AT THE LABORATORY INTERFACE: HIV DISCORDANT FOLLOW-UP

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ABSTRACT

Issue: In 2004, the CDC recommended follow-up antibody testing one month after obtaining preliminary positive rapid HIV tests that do not confirm (i.e., discordant results). In New Jersey, this follow-up includes both antibody and nucleic acid testing (NAT). Patients testing negative at the one month follow-up are deemed to have a 'true' false positive rapid test result. Considerable anxiety is associated with the time lag to resolution and may contribute to the failure of patients to return after one month.

Project: To allow more efficient handling of statewide discordant results, re-designed protocols were introduced at NJ HIV counseling and testing sites focusing on reducing the impediments to discordant resolution. At some sites, serum and plasma are collected together to allow Western blot and/or discordant resolution by NAT. If the Western blot establishes a discordant result, the frozen plasma is immediately sent for NAT testing. The goal is to complete testing before a client returns for confirmatory results. At other sites, plasma sample collection occurs when the client learns of a discordant Western blot result. Both protocols reduce the emotional waiting period, reduce resources used for outreach, and provide faster final disposition to clients. Because NAT is only performed when a discordant result has been documented, testing expenses are not increased.

Results: Despite efforts to encourage clients to return for follow-up, only about half of clients with discordant results historically return for follow-up testing. With protocols designed to reduce inconvenience and turn-around-time, the median time from obtaining a preliminary positive to resolution of a discordant result has been reduced by more than 60% (43 days to 27 days). The number of clients being referred to outreach workers has fallen by nearly 20%.

Lessons Learned: Efforts to resolve discordant results continue to be frustrated by clients who are lost to follow-up. Revised protocols allow for more effective and timely resolution of discordant results and insure that affected clients are more rapidly moved into care. **Issue**: In 2004, the CDC recommended follow-up antibody testing one month after obtaining preliminary positive rapid HIV tests that do not confirm (i.e., discordant results). In New Jersey, this follow-up includes both antibody and nucleic acid testing (NAT). Patients testing negative at the one month follow-up are deemed to have a 'true' false positive rapid test result. Considerable anxiety is associated with the time lag to resolution and may contribute to the failure of patients to return after one month.

BACKGROUND – HIV DISCORDANTS

DEFINITION: **A reactive rapid HIV test followed by a negative or indeterminate Western blot (WB) or immunofluorescent assay (IFA) result.**

TYPE I:

Positive Rapid HIV test, NEGATIVE Western Blot

No bands present

Client is likely to be HIV negative and not to be in an HIV window.

TYPE II

Positive Rapid HIV test, INDETERMINATE Western Blot

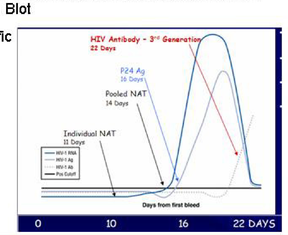
Further evaluation is needed even to assess likelihoods

What Causes Discordants?

