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Short communication

Sensitivity of 8 CE (European Community)-approved rapid disposable tests for anti-HIV antibody detection during and after seroconversion

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We evaluated the sensitivity for the anti-HIV antibody detection of the 8 rapid disposable tests (RDTs) EC approved in 2008.
Methods: A panel of 100 native serum samples collected from HIV-1 subtype B or non-B, HIV-1 group O or HIV-2-infected patient and 3 commercial seroconversion panels were tested. 50 sera from HIV-negative patients were included to blind reading and RDT specificity.
Results: All native samples HIV-1 subtype B were reactive; an HIV-1 non-B subtype gave false-negative results with 3 of the 8 tests. False-negative results on HIV-1 group O samples were observed with one RDT. All the HIV-2 samples were detected. Seroconversion sample reactivity ranged from 60 to 86.7% according to the tests.
Conclusion: Despite their lower performances relative to ELISA tests during the HIV seroconversion period, RDT may be of interest in case of chronic infection.

Rapid disposable tests (RDTs) for HIV infection are used widely in developing countries in order to promote access to treatment. The use of RDT has recently seen a resurgence in industrialized countries, in order to simplify HIV screening in a larger number and variety of points of care (Everett et al., 2009).

Since 2005, medical devices for *in vitro* diagnosis have had to acquire the European Community label (CE) before being allowed on the European market. European Directive 98/79/EC (Directive 98/79/EC, 27 October 1998) requires manufacturers to meet basic design, manufacture and performance standards before such products can circulate freely throughout the European Community. HIV screening tests must also receive a certificate of conformity from an independent body that verifies that their performance complies with a set of technical specifications (Commission decision of 3 February 2009, 2009/108/EC).

The sensitivity of CE-marked RDTs available in France in 2008 (Table A) was tested by using:

- A panel of native serum samples from 94 patients positive in third-generation EIAs and by Western blot (WB): 46 infected by HIV-1 subtype B, 41 by HIV-1 subtype non-B (24 CRF, 3 A, 1 C, 5 D, 1 F, 3 G, 2 H, 1 J, 1 K), two by HIV-1 group O and five by HIV-2. Six native serum samples with an indeterminate WB profile (4 HIV-1 subtype B and 2 HIV-1 CRF02) were also included. HIV subtypes were characterized by pol protease and reverse transcriptase region sequencing and phylogenetic analysis (maximum likelihood method).
- Three commercial seroconversion plasma panels (HIV 12007, HIV 9032 and HIV 9079; Zeptometrix, Buffalo, USA), corresponding to two negative samples, four early seroconversion samples (undetermined or negative WB) and 11 seroconversion samples (WB-reactive for Env gp160 ± Gag).

Objective interpretation with double reading was ensured by including 50 sera from patients negative in a 4th-generation EIA (Genscreen Plus HIV-1/2 Ag-Ab Bio-Rad, Marnes la Coquette, France). The results are summarized in Table B.

All the HIV-negative samples tested negative, except with the Determine HIV-1/2 kit, which was repeatedly positive on one sample. None of the HIV-1 subtype B sera gave false-negative results. In contrast, one of the three HIV-1 subtype A sera was negative in three of the eight tests (Core HIV 1&2, Immunoflow HIV 1–HIV 2,

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Table A
CE-marked rapid test characteristics.

Name (manufacturer)	Sample	Technology	Antigens
Core HIV 1&2 (Core Diagnostics, Birmingham, United Kingdom)	Serum	Lateral flow	p24 subtype O specific synthetic peptide, gp36, gp41
Determine HIV-1/2 (Unipath, Bedford, United Kingdom)	Serum, plasma, whole blood	Lateral flow	Not available
DoubleCheck II HIV 1&2 (Orgenics, Yavne, Israel)	Serum, plasma	Lateral flow/flow through	p24, gp36, gp41
ImmunoComb II HIV 1&2 BiSpot (Orgenics, Yavne, Israel)	Serum, plasma	EIA solid phase	gp36, gp41, gp120
Immunoflow HIV-1HIV2 (Core Diagnostics, Birmingham, United Kingdom)	Serum	Lateral flow	p24-O fusion peptide, gp36, gp41, gp120
INSTI HIV-1/HIV-2 Antibody Test (Biolytical, Richmond, Canada)	Serum, plasma, whole blood	Flow through	gp36, gp41
Retroscreen HIV (Qualpro Diagnostics, Goa, India)	Serum	Lateral flow	p24-O fusion peptide, gp36, gp41, gp120
Vikia HIV 1/2 (BioMérieux, Marcy l'Etoile, France)	Serum, plasma, whole blood	Lateral flow	gp36, gp41

