

In the Footsteps of the WHO HIV Rapid Testing in the US



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CZECHOSLOVAK SOCIETY OF ARTS AND
SCIENCES

SVU

23RD World Congress

Ceske Budejovice

2006

Czech roots: New and Old



Raska, Jr., K, Kim, HC, Raska, III, K, Martin, E, Raskova, J and Saidi, P. Human Immunodeficiency Virus (HIV) Infection in Haemophiliacs: Long Term Prognostic Significance of the HIV Serologic Pattern. Clin. exp. immunol. 77: 1-6, 1989.

US Public Health Policy to HIV

- Prevention strategy
- Currently:
 - Counsel Safe Sex
 - Test for exposure



Goals for Today

- Rapid HIV Testing
 - Differences between Rapid and Conventional HIV Testing
 - Limitations of Rapid Testing
 - The NJ Rapid Testing Experience 2003-6
 - The next step - Rapid HIV Confirmation

Traditional HIV Testing

- Testing technology driven by blood screening needs:
 - Batched, high volume EIA testing
 - Complex equipment
 - Technically demanding
 - Centralized
 - Time-consuming
- Not necessarily more accurate than other formats of testing
- MAJOR issue - client anxiety!

Current Options for HIV antibody screening

- Blood → LAB
- Urine HIV test → LAB
- Orasure HIV 1 test → LAB DAYS

ALL - POSITIVE Antibody Screening must be confirmed by Western Blot confirmation DAYS

- Oraquick Rapid HIV 1/2 test
 - Blood
 - Fingertick
 - OMT - Oral mucosal testing 20 MINUTES
-

- UNFORTUNATELY a PRELIMINARY POSITIVE RAPID HIV TESTS MUST STILL BE CONFIRMED BY A WESTERN BLOT

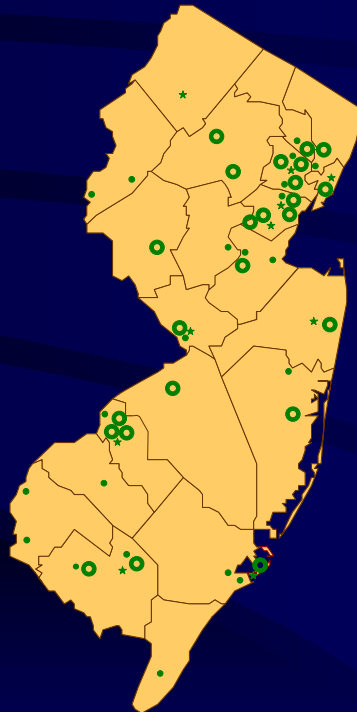
Why do we need rapid HIV testing?

- **Reaching and testing those at risk**
 - **Those unaware of their status**
 - ~ 25% of the 850,000 - 950,000 HIV + people in the United States
 - ~ 40,000 new infections in the US per year
 - ~ 30% who test positive do not receive their results
- **Providing a linkage to care for the HIV infected**
- Reducing the potential for spread by reaching the newly infected sooner
- Stopping the cycle by preventing transmission
 - Perinatal - women in labor
 - AZT will reduce transmission from 25% to 8%

New Jersey Counseling and Testing Sites (CTS)

UMDNJ-RWJMS/ NJ DHSS
AIDS PREVENTION GRANTEES
Primary ● Satellite ● fixed ★ mobile
Pale colors indicate pending sites

AIDS Coalition of Southern New Jersey
Atlantic City Health Department
Bergen County Health Department
Burlington County Health Department
Camden AHEC
Camden County Health Department
Check-Mate
East Orange Health Department
Eric B. Chandler Health Center
FamCare
Henry J. Austin Health Center
Hope House
Horizon Health Center
Hunterdon County Health Department
Hyacinth Foundation
Martin Luther King Outreach
Morristown Memorial Hospital
Newark Community Health Center
NJCRI
Ocean County Health Department
Paterson Health Department
Plainfield Community Health Center
Proceed
Robert Wood Johnson Medical School
Trinitas Hospital



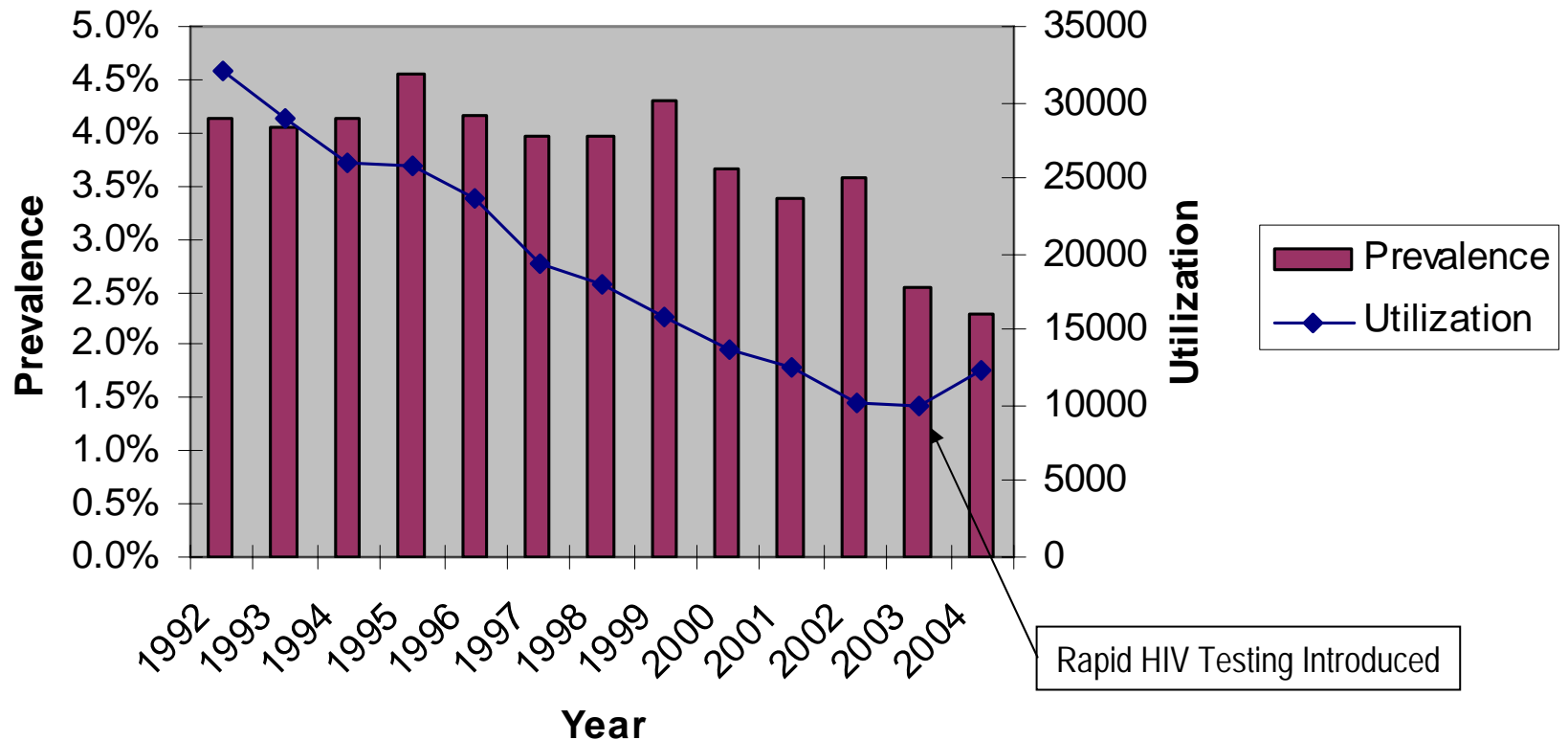
PRIOR to rapid testing:

