HIV Test Technologies, Best Practices, and New Algorithm

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testTEXAS HIV Coalition

TEXAS Department of State Health Services

A Healthy Texas

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

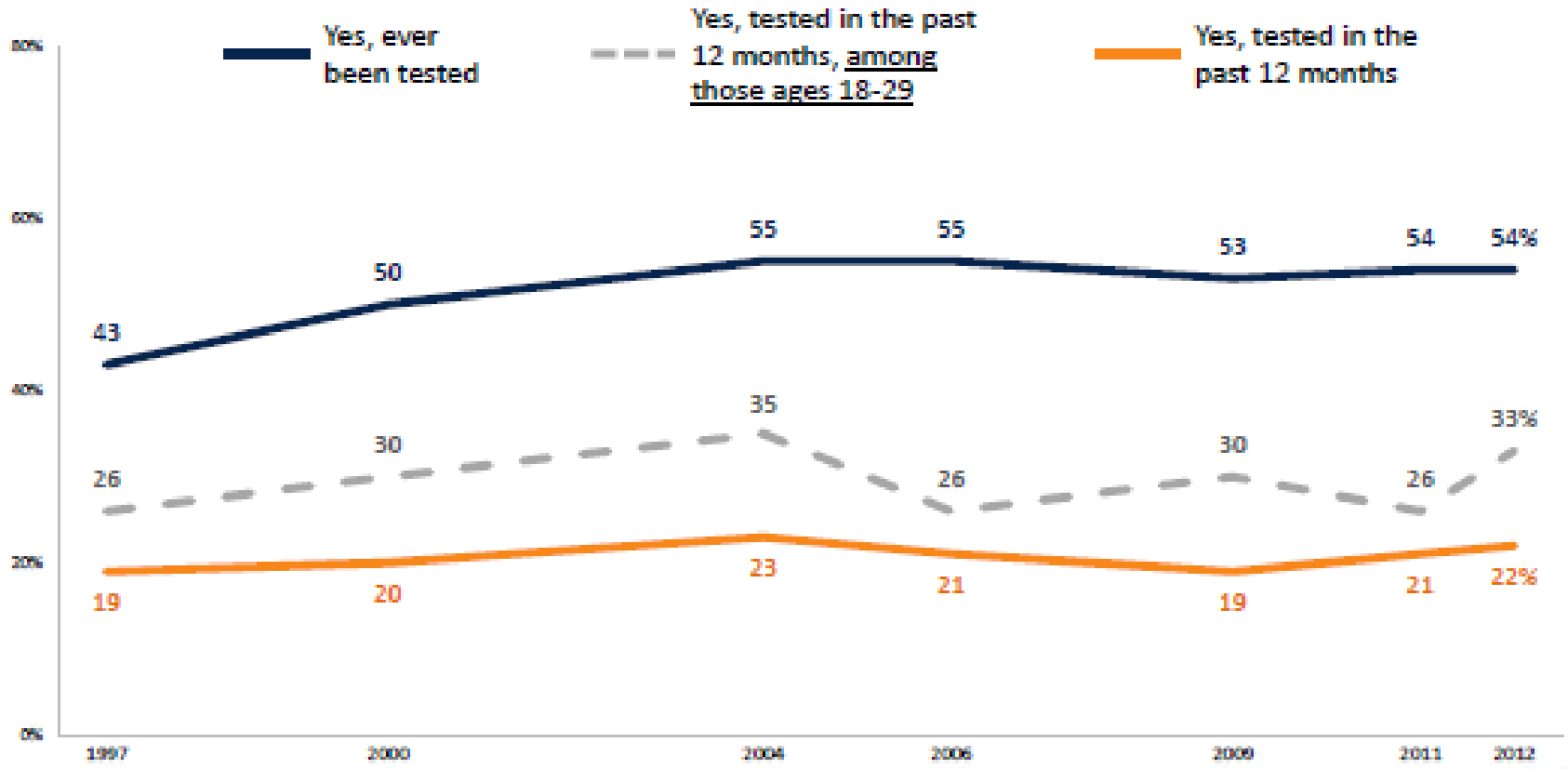
- 1995 – 44% Urgent Health Problem
- 2012 – 10% Urgent Health Problem
- 2006 – 21% concern about what others would think if tested
- **69%** don't think friends would care either way. **9%** think friends would think more of them if tested.

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

SLIDE 33

Reported HIV Testing Rates Relatively Flat, Including Among Young Adults

Among those ages 18-64, percent who say they have been tested for HIV ever and in the last 12 months:



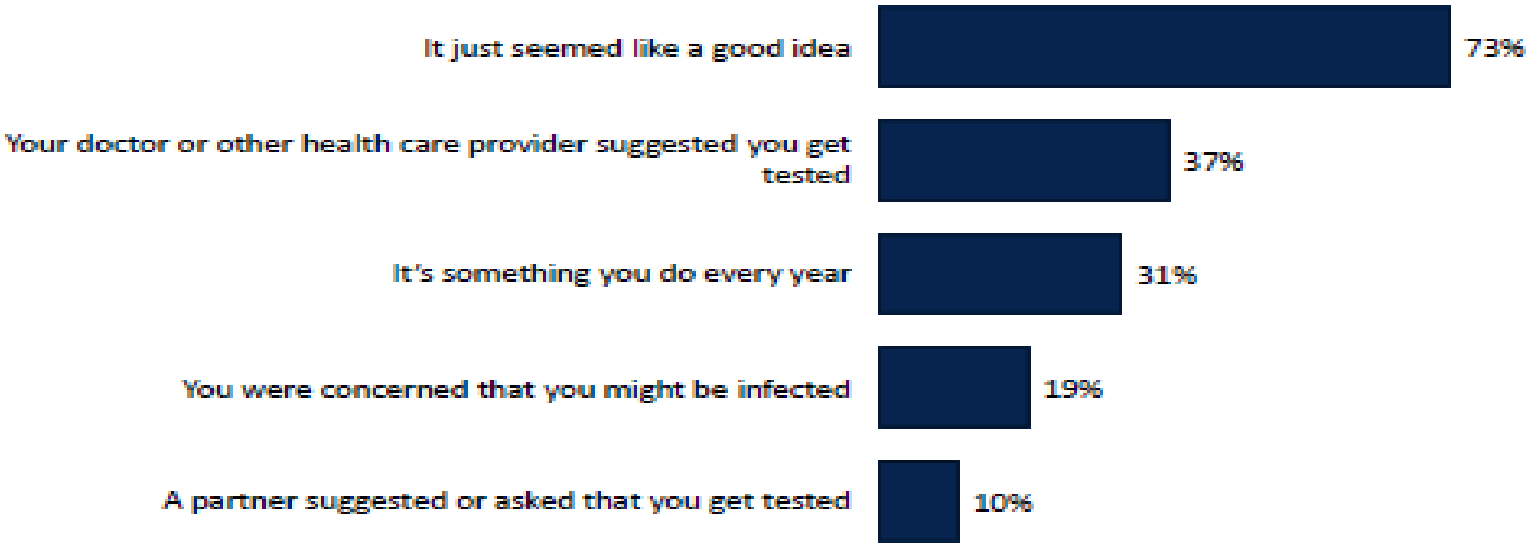
Source: Kaiser Family Foundation surveys

