In the Footsteps of the WHO – Rapid HIV Testing in America

Eugene Martin, Ph.D. *, Gratian Salaru, M.D. ', Sindy M. Paul, M.D., M.P.H.**, Evan Cadoff, M.D.*
* – UMDNJ - Robert Wood Johnson Medical School, New Brunswick, New Jersey
** – New Jersey Department of Health and Senior Services, Trenton, New Jersey

ABSTRACT:

Background: In the United States, only 4 rapid HIV tests have received FDA approval. In excess of 60 rapid HIV tests are now in use worldwide. In some resource-poor countries, confirmatory testing by alternative rapid assays is also in widespread use. In the United States, rapid HIV testing allows preliminary positive results to be recognized in minutes, but still requires traditional confirmation by complex, time-consuming methodologies. In some cases, the reported sensitivity and specificity of rapid tests equals or exceeds that of conventional enzyme immunoassays (EIA) as well as the confirmatory Western blot and/or IFA tests they were intended to confirm. This results in large numbers of negative or indeterminate confirmatory tests that require significant efforts to clarify.

In densely populated states such as New Jersey, efforts to control the spread of HIV relies upon rapid HIV testing in a multitude of venues including outreach centers, satellite facilities, hospital ERs, methadone clinics, perinatal clinics, and increasingly, mobile units. Unfortunately, as many as 30% of preliminary positive HIV clients fail to receive final results because of their unwillingness to return for a second visit and the goal of HIV awareness remains hostage to an aging confirmatory methodology.

Objectives: An alternative method of confirming a rapid HIV test with a second, alternate rapid HIV test has been utilized retrospectively to assess the feasibility of confirming a rapid HIV result with a secondary rapid HIV test.

Methods: Utilizing residual serum samples available in the New Jersey Public Health Laboratory repository between 2004-5 or collected at the time of discordant analysis by staff of NJHIV (2005-6), rapid HIV tests were performed using 4 rapid tests approved for use in the United States including: Oraquick Advanced HIV-1/2 (Orasure, Bethlehem, PA), Multispot HIV-1/HIV-2 Rapid Test (Bio-Rad Laboratories, Redmond, WA 98052), MedMira Reveal Rapid HIV-1 Antibody Test (MedMira Laboratories, Inc, Halifax, Nova Scotia, Canada B3S 1B3) and Uni-Gold (Trinity Biotech plc, Wicklow, Ireland).

Analysis included: Reproducibility of initial finding, concordance with Western blot result and ability to detect an initial false positive result.

Results: Trinity Unigold identified 35/35 discordant specimens, Biorad identified 34/35 discordant specimens and MedMira Reveal identified 22/35 specimens (13 specimens demonstrated sample interference preventing interpretation). Of 355 Western blot confirmed rapid HIV specimens collected between July 1, 2004 and April 19, 2005, 100% concordance was obtained using all three available alternative rapid assays on all specimens tested.

Conclusions: Rapid HIV testing has become a major means of increasing awareness of HIV serostatus in the United States. In 2004, use of a confirming rapid test algorithm in New Jersey would allow an additional 91 HIV positive individuals to learn their definitive status and would assure a better linkage to health care for affected individuals.

THE ISSUES:

Concerns about the significance of false-positive results in low-prevalence populations led the US Public Health Service to require a sequential, two-test algorithm (EIA followed by a Western Blot) to confirm initially reactive rapid HIV results.

Confirmation of preliminary positives by Western Blot is time-consuming, complex and labor intensive. Clients often wait 48-96 hours before receiving a confirmed result, experience enormous anxiety and many fail to return for follow-up.

Among HIV EIA screen positive blood donors 4.8% have false positive Western Blots.

Prior to rapid testing approximately 35% of all patients visiting NJ Counseling and Testing Sites (CTS) for HIV testing failed to receive their results, because they failed to return for a follow-up visit. Currently, more than 97 % of tested clients receive negative results at their initial visit, but 25% of clients who need to return for HIV confirmation *still fail* to return and may not be referred for treatment..

PROPOSED SOLUTION:
CONFIRM A RAPID HIV RESULT WITH A SECONDARY RAPID HIV TEST AT THE TIME OF THE INITIAL SCREENING

THE ISSUES:

Will it detect False Positives as successfully as the Western Blot?

Will it confirm True Positives as effectively as the Western Blot?

Discordant : "Preliminary Positive Rapid HIV" - EIA and/or Western Blot negative or indeterminate

What causes discordants?

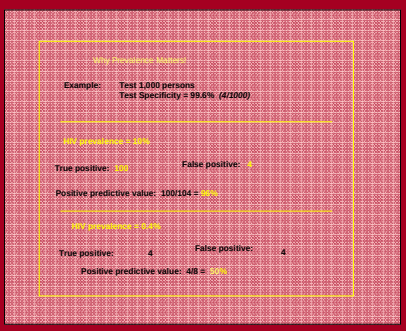
- An evolving infection – HIV screen is positive prior to traditional EIA or Western Blot
- Cross-reacting non-specific antibodies
- Over-reading by testing personnel

HIGHLIGHTS:

- Original OraQuick® results were reproducible in 7 of 8 available serum discordant specimens from 2004 and in 16 of 29 serum specimens collected for discordant analysis between 2005-6. Issue: Oral Oraquick vs. Fingerstick Oraquick?
- One rapid tests (Trinity Uni-Gold ®) successfully identified all 35 Western blot negative specimens as non-reactive and all 355 Western blot positive specimens as reactive.
- The Biorad Multispot® assay correctly identified 34/35 samples as negative with one specimen demonstrating operator-dependent results.
- MedMira Reveal ® assay successfully identified 22/35 discordant specimens properly but experienced significant sample interference using uncentrifuged frozen specimens in the remaining assays.

