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INTRODUCTION

On June, 12, 2006, the New York HIV Research Centers Consortium held its third annual symposium. This forum, held at New York University School of Medicine, addressed Acute HIV Infection (AHI) and speakers included academicians, representatives of the New York City, New York State and New Jersey Health Departments, behavioral scientists, and community representatives. It was attended by over 120 faculty and staff from the 21 HIV research centers in the tri-state region.

Approximately 4,000 new cases of HIV are thought to occur each year in New York City, and approximately 40,000 occur nationwide. Rapid identification of these AHIs could help slow the HIV/AIDS epidemic and may aid in the treatment of these individuals' HIV infections. Despite the importance of AHI for public health, treatment and research, few cases have been identified in the New York region. The purposes of the conference were to:

- Update and educate the research community about AHI
- Provide a forum for the development of potential initiatives and other interventions for:
 - o Identification of AHI;
 - o Prevention of HIV transmission from acutely infected individuals to others; and
 - o The development of an integrated behavioral and biomedical research agenda regarding AHI.

These Proceedings were prepared to further support the purposes of the conference. They include a summary of all presentations, and of a set of action items developed by participants at the end of the conference. Posters representing work related to AHI which is underway by Consortium members, and information about the New York HIV Research Consortium, are included in Appendices.



Why Focus on AHI?

Acute HIV infection can best be described as the interval following the acquisition of HIV infection, but prior to the formation of antibodies traditionally utilized to diagnose the presence of infection. During this period there are very high levels of both HIV viremia and shedding, significantly increasing the potential for subsequent transmission. The issues raised by acute HIV infection are increasingly being addressed by the members of the consortium. Unique aspects of acute HIV infection include the following:

- Given the high viral load, and enhanced risk of transmission, prevention strategies focused on those with acute HIV infection may have significant impact on incident HIV infection.
- Targeting prevention to networks with active disease transmission may be more effective in reducing new infections
- New modalities such as HIV RNA testing in antibody negative specimens may serve as an efficient means to identify those with new infections
- Acute HIV infection provides a unique view of HIV pathogenesis allowing investigators to gain new insights into early infection and subsequent immune response
- The potential exists that early recognition of disease combined with antiretroviral therapy may alter the natural history of HIV infection

Each of these issues was addressed by conference speakers, and many of the conference participants are engaged in research related to AHI.



Clinical Review of Acute HIV Infection

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Exposure to HIV initiates a rapid cascade of clinical events in which HIV penetrates a mucus membrane, interacts with dendritic cells (which initiate an immune response) and within two days has activated CD4⁺ lymphocytes (T-cells) and traveled to lymph nodes. Within three days of exposure, HIV begins to replicate explosively, entering the blood stream and disseminating widely throughout the body. The earliest phase of primary (or acute) HIV infection (AHI) is characterized by very high levels of virus in the blood, which decrease over the first weeks as HIV-specific cellular immune responses, especially the activity of and CD4⁺ and CD8⁺ cells, increase. CD4 counts may decrease slightly and then revert to normal. Primary infection is followed by an often long phase of latency, in which the immune system holds HIV at a set point while CD4⁺ cells begin to decrease. Latency is followed by symptomatic HIV and then clinically defined AIDS, accompanied again by rising viral load.

There is a great need to teach physicians to recognize acute HIV infection. Although up to 92% of patients demonstrate and remember the symptoms of acute HIV infection, the diagnosis is missed 80% of the time by physicians, regardless of the setting. (Nearly half of patients go to their primary care doctor, 31% go to an emergency room, and 21% go to a walk-in clinic.)

Acute HIV infection manifests with flu-like symptoms, including fever (80-90% of the time), pharyngitis (70-90%), rash (40-80%), lymph node enlargement (40-70%), headache, joint and muscle pains, lethargy, nausea, diarrhea, low white blood cell and platelet counts, and sometimes neurologic complaints. There are often genital and/or oral ulcers. Since these symptoms are all common to other diseases, physicians should include acute HIV infection in differential diagnosis.

HIV antibody tests cannot detect acute infection. Viral load peaks during the “window period” prior to detectable levels of antibody on standard HIV tests and begins to fall, nearing a set point as antibodies increase enough to produce a positive test result (seroconversion). Nucleic acid tests should be used to determine viral load, and, although some false positives are possible, a high viral load in an antibody-negative individual is diagnostic of acute infection.

Acute HIV infection is a significant public health risk. Acutely infected people have high levels of virus in both blood and genital secretions, are hyperinfectious, and may be the source of substantial HIV transmission. Earlier identification of HIV might slow the rate of infection as well as reduce risk taking among those infected. People aware of their own HIV status were found to be 53% less likely to have unprotected anal or vaginal intercourse (68% when adjusted for the status of sexual partners).

There may also be clinical health benefits to identification of infection in the primary phase. But many questions remain. Should clinicians treat acute infection? (The preliminary answer is yes, although data are still incomplete.) Will earlier treatment or vaccines that might increase HIV-specific cell immunity alter the course of disease? Should treatment continue after the acute phase? How can physicians help newly infected people develop the immunity of long-term non-progressors? Can screening for acute HIV infection decrease HIV transmission? How can researchers learn more about immune-related diseases?



The Biology of Acute HIV Infection: Virology, Immunology, and Effects of Early Treatment

Fred Valentine, M.D., Director, Center for AIDS Research & Professor of Medicine
New York University School of Medicine

Reviewing the biology of the spherical HIV particle (or virion): its outer viral membrane (envelope) is pierced by many small spikes composed of the glycoprotein gp41 and tipped with gp120. These enable HIV to attach to target cells. A protective matrix, the layer just below the envelope, consists of p17 and encloses the bullet-shaped core (capsid) of p24. The core contains the nucleocapsid (the particle's genome, consisting of two strands of RNA and a p7 protein coat), along with p6 and enzymes important in viral replication: protease (cuts proteins), reverse transcriptase (transforms RNA into DNA), and integrase (integrates DNA into the host cell's genome). One of HIV's nine genes, called gag, codes for the critical structural proteins, p17, p24, p6, and p7. The pol gene codes for the enzymes. Others code for additional viral and regulatory proteins.

HIV replication involves interaction between gp120 and its CD4 receptor on a target cell. The viral envelope fuses with the cell membrane, the capsid enters the cell, and new virus particles (buds) are produced and released.

Current licensed HIV medications attack enzymes (i.e., reverse transcriptase or protease inhibitor) or inhibit viral entry (T-20). Study of the process by which HIV destroys normal immune responses and ways to preserve or re-constitute it are expected to give rise to new treatment and prevention strategies.

The high error (mutation) rate of reverse transcriptase (about one or more per genome per round), rapid HIV replication, (10^6 to 10^7 new infectious virions per day), and frequent genetic recombination (7 to 10 crossovers per genome per round, producing new subtype strains and even recombination of different strains in a single patient) pose major clinical and research challenges. HIV far surpasses the genetic diversity of influenza. Recent recombinants are more successful competitors than earlier genotypes. In Kenya, up to 40% of the many subtypes in circulation are recombinants.

