

HIV Test Technologies, Best Practices, and New Algorithm

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Testing History

- 1985 1st Gen HIV-1 IA
- 1987 HIV-1 WB
- 1990 HIV-2 IA HIV-1 IA DBS
- 1991 2nd Gen HIV 1/2 IA
- 1992 3rd Gen HIV 1/2 IA HIV 1 IFA
- 1994 Oral collection device HIV 1 IA
- 1996 HIV Home Specimen Collection
- Quantitative HIV 1 Viral Load Assay
- 2002 HIV 1 IA Rapid Blood
- 2003 CLIA Waived Rapid IA blood Group O
- 2004 CLIA Waived Rapid HIV 1/2 IA
- Rapid IA Differentiates 1/2
- 2006 Random Access Microparticle CIA
- Qualitative HIV 1 NAT
- 2010 4th Gen Antibody/Antigen
- 2012 CLIA Waived Rapid IA Immediate Results
- Over the counter Rapid IA Oral

Kaiser Study

- 1995 - 44% Urgent Health Problem
- 2009 - 6% Urgent Health Problem
- 2006 - 21% concern about what others would think if tested
- 2010 - 16% concern about what other would think if tested
- 69% don't think friends would care either way. 9% think friends would think more of them if tested.

<http://www.kff.org/kaiserpolls/upload/8186.pdf>

National Strategy

- Identify Undiagnosed Infections
- Increase Access to Care and Improve Health Outcomes for People Living with HIV
- Reduce HIV Related Health Disparities.

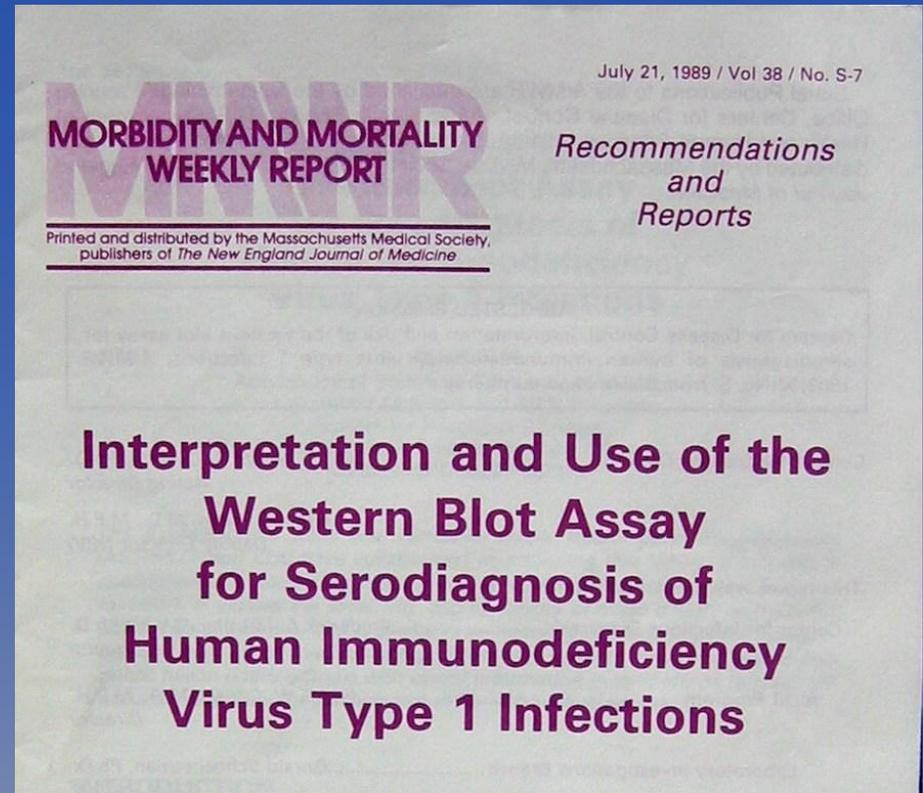
Role of the Awareness of HIV Status

- Approximately 18% of people with HIV are unaware of their HIV status.
- Among those with HIV:
 - Persons unaware are 3.5 times as likely to transmit.
 - Account for 54% (up to 70%) of new infections.
 - Those aware, change behaviors that transmit.
 - ART reduces viral load.

COMMUNITY VIRAL LOAD

Diagnostic Algorithm since 1989

- The Public Health Service recommends that no positive test results be given to clients/patients until a screening test has been repeatedly reactive on the same specimen and a supplemental, more **specific test such as the Western blot** has been used to validate those results.

