

Use of Quantitative Results from HIV Antibody EIAs to Identify Persons in Early Post-Seroconversion Periods

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Abstract

Background: Current HIV-1 antibody tests typically become positive within 2–3 weeks after the onset of acute HIV symptoms. Identifying persons who are within the first 30 to 60 days following seroconversion is potentially useful for treatment, pathogenesis, and epidemiologic studies, as well as clinical decision making and HIV prevention.

Methods: We assembled longitudinal specimen panels from 148 persons in the Acute Infection and Early Disease Research Program (AIEDRP) cohort identified prior to HIV antibody seroconversion with at least two pre-treatment specimens available. A total of 396 pre-treatment specimens were tested using two standard FDA approved EIA HIV-1 antibody tests, the Vironostika HIV-1 (Organon Teknika, OTV) and the Genetics Systems rLAV (Bio-Rad). Signal to cut-off (SCO) ratios ≥ 1.0 are considered positive. We also tested a less-sensitive version of the OTV in which plasma dilution is increased and incubation time decreased; results are in standardized optical density (SOD) units. All specimens were ≤ 180 days of seroconversion. 95% CI were calculated using GEE which adjusted for multiple observations, or the binomial equation if the specificity was 100%.

Results: Sensitivity and specificity (95% CI) for diagnosis of HIV infection of <30 or 60 days duration from seroconversion employing different cut-offs were compared, and key results are summarized below.

Test, cut-off	Sens <30 days	Spec <30 days	Sens <60 days	Spec <60 days
OTV, SCO ≤ 4	57% (47%, 67%)	100% (96%, 100%)	38% (33%, 45%)	100% (94%, 100%)
rLAV, SCO ≤ 4	34% (26%, 43%)	98% (95%, 99%)	24% (18%, 31%)	98% (94%, 99%)
LS-EIA, SOD ≤ 0.2	84% (75%, 90%)	73% (64%, 80%)	68% (59%, 75%)	82% (72%, 89%)
LS-EIA, SOD ≤ 0.5	91% (82%, 95%)	45% (36%, 54%)	84% (76%, 89%)	57% (45%, 68%)

Conclusions: SCO results ≤ 4 on either of two commonly used EIA antibody tests was highly specific for HIV seroconversion of <30 days and can be used to diagnose early HIV-1 infection, at least in sub-type B infections. Sensitivity for detecting early seroconversion is only moderate, especially for the rLAV, due to rapid development of antibody levels above the assay dynamic range. A LS-EIA <0.5 SOD has good sensitivity for detecting seroconversion of <30 days, while a LS-EIA <0.2 had higher specificity with only a modest decrease in sensitivity.

Background

Current HIV-1 antibody tests have been optimized to detect HIV antibody seroconversion early in infection. Tests in current use typically become positive within 2–3 weeks after the onset of acute HIV symptoms. Identifying persons who are within the first one to two months following seroconversion is potentially useful for treatment, pathogenesis, and epidemiologic studies, as well as clinical

decision making and HIV prevention. We aimed to test whether information from standard EIA antibody tests for HIV-1 infection, as well as a less sensitive (or detuned) EIA antibody test could be used to identify persons in this early post-seroconversion period.

Methods

Subjects

We assembled longitudinal specimen panels from the Acute Infection and Early Disease Research Program (AIEDRP) cohort. To be eligible for inclusion, subjects had to be:

- Identified prior to HIV antibody seroconversion, based on either an indeterminate HIV-1 antibody test, or a negative HIV-1 antibody test with an HIV-1 RNA level $>5,000$ copies/ml.
- Have at least two pre-treatment plasma specimens available within 180 days of seroconversion.

Measures

Specimens were tested with the following assays:

- The Vironostika HIV-1 (Organon Teknika, OTV)
- Genetics Systems rLAV (Bio-Rad).
- Signal to cut-off (SCO) ratios ≥ 1.0 are considered positive on the Vironostika and rLAV EIA antibody tests.
- We also tested a less-sensitive (LS) version of the OTV in which plasma dilution is increased and incubation time decreased; results are in standardized optical density (SOD) units. The median time from seroconversion on a standard antibody test to an SOD >1.0 on the LS-EIA is approximately 180 days.