Infection begins when HIV crosses the mucosal epithelium facilitated by trauma, oral exposure, or another infection. It most easily infects activated lymphocytes, especially in the gut, binds to local dendritic cells, is transported to lymph nodes, and encounters CD4⁺ T-cells, as well as macrophages, which it can also infect. Strains of HIV able to replicate in CD4 T lymphocytes and macrophages using the CCR5 co-receptor. Despite the possibility of many genetic variants in a donor, only one quasi-species of HIV is transmitted, usually one using CCR5. Up to 15% of new infections involve the transmission of HIV resistant to one or more drugs.

In untreated HIV infection, the HIV set point is determined during the acute infection phase by mechanisms not yet understood. In the first months, CD4⁺ T-cell levels in the blood may remain close to normal even though large numbers of CD4 cells are being destroyed. Cytotoxic CD8⁺ T-cells develop early in the infection and are able to partially control the level of HIV by killing infected cells. However in spite of their activity, the patients remain infectious to others, and the disease progresses in untreated patients. Although many types of antibody are produced, including those that neutralize HIV, rapid viral mutation outpaces antibody immune responses resulting in "escape mutants", allowing the course of disease to proceed unchecked.



Symptoms begin when CD4 T cell levels have dropped and viral load again rises. In a normal immunologic response, CD4⁺ and CD8⁺ T-cells (lymphocytes) recognize a viral antigen and release cytokines (proteins that act on other cells), and proliferate to generate memory cells. Fewer CD4s leads to fewer CD8s effector cells that can attack the virus. A study of lymphoproliferative response (LPR) to HIV antigen in 120 patients with established HIV disease indicated that most did not respond strongly to HIV antigens gp120 or p24 even though they responded to antigens of other viruses, although long-term non-progressors (LTNPs) with a low viral load, who are infected individuals still asymptomatic after 8 years without ever being treated with drugs had a high LPR response.

Researchers are anxious to learn how LTNPs, (less than 4% of infected people), maintain normal CD4 counts and HIV-specific CD4-dependent proliferative responses, as well as a very low viral load, without treatment, essentially achieving immunologic control of HIV. Untreated patients and those who initiate treatment in established disease cannot contain HIV in this way, even after several years of ART. The working hypothesis is that HIV-specific CD4 proliferative responses are eliminated or inhibited during acute infection.

Although most people with acute HIV infection develop an immunologic response, people who receive treatment during this phase develop a vigorous prolonged LPR and decreased viremia. Some who stop treatment even regain immunologic control of HIV without restarting ART after viral load increases. Patients receiving experimental HIV vaccine also show broad HIV-specific LPR.

It appears that the preservation or loss of the ability of CD4⁺ cells to generate HIV-specific memory cells during the acute and early phase of HIV infection, when viral load set point is also established, is instrumental in determining the course of disease. The fact that a few patients become LTNPs without treatment and some patients treated during acute infection gain immunologic control of HIV even after stopping ART argues strongly that we must learn how this control of HIV occurs. It is imperative that we identify, study and understand the evolution of patients during acute HIV infection.



STAT – The North Carolina Program for Identifying Acute HIV: Implications for STD Programs and Prenatal Screening

Peter A. Leone, M.D., Associate Professor of Medicine, University of North Carolina & Medical Director, NC HIV/STD Prevention and Care, NCDHHS

Clinicians must be educated to consider acute HIV infection (AHI) when patients present with flu-like symptoms. In North Carolina, a recent HIV index case and three subsequently infected patients, all misdiagnosed after coming to physicians in the acute phase of HIV infection, illustrate the current “standard of care”. AHI is often either not considered in the development of a differential diagnosis or appropriate diagnostic tests are not obtained .

The “window period” in HIV is defined as the time between the appearance of HIV in the blood (viremia) and detectable levels of antibody. Seroconversion is defined as an antibody-positive test confirmed by Western Blot. Current ELISA tests do not reliably detect HIV antibodies prior to four to eight weeks, although newer tests may decrease this period. However, HIV has a very short incubation period, from a few days to a couple of weeks, followed by a period of very high viremia lasting about eight weeks. Symptoms begin after viremia begins to rise, so clinicians do not see people in the earliest asymptomatic phase, and antibody tests are often negative on those they do see, although viral load testing is possible. Charting a diagnostic testing timeline: HIV RNA is detectable after the first week of infection and p24 antigen after the second; symptoms often begin between the second and third week; the recombinant peptide ELISA test can be used after the third week, but the viral lysate ELISA may not detect antibodies until the tenth.

There are many compelling reasons for improving acute HIV diagnosis. Early HIV infection is one of the driving forces in the epidemic, perhaps responsible for as much as 30% to 50% of all transmission. There is a 10 to 100-fold increase in transmission risk during the first four to six months of infection. Earlier identification of transmission networks could greatly improve preventive intervention. Patients could also enter care earlier, although it is not yet known whether treatment during the acute phase will improve prognosis. Obstacles to AHI detection are that the diagnosis is rarely considered, that many patients (30%) are asymptomatic, that the symptoms are non-specific for HIV, that lab testing must be directed, and that there must be prompt links to surveillance and partner counseling and referral services.

The North Carolina Screening and Tracing Active Transmission (STAT) Project conducts HIV RNA tests on all blood from public clinics that is antibody negative or Western Blot indeterminate (120,000 tests/year) and reviews all cases that are antibody negative but RNA positive, antibody positive but with a negative HIV antibody test within the previous three months, and antibody positive with symptoms consistent with AHI within the past thirty days. RNA tests are performed on pooled specimens (lowers cost and allows universal screening with no change in specificity), although this method requires large testing numbers, decreases sensitivity, and involves complicated logistics and time to locate patients.

The state has 135 publicly funded community testing sites, which do daily RNA testing on pools of 96 specimens, detecting those with at least 5,000 copies. The program, now in its fourth year, has screened close to 300,000 in a variety of settings and finds 20-25 acute infections per year (a total of 79). It takes on average 11 days from testing to notification; 80% of named partners have been located and tested; more than 40 acute



infection networks have been identified, including those among recent inmates, college students, STD patients, drug users, workplace colleagues, and other groups.

Of patients diagnosed with acute HIV infection at an STD clinic, 78% did not come in for an STD-related visit, although 44% were diagnosed with an STD at the same time. Only about 40% had HIV symptoms at the time of testing. Still, STD clinics are an important entry point for people at high risk for HIV, blood is already being drawn, and the incubation periods of STDs and HIV overlap. HIV testing is done with an “opt out” choice. However, further research is needed to determine whether to screen everyone or just those with symptoms (which symptoms? within what time period?) or those who are high risk. Rapid tests and AHI screening are not mutually exclusive; rapid tests can be used in conjunction with symptom screening.

Concerning women, five of 16 with acute HIV infection were pregnant at the time of testing. All received treatment with HAART, and no infants were infected. However, since three of six HIV+ infants born in NC during this same period had mothers who had tested for HIV antibodies early in pregnancy, it is recommended that all pregnant women be screened for acute HIV infection and have an antibody test early in pregnancy followed by a second one or RNA testing in the third trimester or at delivery.