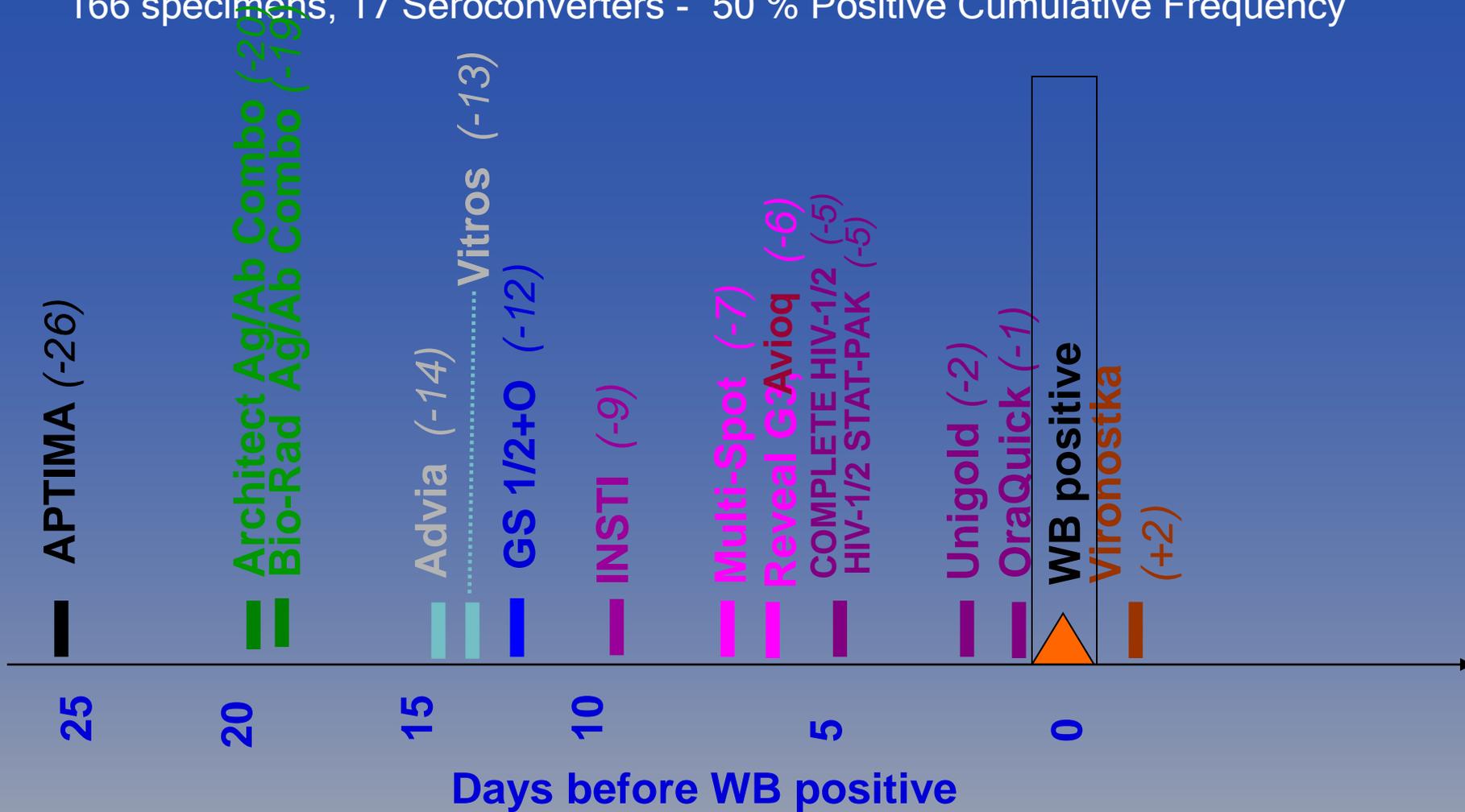


Types of Diagnostic HIV Testing

- 1st and 2nd Generation EIA
- EIA Rapid test kits
- 3rd Generation EIA IgG and IgM Antibody testing
- HIV 1 and 2 Differentiation
- 4th Generation Antibody and Antigen
- Western Blot and IFA
- Viral Nucleic Acids