- Specimens sent to state lab in Trenton
- 2.3-2.6% seroprevalence
- 65% received post-test counseling
- **35% did not return for results**

Rapid Testing started Nov 1, 2003:

- 23 primary sites
- 32 satellite licenses
- Western Blot confirmation at state lab in Trenton
- Over 70 CTS sites, including:
 - Hospitals/EDs
 - FQHCs
 - CBOs
 - Health departments
 - Ten mobile vans
 - Community events

HIV Testing in New Jersey



Performing the Oraquick Rapid HIV test



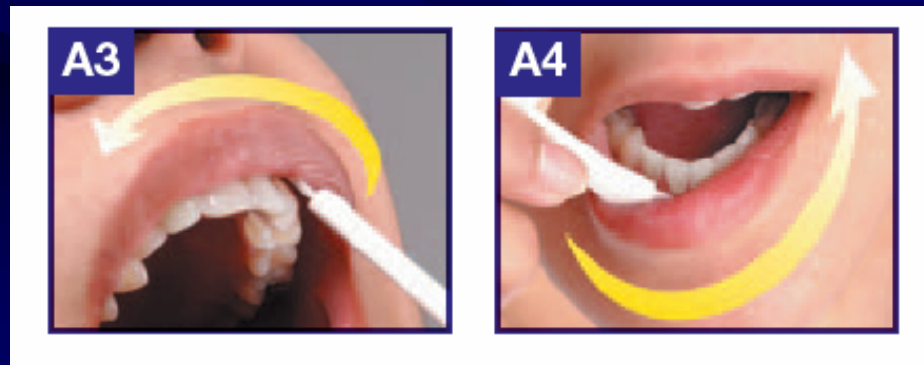
Oraquick Advanced -Specimen Types



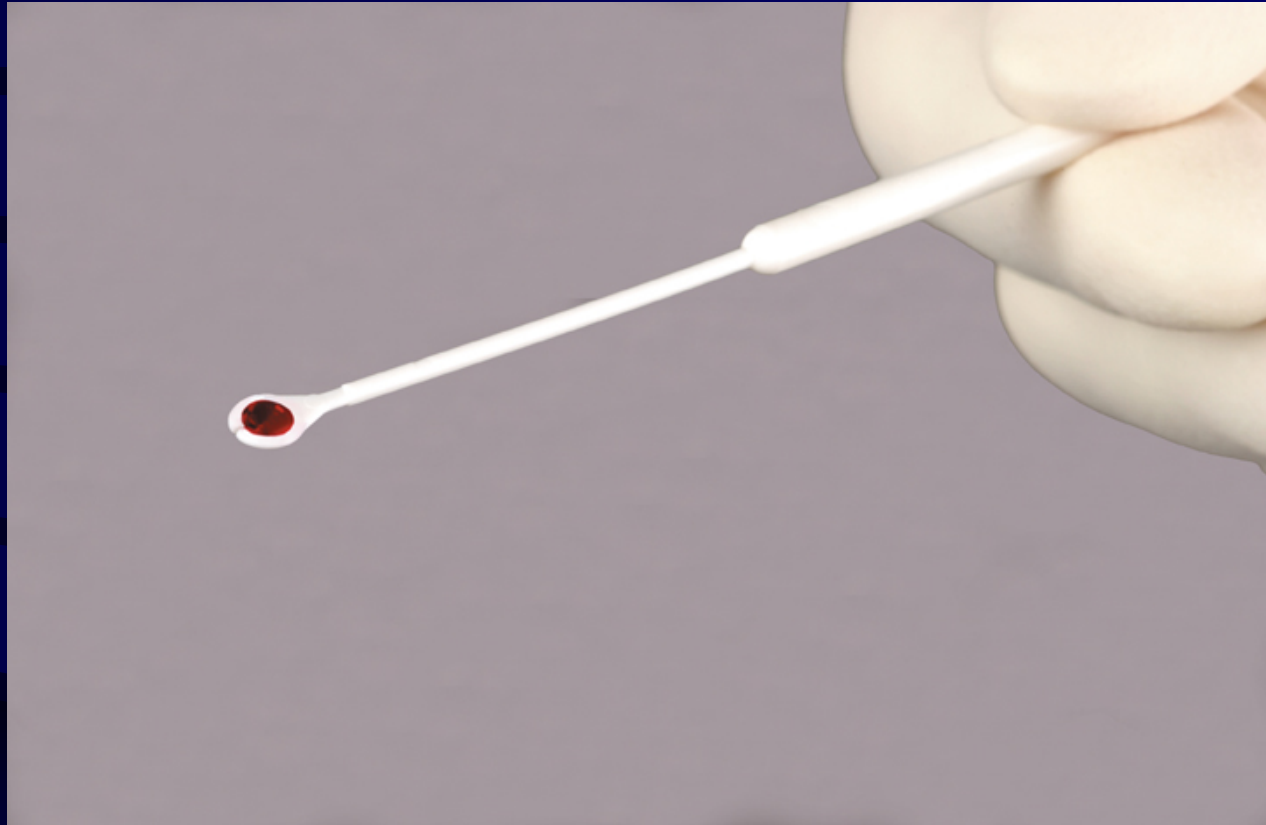
Fingerstick



Wholeblood



Oral Mucosal Transudate



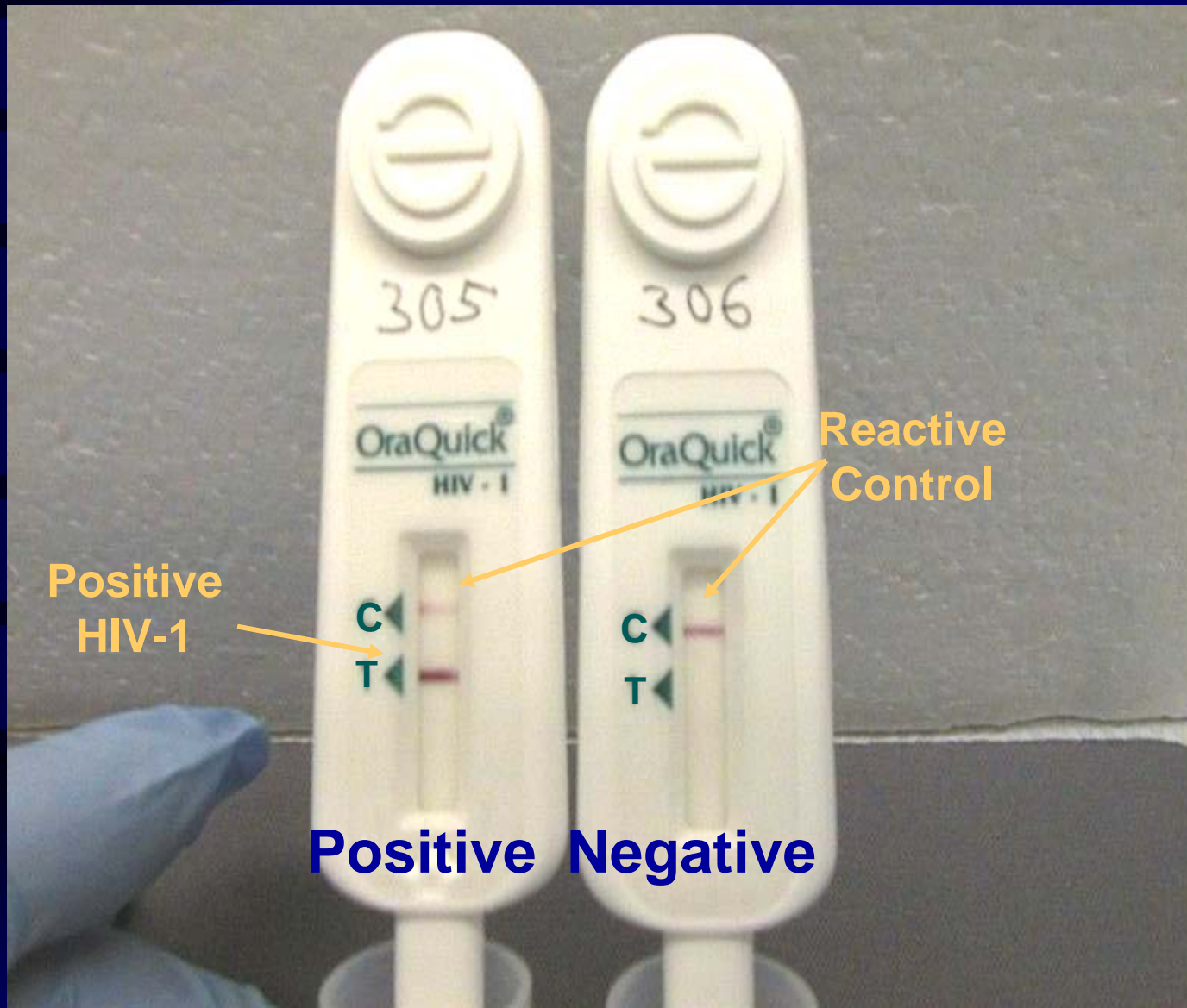
Loop collects 5 microliters of whole blood



