HIV Testing and Prevention Strategies

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A number of presentations at the 15th Conference on Retroviruses and Opportunistic Infections focused on approaches to identify HIV-infected persons for early referral to treatment and prevention. This year's conference also highlighted the challenges we face in developing effective biomedical preventions, with reports on the failure of a candidate HIV vaccine and chronic herpes simplex virus type 2 suppression to prevent HIV acquisition, and the failure of male circumcision for HIV-seropositive men to prevent HIV transmission to their uninfected female partners. On the other hand, there were presentations on progress being made in animal models of microbicides and preexposure prophylaxis and on prevention of HIV transmission through breastfeeding. Several interesting presentations addressed the need to move beyond individual-level interventions into those that target sexual partnerships, communities, and policy changes, as these larger factors are driving the HIV epidemic in the United States and globally.

HIV Testing Programs

Testing programs for HIV are useful in identifying the estimated 25% of persons in the United States who are unaware of their HIV infection and the larger number of persons unaware of their status globally. Testing programs also provide insight into HIV infection rates and risk factors for infection on a population level.

It has been challenging to increase rates of HIV testing in clinical settings in the United States. Heffelfinger (Abstract 533) presented data on 3 programs in emergency departments (EDs) to offer point-of-care rapid HIV testing to medically stable patients 13 years of age or older on an opt-out basis. Each program was developed locally, tested fewer than 10% of patients seen in their EDs, and identified approximately 1% of those tested to be newly diagnosed with HIV infection. Linkage to care was excellent in 2 programs (93% and 100%) and lower in the third (63%). The estimated cost per newly diagnosed patient linked to care was approximately $11,000. Such enhanced testing programs will have to be tailored to the specific needs of the health care setting, but more must be done to improve testing rates and ensure linkage to care for infected persons in all programs.

Greater success in roll-out of testing was reported in a Ugandan antenatal clinic (Abstract 537). During the opt-in period, an average of 549 clinic attendees (82%) were counseled each month and 270 (40%) were tested, of whom 20 (7.3%) per month were HIV-seropositive. In the year after implementation of opt-out testing, 688 (98%) were counseled each month, and 612 (88%) received HIV testing. An average of 36 women per month (5.8%) were found to be HIV-seropositive. This result represented a more than doubling in the proportion of women agreeing to be tested, with a nearly comparable increase in the absolute number of infections detected through this program. The presenters also spoke to the need to maintain a stable supply of test kits.

Cohan and colleagues (Abstract 535a) addressed the impact of switching from standard to abbreviated pretest counseling in an antenatal setting in San Francisco. She presented data from a randomized control trial of 278 women assigned to standard versus abbreviated pretest counseling. Women in the abbreviated counseling arm had slightly lower knowledge scores than those in the standard pretest counseling arm (78.4% vs 83.7% correct, respectively) but similar satisfaction and decision-making scores. These data support efforts to streamline pretest counseling in antenatal settings.

Other presentations focused on implementing testing in hard-to-reach populations. Several focused on HIV testing in Washington, DC, one of the most heavily affected cities in the United States. Castel and colleagues (Abstract 543) reported on the very high rates of late presenters for care. From 1997 to 2006, 66% of AIDS patients in Washington, DC, had received a diagnosis of HIV within 1 year of their AIDS diagnosis, and 53% had been HIV-tested within 1 month of their AIDS diagnosis. Blacks, Hispanics, persons older than 60 years, heterosexuals, uninsured persons, and those born outside of the United States were all more likely than other groups to receive their HIV diagnosis late. Over that 10-year period, there was no substantial improvement in the rates of late testing, pointing to an urgent need to implement new HIV-testing strategies.

In a separate abstract, Castel and colleagues (Abstract 541) presented data on rapid testing of more than 32,000 Washington, DC, residents from June 2006 onward. Approximately 2% (638) of the clients had a positive initial screening result, one-fourth of whom stated they had never been tested before and nearly one-third of whom stated they would not have been tested if it had not been offered.

Malave and colleagues (Abstract 538) presented data on testing in homeless shelters in New York City. Overall, approximately one-half of those offered testing accepted, 1.8% of whom had a preliminary positive test result. Of these, approximately one-half were confirmed seropositive, and an additional 13% were already known to be seropositive. The remainder were largely lost to follow-up or refused confirmatory testing, suggesting that other strategies are needed to help those who screen positive to access care.

Walensky (Abstract 534) sounded a cautionary note about rates of false-positive test results using a particular rapid

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test (OraQuick ADVANCE HIV 1/2 Antibody Test, Abbott Diagnostics). In an ED setting, they found 31 patients to have initially reactive test results, only 5 of whom were confirmed to be HIV-seropositive (positive predictive value [PPV], 16.1%; expected PPV, 75%, based on the manufacturer's specifications). The specificity of the test in this setting (96.9%; 95% confidence interval [CI], 95.7%-98.1%) was significantly lower than published values (99.8%; 95% CI, 99.6%-99.9%). Of the 19 patients with faint lines appearing on the test result, all were ultimately determined to be HIV-seronegative, suggesting that training focus on correct interpretation of faint lines. Western blot results were indeterminate in 50% of those with false-positive responses.

