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Letter to the Editor

Routine Detection of Acute HIV Infection Through RNA Pooling: Survey of Current Practice in the United States

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To the Editor:

Acute human immunodeficiency virus (HIV) infection is a highly infectious and infrequently diagnosed stage of HIV infection that holds promising opportunities for clinical and public health intervention. Several state and local public health agencies are now employing quantitative nucleic acid amplification tests (NAATs) to screen pooled specimens for acute HIV infection.[1]

To describe current nucleic acid amplification testing programs in the United States we collected information from all publicly funded acute HIV detection programs identified through December 1, 2005 (Table 1). We included all publicly funded US programs that used a pooled algorithm, used a qualitative or quantitative NAAT, used screening for acute cases (diagnostic), and supported public-health HIV prevention activities. All government levels (city, county, state, and national) were included in this search. Programs were excluded from the analysis if they performed individual testing (rather than pooled algorithms), employed NAATs for clinical diagnosis rather than screening, were located outside of the United States, or if no preliminary data were available.

Our findings suggest that specimen-pooling schemes varied greatly between programs. The development of existing pooled NAAT protocols requires balancing cost against timeliness while taking into account state or regional budgets and factors related to the testing population and the logistical operation of testing programs.[5,10] Programs using small pools will have faster turnaround time at the expense of a higher cost.

As expected, the yield of NAAT per 1000 specimens tested also varied significantly between different programs. Programs in Los Angeles, San Francisco, Maryland, and Seattle–King County that targeted higher-risk populations (such as gay men and other men who have sex with men and patients from sexually transmitted disease clinics) had a higher diagnostic yield per 1000 specimens tested (6.2–10.5 per 1000) when compared with North Carolina and blood donor programs (0–4 per 1000), whose testing population is similar to the general population. However, by using larger pools when screening populations with lower HIV prevalence, the yield per 100 NAATs was relatively similar among programs (Table 1).

The selection of the initial HIV antibody screening test may have a significant influence over the program cost and productivity. The majority of programs described use either a first- or a second-generation enzyme immunoassay (EIA) (window period ranging between 32 and 39 days). In contrast, blood donor programs are using a more advanced EIA with a shortened window period of approximately 22 days (a more expensive, third-generation IgM-sensitive EIA).[11] The selection of a less-expensive, first- or second-generation EIA allows for a longer window period (10–17 more days than when third-generation EIA is used), and therefore a potentially higher yield for the detection of patients with negative EIA and positive NAAT, with potential cost-effectiveness implications.[12]

Throughout the United States, the use of pooled NAATs to detect acute HIV infection is becoming a popular strategy for the screening of large populations. However, the most efficient approach remains to be determined. Further studies of the performance and cost-effectiveness of NAATs in different populations are required before further recommendations can be provided.

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TABLE 1. Survey of Nucleic-Acid Amplification Testing in Publicly Funded Federal, State, County, and City HIV Testing Programs in the United States