Reasons for Testing

SLIDE 43

'Seemed Like A Good Idea' Is Most Common Reason For Testing

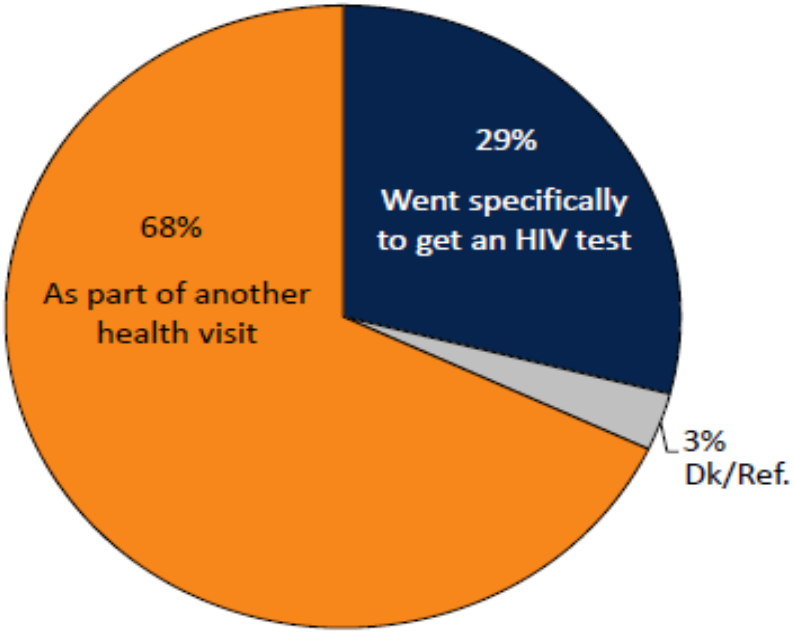
Percent who say each of the following is a reason they got tested for HIV (among the 48% who have been tested for HIV):



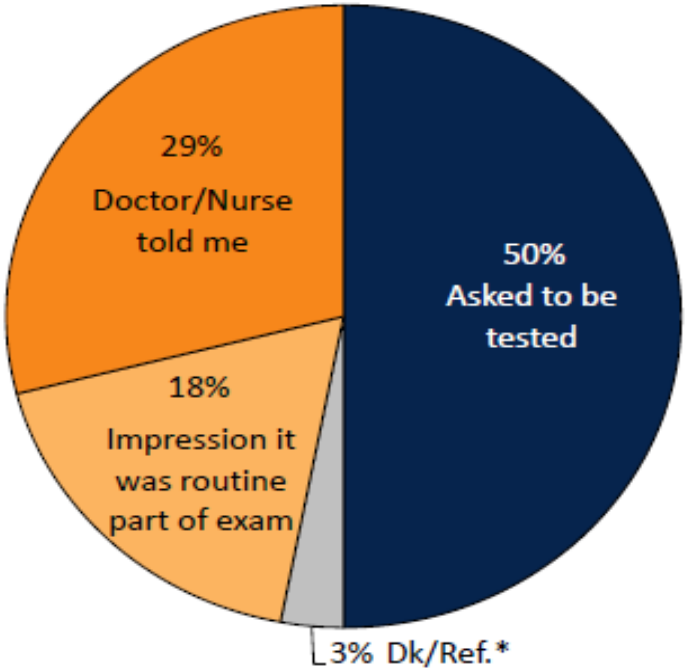
Source: Washington Post/Kaiser Family Foundation 2012 *Survey of Americans on HIV/AIDS* (conducted June 11-24, 2012)

Reported HIV Testing Experiences

The last time you were tested for HIV, did you go to a doctor or a clinic specifically to get an HIV test, or did you decide to get an HIV test as part of another health visit, such as a routine check-up? (Among the 48% who have been tested)



The last time you were tested for HIV, how did you know the test was being done? Did you ask to be tested for HIV, did the doctor or nurse tell you this test was being done, or was it your impression that the test was a routine part of the exam? (Among the 48% who have been tested)



* Includes "Tested as part of blood donation/blood drive (vol.)."

Source: Washington Post/Kaiser Family Foundation *2012 Survey of Americans on HIV/AIDS* (conducted June 11-24, 2012)

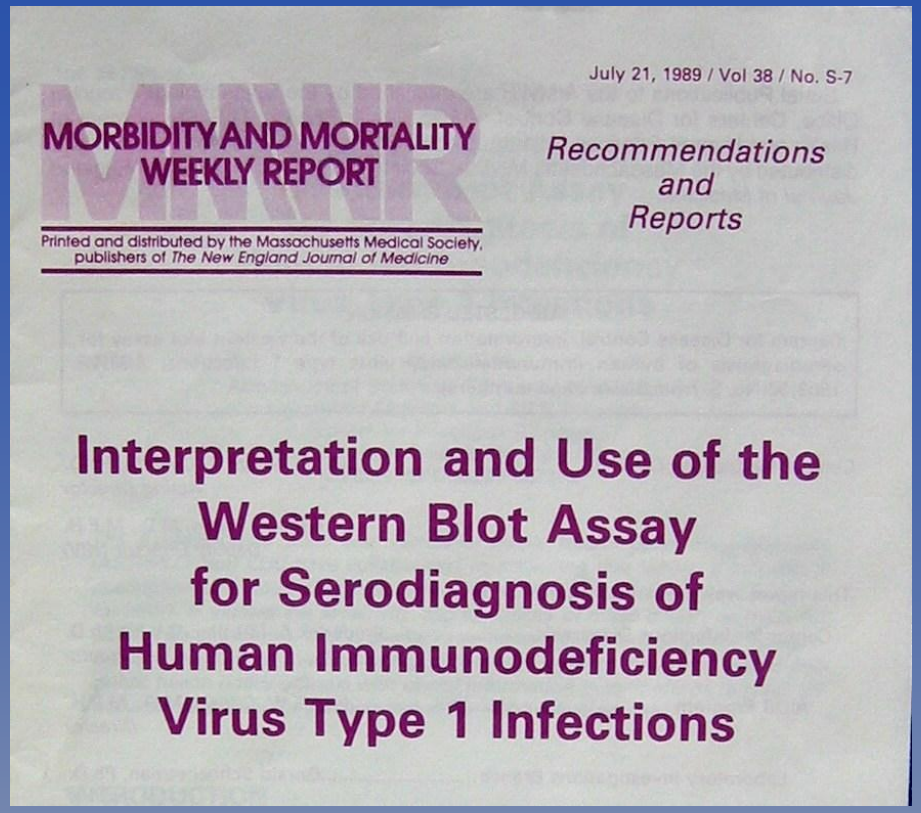
Role of the Awareness of HIV Status

- 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.