Sequence of Test Positivity Relative to WB

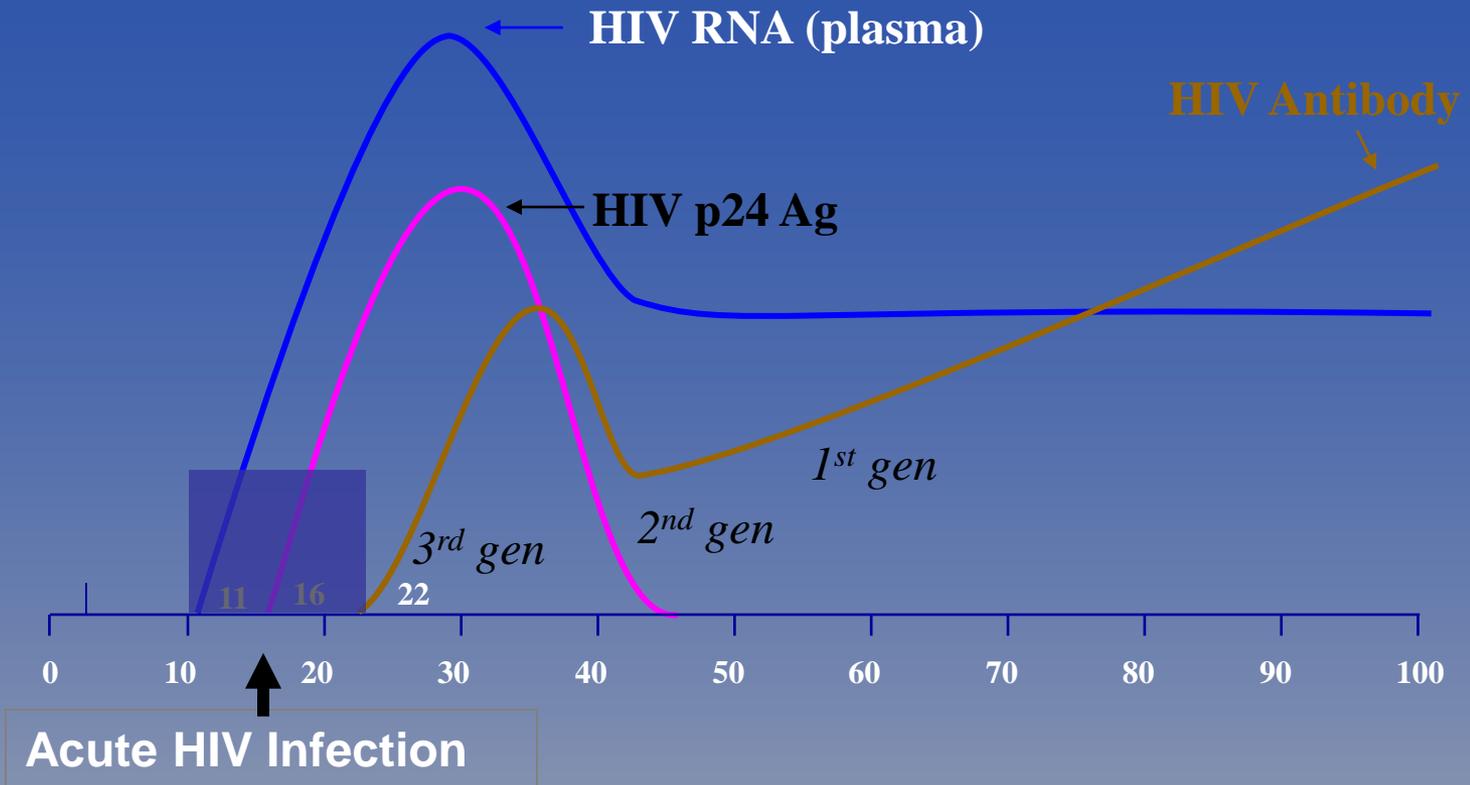
166 specimens, 17 Seroconverters - 50 % Positive Cumulative Frequency