Acute HIV Infection Initiatives in New York State

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New York State, with nearly 167,000 cumulative AIDS cases since 1984 and over 39,000 HIV cases reported since 2000, still leads the nation in HIV/AIDS. Data from 1984 through 2004 indicate that while AIDS diagnoses and deaths peaked in the mid-90s, annual deaths still exceed 2,000, and there are increasing numbers of people living with HIV/AIDS as death rates have fallen and new HIV cases continue to occur. Funding has often not kept pace.

Data presented at the 13th CROI by Hollingsworth suggests that while AHI is responsible for most transmission early in an epidemic, since the acute phase is so short, transmission during the much longer latency phase becomes more important as an epidemic progresses, especially in low risk populations. In an established epidemic, acute infections may account for about 11% of transmission, latent asymptomatic HIV for 68%, and the AIDS phase for 21%.

Still, the high viremia and amplification of transmission risk with co-existing STDs, as well as the potential for more rapid case finding and intervention through partner notification of HIV cases diagnosed in the acute phase, makes diagnosis of acute infection important. The very high (1/30 to 1/200) risk of transmission in the three week acute phase (compared to 1/1000 to 1/10,000 during latent asymptomatic HIV infection) reflects a very high viral load in semen (which can vary from that in blood). The CDC estimates that the 25% of people unaware of their HIV infection are responsible for at least 50% of the 40,000 new infections per year. Both clinical and public health approaches are needed to address AHI.

In NY, the Monroe County STD Clinic Surveillance Demonstration Project (a collaboration of the AIDS Institute, other NY health agencies, and the North Carolina DOH) began in May 2006 to replicate the NC model (16 of 23 acute HIV infections found in NC in a 12-month period were diagnosed at STD clinics). People with suspected acute HIV infections are identified through nucleic acid amplification testing (NAAT), which detects viral RNA, on pooled antibody-negative samples. They are given rapid confirmatory testing, risk reduction counseling, partner notification services, and referrals to care, along with active case finding among their sexual and substance use contacts. The intent is to estimate AHIs among this high risk clinic population, estimate HIV cases among partners, and assess the feasibility and cost of NAAT screening and of enhanced case finding in NY State. However, this method requires a large number of seronegative blood samples, in shorter supply with widespread use of rapid testing and private labs.

The diagnosis of AHI through individual viral load testing requires that patients come to physicians with acute viral syndrome and HIV risk factors, and that physicians consider HIV in the differential diagnosis and follow-up. The NY State consent form may be used to obtain consent to do a viral load test for the purposes of HIV diagnosis, but viral load testing is still not FDA approved for this purpose. There is a need for a cheap, easy screening tool and for further study on the individual and public health benefits of early ART, the interdiction of transmission networks, the cost effectiveness of interventions, and the role of AHI in transmission within a community.



Concerning acute HIV infection and perinatal transmission, in NY the number of HIV-positive women giving birth per year has steadily declined from close to 2,000 in 1988 to about 600 in 2004. Since 1997, the percent of pregnant women aware of their HIV status has increased from 64% to 95%. Mother to child transmissions decreased from 97 in 1997 to 16 in 2004. In chart reviews of the 47 cases of MTCT transmission from 2002-2004 among 2,038 total births to HIV-positive mothers, 12 (25.5%) were found to be due to maternal AHI (mother tested positive after having at least one antibody-negative test during pregnancy or mother had a high plasma HIV RNA level with a negative or indeterminate antibody test). The 12 with documented acute infection during pregnancy had a MTCT rate of 38.7%, compared to 1.7% for the other 35 without documented AHI (although a few mothers may have seroconverted during pregnancy but prior to the first antibody test). Study is needed to determine the roles of factors such as inadequate prenatal care, substance use, STDs, breastfeeding, and immigrant status.

Plans are in progress to increase efforts to engage high risk pregnant women in prenatal care, to educate providers about acute HIV infection during pregnancy, to recommend a routine second antibody test in the third semester, and to do immediate HIV viral load (RNA) and antibody testing for pregnant women with acute HIV symptoms.



Acute HIV Infection in the NY City Metropolitan Area: Rationale for Implementation of AHI Screening in STD Clinics

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The much higher risk of HIV transmission during acute HIV infection compared to the chronic latent stage of infection provides an opportunity for public health intervention. AHI cases are estimated to be responsible for ~20-50% of new HIV infections. Intervening on AHI requires first finding AHI cases. Diagnosis alone is likely to decrease subsequent transmission and diagnosis also provides opportunity for prevention counseling, contact tracing, and early clinical intervention. Strategies for finding AHI cases differ for symptomatic (~50-60%) and asymptomatic people. Symptoms are non-specific, and clinicians usually do not ask about HIV risk when evaluating patient with such non-specific febrile syndromes. Potential public health interventions for symptomatic AHI include 1) provider education to order viral load testing on patients with symptoms consistent with AHI with a history of a high-risk exposure and 2) institutional arrangements to allow for ordering of viral loads on patients who are not documented to be HIV-antibody positive. In contrast, finding asymptomatic AHI primarily requires searching for AHI cases among those seeking HIV testing. This requires testing persons presenting for HIV-antibody testing with pooled viral load or nucleic acid amplification testing (NAAT) also.

Individual NAAT (i.e., unpooled) can identify HIV infection in about 11 days (9-25 day range) when using a test with a 50 copies/ml detection limit. This is often weeks sooner than antibody testing [the newest rapid tests can detect antibodies beginning at ~3 weeks and viral lysate EIAs (enzyme immunoassays) can do so in ~5]. Pooled NAAT allows many specimens to be tested quickly at reduced cost (individual samples tested only if a pool is positive) and allows NAAT screening to be implemented on a large scale. Efforts to detect AHI in North Carolina, San Francisco, Los Angeles, and Seattle indicate that it's very difficult to identify patients with acute retroviral syndrome (ARS) even in high risk settings and support routine pooled NAAT (pNAAT) with HIV testing. In North Carolina, 7 of 23 patients identified with AHI through pNAAT were recognized as having ARS at the time of testing only retrospectively, and 6 more became symptomatic after testing. Experience in several states indicates that use of pNAAT had numerous benefits: 1) increased the number of infections 2) likely prevented infections through index case recognition and prompt contact tracing, 3) identified transmission networks, and 4) facilitated early treatment. Pooled NAAT was found to be cost effective in NC given the high cost of lifetime HIV treatment and has been shown yield the most AHI cases per test when instituted in STD clinics.

To implement NAAT in New York City, the intent is to start with DOHMH STD clinics, initially in Chelsea clinic and then elsewhere, and to join the CDC Acute HIV Infection study. CDC objectives are to assess feasibility and cost effectiveness of pooled NAAT compared to second and third generation antibody assays and rapid tests; identify additional HIV infections; evaluate factors such as pool size and HIV prevalence on NAAT results; describe AHI epidemiology, transmission risks, and clusters; record the outcomes of partner notification; estimate infections prevented; examine HIV resistance in people with AHI; and determine NAAT sensitivity and specificity. The study includes three sites (Los Angeles, Florida, and New York City) and two labs (FL and NY State's Wadsworth Center). In NY, rapid testing will be done in clinics and NAAT in the state lab on a total of 60,000 plasma samples.