July 21, 1989 / Vol 38 / No. S-7

MORBIDITY AND MORTALITY WEEKLY REPORT

Printed and distributed by the Massachusetts Medical Society, publishers of *The New England Journal of Medicine*

Recommendations and Reports

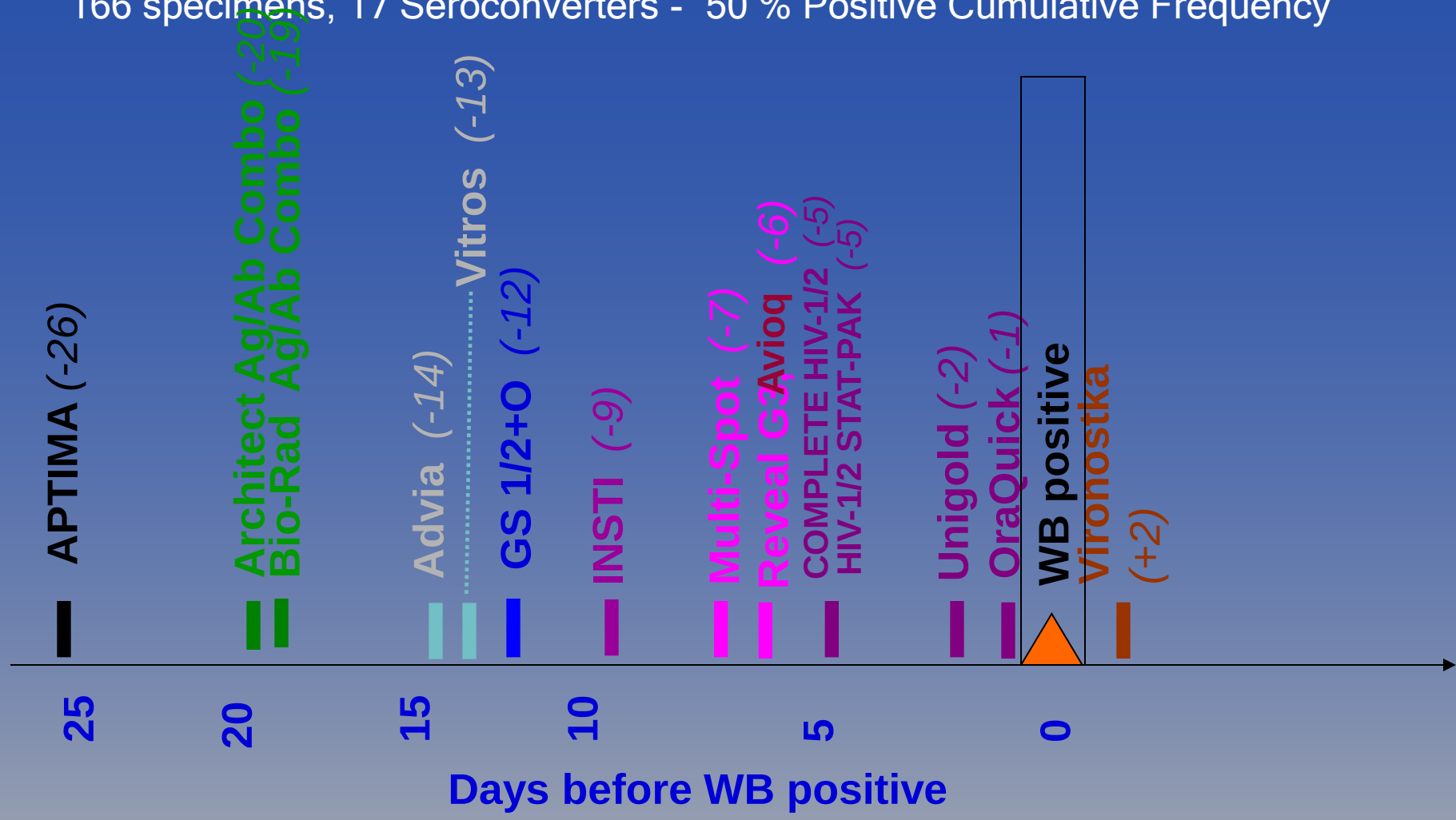
Interpretation and Use of the Western Blot Assay for Serodiagnosis of Human Immunodeficiency Virus Type 1 Infections

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 RNA/DNA

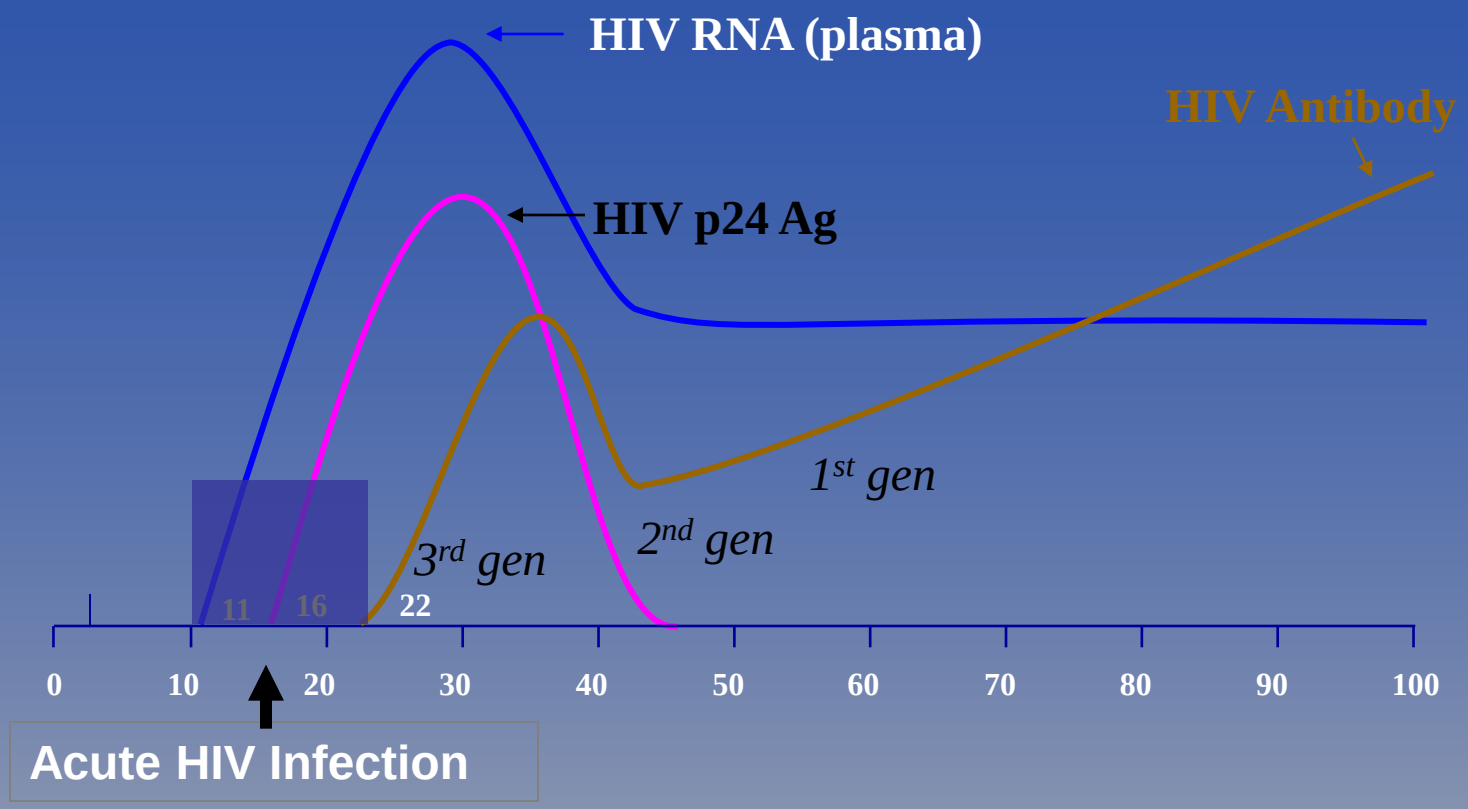
Sequence of Test Positivity Relative to WB