Analysis

- We estimated the seroconversion date in persons with indeterminate antibody test results as the indeterminate test date, plus the median mid-point date between an indeterminate antibody test and the first positive antibody test (7 days).
- In persons with a negative antibody test followed by a positive test, we took the mid-point between these two tests if the interval between tests was ≤ 28 days. If the interval was >28 days, we added 14 days from the date of the negative antibody test with HIV-1 RNA $>5,000$ as the seroconversion date.
- We calculated 95% CI for sensitivity and specificity using GEE, which adjusted for multiple observations, or the binomial equation if the specificity was 100%.

Results

A total of 351 pre-treatment specimens were identified from 139 persons. The initial median HIV-1 RNA \log_{10} was 5.4 copies/ml, and the median CD4+ T-cell count was 529 cells/ μ l. Participants were 91% male, with MSM sexual exposure as the predominant route of transmission.

Table 1: Sensitivity and Specificity

Test, cut-off	Sens <30 days	Spec <30 days	Sens <60 days	Spec <60 days
OTV, SCO ≤ 4	39% (30%, 48%)	100% (98%, 100%)	25% (18%, 33%)	100% (96%, 100%)
rLAV, SCO ≤ 4	22% (15%, 30%)	98% (95%, 99%)	24% (18%, 31%)	98% (94%, 99%)
LS-EIA, SOD ≤ 0.2	80% (71%, 87%)	76% (67%, 84%)	63% (54%, 71%)	84% (75%, 90%)
LS-EIA, SOD ≤ 0.5	90% (82%, 95%)	48% (38%, 58%)	83% (75%, 89%)	63% (50%, 74%)

Figure 1: rLAV EIA Antibody Optical Density (Signal to Cut-Off Ratio) by Days from Seroconversion

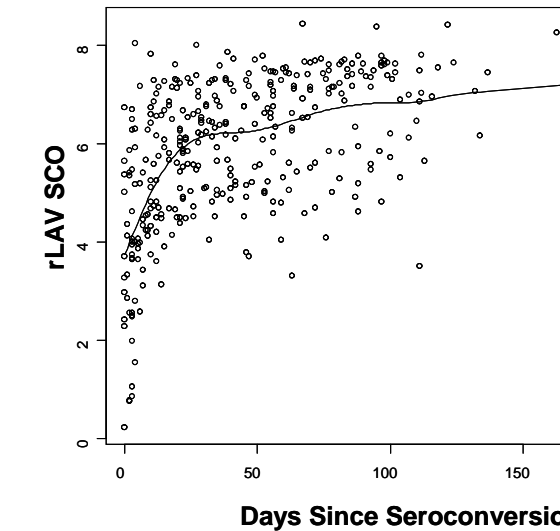
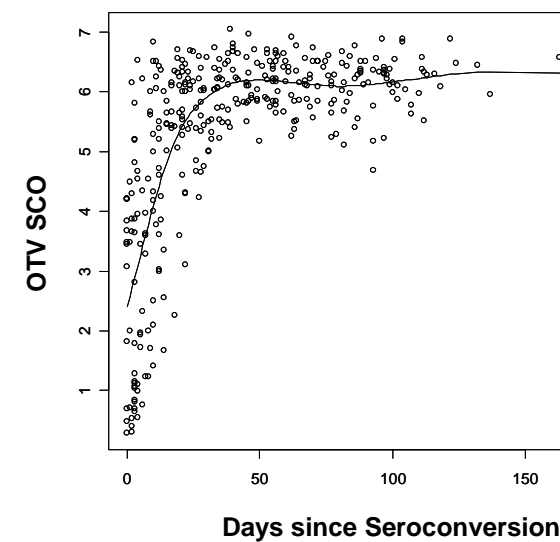


Figure 2: OTV EIA Antibody Optical Density (Signal to Cut-Off Ratio) by Days from Seroconversion



Conclusions

- SCO results ≤ 4 on either of two commonly used EIA antibody tests was highly specific for HIV seroconversion of <30 days and can be used to diagnose early HIV-1 infection, at least in sub-type B infections.
- Sensitivity for detecting early seroconversion using an SCO ≤ 4 on a standard EIA is only moderate, especially for the rLAV, due to rapid development of antibody levels above the assay dynamic range.
- A LS-EIA <0.5 SOD has good sensitivity for detecting seroconversion of <30 days, while a LS-EIA <0.2 had higher specificity with only a modest decrease in sensitivity.

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