	Blood Donor Program[1]			California					
	All	Red Cross Only	North Carolina[6]	Los Angeles[9,10]	San Francisco[2,11]	Seattle–King County	Maryland	Atlanta[7]	Washington DC[8]
Population description	All donations from US labs participating in NAAT screening (98% of tested blood donations)	All donations collected by American Red Cross	All persons seeking HIV testing at 110 publicly funded sites in North Carolina	All men seeking HIV testing at three STD clinics in Los Angeles	All persons seeking HIV testing at San Francisco municipal STD clinic	All MSM seeking HIV testing through Seattle–King County public health facilities	All persons seeking HIV testing at publicly funded sites in Maryland (not Baltimore)	All persons seeking HIV testing at the municipal STD clinic, community testing site or drug treatment clinic	All consenting persons seeking HIV testing at a municipal STD clinic
HIV prevalence per 1,000	0.01554	0.01554	2.13	4.47	17.52	16.4	5.34	3.0	4.1
NAAT study period	Mar 1999–Jan 2002	Mar 1999–Apr 2004	Nov 2002–Oct 2003	Feb–Apr 04	Oct 2003–Jul 2004	Sept 2003–Jun 2006	Oct 2004–Feb 2005	Oct 2002–Jan 2004	Sept 2004–Dec 2005
EIA test used to determine HIV-Ab negative status	3rd generation HIV-1/HIV-2 rDNA EIA (Abbot) Confirmatory: HIV-1 Western Blot (Calypte Biomedical) HIV-2 EIA and Western Blot (Bio-Rad Labs)	3rd generation HIV-1/HIV-2 rDNA EIA (Abbott) Confirmatory HIV-1 Western Blot (Calypte Biomedical) HIV-2 EIA and Western Blot (Bio-Rad Labs)	1st generation HIV-1 EIA Vironostika (bioMerieux) Confirmation: Western blot (Bio-Rad Laboratories)	2nd generation Vironostika HIV-1 Microelisa (bioMerieux) Confirmation: Western blot (Bio-Rad Labs)	2nd generation Vironostika HIV-1 Microelisa (bioMerieux) Confirmation: Western blot (Bio-Rad Labs)	2nd generation HIV-1 EIA Vironostika (bioMerieux) Confirmation: Western blot analysis (Bio-Rad Labs)	2nd generation HIV-1 EIA Vironostika (bioMerieux)	2nd generation Genetic Systems HIV-1 rLAV EIA Confirmation: Western blot analysis (Bio-Rad Labs)	2nd generation OraQuick HIV Test Confirmation: Western blot (Bio-Rad Labs)
NAAT used	Procleix® HIV-1/HCV Assay (Gen-Probe) AND Roche Molecular Systems Cobas Ampliscreen	Procleix® HIV-1/HCV Assay (Gen-Probe)	NucliSens HIV-1 QL assay (bioMerieux) Amplicor HIV-1 Monitor 1.5 assay; Roche Molecular Systems RNA	Amplicor HIV-1 Monitor 1.5 assay; Roche Molecular Systems RNA	VERSANT® HIV-1 RNA 3.0 Assay ((bDNA) Bayer)	Gen-Probe HIV-1 NAT (Gen-Probe)	Not Available	Gen-Probe HIV-1 NAT (Gen-Probe)	NucliSens HIV-1 QL assay (bioMerieux) VERSANT® HIV-1 RNA 3.0 Assay (bDNA) Bayer)
Qual/Quant	Qualitative	Qualitative	Quantitative	Quantitative	Quantitative	Qualitative	Quantitative	Qualitative	Quantitative
Pool size	One stage 16:1	One stage 16:1* 128:1*	Multistage 90:10:1	Multistage 90:10:1	Multistage 50:10:1** 10:1**	Multistage 30:10:1	One stage 20:1	Multistage 48:8:1	One stage 20:1
Patients screened by NAAT	37,164,054	13,200,000	108,667	1,698	2,722	3,439	15,000	2,128	1,553
NAAT performed	NA	NA	NA	28	273	204	NA	104	78
Pos. tests NAAT	12	6	23	1	11	7	0	4	6
EIA yield per 1,000 tests	NA	NA	5.3	8.2	34.0	23.0	34.4	33.5	NA
NAAT yield per 1,000 tests (Pos ÷ tests × 1000)	3.23×10^{-4}	4.55×10^{-4}	0.21	0.58	3.58	2.0	0	1.4	0.5
NAAT per acute case detected	NA	NA	NA	28	25	29	NA	26	13
Increase in diagnostic yield from adding NAAT (%)	NA	NA	4	7.1	10.5	6.2	0	5	10
Indications of cost or cost-effectiveness	1.5 to 4.3 million dollars per QALY	1.5 to 4.3 million dollars per QALY	$3.63 per HIV-1 Ab (−) specimen $3,935 per QALY[12]	NA	$12.78 per specimen $2,314 per case	NA	NA	NA	$2,350 per case

*Pools of 16.1 are used since September 1999; pools of 128:1 were used before September 1999.
**Pools of 10:1 are used since February 2004.

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