For the public health HIV detection and NAAT feasibility study component, all samples will be tested using initial pools of 16 specimens with individual NAAT testing on specimens from positive pools and additional testing on positives to measure viral load and determine test sensitivity related to pool size. Presumptive positives will receive timely confirmatory testing, partner notification, and referrals. Questionnaires and additional specimens will be used for the research components on transmission risks and prevention and to evaluate NAAT performance in comparison with antibody tests. Thus far in 1,000 specimens from Florida and LA, no AHI cases have been identified, but one specimen was antibody-positive and NAAT-negative.

Challenges in New York City include implementation in a system using rapid testing. The need for follow-up will rule out screening of anonymous testers. An AHI/NAAT fact sheet will supplement pre-test counseling so patients are informed about additional testing, possible return visits, and acute retroviral symptoms. IRB, legal, and operational issues will need to be resolved. Since New York City currently uses more sensitive antibody tests that detect HIV earlier than tests used at other sites, the number of AHIs found may be lower. The program will also increase awareness of acute infection among high risk patients through the AHI fact sheet and education regarding the purpose of the new test. A possible next step is the implementation of pNAAT in New York City jails.



AHI: Update from New Jersey

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Although acute HIV infection has not been a focus to date in New Jersey, the state has high HIV prevalence: it is fifth in the U.S. in cumulative reported AIDS cases, third in cumulative pediatric cases, and first in the proportion of women among AIDS cases. Several hundred counseling and testing sites, some opened in the early 1980s, provide 65,000 free confidential and anonymous tests per year and find about one third of new HIV cases. However, overall 35% of people do not return for test results. New Jersey does not have needle exchange programs, and drug treatment programs are administratively part of the state Department of Human Services rather than Health and Senior Services—which gives rise to peculiar regulatory restraints on rapid HIV testing.

Rapid HIV testing is conducted in 23 primary sites and more than 70 satellite sites, including hospitals, local health departments, STD clinics, CBOs, mobile vans, and emergency rooms. As part of a CDC study of rapid HIV testing (called Post Marketing Surveillance-2, or PMS-2) we investigated whether or fluid is as specific as blood testing, when used in actual practice. Testing in emergency rooms has increased recently, with significant numbers of new people tested. This has been a successful effort to reach a new population of at-risk individuals who had not been tested before.

Before rapid testing, only 65% of people tested got their results. With rapid testing, almost all negative patients are getting their results, and post-test, risk-reduction counseling. But even with rapid testing, among those with positive results, still only about 70% of people got their results and post-test counseling—about 30% still did not return for results. The state's Notification Assistance Program only succeeds in locating them 20% of the time, so a fair number of positives are still potentially not receiving appropriate care. A research issue is whether rapid tests could be used to confirm a preliminary positive rapid test result to avoid the wait for Western Blot results. In a retrospective pilot study that we ran in about 16,000 people tested, 355 were positive on both OraQuick and Western Blot tests, 8 were (false) positive on OraQuick but Western Blot negative. A strategy of confirming the initial reactive tests with a second rapid test showed that rapid confirmation may be equivalent to traditional Western Blot. Further prospective studies are planned. On unanswered question, though, is how much benefit will be gained by getting rapid confirmatory results to the 35% of patients who are now not returning for them. Will this population behave differently from those who are motivated and concerned enough to return for their results?

Seroprevalence from an anonymous 2002 survey of more than 3,000 emergency room HIV tests was 10.4% overall (11% for males, 9.6% for females), 60% of whom knew they were positive. About 34% of women and 45% of men had previously not known their status; 15% of women and 13% of men were using ART; and 50% of women, 41% of men had diagnosed HIV but were not using ART. The acute infection rate is unknown. Data collected from rapid HIV testing in several emergency rooms shows that of close to 5,500 patients tested, 98.6% received the results. Seroprevalence was 2.8%, compared to 1.9% in non-emergency settings; 120 of 154 positives (77.9%) were newly diagnosed; and 76.7% of these new positives got confirmation test results. This increased yield compared to traditional testing has supported the efforts in increase emergency department testing. Because of this high prevalence and higher yield of new cases, we are planning further



studies to look at the prevalence of AHI in this population. We still do not know acute infection rate in emergency settings and elsewhere, or how many AHI patients would receive NAAT results.



Controlling AHI Transmission: Issues Related to Risk Networks, Social Networks, and other Social Influences

Samuel R. Friedman, Ph.D., Director, Social Theory Core, Center for Drug Use and HIV Research & Senior Research Fellow, National Development and Research Institutes, Inc.

To understand HIV epidemics, it is essential to examine how risk networks transmit infection between individuals and within communities and groups. One hypothesis with some support is that long-term HIV-infected people with high HIV antibody levels can be a type of “firewall” keeping acute HIV infection from reaching the uninfected. In a study in the 1990s of injecting drug users in Bushwick, Brooklyn, it seemed that this situation had produced a group (“herd”) immunity. This partial group immunity may, however, have been weakened by a later decrease in overall HIV prevalence among drug injectors (due in part to syringe exchange programs) from approximately 50% in 1990 to approximately 15% currently.

The implication is that AHI may be more important in new epidemics or where prevalence is low and where high risk behavior networks operate concurrently. Social networks, norms, and processes affect behavior. Prevention strategy must trace not only sexual and drug use contacts but social connections as well.

The more important that AHI is in an epidemic, and the shorter the acute infection phase is, the more focus there should be on individuals at risk compared to public health systems. We suggest that AHI-driven epidemics can be addressed by grassroots action if people at high risk (and their social networks) understand AHI symptoms, the fact that AHI can occur without symptoms, and encourage those potentially infected to get tested—particularly if those who think they might be infected trust the health care system and can very rapidly and easily obtain testing for AHI. Current individual-focused and more institutionally-dependent strategies include standard prevention for HIV-positives, which may reduce transmission and thus AHIs to the extent that it can locate newly-infected people quickly—but will be ineffective at reducing AHI-driven infection if positives are detected only after they have seroconverted. Serosorting and altruism by positives, including those with AHI, can be effective—but, again, only works once those who are newly infected become aware of this fact. Serosorting by negatives is dangerous (unless there is absolute monogamy and/or solitary injection practices) because people with AHI usually believe themselves to be negative. Routine HIV testing, even with viral load assessment, is unlikely to identify many people with AHI in time to prevent transmission, especially in epidemic outbreaks. (It often takes weeks just to get a doctor’s appointment, and there is insufficient capacity to meet a rapidly expanding demand for testing.)