Modified from Masciotra et al, J Clin Virol 2011

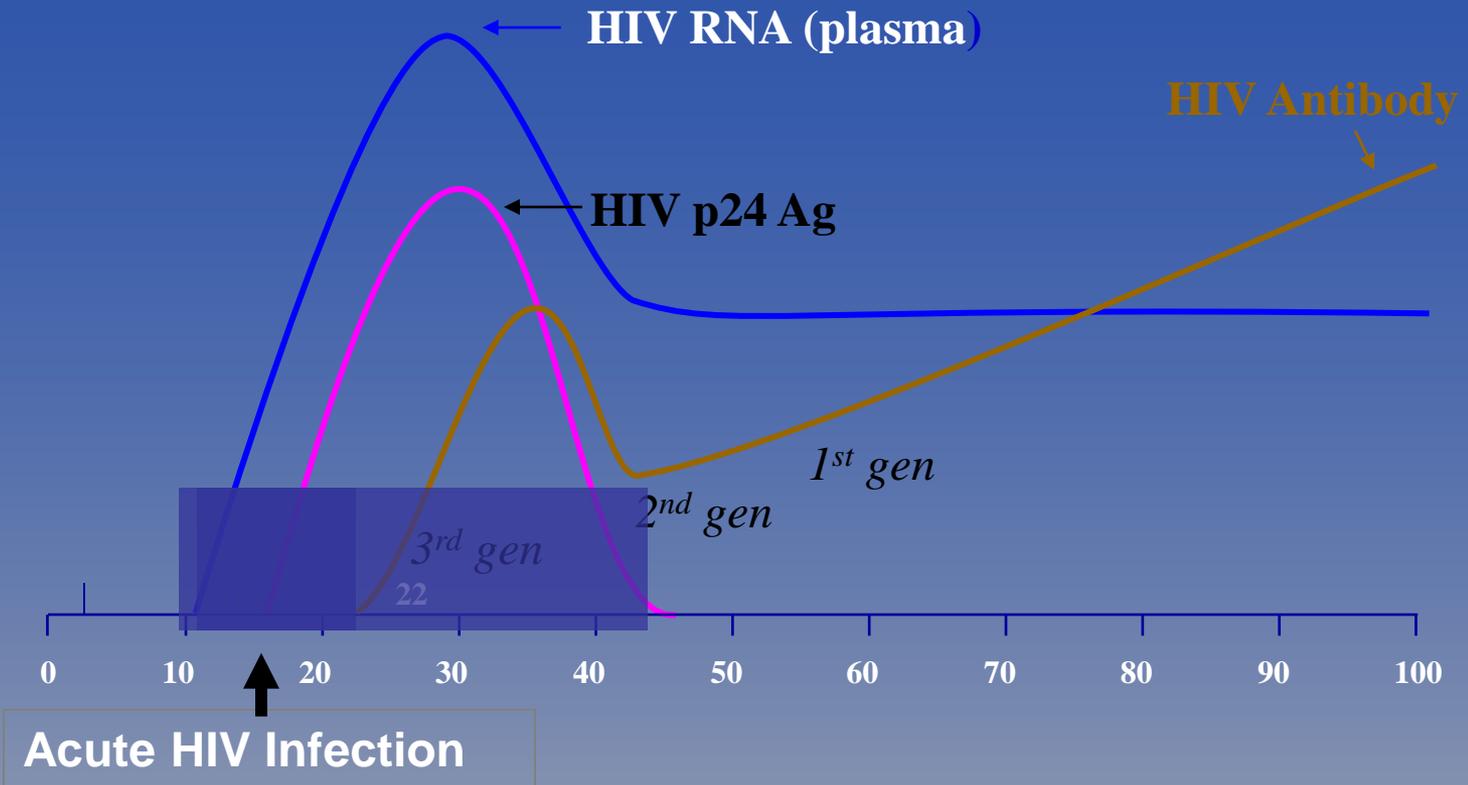
and Owen et al, J Clin Micro 2008

Window Period and HIV Infection



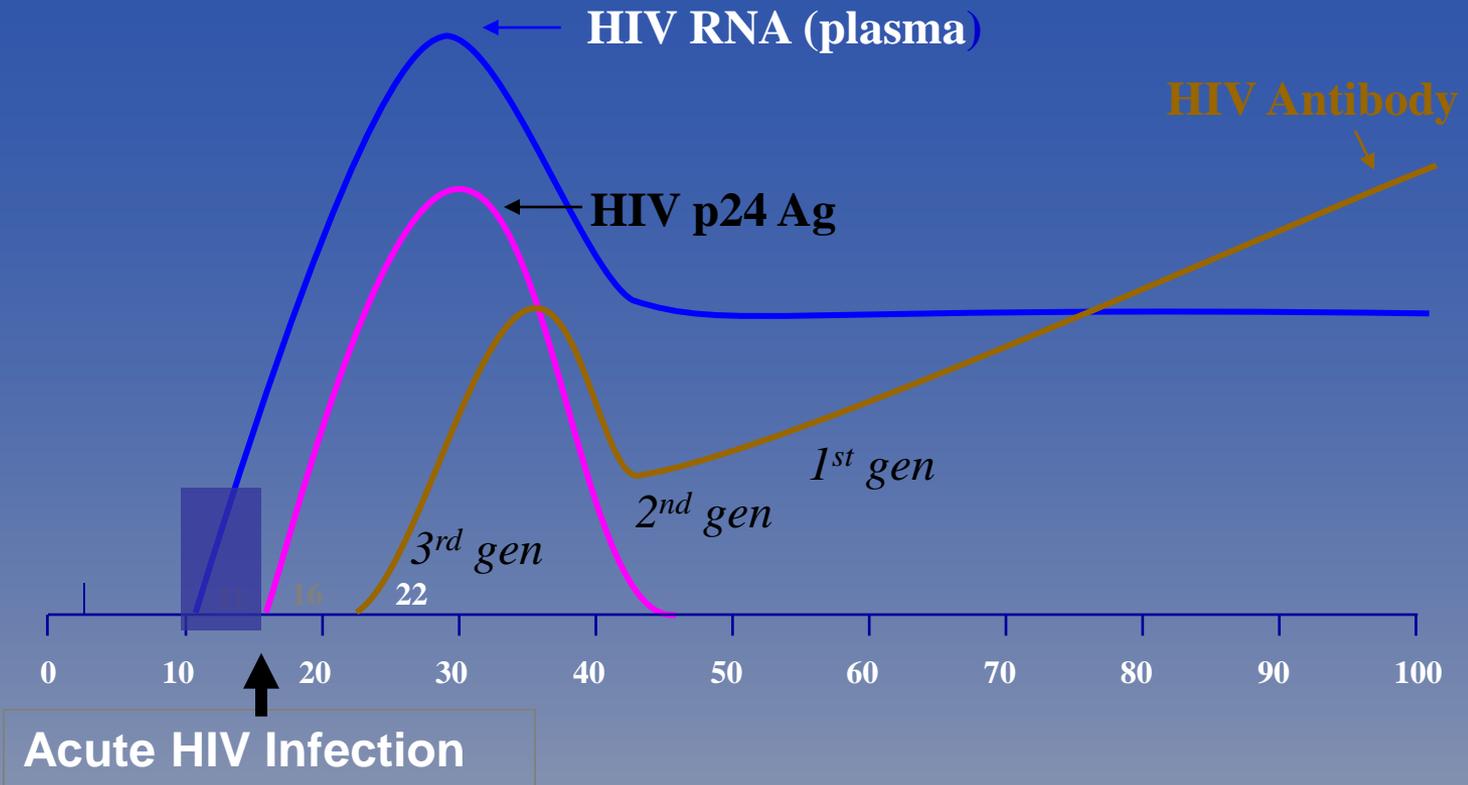


Windows



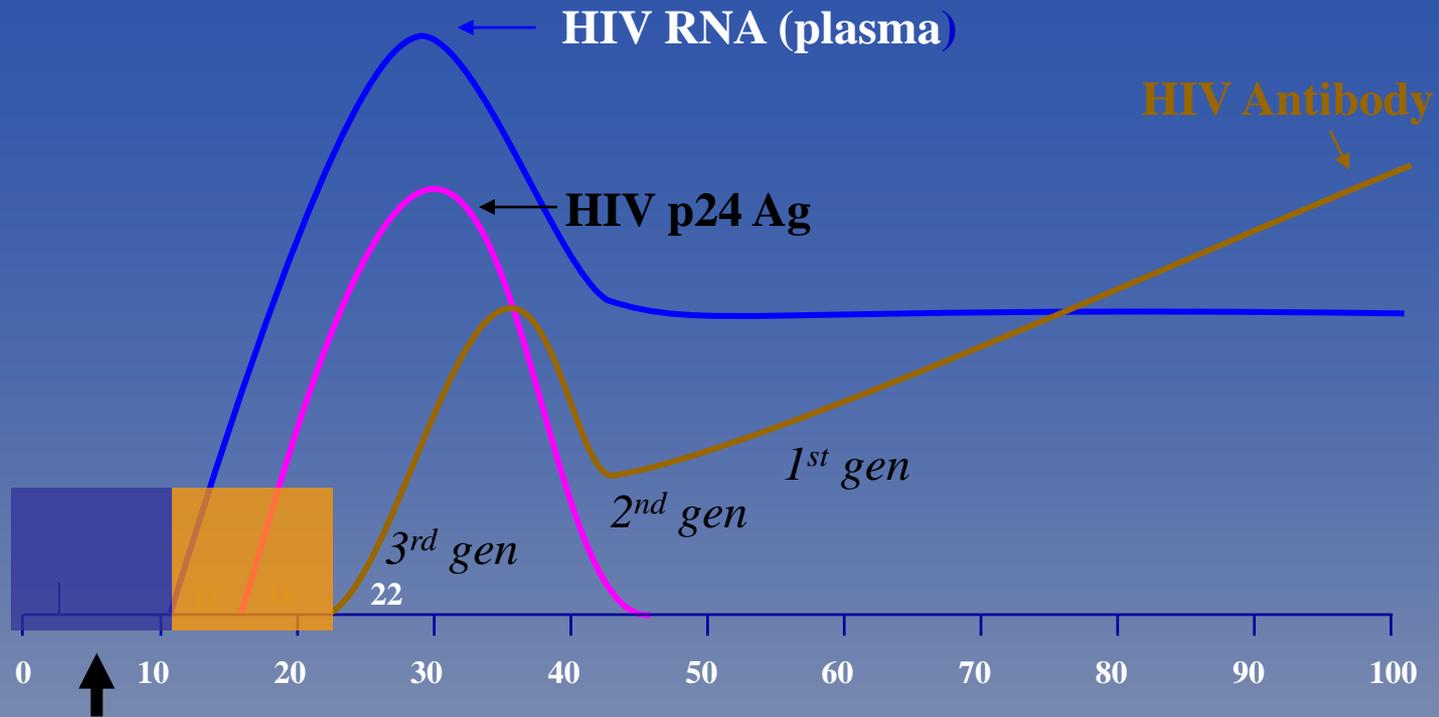


Windows



Acute HIV Infection

We Can't Close the Window



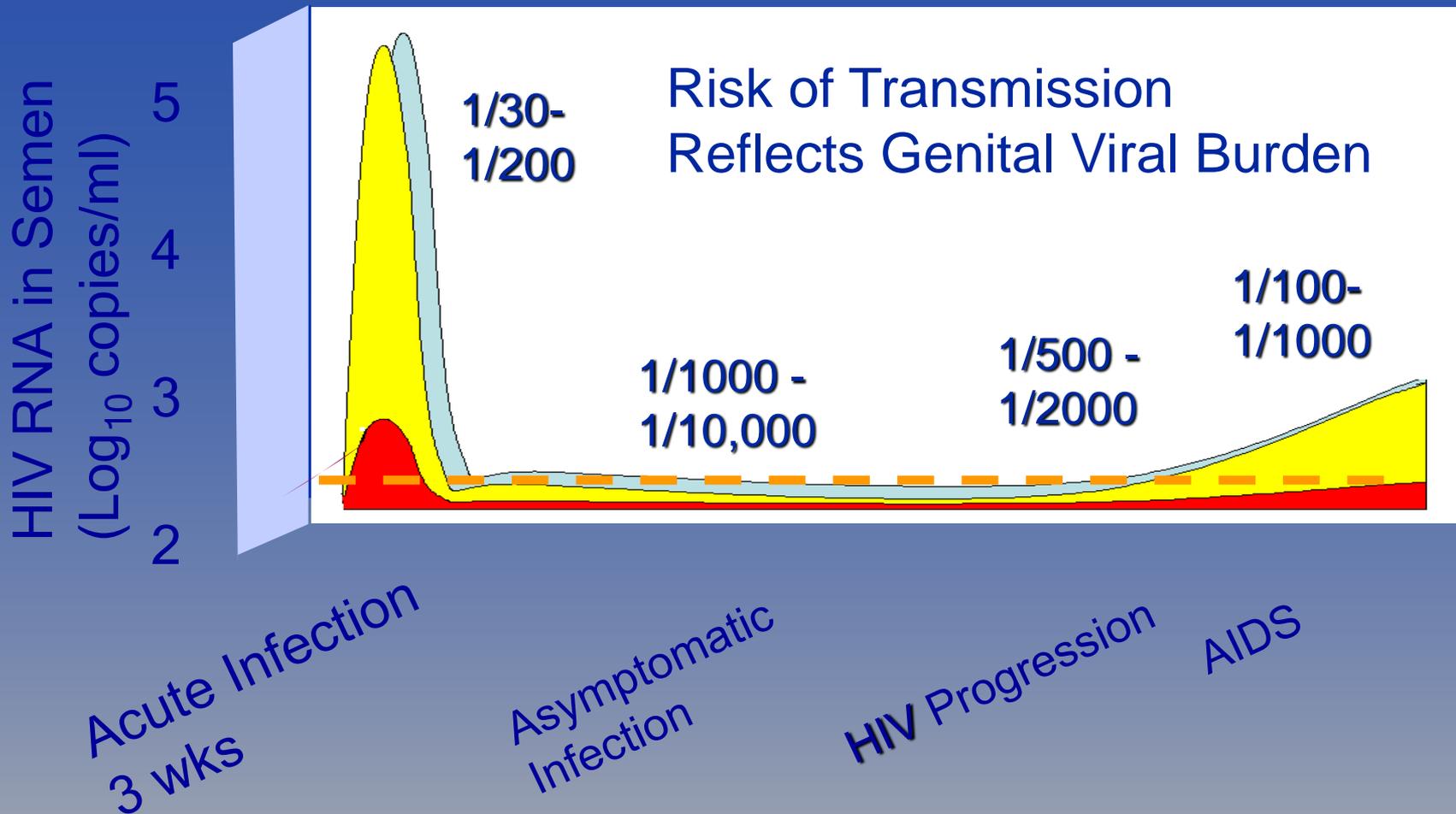
Infection
Undetectable

Clinical Syndrome of Acute HIV

- 40-90% develop symptoms of Acute HIV
- 50%-90% with symptoms seek medical care
- Of those diagnosed with Acute HIV, 50% of patients seen at least 3 times before diagnosis

- Kahn et al, NEJM 1998
- Weintrob et al, Arch Int Med
2003

Risk of Sexual Transmission of HIV