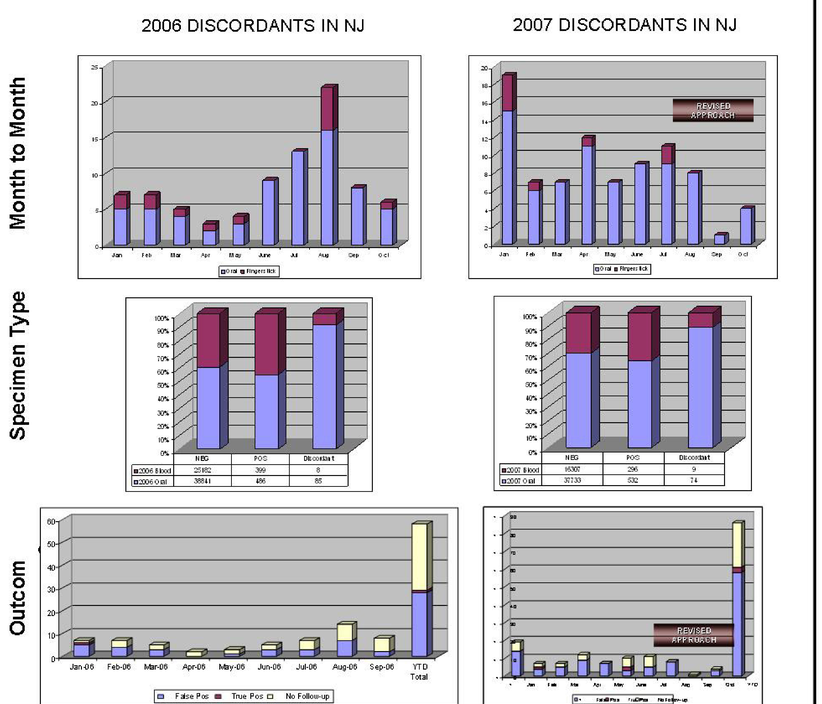
- An evolving infection – HIV screen can turn positive sooner than traditional EIA or Western Blot
- Cross-reacting non-specific antibodies
- Over-reading by testing personnel

LIMITATIONS OF RAPID HIV TESTING:

Antibody Detection is not Viral Detection and it lags exposure to the virus

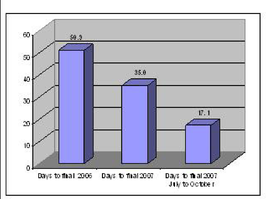


DISCORDANT FREQUENCY

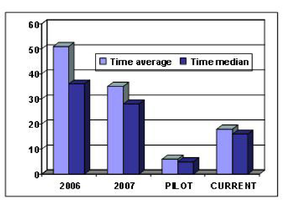


DISCORDANT FOLLOW-UP

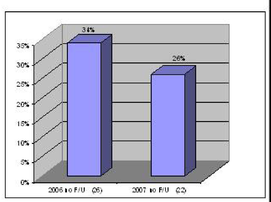
Days to Resolve a Discordant Result



Approaches to Discordant Resolution



Lost to Follow-up



In 2006, **thirty-four percent** of clients experiencing a discordant result were lost to follow-up. In 2007, in association with the dramatic reduction in time to resolution, an 8% reduction in the number of clients being lost to follow-up occurred in the July → October timeframe.

APPROACHES TO DISCORDANT RESOLUTION

INITIAL APPROACH [2004→ May 2007]

After an initial positive rapid HIV result:

- A PRELIMINARY POS form is returned via fax to NJ HIV
- NJHIV staff contact counselor
- After receipt of WBs results: FORM indicating DISCORDANT STATUS is faxed in

Site coordinator contacted to coordinate collection of follow-up specimens.

Professional staff are available to counsel counselor and/or patients.

Follow-up visit scheduled ~4 WEEKS:

Venipuncture - collect SST, white top, & purple top tubes.

- Centrifuge and prepare specimen
- Ship to reference laboratory
  - Repeat HIV1/2 EIA
  - HIV1 Western blot
  - Ultrasenstive Quantitative RNA PCR
  - Qualitative HIV PCR

PILOTED APPROACH – [4 sites; May-June 2007]

At the time serum is obtained to perform a Western blot assay

COLLECT:

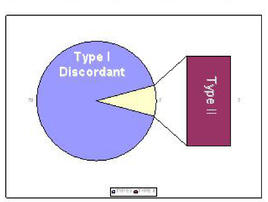
- Additional Pearl White-Top *Plasma* Preparation Tube (PPT)
- Spin (*on-site*) and store *inverted* in a freezer at <-10 ºC to separate plasma from cells.
- **If the serum specimen fails to confirm**, the frozen white top tube is collected by staff from NJ HIV and sent frozen overnight to ARUP laboratories (Salt Lake City, Utah) for:
- HIV Ultra Sensitive Quantitative (0055601)
  - PCR using the FDA approved Roche AMPLICOR HIV-1 MONITOR® Test, version 1.5.
  - Analytic measurement range of this assay is 1.7-5.0 log copies (50 to 100,000 copies/mL).
- HIV1/2 WB w/ reflex to WBlot (0051160)

