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Finding those at risk: Acute HIV infection in Newark, NJ

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ABSTRACT

Background: A screening strategy combining rapid HIV-1/2 (HIV) antibody testing with pooled HIV-1 RNA testing increases identification of HIV infections, but may have other limitations that restrict its usefulness to all but the highest incidence populations.
Objective: By combining rapid antibody detection and pooled nucleic acid amplification testing (NAAT) testing, we sought to improve detection of early HIV-1 infections in an urban Newark, NJ hospital setting.
Study design: Pooled NAAT HIV-1 RNA testing was offered to emergency department patients and outpatients being screened for HIV antibodies by fingerstick-rapid HIV testing. For those negative by rapid HIV and agreeing to NAAT testing, pooled plasma samples were prepared and sent to the University of Washington where real-time reverse transcription-polymerase chain reaction (RT-PCR) amplification was performed.
Results: Of 13,226 individuals screened, 6381 had rapid antibody testing alone, and 6845 agreed to add NAAT HIV screening. Rapid testing identified 115 antibody positive individuals. Pooled NAAT increased HIV-1 case detection by 7.0% identifying 8 additional cases. Overall, acute HIV infection yield was 0.12%. While males represent only 48.1% of those tested by NAAT, all samples that screened positive for HIV-1 RNA were obtained from men.
Conclusion: HIV-1 RNA testing of pooled, HIV antibody-negative specimens permits identification of recent infections. In Newark, pooled NAAT increased HIV-1 case detection and provided an opportunity to focus on treatment and prevention messages for those most at risk of transmitting infection. Although constrained by client willingness to participate in testing associated with a need to return to receive further results, use of pooled NAAT improved early infection sensitivity.

1. Background

In New Jersey, more than 100,000 individuals [1] are screened annually for human immunodeficiency virus (HIV) using rapid tests that detect antibodies to HIV. Unfortunately, antibody assays possess a limited ability to detect acute HIV infection (AHI) [2].

AHI [3] is characterized by active viral replication, shedding [4], increases in viral load in blood [5] and genital fluids [6] and a high degree of infectivity [7,8]. During the first 5 months of infection, the probability of transmission (per coital act) has been estimated to be 8–10 times higher than during asymptomatic infection [9]. Primary infection is 26 times more infectious than the asymptomatic phase [10] that follows. By some estimates, AHI accounts for the transmission of up to 50% of all new HIV infections [11].

Screening for AHI provides opportunities for early linkage to care and treatment, with benefits ranging from immune system preservation to decreased onward transmission of HIV [12]. Since many HIV-infected individuals are known to take active measures to reduce their risk of infecting others upon learning of their infection [13], the identification of those in the midst of infection can have important consequences.

First used to detect the presence of HIV RNA during the seronegative period among blood donors [14], pooled nucleic acid amplification testing (NAAT) has been used in conjunction with several generations of HIV-1 immunoassays [15–18], to identify acutely infected individuals and reportedly increases case detection beyond that of even the most sensitive, third generation immunoassays [19]. Unfortunately, pooled NAAT testing is also labor intensive, time-consuming, costly and complex [20].

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[1] On July 1, 2013, the New Jersey Medical and Health Sciences Education Restructuring Act took effect, integrating Rutgers, The State University of New Jersey, with all units of the University of Medicine and Dentistry of New Jersey (formerly UMDNJ).

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Newark is the epicenter of the HIV epidemic in New Jersey. Minorities account for 76% of adult/adolescent cumulative HIV/AIDS cases and 77% of all persons living with HIV/AIDS. In the US, African-Americans have among the highest racial or ethnic HIV prevalence [21] and the highest incidence [22] (68.9 new cases per 100,000 populations) – 7.9 times the rate in whites.

Among African-American females, heterosexual contact with a person known to have, or to be at high risk for HIV infection is associated with an estimated 87% of all new infections. The rate of new HIV infections for black females (38.1 per 100,000) is 20.1 times the rate for white females (1.9 per 100,000) [10].

Among males in the US, African-American male-to-male sexual contact is responsible for an estimated 72% of new HIV infections and accounted for 45% of new HIV infections (ages 13–24). The rate of new HIV infections (103.6 per 100,000 populations) was 6.6 times the rate for white males (15.8 per 100,000 populations) and the highest of any racial/ethnic subgroup [10].

Injection drug use and their sexual contacts have traditionally been a major mode of HIV exposure in Newark. While the proportion exposed through injection drug use (IDU) is lower than in the past, the proportion of cases exposed through sexual contact is increasing [23].

Among factors affecting HIV transmission [24], a high viral load [25] particularly during the earliest phase of the infection, before the appearance of any significant antibody, response is important [26–28]. Pilcher and Cohen [29] estimate the risk of heterosexual transmission per coital act to be between 1/30 and 1/200 during the acute phase of an HIV infection compared to a risk of 1/1000 and 1/10,000 during the later, asymptomatic phase of the infection.