Cohen MS, et al. *J Infect Dis.* 2005

Limitations of the 1989 Algorithm

- Western blot is less sensitive during early infection than most screening tests in current use
- Antigen/antibody combo tests can detect most antibody-negative persons during highly infectious acute infection stage
- Because of cross-reactivity, >60% of persons with HIV-2 infection misclassified as HIV-1 by Western blot

HIV-2 Infection

- **Remains uncommon in U.S., but**
 - Does not respond to NNRTIs, some PIs (first line therapy)
 - Undetectable by HIV-1 viral load tests
- **Misclassification by HIV-1 Western blot:**
 - 54/58 (93%) HIV-2 patients tested had positive HIV-1 WB (NYC)*
 - 97/163 (60%) HIV-2 cases reported had positive HIV -1 WB (CDC)**
- **HIV-2 often diagnosed after immunologic deterioration in patient with negative viral load**

**Torian et al, Clinical Infectious Disease 2010*

***MMWR July 2011*

2010 HIV Diagnostics Conference: CDC/APHL Proposed New Testing Algorithm

Schematic Version of Recommended Algorithm

4th generation HIV-1/2 immunoassay

(+)

(-)

Negative for: HIV-1 and HIV-2 antibodies and p24 Ag

HIV-1/HIV-2 antibody differentiation immunoassay

HIV-1 (+)

HIV-1 (-)

HIV-1 (+)

HIV-1 (-) or indeterminate

HIV-2 (-)

HIV-2 (+)

HIV-2 (+)

HIV-2 (-)

HIV-1 antibodies detected

HIV-2 antibodies detected

HIV antibodies detected*

HIV-1 RNA

RNA(+)