Insert loop into vial and stir



Test develops in 20-40 minutes



Positive Negative

Read results



Non-reactive



Reactive

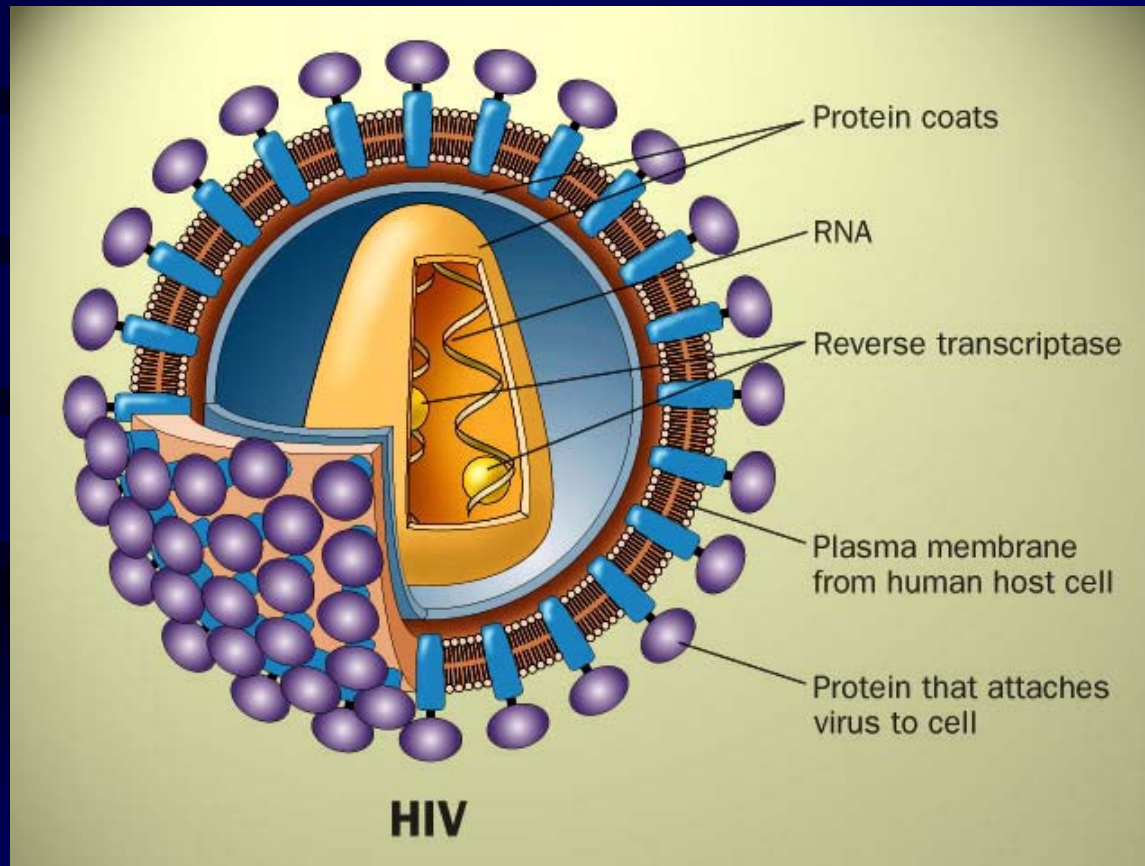
Invalid



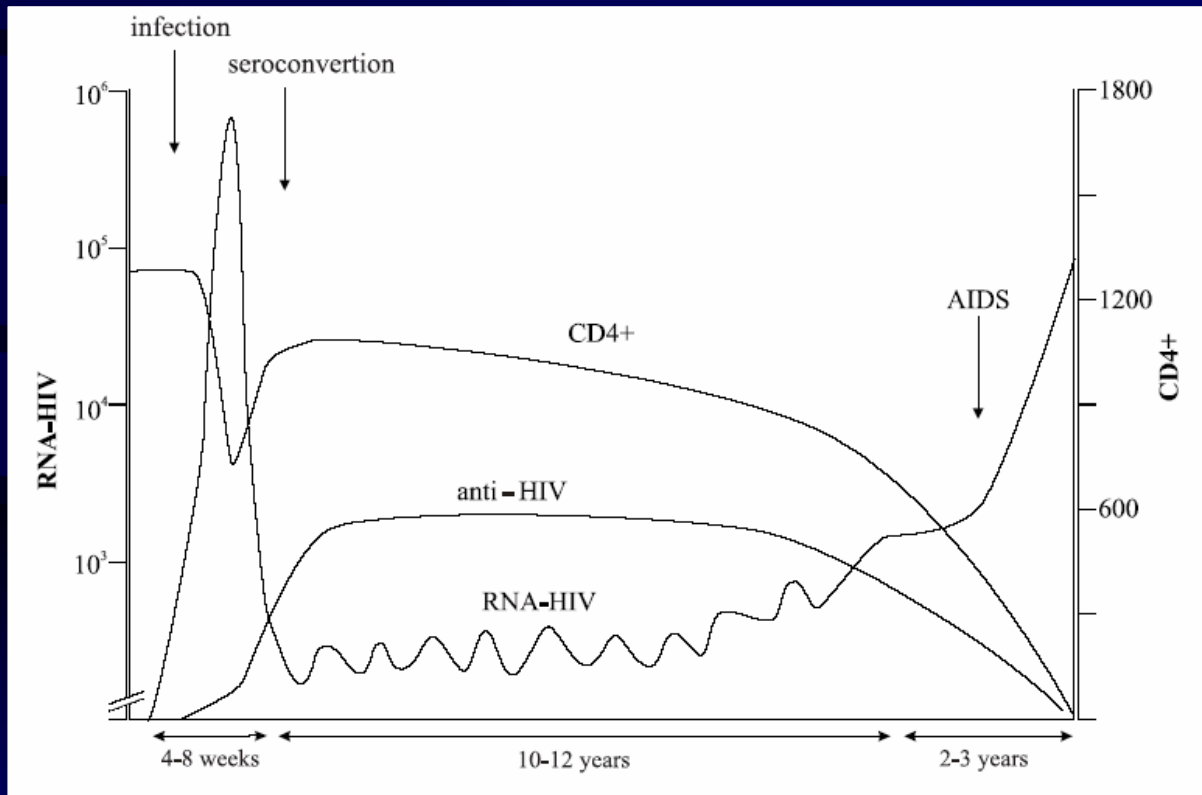
Basics

- What Can the Rapid HIV Test Measure?
 - Antibodies to HIV
- What Can It NOT Measure?
 - The HIV virus/RNA or DNA
- How Sensitive Is It?
 - At least as sensitive as more complex EIA technology used in hospitals and laboratories
 - In some cases it is more sensitive than the confirmatory test used to validate its results.