CONCLUSION:

- A rapid, alternative confirmatory algorithm has been used to retrospectively confirm Oraquick® HIV positive findings in New Jersey over a three year period.
- A ***waived algorithm*** based upon initial Oraquick® HIV screening and confirmatory testing by Trinity Unigold™ Recombigen confirmed all Western Blot positive specimens while excluding all false positives identified by the initial Oraquick® screen.
- A rapid testing strategy that provides a complete answer in a single visit would allow Counseling and Testing personnel to more effectively guide HIV + patients into treatment, while avoiding the nearly 25% of HIV + clients who are lost to follow-up.



TAKE HOME MESSAGES:

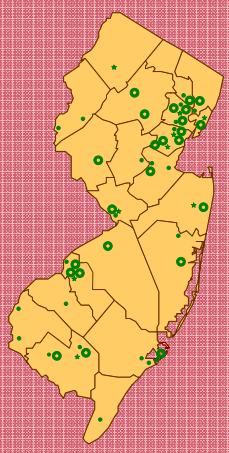
• A retrospective rapid test algorithm performed successfully at a prevalence rate of ~2%.

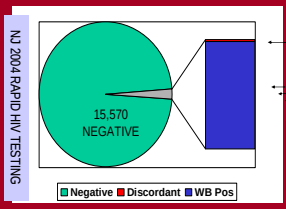
• *Concern about the impact of the US HIV prevalence rate on the Positive Predictive Value of a rapid HIV test is actually less important in some US urban centers where prevalence is relatively high among the tested population than the unwillingness of clients to return to hear the final word on whether they're HIV positive.*

• *The retrospective performance of an HIV rapid test algorithm suggests that*
  - *A rapid test algorithm would work very well in NJ*
  - *HIV Positive clients will be entered into care sooner*
  - *More HIV Positive clients will know their status with less anxiety and at least equal reliability as clients tested by traditional confirmatory methods.*

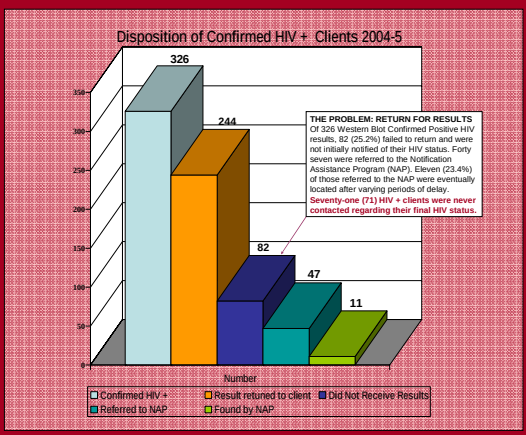
UMDNJ-RWJMS/ NJ DHSS
AIDS PREVENTION GRANTEES
Primary Satellite fixed mobile
Pale colors indicate pending sites

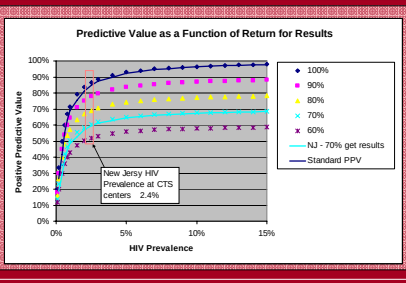
AIDS Coalition of Southern New Jersey
Atlantic City Health Department
Bergen County Health Department
Burlington County Health Department
Camden AHEC
Camden County Health Department
Check-Mate
East Orange Health Department
Eric B. Chandler Health Center
FamCare
Henry J. Austin Health Center
Hope House
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





TOTAL TESTS 7/1/04 – 4/19/05	HIV PRELIM POSITIVE	WESTERN BLOT – Discordants
15,923	363 (2.3 %)	10 (3.4% of Prelim Pos. – 0.07% Overall)



THE PROBLEM: RETURN FOR RESULTS
Of 326 Western Blot Confirmed Positive HIV results, 82 (25.2%) failed to return and were not initially notified of their HIV status. Forty seven were referred to the Notification Assistance Program (NAP). Eleven (23.4%) of those referred to the NAP were eventually located after varying periods of delay.
Seventy-one (71) HIV + clients were never contacted regarding their final HIV status.

	2004 8 Western Blot negative/IND	2005-6 29 PRESUMED Western Blot negative/IND	2004 355 Western Blot POSITIVE (True Positive OraQuick)
OraSure OraQuick	7 positive 1 negative	16 positive 13 negative	355 positive
Trinity Uni-Gold	8 negative	27 negative 2 Prelim Pos.	355 positive
BioRad Multispot	7 negative 1 positive	27 negative 2 Prelim Pos.	354 positive 1 QNS
MedMira Reveal	8 negative	14 negative 1 Prelim Pos. 14 sample interference	340 positive 0 negative 15 sample interference
FINAL	6/6 negative Western Blot 6/6 negative viral load	1 Positive/+ Viral Load 1 WBlot Indeterm/ + Viral Load