CURRENT APPROACH [July 2007 →]

- NJHIV personnel are notified of the date a discordant result will be shared with client. Personnel are present at draw.
- Pearl White-Top *Plasma* Preparation Tube (PPT) collected
- Transported to NJHIV laboratory
  - Spun, ***inverted*** and frozen in freezer at <-10 ºC to separate plasma from cells.
- Sent frozen overnight to ARUP laboratories (Salt Lake City, Utah) for testing as piloted in May-June, 2007.
- See DISCORDANT FOLLOW-UP

2007 DISCORDANT DESCRIPTION

DISC	TOTAL TESTED	T<C	EIA POS	WB INDETER	TRUE POS	FALSE POS	LOST TO FOLLOW-UP
85	38,265	79	3	7	2	59	26
	THROUGH OCTOBER, 2007	93%	3.53%	8.24%	2.35%	69%	31%



In 2007, 91.76% of all New Jersey discordant results were Type I Discordants i.e. (EIA negative, WB – no bands)

DISCUSSION

Discordant results create difficulties for CTS programs. Devising an effective strategy to permit resolution of these testing anomalies needs to be based on both practical and theoretical considerations.

Rapid HIV discordants have been broadly characterized as either Type I (Western Blot negative) or Type II (Western Blot indeterminate). In New Jersey, the vast majority (91%) are Type I discordants. In 2007, during rapid HIV testing, 93% of discordant specimens were described as having a T line that was weaker than the C line. Of 85 discordants observed in 2007 YTD, only 3 discordant results were associated with a reactive EIA result (3.53%). None of the Type I discordants was associated with a positive EIA – initial reactive, followed by a duplicate repeat in which one or more specimens was reactive.

From a programmatic vantage point, the inability to follow-up on 31% of clients with a discordant result, represents an enormous challenge. When a client fails to return for additional testing, it is possible that an HIV infected client will:

- Not be initially linked to care
- Continue to place others at risk of infection during a time when they are most at risk of transmitting the virus.

The current data suggests that scheduling return client visits 4 weeks after obtaining a discordant result results in a failure to conclude a discordant investigation in more than 1/3 of the investigations! To improve this situation we attempted to collect and process follow-up specimen at the time specimens were to be drawn for confirmatory testing.

RESULT: some CBO sites had major difficulties collecting and preparing specimens for shipment. --- **PILOTED APPROACH**

This led to the **CURRENT APPROACH.**

- Obtain the follow-up specimen during a second meeting held to tell the client of his confirmatory results.
- This approach allows NJHIV to assist with the proper preparation of specimens and follow-up on discordant results in an expeditious and to allow the program to perform nucleic amplification testing if necessary accurate characterization of discordant results can be assured with only a minimal risk that the technology will fail to detect an evolving infection.

CONCLUSIONS

1. The vast majority of discordant results (>90%) in New Jersey are associated with EIA non-reactivity and negative Western blots
2. Follow-up of clients with discordant results is important. Between 2-3% will seroconvert and become HIV positive. Clients with positive results needed to be linked to care and need to be counseled regarding the risk of HIV transmission
3. Loss of clients to follow-up is a major problem. In 2006 – 34%. In 2007 – 31%.
4. In mid-2007, revised protocols were develop to focused on reducing the time to resolve a discordant result and collecting specimens earlier in the resolution process
5. This led to:
   - Decrease in the time to resolve a discordant result - 50.9 to 17 days
   - Decrease in number of clients lost to follow-up: 8% in the first 4 mos.

NJ RAPID HIV SUPPORT PROGRAM

The NJ Rapid HIV Program is a large, centralized QA program. NJ HIV technical support consists of physicians, scientists nurses and medical technologists who specialize in supporting the entire state-wide rapid HIV testing staff.

The NJ Rapid HIV Program was the 2006 winner of the ASTHO Vision Award.