HIV/AIDS SENTINEL PROVIDERS' NETWORK NEWSLETTER

Public Health
Seattle & King County
HEALTHY PEOPLE. HEALTHY COMMUNITIES.
City of Seattle King County

Spring/Summer 2007; Vol. 17; No.2 HIV/AIDS Epidemiology (206) 296-4645

False-Negative Rapid HIV Tests in Early HIV Infection

: The following is an update of a Clinical Observation letter in press in Annals of Internal Medicine[1]. HIV antibody tests have varying "window periods" after HIV acquisition when persons may have very high HIV RNA levels, but antibodies to HIV cannot be detected. Commonly-used antibody tests -- 1st and 2nd generation enzyme immunoassays (EIAs) -- have window periods that last at least 4-6 weeks after HIV acquisition. Rapid HIV antibody tests are generally considered to be at least as sensitive as 1st and 2nd generation EIAs in detecting individuals with recent HIV infection[2-4]. In the fall of 2003, Public Health - Seattle & King County (PHSKC) began to offer rapid HIV antibody testing for men who have sex with men (MSM) and started routinely testing antibody-negative MSM for acute HIV infection using pooled HIV nucleic acid amplification testing (NAAT). Because many MSM who are screened for HIV infection with rapid HIV antibody tests have a blood sample sent to the PHSKC laboratory for further testing, we have been able to detect cases of false-negative rapid HIV antibody test results.

In November 2005, PHSKC identified an individual with early HIV infection after he tested HIV-negative by the OraQuick Rapid HIV-1 Antibody Test (OraQuick, OraSure Technologies, Inc, Bethlehem, PA) on a finger-stick blood sample. He tested HIV NAAT-positive, but he surprisingly also had anti-HIV antibodies detected by a 1st generation EIA. Since this case, PHSKC has used either a 1st or 2nd generation EIA on samples from MSM who test OraQuick-negative prior to pooling for HIV NAAT. Between 11/2005 and 6/2007, PHSKC identified seven HIV-infected MSM who were OraQuick-negative and 1st or 2nd generation EIA-positive.

The seven men were mostly young, Caucasian MSM. There is no evidence of epidemiologic links among the group, and they do not uniformly represent a group of MSM at high risk for HIV infection. The false-negative OraQuick tests were performed on both oral fluid and finger-stick blood samples, and test kits came from more than one lot. Three had tested HIV-negative 1-3 months prior to their discordant testing. At the time of the false-negative OraQuick result, all seven had a positive Western Blot assay, but none had anti-gp41 detected on his Western Blot assay.

Discussion: Despite reports of equivalent sensitivity between rapid HIV antibody testing and EIAs during early HIV infection[2-4], we have identified seven men with definite or probable early HIV infection who had false-negative rapid HIV test results but had HIV antibodies detected by an early generation EIA. These seven men represent 6% of 111 HIV antibody-positive men who were tested by OraQuick in three PHSKC-funded sites since 2003. It is especially concerning to us that all seven men had likely been recently infected at the time of their discordant testing. OraQuick could have reduced sensitivity in early HIV infection because the assay uses only synthetic gp41 (whereas EIAs use viral lysate with multiple antigens), and antibody development to gp41 may occur after p24 or gp120/160 (S. Holte, personal communication.).

On the other hand, it could be possible that all seven false-negative test results were due to operator error. We used OraQuick to re-test frozen specimens from three of these cases, and all three test results had a very faint test line. It is unclear if additional personnel training could prevent future errors, because faint test lines should be interpreted with caution due to their association with false-positive test results[5-7].

PHSKC seems to be the first public health HIV testing program to identify this problem with false-negative OraQuick results, perhaps because we may be the only health department that performs EIAs on OraQuick-negative testers prior to pooling for HIV NAAT. We do this because preliminary positive EIA results can be available to HIV-infected, OraQuick-negative MSM 1-2 weeks before results of HIV NAAT.