2. Objectives

Utilizing a second generation rapid HIV test and NAAT pooling, we sought to assess the frequency of AHI in an emergency room and an outpatient testing site in Newark, NJ.

3. Study design

Routine HIV testing was offered to patients in the emergency department (ED) daily from 7 am to 11 pm and those who walked in and requested testing. The following patients were not routinely screened: <13 years of age, psychiatric illness, trauma, mental status changes, critically ill patients (e.g. chest pain, difficulty breathing, etc.).

All individuals underwent initial screening for HIV antibodies (13,226) utilizing a rapid HIV-1/HIV-2 antibody test, the Clearview HIV 1/2 STAT-PAK (Alere North America, Inc., Princeton, NJ). Between February 2010 and January 2012, pooled NAAT testing was also offered to emergency department (ED) patients and outpatients (OP) seen at University Hospital, a large, urban hospital in Newark, NJ.

For those negative by rapid HIV and agreeing to NAAT testing (6845–52.2%), plasma samples were collected, centrifuged and stored frozen until a 27 sample batch could be pooled and transported, frozen, to the University of Washington Department of Laboratory Medicine. Real-time reverse transcription-polymerase chain reaction (RT-PCR) amplification was performed at the University of Washington, to assess HIV RNA (dynamic range for HIV RNA detection by Real-Time RT-PCR, 30–1,000,000 copies/mL).

4. HIV-1 RNA pooling by matrix method

Four 125 mcL aliquots from each of 27 seronegative plasma specimens were placed into a single tube representing the total pool and into three respective sub-pool tubes from among nine sub-pool tubes representing a three-dimensional matrix comprised of three rows ($x = 1, 2, 3$), three columns ($y = 1, 2, 3$) and three levels ($z = 1,2, 3$); whereby each of the nine sub-pool tubes represent the sum of nine aliquots from each row, column and level. Thus, each unique specimen with its (x, y, z) coordinate could be identified from among the expected patterns of tube reactivity for this size of matrix. For example, a specimen with the matrix-pool coordinate (1, 2, 3) would contribute 125-mcL aliquots to the 27-member pool tube and into each of three sub-pool tubes representing row 1, column 2 and level 3, respectively. Should this specimen have detectable HIV-1 RNA, then these three tubes would be reactive for HIV-1 RNA and the pattern of this tube reactivity would deconstruct to identify the unique specimen with the matrix coordinates (1, 2, 3). The expected pattern of reactivity for up to three positive samples for this size of matrix-pool should deconstruct accordingly, otherwise a pre-analytical dilution error was suspected and the dilution schema considered invalid and required repeating. In this schema, a reactive specimen was considered presumptively positive for HIV-1 RNA and the original specimen was re-tested to confirm the matrix-pool result. This matrix-pooling method and earlier variants for detection of AHI have been in place at the University of Washington Retrovirus Laboratory and Public Health – Seattle King County, Seattle, WA for several years [30].

Typically, the turn-around-time from specimen acquisition to result delivery took 7–10 days.

AHI case definition: All RT-negative/NAAT-positive results that had detectable viral loads were considered presumptive AHI cases. Persons with presumptive AHI had specimens drawn for follow-up confirmatory testing on the day they received their test results. Follow-up plasma specimens underwent EIA, WB, and viral load testing at University Hospital, Newark, NJ.

AHI case notification: NJ-certified counselors notified presumptive AHI cases of their results and arranged follow-up visits with infectious disease specialists (Fig. 1).

5. Results

Of 13,226 individuals screened, 6381 (48.2%) agreed to rapid HIV testing alone (3587 female, 2794 male), while 6845 (51.8%), (3554 female 3291 male), agreed to rapid testing plus additional NAAT screening of seronegative specimens. More females than males agreed to additional testing (51.9% vs. 48.1%).

As shown in Table 1, rapid testing alone identified 115 antibody positive individuals (0.87%). Of the total, 75 (65.2%) were male and 40 (34.8%) were female. Almost half of the men, 33/75 (44.0%), testing positive by rapid HIV reported male-to-male sexual activity (MSM) as a transmission risk factor. Overall, 33/115 (28.7%) of all

Table 1
Summary – rapid HIV screening supplemented with pooled NAAT testing (B/W reproduction).

Rapid HIV screening supplemented by pooled NAAT testing February 2010–January 2012							
Description	Rapid tested	Rapid and NAAT tested	AHI	HIV Ab+	%HIV Ab+	%Increase in yield	%Yield AHI
HIV Ab− adults receiving testing and counseling at a high risk urban hospital in Newark, NJ	13,226	6845	8	115	0.87%	7.0%	0.12%