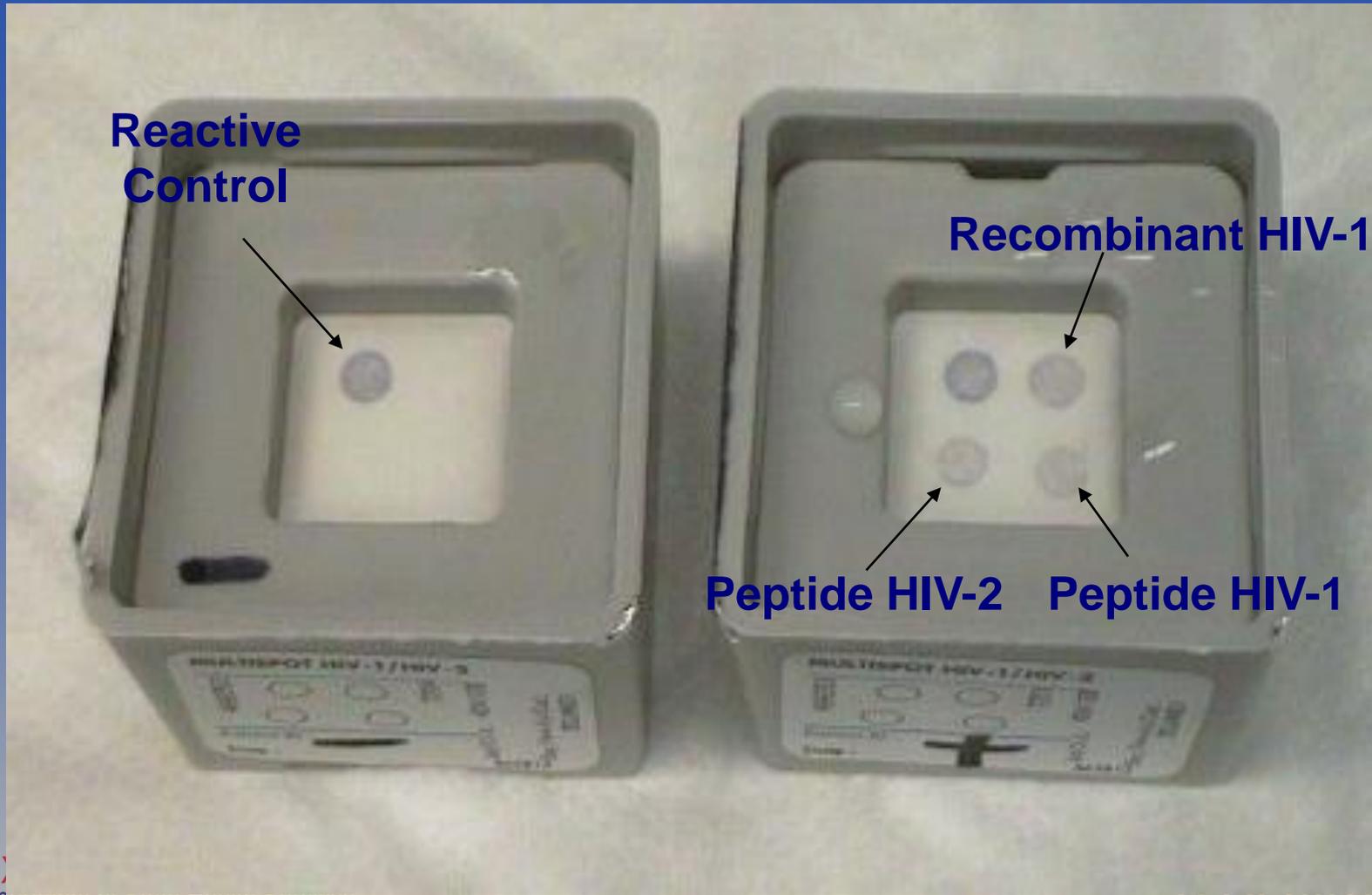
Acute HIV-1 infection

RNA (-)

Negative for HIV-1

**Additional testing required to rule out dual infection*

FDA-approved HIV-1/HIV-2 Antibody Differentiation Assay



New HIV Testing Algorithm Results

Lab Report Language

Interpretation

Negative. HIV-1 p24 antigen, HIV-1 and HIV-2 antibodies not detected.

If client did not have risk in the two weeks before the test or since, client does not have HIV.

Positive. HIV-1 antibodies detected.

The client has HIV-1.

Positive. HIV-2 antibodies detected.

The client has HIV-2.

Positive. A reactive HIV antigen/antibody test and a positive HIV-1 RNA test indicate acute HIV-1 infection.

The client has HIV-1 and the test result indicates that s/he was recently infected (likely infected 2-8 weeks before taking the test).

Negative. HIV antibodies not detected. No detectable HIV-1 RNA. HIV-2 infection cannot be excluded.**

The client does not have HIV-1. The client should be retested in two weeks to rule out possibility of acute HIV-2.

How to submit specimens for new algorithm

- 4th Gen; HIV 1, 2 Antigen/Antibody
 - No more than 5 days cold.
 - Gold top, tiger top, spin before submit. NO DRY BLOOD SPOT.
 - Reactive samples run in duplicate.
- MultiSpot HIV 1/2 Differentiation
 - Reflex from reactive 4th Gen.
 - 10 minute average run time. Read immediately once test completed.
 - DSHS Lab Costs: MS \$40.74, WB Serum and DBS \$277.23, oral fluid \$324.74.

Discordant Results

- Nucleic Testing
- Resolves HIV 1 infections
- Dallas and Houston Health Departments

Seattle/King County Best Practice Study

- Compare four point of care tests to determine ability to identify early infection in real time.
- 2/2010 - 11/2012 -Recruited 2144 HIV negative MSMs
- STD clinic, Gay Men's Health, Primary Health

HIV Test Results among 2144 MSM enrolled Feb 2010 - Nov 2012

	STD Clinic & Gay City n=2127	PIC n=17	Total n=2144
Concordant Rapid Positive Tests	56 (81%)	9	65
Discordant FDA-approved Rapid Tests	3 (4%)	7	10
All Rapids Negative / EIA Positive	3 (4%)	1	4
Acute (EIA Neg / NAAT Pos)	7 (10%)	0	7*
Total HIV Positive	69 (3.2%)	17	86

*Includes one person with reactive p24 Ag on Determine (#4 below)