Also, because HIV NAAT is not performed on the pooled samples that include a positive test, If our results are confirmed, widespread use of OraQuick or other rapid HIV antibody tests could have deleterious public health effects if they are consistently less sensitive or more prone to operator error during early HIV infection. Individuals are more infectious after HIV acquisition than during established infection[8], may be incorrectly reassured by a recent negative HIV test result, and therefore may not change their behaviors to protect their partners. On the other hand, in some settings, rapid testing may allow more people to get HIV antibody test results because preliminary results can be given in less than an hour[9]. If programs elect to offer rapid HIV antibody testing instead of standard EIAs, PHSKC recommends that pooled HIV RNA testing should be integrated with rapid HIV antibody testing for populations at high risk of HIV acquisition to prevent false-negative test results associated with rapid HIV antibody testing (In Seattle, this group is primarily MSM). Clinicians should counsel populations at low risk of HIV acquisition that the window period exists, and it may be longer for rapid HIV antibody testing than is commonly thought.

1. Stekler J et al. *Ann Intern Med.* 2007, in press.
2. Kuun E et al. *Vox Sang.* 1997;72:11-15.
3. Samdal HH et al. *Clin Diagn Virol.* 1996;7:55-61.
4. Beelaert G et al. *J Virol Methods.* 2002;105:197-206.
5. Jafa K et al. *PLoS ONE.* 2007;2:e185.
6. Delaney KP et al. *AIDS.* 2006;20:1655-60.
7. Wesolowski LG et al. *AIDS.* 2006;20:1661-6.
8. Wawer MJ et al.. *J Infect Dis.* 2005;191:1403-9.
9. Spielberg F et al. *J Acquir Immune Defic Syndr.*2005;38:348-55.

Routine HIV Screening: On 9/22/06 the CDC updated recommendations concerning HIV testing in its MMWR (Morbidity and Mortality Weekly Report). The main new recommendation CDC conveyed was that since about a quarter of the estimated million or so people living with HIV in the United States are believed to be yet unaware of their infection, HIV testing should become routine, and every man, woman, and child between the ages of 13 and 64 should be tested at least once. The CDC wants testing to be done only with the patient's awareness so that patients could 'opt-out' of or decline testing. Persons who engage in on-going risk for acquiring HIV should be tested repeatedly, generally at yearly intervals, depending on their risk.*

this additional step actually costs less money.

CDC recommends that broad-scale screening be implemented in all primary care settings, including hospitals, ERs and urgent care settings, jails and prisons, large and small clinics, and private offices. Only after a clinical setting showed that its prevalence of HIV was less than 1 case in 1,000 would it be reasonable for the clinic to cease routine testing for HIV.

Dr. Bob Wood, of the HIV/AIDS Control Program for Public Health Seattle & King County brought these new recommendations to King County Medical Society's Public Health Liaison Committee on 10/11/06, and at the KCMS Board meeting on 6/11/07 the Board decided to endorse this new CDC strategy to help more persons with HIV become aware of their infection. Dr. Maxine Hayes, State Health Officer, has worked with others in the State Department of Health to develop educational materials for providers and brochures for patients, available on the department's website: www.doh.wa.gov/cfh/HIV_AIDS/Prev_Edu/default.htm).

* Currently Public Health - Seattle & King County recommends that HIV testing for men who have sex with other men (MSM) occur at least every 6 months. MSM who have any bacterial STD, those using methamphetamine, and those who admit to unprotected sex with persons of unknown or sero-discordant HIV status are at greatest risk for acquiring HIV, and should be urged to test every 3 months.

New HIV/AIDS Case Report Form:

Due to the dynamic nature of the local HIV epidemic, the HIV/AIDS case report used by Washington State is revised periodically. This summer a new version will be implemented that includes:

- Simplified testing history questions
- For foreign born individuals, length of residence in the U.S.
- Information about the first resistance test
- Start date of antiretrovirals
- Revised partner notification/partner counseling and referral (PCRS) section
- Addition of methamphetamine use

These changes will help us better monitor HIV drug resistance, estimate HIV incidence, monitor patterns in HIV treatment, and manage PCRS.