Table B
Number of discordant results on serum samples.

HIV-positive sera ($n=100$)					HIV-negative sera ($n=50$)	
HIV-1				HIV-2 ($n=5$)		
Group M			Group O ($n=2$)			
Subtype B ($n=46$)	Non-B subtypes ($n=41$)	Samples with indeterminate WB ($n=6$)				
0	1 subtype A Core HIV 1&2 Immunoflow HIV-1/HIV-2 Retroscreen HIV	0	2Core HIV 1&2	0	1	Determine HIV 1/2

Table C
Results for commercial seroconversion plasma panels.

Panel	Sample	Timing	Status	Negative test(s)	Percentage of positive tests
9079	10	13/12/99	Negative	All	0%
9079	11	18/12/99	Early seroconversion	Determine, DoubleCheck, ImmunoComb, INSTI, VIKIA	38%
9079	12	20/12/99	Seroconversion	ImmunoComb, VIKIA	75%
9079	13	26/12/99	Seroconversion	None	100%
9079	14	28/12/99	Seroconversion	Core	83.8%
9079	15	02/01/00	Seroconversion	Core	83.8%
9032	8	30/07/98	Early seroconversion	All	0%
9032	9	04/08/98	Early seroconversion	Determine, DoubleCheck, ImmunoComb, VIKIA	50%
9032	10	11/08/98	Seroconversion	ImmunoComb	83.8%
9032	11	13/08/98	Seroconversion	None	100%
9032	12	24/08/98	Seroconversion	Core	83.8%
9032	13	26/08/98	Seroconversion	None	100%
12007	4	22/10/99	Negative	All	0%
12007	5	24/10/99	Early seroconversion	All	0%
12007	6	29/10/99	Seroconversion	None	100%
12007	7	31/10/99	Seroconversion	None	100%
12007	8	05/11/99	Seroconversion	None	100%

and Retroscreen HIV). This sample was fully reactive by Western blot (New lav blot 1, Bio-Rad, Marnes la Coquette, France). The two HIV-1 group O samples were negative with one of the kits (Core HIV 1&2). All the HIV-2 samples were detected, but there was very strong HIV-1/HIV-2 cross-reactivity with the three kits capable of distinguishing the type of infection.

The six native samples with indeterminate WB profiles were positive in all the tests.

None of the kits detected all the early seroconversion samples, and only five of the eight kits were positive on all the seroconversion samples (Table C).

One test (Core HIV 1&2) was positive during early seroconversion on panels 9032 and 9079 but repeatedly negative on following serial samples. False-positive results for the early samples or an hook-effect on the latter samples are the most likely explanations for these results.

The overall detection rate for both early commercial seroconversion and seroconversion samples ranged from 60% to 86.7% according to the test.

Finally, it should be noted that two tests (Retroscreen HIV and Immunoflow HIV 1–HIV 2), although identical, are marketed under different names and by different distributors, which is a source of confusion when establishing a combinatory algorithm for the end-user.

The use of these tests by healthcare professionals outside of medical facilities has been recommended in order to extend screening cover (Centers for Disease Control and Prevention (CDC), 2007; Guenter et al., 2008). Rapid tests, despite their lower sensitivity relative to ELISA tests during the primary phase of infection, may be suited for this purpose in case of chronic HIV-1 group M infection (Delaney et al., 2006; Wesolowski et al., 2006). It is important to obtain more comparative data on their capacity to detect antibodies against locally circulating HIV strains at different stages of the infection, not only in sera and plasma but also in whole blood and saliva.

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