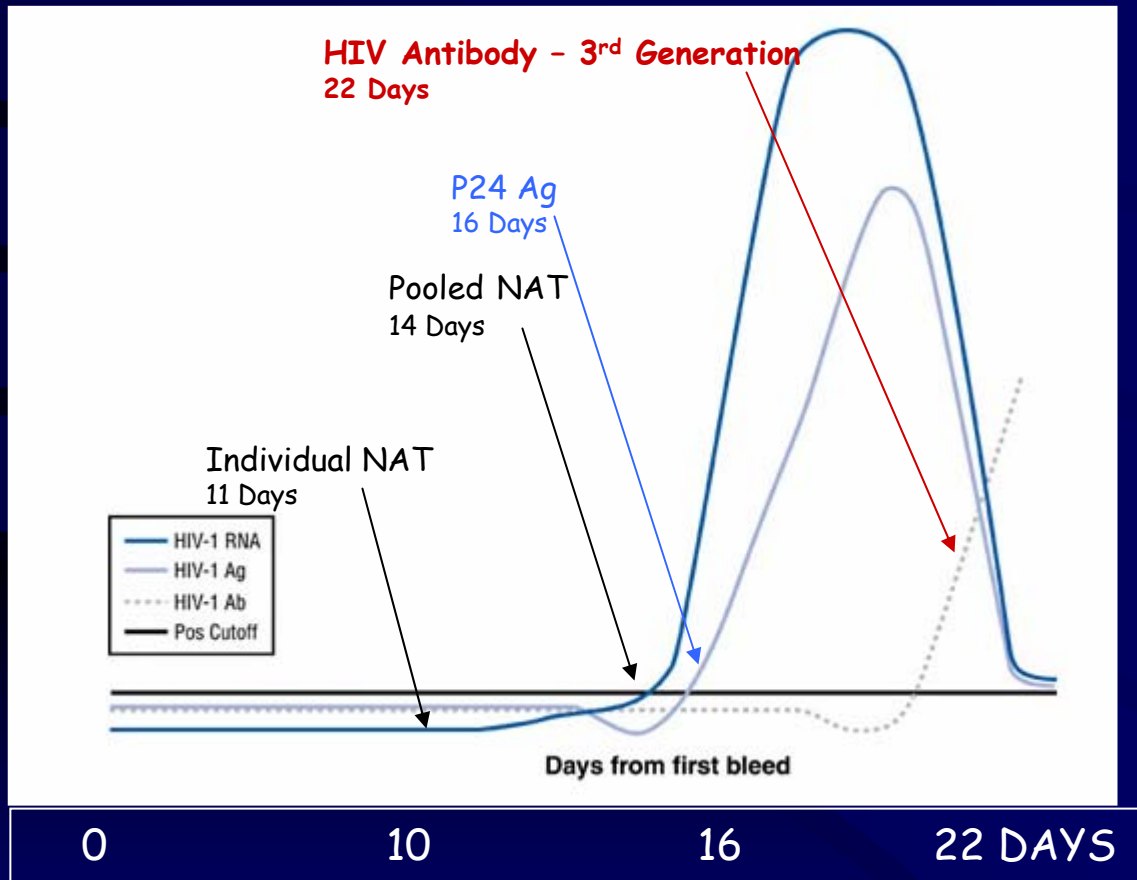
HIV Schematic



The Natural History of HIV Infection



Viremia During Early HIV Infection



- Ramp-up Viremia Doubling Time = 21.5 hrs
- Peak Viremia $10^6 - 10^8$ gEq/mL
- Viral set-point $10^2 - 10^5$ gEq/mL
- WINDOW
 - Antibody - 22 Days
 - Antigen - 16 Days
 - Pooled NAT - 14 Days
 - Individual NAT - 11 Days

CDC PMS-2 Survey 2005

TYPE of Rapid Test	Number Tested	Specificity (Probability test – when patient -)	Positive Predictive Value (Probability patient + when test is +)
BLOOD	135,724	99.98% (range: 99.73% -100%)	99.24% (range: 66.27% - 100%)
ORAL	26,066	99.89% (range: 99.44% - 100%)	90.00% (range: 50.0% - 100%)

February, 2006

Rapid Diagnostic HIV Assays

- **ADVANTAGES:**

- No transportation expense or delay
- Minimal equipment requirements
- Whole blood, finger-stick or oral specimens
- Easy to interpret
- No additional laboratory personnel expense.
- Negative results can be reported immediately

- **DISADVANTAGES:**

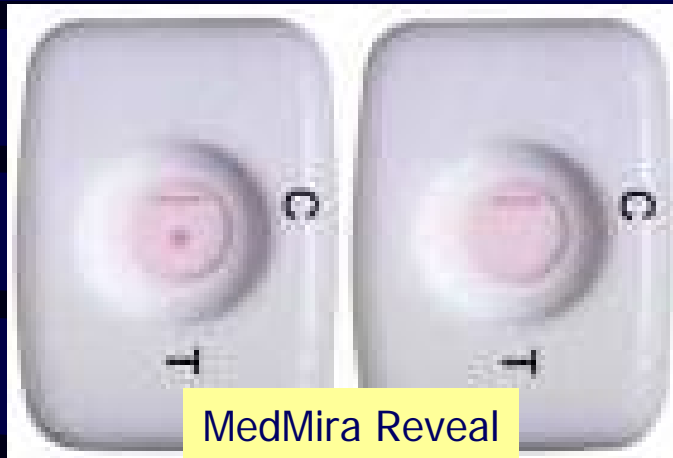
- Detects antibodies, not the virus
- A positive result requires confirmation by Western blot
- Temperature limitation on storage and transport

Rapid HIV procedures

- Worldwide > 60 rapid diagnostic tests
- US – 4 FDA approved rapid tests
 - 2 Moderate complexity – *lab only*
 - MedMira HIV 1
 - Biorad HIV 1 & 2
 - 2 CLIA-waived tests –
 - Oraquick HIV1 & 2 *Pursuing Over the Counter Approval*
 - Unigold HIV 1