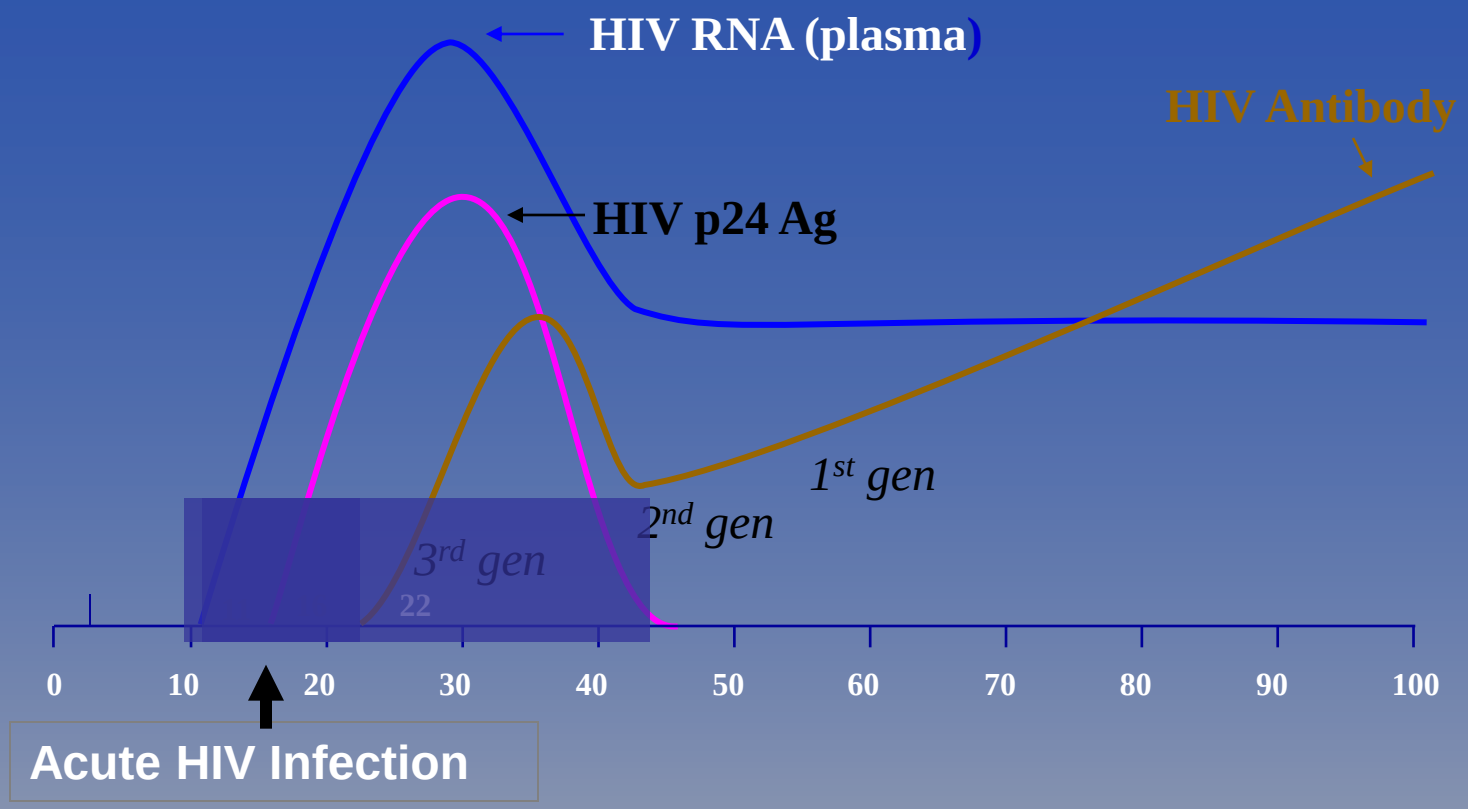
166 specimens, 17 Seroconverters - 50 % Positive Cumulative Frequency

