Acute HIV infection: Improved algorithms for HIV testing.

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Acute HIV Infection: Improved algorithms for HIV testing


Keywords: Acute HIV Infection, HIV testing, Western Blot, HIV-RNA

Identification of Acute HIV Infection (AHI) has direct implications for the safety of blood products, HIV prevention, due to patient high infectiousness and HIV treatment. Antiretroviral therapy at this stage allows for potential immunological and viral advantages and latent reservoirs reduction [1]. Recently published CDC recommendations for HIV testing suggest that 4th generation (4thG) immunoassays (IAs) for the combined detection of HIV p24-antigen and HIV-antibody should become the standard of care for HIV testing because they are more sensitive than 3rd generation assays [2,3]. The same guidelines suggest that confirmation of HIV screening reactivity should be assessed by the detection of viral genome (HIV-RNA) instead with Western Blot (WB) due to the significant less sensitivity of WB in the early stages of HIV infection. In contrast to other 4thG IAs, a recently CE approved HIV assay, the LIAISON-XL Murex HIV Ab/Ag (DiaSorin, Saluggia, Italy) offers the advantage of a signal discrimination between HIV-p24 and HIV-antibody reactivity.

In the year 2013, at the laboratory of Microbiology and Virology, Infectious Diseases Department, University of Torino, Italy, 15,412 HIV tests were routinely performed (HIV infection rate: 1.8%), with the following procedure: HIV screening with 4thG ARCHITECT HIV Ag/Ab Combo (Abbott Diagnostics, Rome, I), re-testing reactive samples with LIAISON-XL, confirmation of screening results with WB (HIV-1, BIO-RAD, Milan, I) and/or HIV-RNA (CAP/CTM HIV-1, v2.0, Roche Molecular Diagnostic, Branchburg, NJ, USA). ARCHITECT and LIAISON-XL analytical sensitivity according to WHO p24 (NIBSC 90/636) and French National Reference (SFTS 2007) HIV standards is 17.8 and 22 pg/ml, respectively (1.032 and 0.873 IU/ml) [4]. Following latest CDC recommendations, we reviewed AHI identified in the year 2013 (15 patients, corresponding to 5.4% of new HIV infections) defined by a positive HIV-RNA and a non-reactive/indeterminate WB [1].
The two 4thG IAs correctly identified AHI infection in all patients (average age: 40 years ± 11; CD4+ cell count: 477 ± 209/uL; HIV-RNA median level: 942,295, range 95,295 - >10 million copies/mL). By LIAISON-XL HIV-antibodies and p24 were positive in 10/15 and 11/15 AHI, respectively (sensitivity: 67 and 73%). Fiebig stage II and III [5] were identified in 5/5 and 3/3 patients (HIV-RNA > 500,000 and > 300,000 copies/mL, respectively). WB was negative in Fiebig stage II and III patients (n=8) and indeterminate in Fiebig stage IV (7 patients) (Table 1). p24 correlation with HIV-RNA was good (r=0.822, p=0.0002, 95% CI 0.535-0.939).

In conclusion, 4thG IAs are very sensitive for the detection of AHI and they enhance the early detection of HIV infection during the acute phase, when substantial HIV transmission occurs, thus representing an important advance in HIV testing to address HIV public health burden. Confirmation of their results should not include WB, but the detection of HIV-RNA due to the lack of WB sensitivity in the early stages of HIV infection. Recently commercialized 4thG IAs allowing signal discrimination between reactivity due to p24 and HIV antibody offer the advantage of a better classification of AHI. This is certainly an added value in situations where HIV-RNA testing is not available.

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References


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### Table 1

Characteristics of the 15 patients with AHI.

<table>
<thead>
<tr>
<th>ID</th>
<th>Age years</th>
<th>Sex</th>
<th>Risk Factor</th>
<th>CD4/ul</th>
<th>ARCHITECT Ag/Ab Combo S/CO ratio</th>
<th>LIAISON-XL HIV-p24 Antibody S/CO ratio</th>
<th>LIAISON-XL Antibody S/CO ratio</th>
<th>HIV-RNA copies/mL</th>
<th>Fiebig stages</th>
<th>HIV GENOTYPE</th>
<th>WB</th>
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<td>1</td>
<td>37</td>
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<td>25</td>
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</tbody>
</table>

ARCHITECT and LIAISON-XL non reactive samples for S/CO (Cut-off) ratio ≤ 1.
IND: Indeterminate WB pattern according to CDC interpretative criteria.
Na: Not available.