HIV Rapid Test Formats

HIV 1 Only



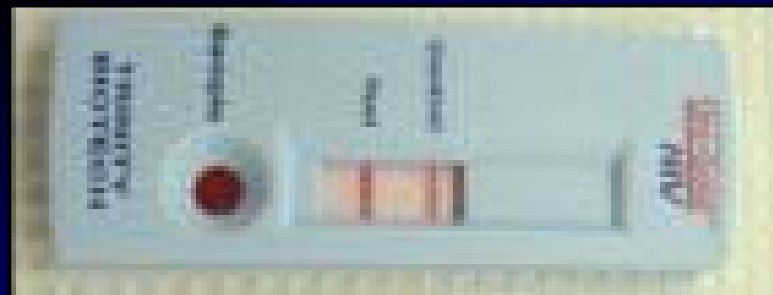
MedMira Reveal

HIV 1 & 2



Bio-Rad Multispot

Moderate Complexity



Trinity Uni-Gold

CLIA-waived Complexity



Oraquick Rapid

When technology collides with tradition

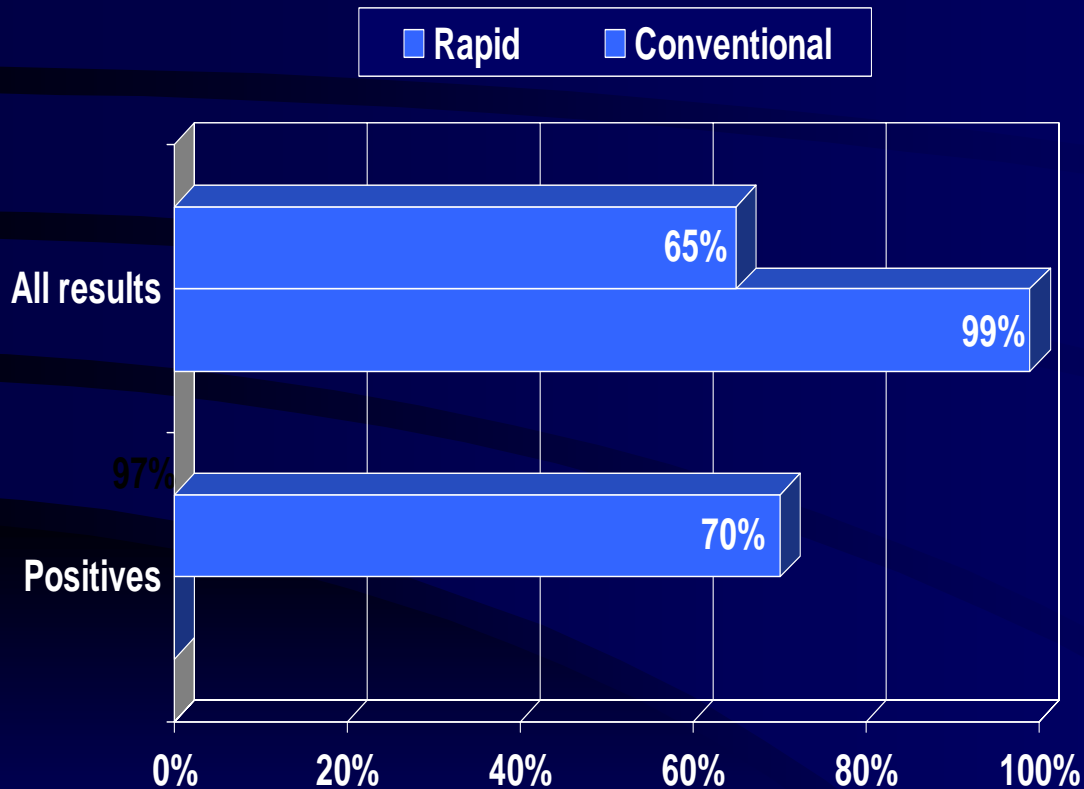
- ALL laboratory tests have a
 - A sensitivity - i.e. the ability to call a true positive, positive
 - A specificity - i.e. the ability to call a true negative, negative
- With tests as important as an HIV test, the results are made more reliable by running a second test, a confirmatory test
 - traditionally the Western blot.

When technology collides with tradition

- In resource poor countries, the WHO has recommended confirmation of **POSITIVE rapid HIV** tests with a second, alternative rapid test when HIV prevalence exceeds 10%.
- In resource rich countries, confirmation of **POSITIVE** rapid HIV tests still occurs using a traditional western blot procedure.
- This may not be warranted based upon the outcome of a recently completed retrospective study we have conducted.

Can a second rapid HIV test
confirm preliminary positives
as effectively as a Western
Blot?

Clients receiving post-test counseling

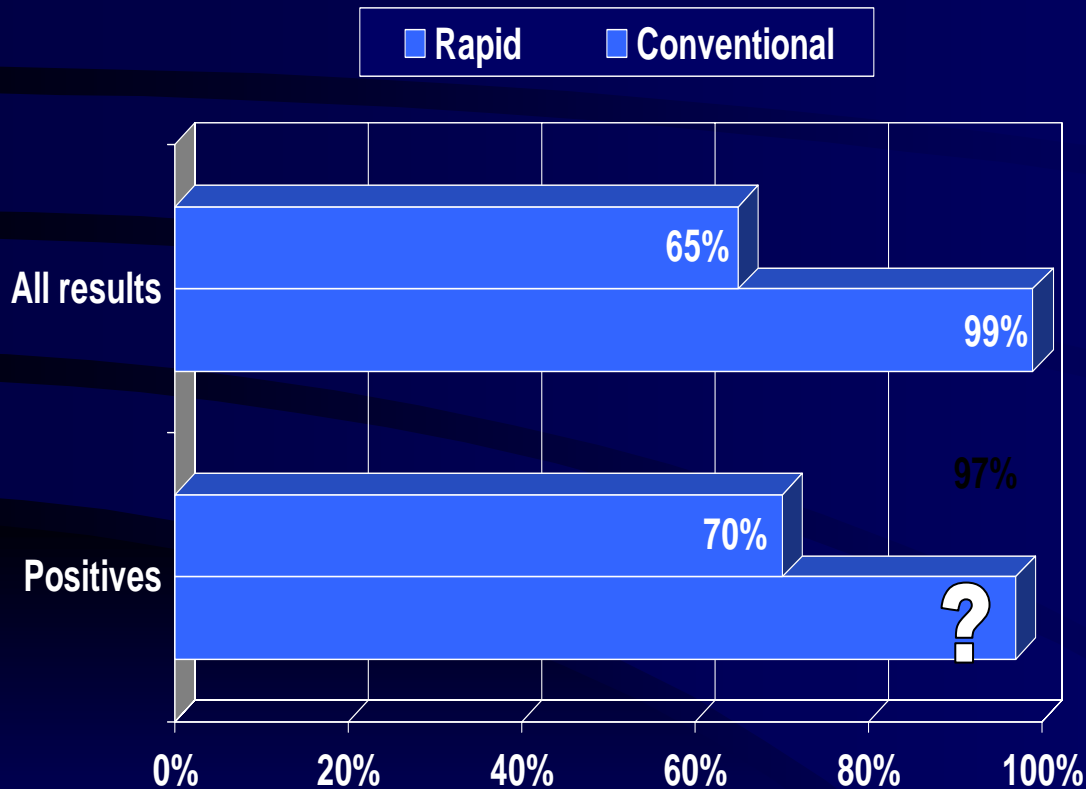


Marked improvement with introduction of rapid testing

Preliminary positives:

- 7.1% refused blood draw for confirmation
- 25.8% of those drawn did not return for results
- 70.1% of confirmed positives got their results and post-test counseling

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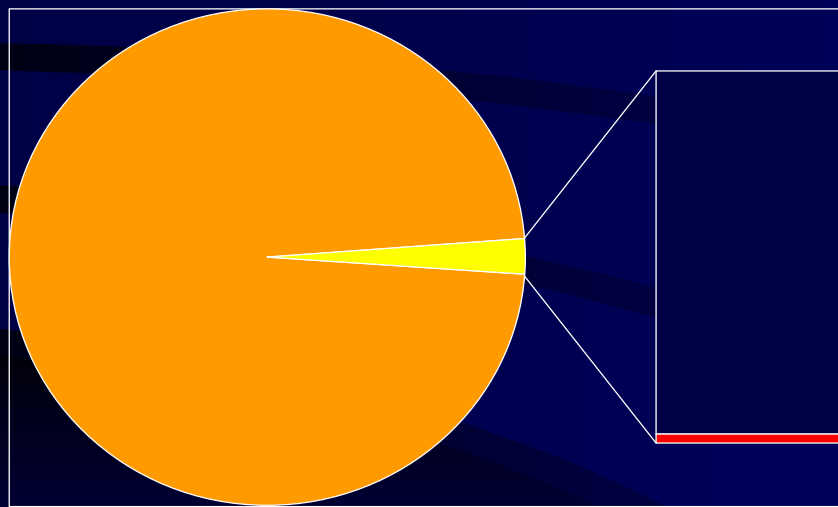
Can we extend our success to preliminary positives?

Question

- Can rapid immunoassays confirm testing results as well as the 'gold standard' Western Blot?

Rapid confirmation trial

July 1, 2004 through April 19, 2005



■ Negative □ WB Pos ■ Discordant

- 15,923 OraQuick tests statewide
- 363 prelim positive samples to state lab for confirmatory testing
 - 355 Western Blot positive
 - 8 Western Blot negative

Rapid confirmation trial

- All 8 Western Blot negative clients:
 - Part of CDC Post-marketing surveillance study
 - Negative on follow-up at least 4 weeks later, both antibody and nucleic acid testing
 - 4 of 7 tested reacted with non-viral components of OraQuick device

All 8 were false positive OraQuick tests

Rapid confirmation trial

All samples run by:


- Trinity Uni-Gold
- BioRad Multispot
- OraSure OraQuick
- MedMira Reveal




2004 Confirmatory test results

	8 Western Blot negative (False Positive OraQuick)	355 Western Blot positive (True Positive OraQuick)
OraSure OraQuick	8 positive	355 positive
Trinity Uni-Gold		
BioRad Multispot		
MedMira Reveal		
Followup of > 1 month	8 negative Western Blot 8 negative viral load	


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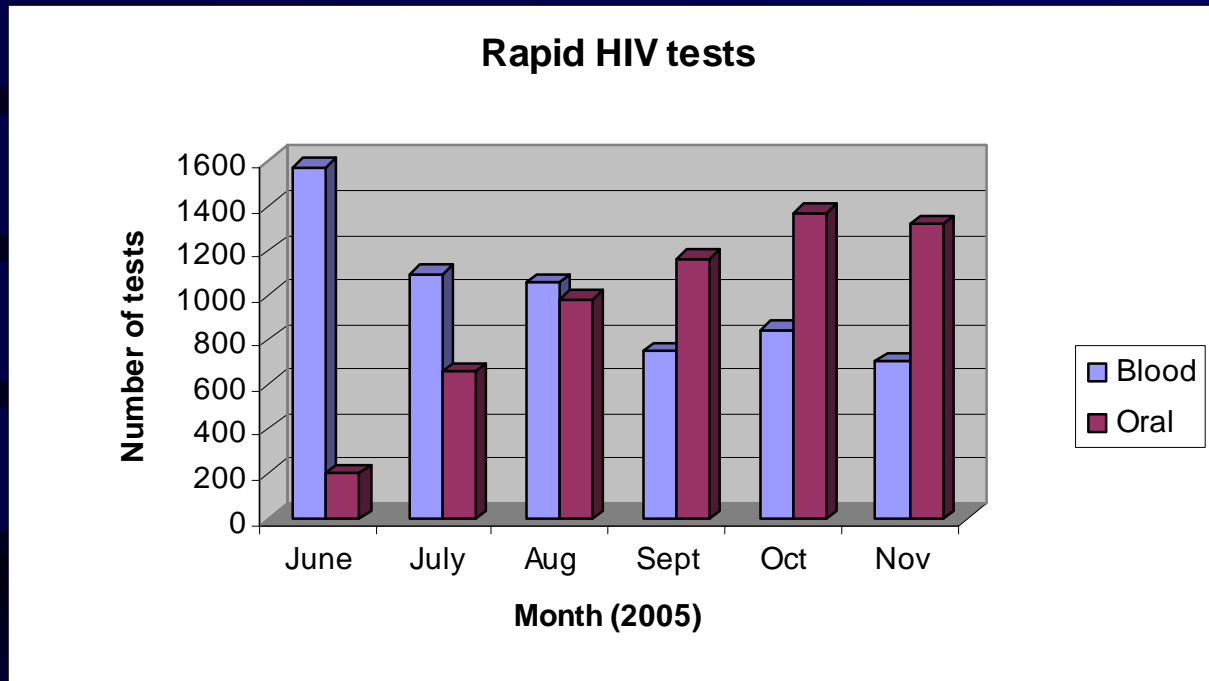
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Trinity Uni-Gold	8 negative	355 positive
BioRad Multispot	7 negative 1 positive	354 positive 1 QNS
MedMira Reveal	8 negative	340 positive 15 sample interference
Followup of > 1 month	8 negative Western Blot 8 negative viral load	

2005 - Shift in testing from Fingerstick to OMT



Rapid HIV Testing Statewide at Publicly Funded Counseling and Testing Sites: A Successful Statewide Initiative in New Jersey