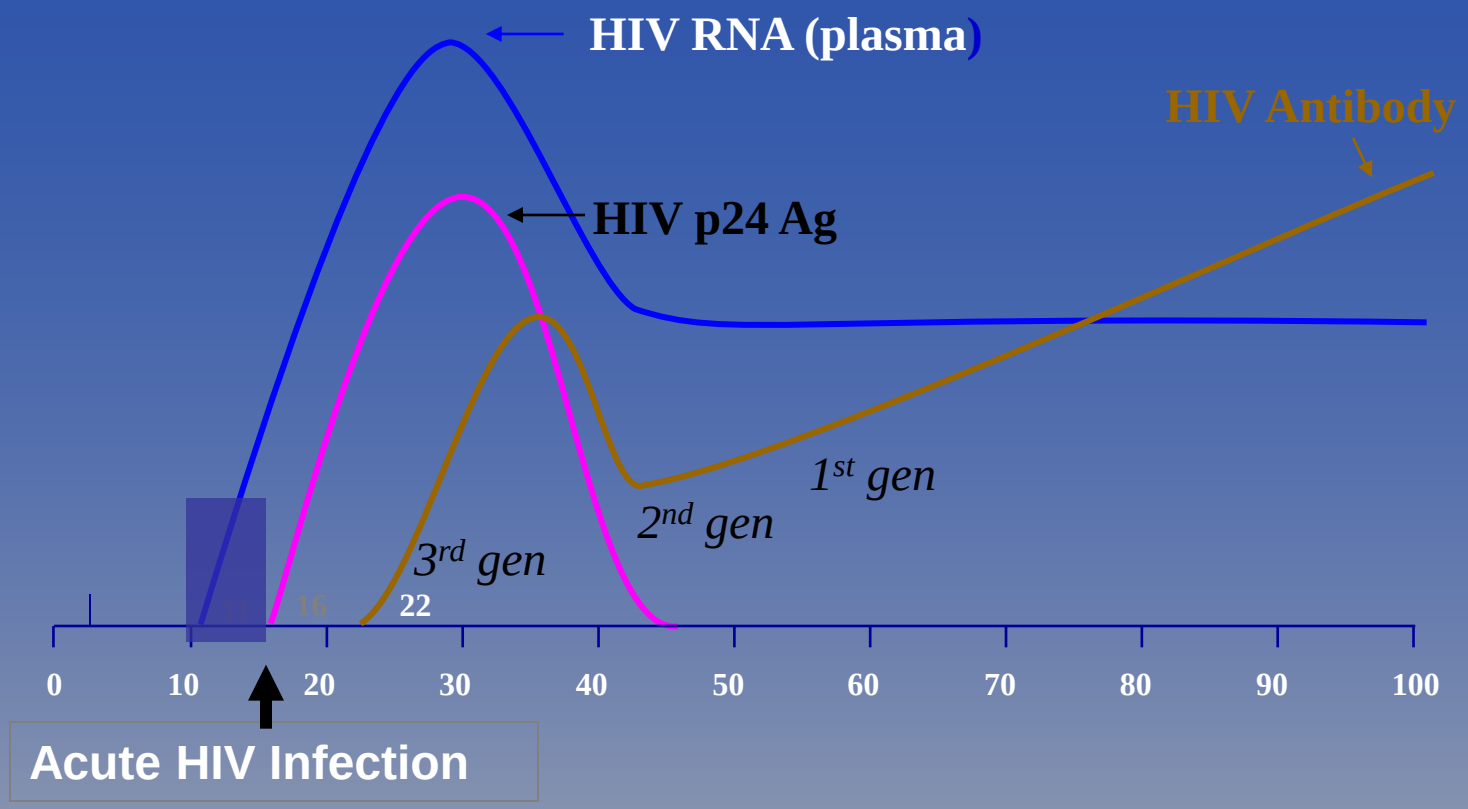


Modified from *Masciotra et al, J Clin Virol 2011* and *Owen et al, J Clin Micro 2008*

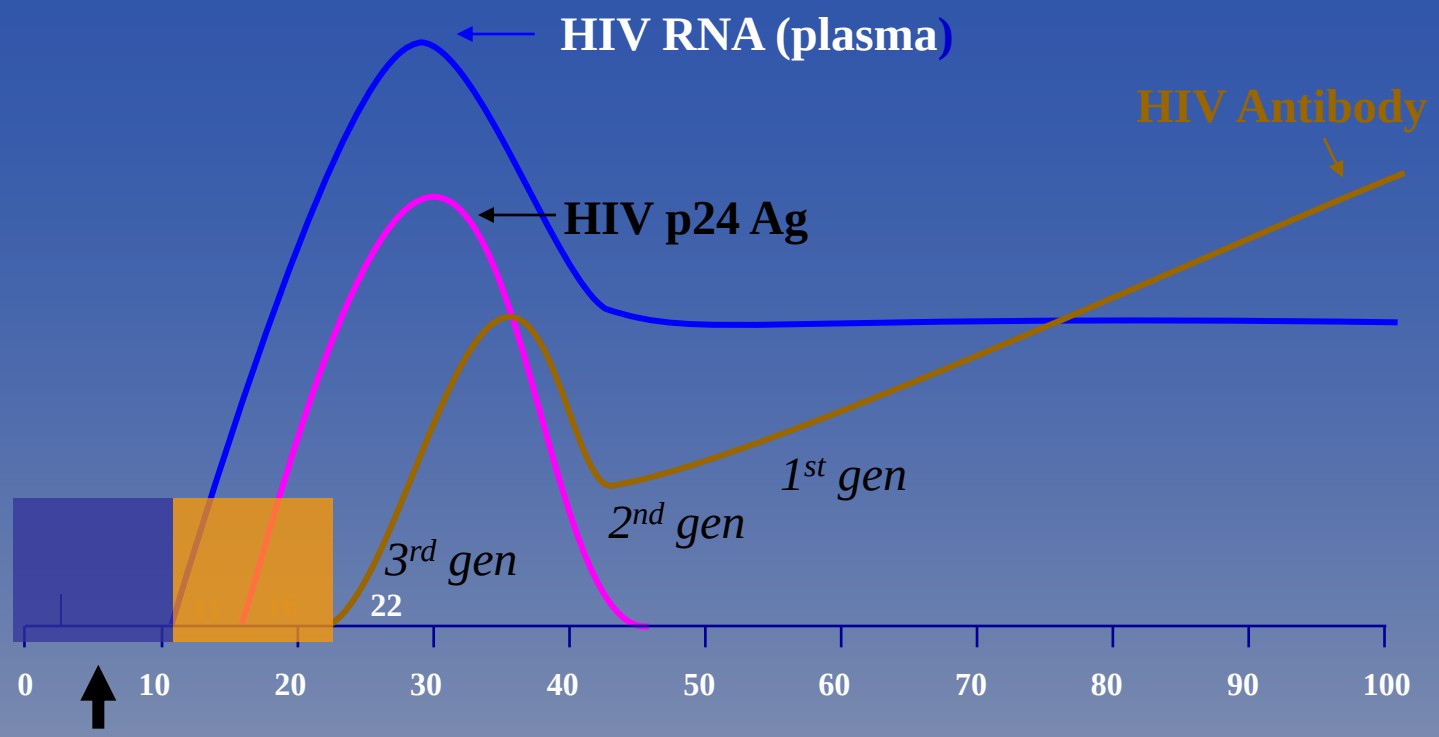
Window Period and HIV Infection




HIV RNA (plasma)
HIV Antibody
HIV p24 Ag
1st gen
2nd gen
3rd gen
0
10
20
30
40
50
60
70
80
90
100
Acute HIV Infection


HIV RNA (plasma)
HIV Antibody
HIV p24 Ag
1st gen
2nd gen
3rd gen
16
22
0
10
20
30
40
50
60
70
80
90
100
Acute HIV Infection