Public health can, however, initiate comprehensive community education about AHI, its risks and importance, and its clinical manifestations. Communities can be encouraged to do their own surveillance by encouraging people who test newly positive to let this be known or by noticing that some members have AHI symptoms—and then have social networks be ready to carry the message that someone in the community may have AHI so everyone can take precautions. Barriers to testing and obtaining test results should be eliminated so that tests are free, convenient, and non-threatening—which requires serious ongoing research on and understanding of what people perceive as threats, which currently probably includes name reporting or government surveillance. There is no data, for example, about how communities are really reacting to New York City’s strategies for routine HIV testing and what community members (as partially distinct from community organizations) think is important. Social network and contact tracing can be useful to the extent that they do not interfere with active community education and norm changing efforts concerning AHI prevention.



(Neighborhood people often recognize those known to do HIV tracing, which can inhibit test seeking and contact naming.)

Communities and individuals can also take important steps to protect themselves by reducing stigma and other barriers to disclosure of HIV status and AHI symptoms, by being supportive of those who do disclose, and by alerting others to the presence of AHI in the area. People can help those with suspected or confirmed HIV exposure or AHI to reduce or stop high-risk sexual and drug use risk behavior immediately by decreasing the number of partners, always using condoms, and never sharing injection equipment, or even by abstaining completely for a couple of months. Similarly, those in a local social environment where recent infections are known or believed to have occurred can similarly reduce their risk for a limited period. This is different than urging permanent abstinence. Delaying transmission can forestall an AHI outbreak.

Both public health and community AHI prevention strategies, including the rapid location of AHI cases, depend on trust and the establishment of safety norms within networks. Factors that disrupt or threaten social networks, such as gentrification, aggressive policing, and security measures that invade privacy, may weaken AHI prevention. In New York City, HIV is spreading but not nearly at the rate of the 1970s; on the other hand, as seroprevalence has declined in some communities, the “herd immunity” has disappeared. And HIV is still spreading very rapidly in many areas of the world. A great deal more research, as well as action, is needed.



The HIV Prevention Spectrum: Behavioral, Psychosocial, and Structural Barriers to AHI Detection

Robert H. Remien, Ph.D., Research Scientist, Associate Professor of Clinical Psychology, HIV Center for Clinical and Behavioral Studies, New York State Psychiatric Institute and Columbia University

The prevention opportunity afforded by AHI presents the challenge of working in an interdisciplinary way to effectively use evolving technology and to shape policy, practice, and community awareness. Since reducing HIV transmission during the primary infection stage has the potential to significantly alter the epidemic, and since tests are available to detect early infection, the task is to examine issues that may impede effective primary stage behavioral interventions.

A medical strategy depends on aware, symptomatic patients who seek health care and HIV testing from educated providers motivated to do risk assessments and the existence of policies and procedures for appropriate testing. A public health strategy requires blood samples, pooled testing procedures, AHI counseling protocols, and effective contact tracing. Traditional prevention efforts target the general population, high-risk populations, and people who are HIV-positive.

Behavioral, psychosocial, and structural obstacles to the ideal sequence of steps from HIV risk behavior to identification of acute infection and access to appropriate medical care and risk reduction education provide additional opportunities for intervention. Individuals may fail to recognize possible HIV exposure and/or may not have knowledge of or access to testing. They may not be aware of or have access to non-occupational post-exposure prophylaxis (nPEP) or assume they must wait out a three month window period to have antibody testing following a known risk episode, may use rapid testing without follow-up, or may assume that what they have is the flu when symptomatic with an acute HIV infection. Providers may lack knowledge, time, or interest in discussing HIV risk with patients or may not have access to appropriate tests or reimbursement. Test results might not be timely or accurate. Contact tracing and partner notification may not be effective or the index patient may not remain in care.

There are ongoing studies but no systematic research or data yet about the level of awareness of AHI risk among high risk groups. A study of nPEP awareness among HIV-negative partners in serodiscordant relationships (Smart Couples Study, Remien et al) found only 5% with name recognition and 27% with some knowledge of the concept. Awareness was unrelated to sexual risk behavior. In a study of men having unprotected sex with partners met through the internet (Frontiers in Prevention Study, Carballo-Diequez et al), few knew that infectiousness varied and more guessed that infectiousness was lower than higher during early infection. Despite STD transmission events within their close network of sexual partners, study participants were confident of a low HIV risk since they have frequent antibody testing. They await the advent of rapid home testing that they believe will allow instant serosorting and will influence sexual behavior such as condom use.

To increase the likelihood of AHI detection, the general public, at risk populations, and providers must be re-educated about the course of HIV infection, the timing and availability of HIV tests, and AHI symptoms and transmission risk. Providers must also gain increased comfort and skills for risk assessment and learn policies and procedures for AHI testing.



As part of a six-site NIMH study, the HIV Center at the New York State Psychiatric Institute and Columbia University will recruit 60 people with AHI and conduct quantitative and qualitative interviews (initial and two-month follow-up). The intent is to assess the feasibility of detecting and enlisting AHI patients in prevention research, study social and psychological factors in recent HIV transmissions, and determine sexual behavior, substance use, and psychological state of people with AHI.

Major prevention challenges for public health are to identify AHI cases, determine the cost effectiveness of detecting AHI and preventing transmission in a variety of settings (i.e., prenatal, substance use, other countries), and promote rapid antibody testing without increasing AHI transmission risk. It will be critical to train providers and counselors to do AHI post-test counseling for individuals who test both positive and negative. Interdisciplinary collaboration in this work must include basic, clinical, and behavioral researchers; policy makers; public health officials; providers; testing personnel; CBO program staff; and people at risk for HIV.



Community Perspectives

Daniel Raymond, Policy Director
Harm Reduction Coalition

The prospects for AHI detection can be informed by comparison with acute hepatitis C. There are at least 25,000-30,000 new hep C cases per year in the U.S., mostly in intravenous drug users (IDUs). Hep C is very treatable in the acute phase, and there could be a compelling case for identifying cases early and treating it aggressively. But that is not happening. There are problems with side effects, toxicity, cost, and adherence. With AHI, there seems to be no great advantage to individuals to be identified and treated early. Some studies have shown an early treatment benefit, but it has not been durable and has not been shown to affect the ultimate course of disease. There may, in fact, be a disadvantage since early initiation of HIV medications (five to ten years earlier than the current norm) may limit a patient's medication options later.

Predicting the potential for public health benefit from AHI detection is complicated. In syringe exchange programs (SEPs), HIV incidence is stable in the context of very high testing rates (80-90%), syringe access and prevention education. There are not many new HIV diagnoses at SEPs because these programs attract people at high risk and effectively decreases their risk. But SEPs do not directly reach the majority of injection drug users, creating a paradox for AHI detection: the people we can reach are the least likely to become acutely infected, and the bulk of new infections will not be detected since they occur in people we do not directly reach.