Sindy M. Paul, M.D., M.P.H. *, Evan Cadoff, M.D. **, Eugene Martin, Ph.D. **, Maureen Wolski*, Lorheta Nichol*, Rhonda Williams*, Phil Bruccoleri*, Aye Maung Maung*, Rose Marie Martin, M.P.H. *, Linda Berezny RN*, Charles Taylor*

New Jersey Department of Health and Human Services * and UMDNJ – Robert Wood Johnson Medical School

2006 Confirmatory test results

	29 Presumed Western Blot negatives	
OraSure OraQuick	16 positive 13 negative	Orasure Oraquick OMT sampling introduced?
Trinity Uni-Gold	27 negative 2 positive	
BioRad Multispot	27 negative 2 positive	
MedMira Reveal	14 negative 1 Positive 14 sample interference	
Follow-up	2 specimens presumed to be negative were not WBlot NEGATIVE	<i>- 1 evolving band pattern of an HIV positive, the other a true positive that had been accidentally stored in the discordant repository</i>

A second rapid HIV test
can confirm a positive Oraquick result
as reliably as a Western Blot.

Western blot Limitations

- 7.1% of positives could not be confirmed because specimens were not collected
- 25.8% did not return for results of confirmatory Western Blot
- ONLY 70.1% of confirmed positives got their confirmed result!!

- Western Blot confirmation has an **effective** sensitivity as low as 70.1%

Using OraQuick with Uni-Gold confirmation:

- Matched OraQuick with Western Blot confirmation in 100% of 15,923 clients studied
- Every false positive was identified by a rapid confirmation algorithm between 2004-2006
- Consequences:
 - Rapid confirmation may virtually eliminate the non-returns
 - **Effective** sensitivity may approach 99-100%
 - Counseling, contact elicitation and referral for treatment can be done immediately
 - In NJ, at least 200 HIV + individuals will definitively know their status

Next steps

Prospective evaluation of a rapid testing algorithm

- What will be the real world performance of a rapid test in a confirmatory setting
 - Does reducing the delay really improve the linkage to care
 - Does post-testing counseling impact positively on prevention messages

TAKE HOME MESSAGE:

- Client anxiety about the outcome of a rapid test matters greatly.
- Delay in reporting final results discourages anxious clients from being tested.
- Rapid HIV technology appears able to provide rapid turnaround with equivalent reliability and sensitivity as traditional HIV testing.

Thanks To:

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- Evan Cadoff, MD*
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- Vivian Shih, BS
- Jake Nelson
- Lisa May

All the site coordinators
and counselors



NJDHSS/DHAS

- Sindy Paul, MD, MPH*
- Linda Berezny, RN
- Rose Marie Martin, MPH
- Maureen Wolski, BS
- Aye Maung Maung

NJDHSS/PHEL

- Kenneth Earley
- Kanjana Garcia

END OF TALK



HIV Testing Over 25 Years

- 1980's - HIV a mystery uncertain and unsure

Raska, Jr., K, Kim, HC, Raska, III, K, Martin, E, Raskova, J and Saidi, P. Human Immunodeficiency Virus (HIV) Infection in Haemophiliacs: Long Term Prognostic Significance of the HIV Serologic Pattern. *Clin. exp. immunol.* 77: 1-6, 1989.

- Immediate public health goal - protect the blood supply

- Antibody detection

The first assays:

- Relative insensitive and relatively non-specific
- The FDA mandated that confirmatory testing of every result must occur before a result was declared final

- 1990's - understanding the dimensions of infection, the temporal course of infection

- P24 Antigen detection

- Polymerase Chain Reaction/NAT

HIV Screening

- Choice of the test should be driven by risk assessment:
 - To know one's status in a public health setting - HIV Antibody
 - High risk exposure - PCR (NAT)

What is a rapid HIV test?



Oraquick Rapid HIV1/2

- Performed and interpreted at the site of care/counseling
- Varying formats:
 - Venipuncture Blood
 - Fingertick
 - Oral
 - Plasma
- Varying complexity
 - CLIA-waived → Moderate complexity
- 20 mins or less to a result

BBI Seroconversion Panel Results:

Member #	Days since first bleed	EIA	Western blot	Viral load	Rapid test
PRB959-01	0	0.1	No bands	2×10^5	N
PRB959-02	7	0.1	No bands	$>8 \times 10^5$	N
PRB959-03	9	0.2	No bands	$>8 \times 10^5$	N
PRB959-04	14	1.8	p24, gp160	8×10^5	P
PRB959-05	19	7.3	p24, gp160	5×10^5	P
PRB959-06	21	7.6	p24, gp160	3×10^5	P
PRB959-07	26	7.8	p24, gp160	$>8 \times 10^5$	P

Rapid confirmation trial

- **Repeat OraQuick** (CLIA waived for whole blood or oral fluid)
 - All samples reproduced
 - Not approved for serum testing, or stored samples
- **UniGold** (CLIA waived for whole blood, CLIA moderate for serum)
 - All samples matched Western Blot
 - Study used serum, clinics would perform whole blood testing
- **Multispot** (CLIA moderate for serum/plasma)
 - 1 false positive
- **Reveal** (CLIA moderate for serum/plasma)
 - No false positives, or false negatives
 - Several unreadable samples

Rapid HIV Testing in New Jersey

- The rapid HIV program in NJ is one of the largest, centralized rapid HIV testing programs in the country
- Current locations (117) (2/2006):
 - County health departments
 - Sexually transmitted disease clinics,
 - Family planning programs,
 - Federally qualified healthcare centers,
 - TB clinics,
 - Hospital-based programs - 13 ERs (8 counties)
 - Prenatal clinics, and
 - Outreach through mobile vans.

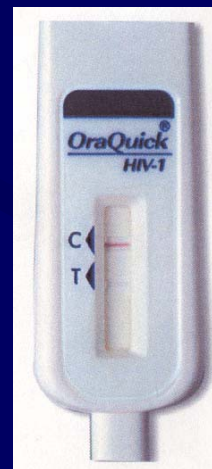
What is a rapid HIV test?



20 MINUTES



Preliminary
Positive



Negative