We Can’t Close the Window



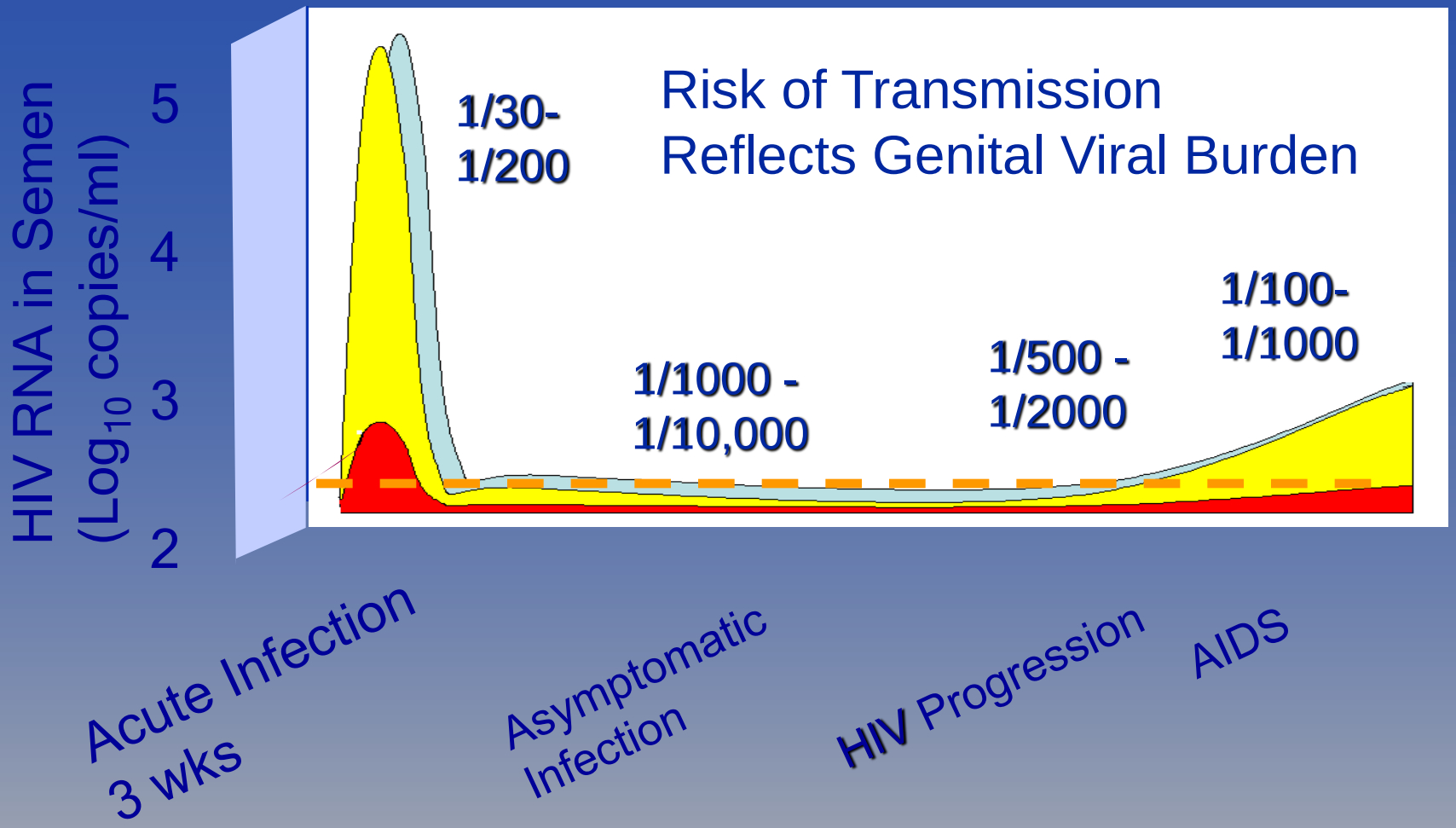
Infection Undetectable

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

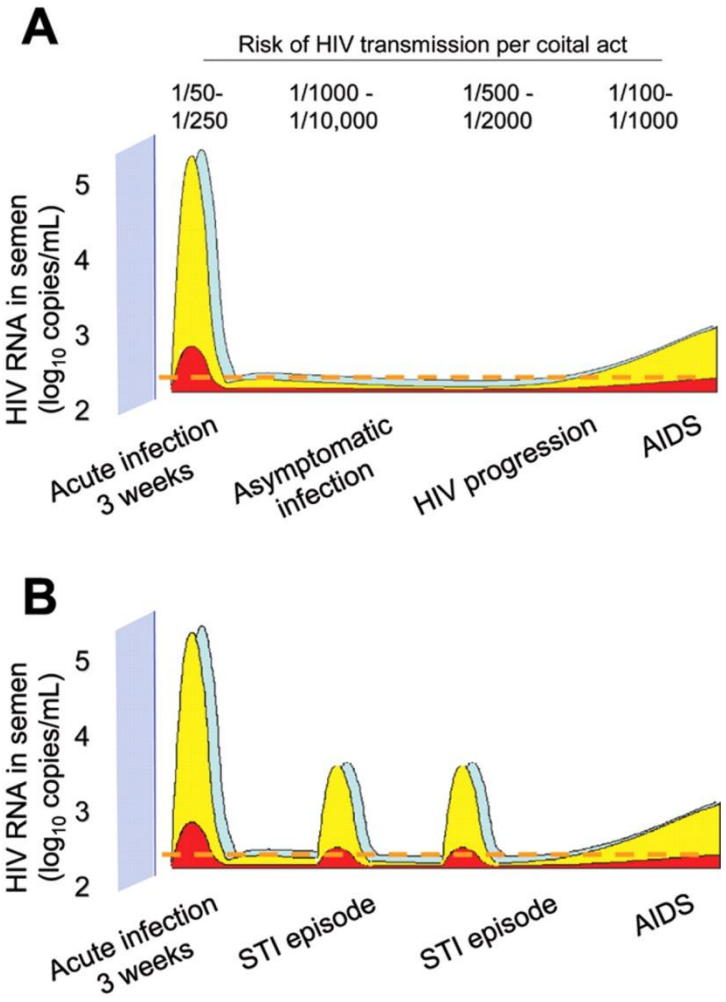
- Kahn et al, NEJM 1998
- Weintrob et al, Arch Int Med 2003

Risk of Sexual Transmission of HIV



Cohen MS, et al. J Infect Dis. 2005

Prediction of the efficiency of HIV transmission according to HIV burden in the genital tract.



Cohen M S , and Pilcher C D J Infect Dis. 2005;191:1391-1393

© 2005 by the Infectious Diseases Society of America

The Journal of Infectious Diseases

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 infections acute infection stage,
- Because of cross-reactivity, >60% of persons with HIV-2 infection misclassified as HIV-1 by Western blot

