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Acute HIV Infection: Improved algorithms for HIV testing

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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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Competing interests

None declared.

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Table 1

Characteristics of the 15 patients with AHI.

ID	Age *years*	Sex	Risk Factor	CD4/ul	ARCHITECT Ag/Ab Combo S/CO ratio	LIAISON-XL HIV-p24 S/CO ratio	LIAISON-XL Antibody S/CO ratio	HIV-RNA *copies/mL*	Fiebig stages	HIV GENOTYPE	WB
1	37	M	MSM	222	1.74	2.6	160	586,295	III	B	Negative
2	31	M	MSM	502	1.62	Negative	25	336,000	III	B	Negative
3	31	M	MSM	377	2.12	2	Negative	502,802	II	B	Negative
4	50	M	MSM	561	41	Negative	56	301,154	IV	Na	IND
5	42	M	Etero/bisex	270	28.9	29	Negative	740,881	II	B	Negative
6	38	F	Etero/bisex	749	92	Negative	22	95,295	IV	B	IND
7	40	M	MSM	452	129	168	Negative	>10,000,000	II	B	Negative
8	37	M	MSM	788	35	Negative	43	1,802,927	IV	Na	IND
9	40	M	MSM	447	190	105	39	>10,000,000	III	B	Negative
10	45	M	MSM	566	88	1.25	41	288,769	IV	B	IND
11	49	M	MSM	39	88	5.4	36	3,955,236	IV	CRF02_AG	IND
16	69	M	MSM	705	116	51	Negative	>10,000,000	II	A	Negative
13	25	M	MSM	Na	373	1.85	106	410,000	IV	B	IND
14	48	M	MSM	335	39	16	35	6,019,484	IV	B	IND
15	28	M	MSM	503	1.76	1.27	Negative	1,144,212	II	Na	Negative

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