Delaney and colleagues (Abstract 535b) addressed challenges with rapid-testing algorithms requiring that patients return for results of laboratory-based confirmatory tests. He presented data from 3043 clients tested at 8 counseling and testing sites and 8570 patients screened in 2 EDs; each site used its own algorithm using results of multiple rapid tests to identify and confirm HIV infection at point of care. Overall, 101 clients (0.9%) tested initially seropositive, 78 of whom were seropositive on all confirmatory tests and were referred immediately for care. This approach limits the need for confirmatory laboratory-based tests to those with discordant test results on rapid tests, and allows for rapid referral of most newly identified HIV-infected persons into care.

HIV Vaccines

Data were presented at this year's conference on the STEP Trial, a test-of-concept vaccine trial conducted by the HIV Vaccine Trials Network, the National Institute of Allergy and Infectious Diseases, and Merck & Co, Inc. (Abstracts 88LB and 89LB). This trial enrolled 3000 HIV-seronegative volunteers from 34 sites in the Americas and Australia to evaluate the efficacy of a trivalent adenovirus type 5 (Ad5) vaccine (Merck) to prevent HIV acquisition, lower early viral load setpoint, or both.

Abstract 88LB focused on efficacy results from an interim analysis of the 1500 volunteers with low preexisting Ad5 neutralizing antibody (NAb) as well as post hoc analyses on the entire group. Vaccinations in the trial were halted when data from the first interim analysis crossed prespecified futility boundaries for both the infection and viral load endpoints. In those participants with baseline Ad5 NAb titers at or below 200 units, HIV infection rates were 2.92 per 100 person-years in vaccine recipients and 2.51 per 100 person-years in placebo recipients. Mean plasma HIV RNA levels at approximately 3 months postdiagnosis of infection were 4.61 $\log_{10}$ copies/mL in vaccinees and 4.41 $\log_{10}$ copies/mL in placebo recipients. Only 1 infection was seen in a woman, so post hoc analyses were limited to male study participants regardless of baseline Ad5 titer.

Post hoc analyses revealed an increased number of HIV infections in vaccine versus placebo participants (49 vs 33 infections, respectively). The increased infection rate in vaccinees appeared to be concentrated in male participants who were both uncircumcised and Ad5-seropositive (Ad5 NAb > 18 units). In various multivariate models, the estimated increased risk associated with receiving the vaccine (relative hazard) for men who were both uncircumcised and Ad5-seropositive ranged from 4.2 to 4.8, fairly consistent along a spectrum of multivariate models.

On the other hand, there was no evidence of increased risk to vaccinees in the subpopulation who were both circumcised and Ad5-seronegative, with relative hazards ranging from 0.6 to 0.8 in multivariate models. Hazard rates for the subgroups of men who were either uncircumcised or Ad5-seropositive (but not both) were intermediate between these 2 groups. The vaccine did not cause infection itself but may have made study participants more susceptible to infection if later exposed. Additional analyses are being conducted to rule out other potential confounders, such as herpes simplex virus (HSV)-2 status, human leukocyte antigen type, and sexual network clusters.

Robertson (Abstract 89LB) presented the initial laboratory data exploring reasons for lack of protection from the vaccine as well as potential mechanisms for increased risk of HIV acquisition among vaccinees. The vaccine was immunogenic, generating positive interferon gamma (IFN-γ) enzyme-linked immunospot assay responses in more than three-fourths of study participants with low preexisting Ad5 immunity (NAb < 200 units) and more than one-half of study participants with high preexisting immunity (NAb > 200 units). Similarly, results of intracellular cytokine staining confirmed that the vaccine generated both CD8+ and CD4+ cell responses, and those with preexisting Ad5 immunity had lower levels of response. There was no substantial difference between immune response in those who later became HIV-infected and those who remained HIV-uninfected, suggesting that the quantity, quality, breadth, or homing of the immune responses generated by this vaccine were insufficient to confer protection.

In exploring potential mechanisms for increased HIV-acquisition risk, there appeared to be no difference between vaccinees and placebo recipients in the level of activated CD4+ T cells in peripheral blood. The CD4+ and CD8+ T-cell responses to an empty Ad5 vector were lower in participants with preexisting Ad5 NAb titers over 200 units, failing to provide an explanation for increased HIV-infection rates in this group. Additional studies are underway or being planned to explore both the vaccine's failure to protect and the potential for increased HIV-acquisition rates. A process for soliciting the input and engagement of the broad scientific community was also described.