HIV-2 Infection

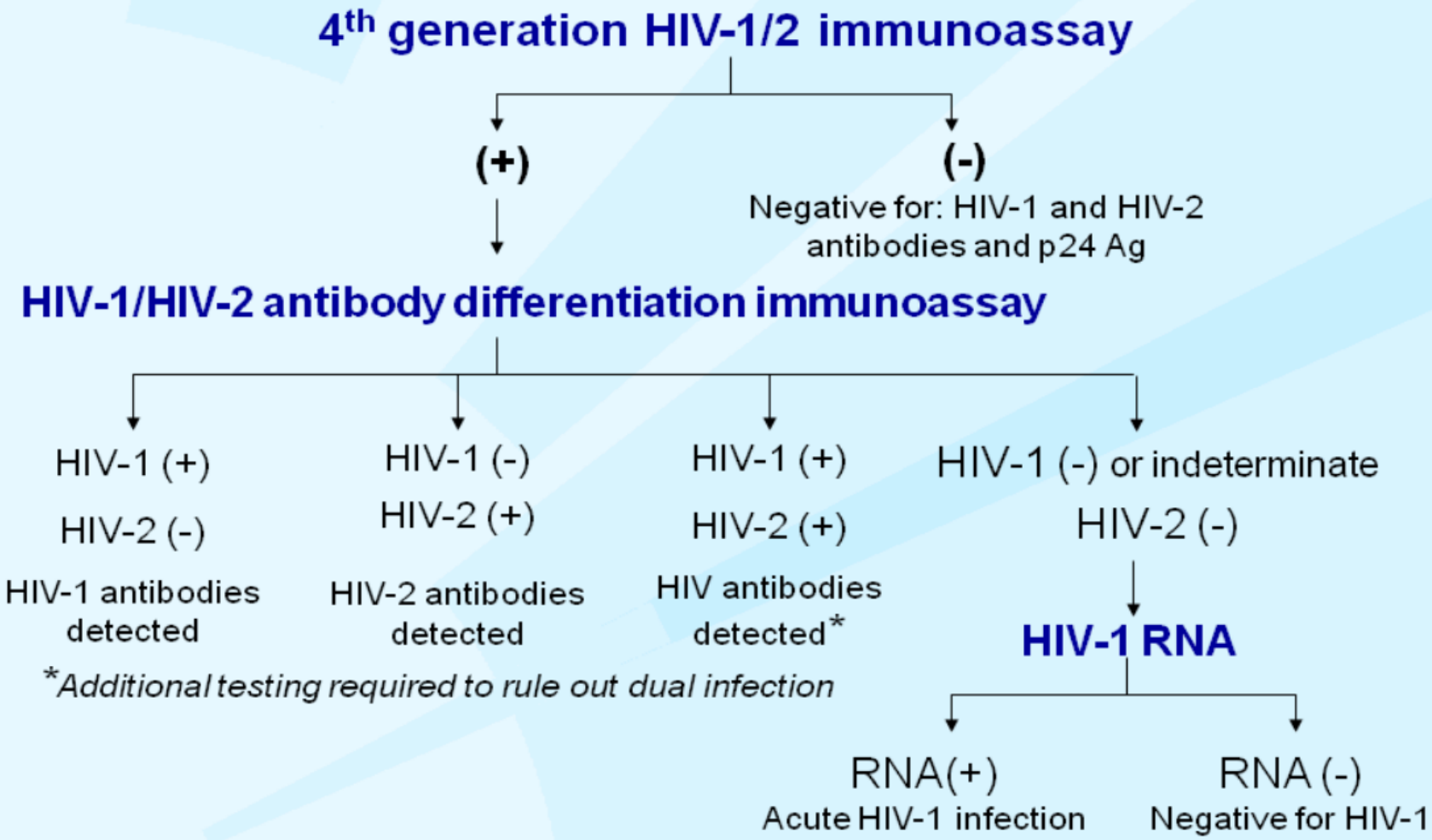
- **Remains uncommon in U.S., but**
  - Does not respond to NNRTIs, some PIs (first line therapy)
  - Undetectable by HIV-1 viral load tests
- **Misclassification by HIV-1 Western blot:**
  - 54/58 (93%) HIV-2 patients tested had positive HIV-1 WB (NYC)*
  - 97/163 (60%) HIV-2 cases reported had positive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

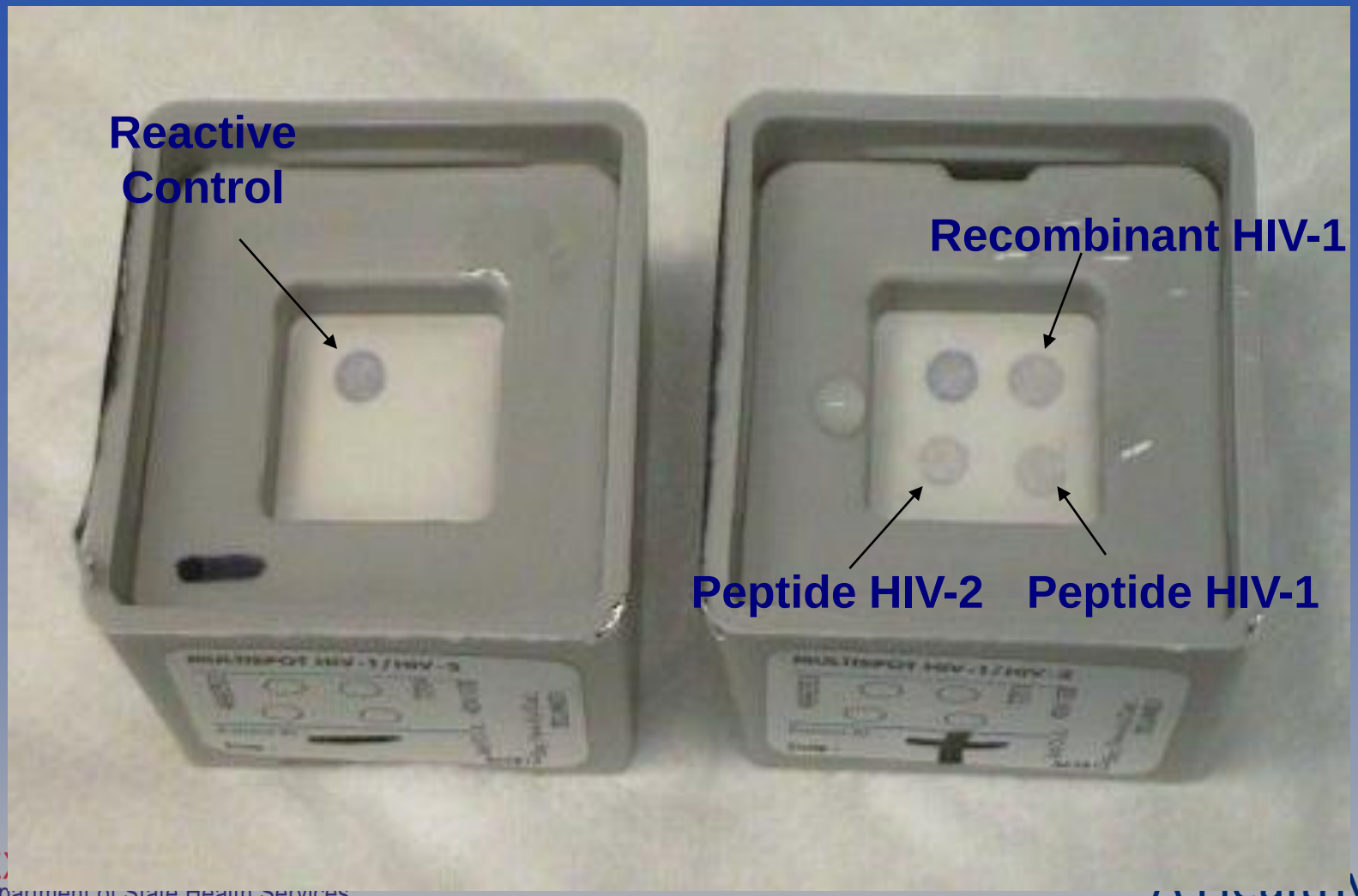
2010 HIV Diagnostics Conference: CDC/APHL Proposed New Testing Algorithm

Schematic Version of Recommended Algorithm



*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 for Patients
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.