However, many acutely infected injection drug users may be connected through peer or social networks to people we do reach through SEPs and other services. Further consideration of risk networks, management of risk, and safety negotiation is important. Social networks can be used to promote community and public health goals, which are not necessarily the same. Currently, for example, syringe exchange programs (SEPs) cannot legally dispense needles for use by other drug users through secondary exchange, limiting their ability to implement network based interventions (e.g., encouraging SEP participants to disseminate information about risk reduction, or symptoms of AHI). Thus social network interventions may aid in detecting AHI in drug injectors. However, some of the evidence and assumptions regarding the public health value of identifying AHI derived from research on sexual transmission may not automatically apply to transmission through shared injection equipment. While there is a reasonably well-documented relationship between viral load and risk of HIV transmission through sexual behavior indicating that risks are highest during the acute phase of infection, this correlation has not been explored in relation to intravenous drug use. Similarly, in settings with relatively low HIV incidence among drug injectors, as in New York, new infections may predominantly occur sporadically rather than appearing as clusters connected to an acutely infected index case. The symptoms of AHI are also common for many reasons in drug users, the homeless, and other groups, making detection strategies based on community education about symptom recognition problematic.

One final consideration is how AHI initiatives fit into the current HIV testing milieu. People test for different reasons and have various testing patterns: some because they have started a new relationship, some because they have engaged in risk behavior, others because they happen to be near a test site or are regular, serial testers. Anticipation of a positive test result often elicits feelings of anxiety, shame, guilt, and responsibility. They are related to issues of self-identity and relationships with others, including domestic violence. AHI detection doesn't simply represent a new technology or surveillance strategy; it transforms the meanings and



experiences of HIV testing and HIV status. Whereas the availability of rapid testing eliminates the week spent waiting for results, AHI will now reintroduce a waiting period for test result confirmation. Moreover, an emphasis on community awareness and education about AHI could potentially usher in a sense of uncertainty, where individuals at recurrent risk can never feel secure in the perception that they remain HIV-negative. Such a shift would likely have implications, including potentially deleterious ones, for people's investment in adopting and maintaining risk reduction strategies. These factors and consequences must be explored through research as AHI detection efforts expand.



Action Items

At the closing session of the conference, a discussion was held to identify action items. The actions recommended can be grouped into three primary areas:

1. Educate various audiences regarding AHI
 - Communities, especially high risk communities, about acute HIV infection and its symptoms; messages must be simple and clear and provide motivation for action
 - Health care providers, including medical students and physicians; in addition to education specific to AHI, clinicians need training regarding how to talk with patients about their sexual risk behaviors
2. Develop testing technology
 - Make viral load testing more routine and efficient in laboratories and hospitals
 - Further develop the technology for rapid AHI testing
3. Conduct research to:
 - Determine effective prevention messages for various audiences (prevention of HIV acquisition and transmission)
 - Assess impact of messages regarding AHI on various communities



APPENDICES

Conference Posters Abstracts

- New York HIV Research Centers Consortium
- Mission Statement and Consortium Contact Information
- Consortium Membership



HIV Pre- and Post- Exposure Prophylaxis Among Patrons of a High Risk Commercial Sex Venue

Demetre Daskalakis, M.D.; Kyle T. Bernstein, Sc.M.; Ph.D., Robert Hagerty; Richard Hutt, R.N.; Timothy Neithercott; Richard Silvera; Michael Marmor, Ph.D.; Fred Valentine, M.D.
New York University School of Medicine

Background. Non-occupational post-exposure prophylaxis (PEP) may be effective in preventing HIV transmission and acquisition among men at high risk for infection.

Objectives. To describe the knowledge of and reported use of pre and post-exposure prophylaxis for HIV among men who have sex with men (MSM) attending two New York City bathhouses.

Methods. An ongoing enhanced HIV screening project in two New York City bathhouses began in February, 2006. MSM visiting these venues are offered rapid HIV testing as well as PCR testing for acute HIV infection. Participants also undergo risk reduction counseling and a standardized face-to-face interview regarding sexual and drug using behaviors.

Results. As of March 21, 2006, 43 MSM have participated and been tested for HIV. HIV seroprevalence was 7% (95% CI: 1.5%-19.1%). The median age of participants was 37 years (range: 22-76); 17% were African-American, 28% Latino, and 35% White. Seven (16.3%) reported currently being married to a female. Twenty-three (53.5%) reported they would not likely have been tested for HIV in the following month if testing was not offered at the bathhouse. The median number of sexual partners in the past 90 days was 10 (range: 0-80) and 80% reported these venues as the primary place to meet sex partners. The median partners/hr spent at the bathhouse was 0.33 (range: 0-2). Only 12% had ever heard of PEP, and the 1 person reporting using PEP was a medical provider. None of the participants reported use of pre-exposure prophylaxis.

Conclusions. This high risk population most likely to benefit from PEP, was largely unaware of its existence. Outreach regarding PEP to men attending bathhouse and other commercial sex venues (CSV) may be a productive primary and secondary prevention strategy.

Implications for Programs, Policy, and/or Research. CSVs may be a unique health care site for interaction with high risk individuals. Screening for STIs in the population is warranted.

Measurable Learning Objectives. By the end of the presentation participants will be able to describe the knowledge and use of PEP among high risk men at New York City CSVs.



Is Anal Receptive Sex Declining as a Route of HIV Transmission among Men Who Have Sex With Men?

Richard Hutt, R.N.; Michael Marmor, Ph.D.; Demetre Daskalakis, M.D.; Charles Gonzalez, M.D.; Robert Hagerty; Richard Silvera; Fred Valentine, M.D.
New York University Medical Center

Background. Men who have sex with men (MSM) have adopted various strategies to reduce their risk of human immunodeficiency virus type 1 (HIV) infection. In light of the known high risk of HIV infection associated with unprotected receptive anal sex, some men may have chosen to reduce this behavior while continuing other unprotected sexual activities. If so, risk factors for HIV acquisition may have changed from those observed earlier in the HIV epidemic. This change may be easiest to observe among persons with acute and recent HIV infection.

Objectives. To describe the behaviors associated with HIV acquisition among persons with acute or early HIV infection.

Methods. Subjects were participants in an ongoing project designed to identify acute or recent HIV-infections. Acute infection was defined as negative HIV-antibody status on the OraQuick rapid assay and positive RNA PCR. Recent infection was defined as positive on the OraQuick rapid assay and recent status as indicated by the STAHRs, or detuned assay. Sexual behaviors and risks for HIV infection were obtained by face-to-face interviewing with a structured questionnaire.

Results. Data is currently available on 11 participants. Ten chose to join the clinical trial. Five participants were identified as acutely infected and 6 as recently infected. HIV acquisition appeared to be by unprotected insertive anal sex in 4 individuals, insertive vaginal sex in 1 and unprotected oral sex in another. Only 45% (5/11) reported receptive anal sex in the period consistent with HIV infection.

Conclusions. Initial assessment of this small number of study enrollees suggests less receptive anal intercourse among acute and recent HIV infections than expected from epidemiologic studies conducted earlier in the HIV epidemic. Subjects at risk for HIV infection may be reducing their involvement in receptive anal intercourse allowing the potential for HIV transmission by other routes to become apparent. Further study and assessment may be helpful. Circumcision status information will be collected.



Recruitment for a Clinical Trial of Acute and Recent HIV-Infection

Richard Silvera, Demetre Daskalakis, M.D.; Charles Gonzalez, M.D.; Robert Hagerty; Richard Hutt, R.N.; Gary Carlisle, R.N.; Fred Valentine, M.D.; Michael Marmor, Ph.D. New York University School of Medicine

Background. Few cases of acute/recent HIV-infection are identified despite thousands of suspected cases annually in the New York City area.