Care and Prevention (CAP): The Care and Prevention (CAP) project started conducting patient interviews in January 2007 and we completed 338 interviews at eleven

different sites. CAP is a CDC-sponsored expanded surveillance project. Its aims are to 1) monitor HIV-associated presentation, outcomes, and treatments; including how many people are receiving the recommended care for HIV, including HAART, OI prophylaxis, PPD screening, vaccinations, hepatitis screening, etc; 2) identify barriers to care; 3) examine morbidity still experienced by HIV-infected persons in the HAART era; 4) measure adherence to, acceptance of, and adverse effects of therapy; and 5) examine many facets of HIV prevention including condom use, serosorting, disclosure of HIV status, where sexual partners meet each other (internet, baths, etc.) and numbers of partners met at each location.

Data are collected by chart review and interview. Chart review data include HIV-related treatments, diagnoses, and laboratory values. The interview asks patients about their health-care seeking and other behaviors impacting HIV care, such as adherence to HAART. Patients were compensated $20 for their time. Thanks to all the CAP providers and participants.

Data collection for CAP ended on June 1st and we are now focused on getting the 2007 round of the Medical Monitoring Project (MMP) up and running. For this cycle of MMP, 17 King County providers are participating. We hope to have the random selection of patients drawn from the participating sites by early July to begin interviews soon afterwards. If you have any questions about CAP or MMP, please contact Elizabeth Barash at 206-296-2907.

HIV/AIDS Epidemiology Brown-bags.

These meeting occur approximately monthly, Tuesday lunchtimes, usually at the 3rd floor 400 Yesler building. For more information, to be added to the mailing list, or to suggest a speaker or topic, please call Elizabeth Barash at 296-2907.

Clinical Conferences & Lunchtime Talks.

Clinical conferences are usually the 3rd Tuesday of each month 8am to 9am at the HMC Research and Training Building. Brown-bag lunchtime talks are usually held on Fridays from 12 noon to 1pm. For more information on the AIDS Clinical conferences, including CME, contact Dennis Torres at 206-731-6972.

EPIDEMIC AT A GLANCE: AIDS CASES

	Cumulative AIDS Cases	AIDS Deaths	Persons living with AIDS
Seattle-King County (actual reports, 5/31/06)	**7,551**	**4,151**	**3,400**
Washington State (actual reports, 5/31/06)	**11,844**	**6,354**	**5,490**
United States (estimated, 12/31/05)	**988,376**	**550,394**	**437,982**

HIV CASES (WITHOUT AIDS)

	Cumulative HIV non-AIDS Cases	HIV non-AIDS Deaths	Persons living with HIV non-AIDS
Seattle-King County (actual reports, 5/31/06)	**4,902**	**118**	**2,784**
Washington State (actual reports, 5/31/06)	**4,459**	**203**	**4,256**
United States (estimated, 12/31/05)*	**249,950**	**11,811**	**238,139**

*.Based on 38 states and 5 US territories with long-standing confidential name-based HIV reporting, not including WA

TOTAL HIV/AIDS CASES

	Cumulative HIV & AIDS	HIV & AIDS Deaths	Persons living with HIV /AIDS
Seattle-King County (actual reports, 5/31/06)	**12,453**	**4,269**	**6,156**
Washington State (actual reports, 5/31/06)	**16,303**	**6,557**	**9,746**
United States (estimated, 12/31/05)**	**1,231,105**	**553,394**	**677,670**

*.Based on 38 states and 5 US territories with long-standing confidential name-based HIV reporting, not including WA

To report AIDS and HIV disease cases or to order reporting forms and information, call Faythe Crosby at (206) 296-4645

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