Texas Department of State Health Services
Physical Address: 1100 West 49th Street Austin, TX 78756

Austin Laboratory
PO Box 149347
Austin, TX 78714-9347
888-963-7111 Ext. 7318
CLIA: 45D0660644

Internal Use Only

Provider:

LIMS Report #:

Sample #: AMS1200051 (578207)

Source: Serum

Additional Info:

Billing Comment:

Specimen Note:

Collected By:

Date Collected:

Date Received: 10/11/2012 8:36 am

Date Reported:

Test	Result
HIV Combo Ag/Ab EIA	Reactive
Multispot HIV-1/HIV-2 Rapid EIA	HIV-1 Reactive

Note:

1. Reference Ranges = Nonreactive
2. The HIV testing is not, in and of itself, diagnostic for HIV infection and should be considered in conjunction with other laboratory test results, clinical presentation and patient history. Only a physician should interpret the results.
3. The assay may also be used as an aid in the diagnosis of HIV-1 and/or HIV-2 infection in pediatric subjects (i.e, children as young as 2 years of age).
4. HIV screening performed by the 4th generation HIV Combo Ag/Ab EIA test for HIV detection do not distinguish between the presence of HIV antibodies or antigen in a sample. Additional supplemental tests will be automatically performed to verify the presence of HIV-1 p24 antigen or antibodies to HIV-1 or HIV-2.
5. A person who has antibodies to HIV-1 is presumed to be infected with the virus, except a person who has participated in an HIV vaccine study may develop antibodies to the vaccine and may or may not be infected with HIV.
6. Nucleic Acid Amplification Test (NAAT) is performed by an outside laboratory in Dallas and the final report is attached if this test was performed.

HIV Screening, multispot HIV-1/HIV-2 rapid test, and NAAT results interpretation:

HIV Combo Ag/Ab EIA	Multispot	Interpretation
Nonreactive	*(not performed)*	No serologic evidence of infection with HIV. Cannot exclude incubating or early HIV infection. Submit second sample in 3-4 weeks if clinically indicated.
Reactive	HIV-1	**Presumptive evidence of HIV-1 infection:** Based on EIA and MS HIV-1 Ab positive results, probable active HIV-1 infection. (NAAT is not indicated per CLSI guidelines). **Refer to physician for care.**
Reactive	HIV-2	**Presumptive evidence of HIV-2 infection:** Based on EIA and MS HIV-2 Ab positive results, probable active HIV-2 infection. (NAAT is not indicated per CLSI guidelines). **Refer to physician for care.**
Reactive	Nonreactive or Indeterminate / Undifferentiated	**Possible acute infection:** Based on EIA and MS results, possible acute HIV infection (AHI). Test for NAAT to rule out AHI; if reactive, possible AHI. **Refer to physician for care**. If NAAT is nonreactive or not tested, submit second sample in 3-4 weeks to rule out HIV infection.

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Reactive	HIV-2	**Presumptive evidence of HIV-2 infection:** Based on EIA and MS HIV-2 Ab positive results, probable active HIV-2 infection. (NAAT is not indicated per CLSI guidelines). **Refer to physician for care.**
Reactive	Nonreactive or Indeterminate / Undifferentiated	**Possible acute infection:** Based on EIA and MS results, possible acute HIV infection (AHI). Test for NAAT to rule out AHI; if reactive, possible AHI. **Refer to physician for care**. If NAAT is nonreactive or not tested, submit second sample in 3-4 weeks to rule out HIV infection.

Specimen Collection

- 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.

Discordant Results

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

Non-Reactive and Indeterminate WB NAAT Testing

	2011	AHI	2012	AHI	2013	AHI
Fort Worth Hospital	47	4	49	4	13	3
Beaumont Hospital	0	0	8	1	1	0
Private Dallas Hospital	2	1	6	3	3	0
Texarkana Hospital	0	0	1	1	0	0
Ft. Worth/Arlington Hospital					2	0
Dallas Hospital					1	0
Total:	49	**5**	64	**9**	20	**3**

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

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

Joanne Stekler[1,2], Aric Lane[1], Joshua O'Neal[3], Matthew R. Golden[1,2]

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

	OraQuick Oral Fluid	OraQuick Fingerstick	Uni-Gold	Determine	EIA or 4th 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*			

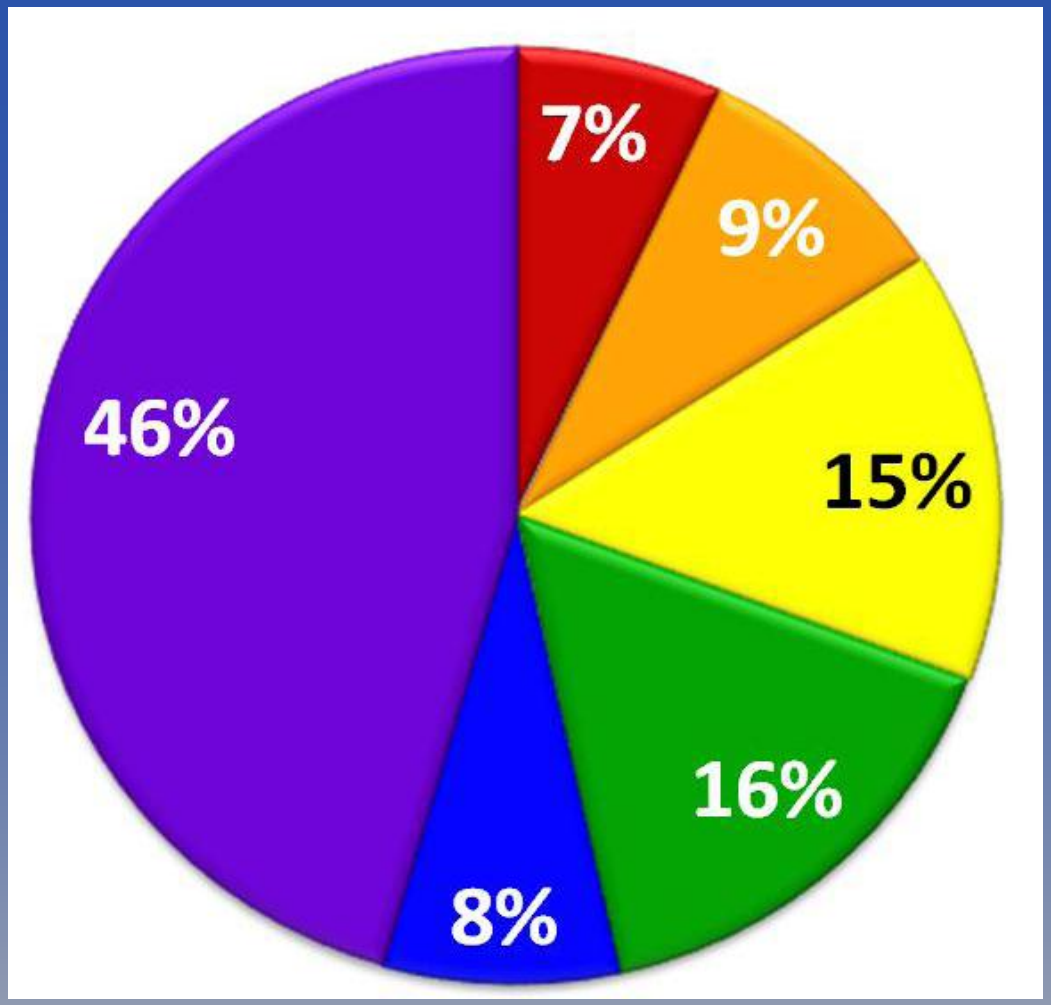
ND: not done

*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

The AMERICAN MEDICAL ASSOCIATION ETHICS POLICY states that a physician's duty to promote patient welfare and to improve the public's health are fostered by routinely testing their adult patients for HIV.

www.ama-assn.org/go/cdjareports

TEXAS
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(512) 533.3094

Questions?