Objective: To describe a campaign targeted at identifying acute/recent HIV-infections among high risk men who have sex with men (MSM).

Methods: NYU School of Medicine began a program for diagnosis and treatment of acute/recent HIV-infection in June, 2005. Internet banners, print advertisements, and cards describing the symptoms of acute HIV infection have been distributed targeting high risk MSM. Respondents undergo a scripted telephone questionnaire within 24 hours of inquiry. Those suspected of exposure are scheduled for HIV antibody and RNA PCR testing and counseling. HIV-positive subjects are offered entry into treatment or observational studies.

Results. As of 4/19/2006, 131 people (m=113, f=14) contacted the project. 109 (m=97, f=12) made appointments of whom 72 (m=69, f=3) presented. Median age of callers was 33 (range=18-71). Among male callers 51.3% (58/113) were recruited via print, 20.4% (23/113) via internet, 9.7% (11/113) via cards, 4.4% (5/113) via other methods, and 14.2% (16/113) did not recall. 74.1% (43/58) of male callers recruited via print reported unprotected sex (anal or oral with ejaculation) compared to 52.7% (29/55) of those recruited by other methods ($p=0.015$). Prevalence of reported sexually transmitted infections (STIs) in the past year were: 3.1% (4/131) gonorrhea, 2.3% (3/131) chlamydia, 2.3% (3/131) syphilis, 1.5% (2/131) genital warts, 1.5% (2/131) genital herpes, and 1.5% (2/131) parasitic STIs. Callers age 30-40 were more likely than callers of other ages to report an STI in the previous year ($p=0.001$). 14.2% (16/113) of male and 14.3% (2/14) of female callers did not report high risk exposures and were not scheduled. Of those scheduled, 66.1% (72/109) presented. Callers who reported unprotected anal or oral sex with ejaculation were more likely to present than those who did not ($p=0.001$). Of those who presented, 5.6% (4/72) were acutely or recently HIV-infected.

Conclusions. Recruitment targeted at high risk MSM may be an effective method of identifying acute/recent HIV-infections. It is unclear why STIs appear more frequently among 30-40 year olds but the data suggests that this group may need additional prevention efforts.



Acute HIV Infection: Where It All Begins, and Where the Outcome May Be Determined: An Ongoing Clinical Study of HIV-Specific Immune Responses and Virologic Control

F. Valentine, M.D.¹; C. Gonzalez, M.D.¹; D. Daskalakis, M.D.¹; M. Marmor, Ph.D.¹; M. Poles, M.D., Ph.D.¹; N. Bhardwaj, M.D., Ph.D.¹; D. Littman, M.D., Ph.D.¹; F. Siegal, M.D.²; W. Borkowsky, M.D.¹; H. Burger, M.D.³; R.P. Sekaly, Ph.D.⁴; J.P. Routy, M.D.⁵ New York University School of Medicine¹; St. Vincent's Medical Center², NY; Wadsworth Center, Albany³; University of Montreal⁴; McGill School of Medicine⁵

Background. After the initial relatively asymptomatic weeks of infection the subsequent course of HIV in the absence of antiretroviral therapy is characterized by the lack of HIV-specific CD4 T cell responses and a quite variable rate of progressive disease in most patients. An occasional individual emerges from the acute infection with a low level of HIV, little decrease in CD4 cells, and no signs of immunodeficiency for many years, without ever receiving antiretroviral drugs (a long-term nonprogressor-LTNP). Host genetics and viral variants can contribute to heterogeneity of outcome, but anti-HIV immune responses may play a critical role in controlling HIV in the LTNP.

Experimental design. The NIH has funded a large grant for detailed immunologic and virologic studies of acute and recent HIV infection with goals of: 1) defining types of HIV-specific immune responses associated with becoming a LTNP, 2) determining how often starting antiretroviral drugs during acute infection preserves effective anti-HIV immunity, 3) whether the additional enhancement of HIV-specific immune responses with a vaccine results in more individuals behaving like LTNP and controlling HIV after discontinuing antiretroviral drugs.

A critical requirement of this study is to identify individuals as early as possible after infection. Potential participants receive free rapid antibody and PCR tests for HIV. They may elect to receive antiretroviral drugs, or to remain untreated during their early infection. Although a combination of drugs is provided free, patients may elect to receive any effective combination of drugs.

Immunologic measurements include: enumeration of subtypes of lymphocytes, Dendritic Cells; studies of functional responses of T cells to HIV antigens and peptides by multiple parameters; class II tetramers; sequential HIV sequencing to monitor viral epitopes; antigen presentation by DCs; interferon- α ; lymphocyte activation and apoptosis, and thymic output of T cells using α/β TREC ratios. Measurements are repeated during resolution of the acute infection, and sequentially. **Virologic control** is assessed by careful monitoring of viral load and CD4 cells during a supervised discontinuation of antiretroviral drugs after one year of therapy, with predetermined rules for restarting drugs as needed.

Preliminary data indicates that some individuals treated during acute and recent HIV infection will develop HIV-specific CD4 T cell responses and control HIV viral load even after discontinuing antiretroviral therapy. Immunologically, these individuals appear to resemble LTNPs.

Conclusions. In contrast with patients initiating antiretroviral therapy during established HIV infection, individuals treated during acute infection may control HIV after discontinuing drug therapy. Many additional patients must be studied to determine exactly what patterns of immune responses are responsible for this control of HIV.

To enroll a potential acute or recent infection call 212-263-3544.



The CNS in Acute and Early HIV infection: The CHARTER Study

Susan Morgello, M.D.; David M. Simpson, M.D.; Munib Mundia, M.D.; Anita Rau, B.A.; Letty Mintz, N.P. The Mount Sinai School of Medicine

Experimental models and natural history studies in man suggest early penetration of the CNS in HIV infection. However, there is a dearth of information regarding the effect of HAART on this phenomenon, or the relevance of early therapy to long term CNS outcomes. The CNS HIV Anti-Retroviral Therapy Effects Research (CHARTER) study is a longitudinal, observational, multi-site study focused on the characterization of HIV-related nervous system disorders, and their relationship to anti-retroviral therapies. In recognition of the important questions regarding the potential for early formation of CNS viral reservoirs, CHARTER is currently opening a sub-study for the evaluation of individuals with acute or early HIV infection. Eligibility criteria for subjects include: 1. acute (within 6 weeks) or early (within 1 year) HIV infection; and 2. either naïve to anti-retroviral therapy or within 2 weeks of its initiation. Subjects will be asked to complete a screening visit to document their eligibility, unless they are enrolled in another acute/early infection protocol (as, for example, the Acute Infection and Early Disease Research Program – AIEDRP). Once enrolled in CHARTER, at baseline subjects will undergo a 20 minute neuropsychological testing battery, psychiatric and substance use screens, a neurologic evaluation, phlebotomy, urine toxicology, and a buccal swab. If willing, subjects will be asked to undergo a lumbar puncture, neuroimaging (MRI/MRS), and an extended neuropsychological battery. Subjects will be followed at 6 month intervals with all clinical modalities (neuropsychologic, psychiatric, neurologic, and laboratory assessments) except neuroimaging, which will be performed on an annual basis. With this pilot program, we hope to begin the documentation of early CNS events in HIV infection, with the long term goal of determining what therapeutic decisions give rise to optimal neuromedical outcomes.