Oral Fluid is Inferior to Fingertick Point-of-Care HIV Tests Among Seattle MSM

Joanne Stekler^{1,2}, Aric Lane¹, Joshua O'Neal³, Matthew R. Golden^{1,2}

Results of study HIV tests among 11 HIV+ MSM with discordant results

	OraQuick Oral Fluid	OraQuick Fingertick	Uni-Gold	Determine	EIA or 4 th gen	HIV RNA (copies/mL)
1	+	+	—	ND	+	140,000
2	—	+	+	ND	+	
3	—	+	+	ND	+	128,000
4	—	—	—	—/+	—	5.7 million
5	—	—	+	ND	+	12.8 million
6	—	—	+	+/-	+	21,000
7	—	+	—	+/-	+	719,000
8	—	+	+	+/-	+	436,000
9	—	+	+	+/-	+	33,000
10	—	+	+	+/-	+	
11	—	+	+	+/-	+	32,000
		p=0.02*	p=0.04*			

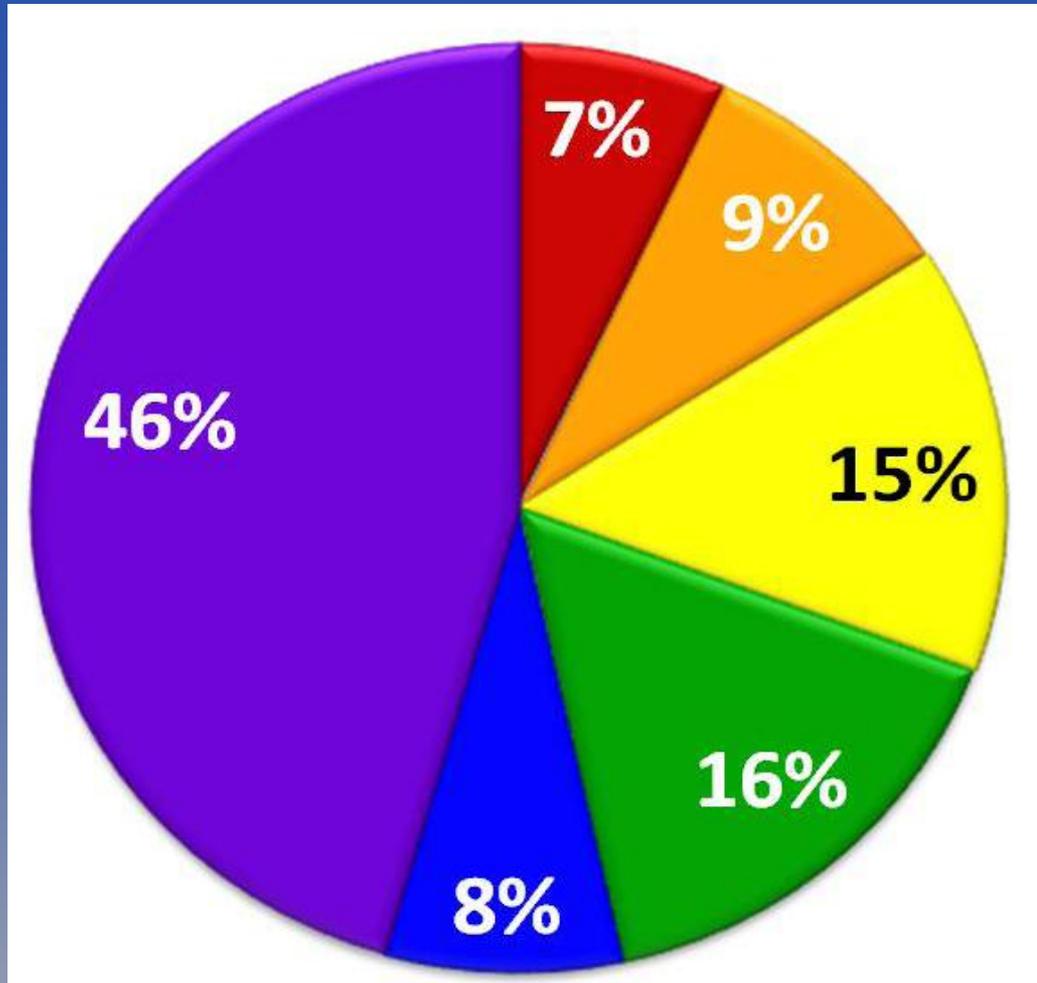
ND: not done

*Compared to OraQuick performed on oral fluids

Patient Survey Collection Preference and Test Trust

- “On a scale from 1-5, which HIV test(s) would you prefer, based solely on the specimen collection method(s)?”
- “Among all of the tests that have been done today, on a scale from 1-5, which HIV test(s) do you trust most to correctly tell you whether you are truly HIV-positive or HIV-negative. Answer this question based on today's visit, your recent potential exposures, the test, the test window period, and specimen collection method.”

“Taking all factors into account, if you could only get one HIV test today, which test would you get?” (n=120)



- OraQuick OF
- OraQuick FS
- UniGold
- Determine Combo
- EIA
- RNA

http://www.hivforum.org/storage/hivforum/documents/_2012NationalSummit_Posting/a_079_stekler.pdf

Transition to Best Practices

- Current Test Technology Used
- Patient Population
 - Who is likely to have acute infection?
- Staff training
 - Technology
 - Specimen Collection
 - Messaging/Counseling
- Administration
- Budget

Resources

- www.aphl.org/aphlprograms/infectious/hiv/Pages/HIV-Diagnostic-Testing-Algorithm.aspx
- www.hivtestingconference.org
- www.hivforum.org/index.php?option=com_content&task=view&id=774&Itemid=92



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Questions?