic	166	0	2 (1.2%)	2 (1.2%)
<b>Total</b>	<b>590</b>	<b>1 (0.2%)</b>	<b>6 (1.0%)</b>	<b>7 (1.2%)</b>

# Yale Referrals

- YNHH ED: 3 suspected cases
  - 2 did not come to referral appointment
  - 1 hospitalized with TB and found to have chronic HIV infection
- Nurse from Lawrence and Memorial Hospital referred a known AHI case

# Case identified by screening at SCRC

- 34 year-old Hispanic white male
- Positive rapid test
- Negative western blot
- HIV RNA: >500,000 copies/ml
- Symptoms
  - Severe headache
  - 10 pound weight loss
- Probable source of infection: HIV-infected wife

# Known AHI case referred by nurse at Lawrence & Memorial Hospital

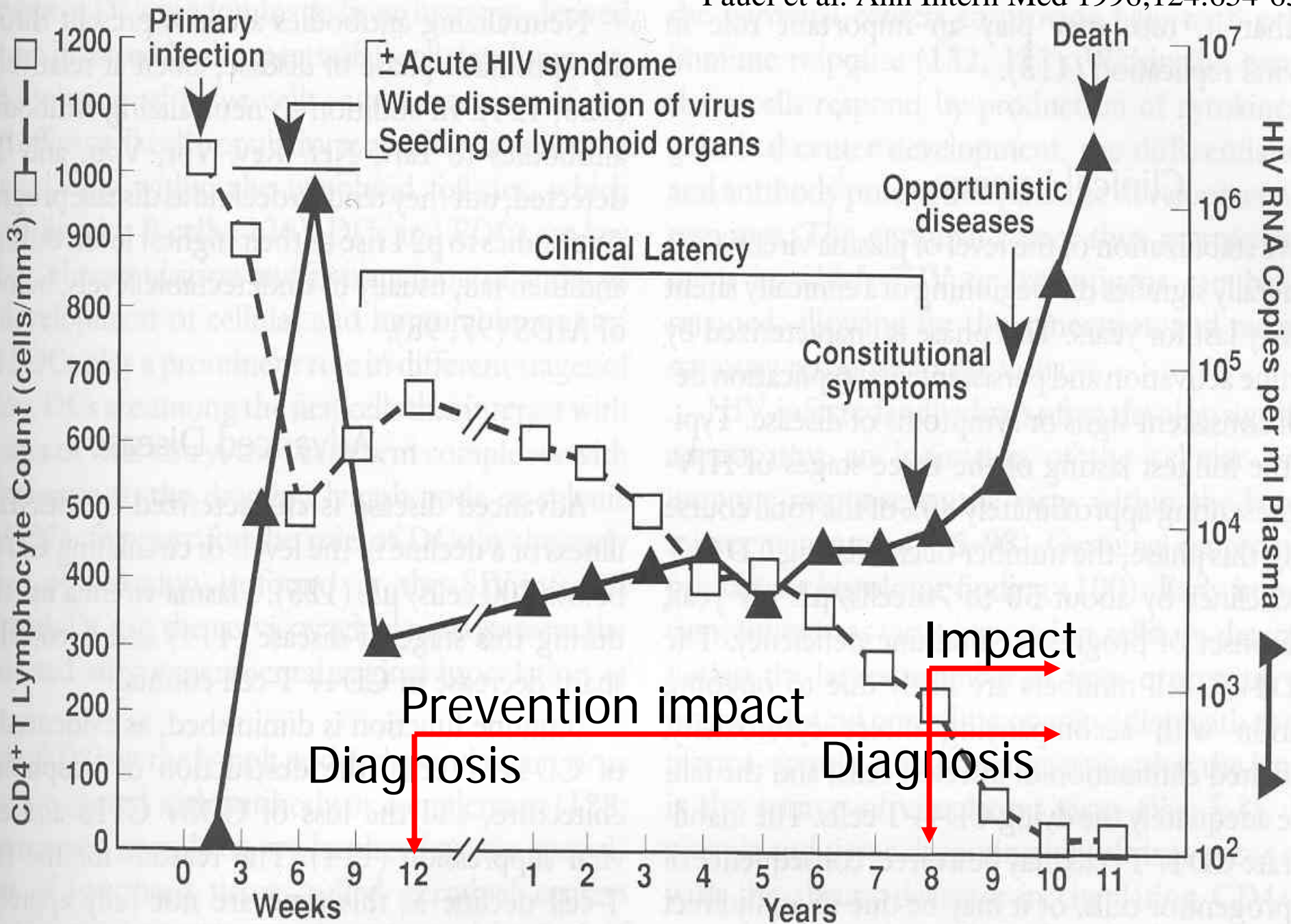
- 34 year-old non-Hispanic white female
- Admitted to hospital with fever, diarrhea, abdominal pain, pain on swallowing, headache, low back pain, ulcers of tongue and esophagus, rash on trunk and extremities
- Negative rapid test
- HIV RNA: >750,000 copies/ml
- Probable source of infection: binged on alcohol, crack and sex with an HIV-infected IDU

# Lessons

- Need for orders of magnitude higher screening volumes at multiple sites
- Need for routine opt-out testing
- Use rapid test (as opposed to conventional ELISA) in conjunction with HIV RNA test to avoid delays in diagnosis
- Need for point-of-care HIV testing in EDs
- Need for physician education about AHI

# Can we diagnose enough AHI to make a difference in prevention?

- Limitations of primary care settings:
  - 25% - 50% of AHI cases are asymptomatic
  - An unknown proportion of symptomatic cases do not seek medical care
  - Diagnosis is challenging: nonspecific symptoms
- Limitation of C&T sites:
  - Narrow window period for diagnosis (a week to a month)
- Diagnosis of AHI should be seen as one tactic within strategy of earlier diagnosis of HIV infection



# Goals for Connecticut

- Increase diagnosis of AHI in primary care settings through clinician education
- Add HIV RNA test (or p24 antigen test) to standard HIV testing protocol at C&T sites