A Multisite Initiative to Understand the Social and Psychological Context of Acute HIV Infection

Robert H. Remien, Ph.D.¹; Robert Dubrow, M.D., Ph.D.²; Jennifer Hirsch, Ph.D.¹; Michael Stirratt, Ph.D.¹; Mark Bradley, M.D.¹; Kenneth Mayer, M.D.³; Wayne Steward, Ph.D.⁴; Hong-Ha Truong, Ph.D.⁴; David Seal, Ph.D.⁵; Anke A. Ehrhardt, Ph.D.¹; Igor Grant, M.D.⁶; Jeffrey A. Kelly, Ph.D.⁵; Michael Merson, M.D.²; Steven Morin, Ph.D.⁴; Mary Jane Rotheram-Borus, Ph.D.⁷

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Program Goals/Objectives. This multi-site study entails formative research on which to base interventions for preventing HIV transmission during acute HIV infection (AHI). Objectives are to (1) determine the feasibility of detecting and recruiting acutely infected individuals for prevention research, (2) document the social and psychological context of recent HIV transmissions, and (3) assess sexual behavior, substance use and mental health among individuals diagnosed with AHI. This multi-site initiative is coordinated and funded by NIMH at six AIDS prevention centers [NYSPI/Columbia University, Yale University (in collaboration with Brown University), Medical College of Wisconsin, UCLA, UCSD, and UCSF].

Background. AHI is associated with high viral loads, and modeling suggests that this early phase of infection, before the virus is detected by traditional antibody testing, is a driving force in heterosexual transmission in Sub-Saharan Africa as well as in concentrated US epidemics. Given the likelihood of high transmissibility during AHI, it is imperative that we understand its associated psychosocial experiences in order to devise effective prevention strategies.

Program Description/Methods. Each of the six sites will enroll 10 individuals with AHI. Participants will be 18 years or older and diagnosed with AHI (presence of HIV RNA by nucleic acid amplification testing and a negative or indeterminate HIV antibody test result by standard enzyme immunoassay or Western blot). Participants complete both semi-structured qualitative interviews and structured behavioral and psychological assessments at two time points: within two weeks of AHI detection and at 8-week follow-up. The interviews explore the context of transmission, circumstances of AHI detection, and experiences since detection. The structured assessments determine mental health and sexual and drug use behavior in the two months before and after detection of AHI.

Challenges Encountered and/or Lessons Learned. Enrollment and data collection is in process. Progress to date suggests multiple barriers to the identification and recruitment of AHI cases. We are working to document, understand, and overcome these barriers to achieve our recruitment goals.

Next Steps and/or Recommendations. Effective risk reduction interventions for individuals with AHI could significantly decrease new infections. This multi-site collaboration will provide a strong foundation for intervention development by improving understandings of AHI detection, the social and psychological context of recent HIV transmissions, and appropriate timing and mode for intervention delivery.



Current Research on Acute HIV Infection
 by New York HIV Research Centers Consortium Member Centers
 (as of February 2006)

<i>Center</i>	<i>Type(s) of Research</i>	<i>Contact Information</i>
Aaron Diamond AIDS Research Center (ADARC)	-Basic Laboratory Science -Clinical/Biomedical Science	Martin Markowitz, MD Clinic Director and Principal Investigator on Acute Infection and Early Disease Research Program Grant mmarkowitz@adarc.org
Center for AIDS Research (CFAR), New York University School of Medicine	-Basic Laboratory Science -Clinical/Biomedical Science -Behavioral/Prevention Science	Fred Valentine, MD Director of NYU CFAR fred.valentine@med.nyu.edu
Center for Interdisciplinary Research on AIDS (CIRA), Yale University School of Medicine	-Clinical/Biomedical Science -Behavioral/Prevention Science	Robert Dubrow, MD, PhD Associate Clinical Professor, Yale School of Public Health robert.dubrow@yale.edu
HIV Center for Clinical and Behavioral Studies, NYS Psychiatric Institute and Columbia University	-Behavioral/Prevention Science	Patricia Warne, PhD Associate Director paw6@columbia.edu
HIV Center for Women and Children, SUNY Downstate Medical Center	-Clinical/Biomedical Science -Epidemiological/Public Health	Jack A. DeHovitz, MD, MPH Director Jack.DeHovitz@downstate.edu
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New York State Department of Health	-Basic Laboratory Science -Epidemiological/Public Health	James M. Tesoriero, PhD Director, Office of Program Evaluation and Research jmt07@health.state.ny.us



New York HIV Research Centers Consortium Mission Statement

The New York HIV Research Centers Consortium is a collaborative project of HIV research centers in the greater New York area. The mission of the Consortium is to enhance scientific knowledge of the HIV/AIDS epidemic and related issues by facilitating inter-institutional, multi-disciplinary collaborations by scientists affiliated with HIV research centers in the New York region. There are currently 21 member Centers in the Consortium.

The aims of the Consortium are:

1. To promote inter-institutional exchange of information about our work
2. To foster inter-institutional, multidisciplinary collaboration
3. To enhance the dissemination of knowledge to public policy makers, researchers, and HIV-affected communities
4. To promote the application of knowledge obtained to the New York area and to other domestic and international populations

For information on the Consortium, please contact a member of the Steering Committee:

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New York HIV Research Centers Consortium (June 2006)

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AIDS Research Program, Montefiore Medical Center

Baron Edmond de Rothschild Chemical Dependency Institute (CDI), Beth Israel Medical Center

Center for AIDS Research (CFAR), New York University School of Medicine

Center for Drug Use and HIV Research (CDUHR), National Development and Research Institutes, Inc.

Center for Health/HIV Intervention & Prevention (CHIP), University of Connecticut

Center for Health, Identity, Behavior & Prevention Studies (CHIBPS), Department of Applied Psychology, New York University

Center for HIV/AIDS Educational Studies and Training (CHEST), Hunter College

Center for Infectious Disease Epidemiologic Research (CIDER), Columbia University Mailman School of Public Health

Center for Interdisciplinary Research on AIDS (CIRA), Yale University School of Medicine

Center for Urban Epidemiologic Studies (CUES), New York Academy of Medicine

Columbia University, Center for AIDS Research (CU-CFAR)

Harlem Health Promotion Center, Columbia University Mailman School of Public Health

HIV Center for Clinical and Behavioral Studies, NYS Psychiatric Institute & Columbia University

HIV Center for Women and Children, SUNY Downstate Medical Center

Hunter College Center for Community and Urban Health

Mount Sinai Center for AIDS Research

New York City Department of Health and Mental Hygiene, HIV Epidemiology Program

New York State Department of Health, Office of Program Evaluation and Research, AIDS Institute

Social Intervention Group (SIG), School of Social Work, Columbia University