Two plenary lectures described the challenges posed in developing an HIV vaccine and urged 2 related, but somewhat different paths forward. Desrosiers (Abstract 91) summarized the obstacles facing development of a successful HIV vaccine and argued that efforts should focus on basic discovery, particularly efforts to create broadly neutralizing antibodies. He also argued that efficacy trials that produce

negative results could have a negative impact on the research field, and that a high threshold of protection in stringent simian immunodeficiency virus (SIV) challenge models be attained before moving new candidates into efficacy trials.

Nathanson (Abstract 92) also argued for the need to devote additional thought and resources into basic discovery. He urged that new, innovative mechanisms be developed to stimulate and fund high-risk research of novel ideas, and he used as an example strategies that focus on development of broadly neutralizing antibody. In contrast to Desrosiers, Nathanson pointed out that the predictive value of nonhuman primate challenge models is still unknown. He recommended that a hierarchy of nonhuman challenge models be built and validated through data generated from human efficacy trials. He also urged that nonvaccine prevention efforts be moved forward aggressively, as the global epidemic needs efforts now to stem the tide of new infections.

Herpes Suppression

Celum and colleagues presented final data from a randomized, placebo-controlled trial of HSV suppression in HSV-2-seropositive, HIV-seronegative men and women in Peru, the United States, Zambia, Zimbabwe, and South Africa (Abstract 32LB). The HIV Prevention Trials Network 039 study evaluated the use of 400 mg of acyclovir, given twice daily, to prevent HIV acquisition in 1871 men who have sex with men (MSM) and 1380 heterosexual women. Seroincidence rates of HIV were 3.9 per 100 person-years in the acyclovir arm and 3.3 per 100 person-years in the placebo arm (relative risk [RR], 1.16; 95% CI, 0.83-1.62).

There were no significant differences in vaccine efficacy by sex, adherence measures, or history of clinical genital ulcer disease. The rate of clinical genital ulcers decreased by 37% in the acyclovir arm. Surprisingly, the amount of viral shedding from these ulcers was reduced by acyclovir only in the United States but not in the Peruvian or African cohorts. Although adherence appeared to be excellent as measured by pill count and self-report, additional efforts are underway to uncover potential over-reporting on adherence measures or differing drug pharmacokinetics in these different populations. A companion trial is underway to explore the potential for HSV suppression in HIV-infected persons to prevent HIV transmission; results from this trial are expected within 1 year.

Male Circumcision

A number of ecological and observational studies previously suggested a beneficial effect of male circumcision in preventing HIV acquisition in heterosexual men. Then, over the past several years, results from 3 randomized controlled trials in South Africa, Uganda, and Kenya demonstrated that adult male circumcision cut the rate of HIV acquisition by 60% in heterosexual men. This year's conference included new data on beneficial effects of male circumcision for HIV-seronegative men and their female partners but also concerns about potential harm to the female partners of HIV-seropositive men who are circumcised as adults.

Tobian and colleagues (Abstract 28LB) presented data from the randomized controlled trial of adult male circumcision in Rakai, Uganda. In that trial, HIV-seronegative adult men underwent randomization to immediate male circumcision (intervention arm) or circumcision delayed for 24 months (control arm). Circumcision was associated with a 24% reduction in HSV-2 acquisition among the 3516 men who were HSV-2-seronegative at enrollment. Acquisition rates of HSV-2 were 8.2% in the intervention arm and 10.8% in the control arm (RR, 0.76; 95% CI, 0.60-0.96).

Tobian also reported a significant decrease in sexually transmitted infections in the 1608 married women linked to male study volunteers, including a 24% reduction in genital ulcer disease (RR, 0.76; 95% CI, 0.60-0.97), 47% reduction in trichomoniasis (RR, 0.53; 95% CI, 0.33-0.85), and 20% reduction in bacterial vaginosis, (RR, 0.80; 95% CI, 0.71-0.89). The prevalence of severe bacterial vaginosis, development of bacterial vaginosis, and persistence of bacterial vaginosis were also reduced in intervention wives compared with control wives. All of these factors may have favorable effects on HIV acquisition rates in this population.

Wawer and colleagues presented data on a companion trial of male circumcision among HIV-seropositive men in Rakai, Uganda (Abstract 33LB). In this study, 922 HIV-seropositive men with CD4+ counts at 350 cells/μL or higher underwent randomization to immediate circumcision or circumcision delayed for 24 months. Of this group, 770 were married and 566 wives enrolled, 245 of whom were HIV-seronegative.

Among the 245 HIV-seronegative women, HIV infection rates were somewhat higher in the wives of men in the male circumcision arm than in wives of men in the intervention arm (14.4% vs 9.1%; incidence rate ratio, 1.59; 95% CI, 0.7-4.3), although these differences were not statistically significant. In the first 6 months of follow-up, HIV incidence was 27.3 per 100 person-years in wives of men in the circumcision arm and 17.8% in wives of men in the control arm, dropping in the 6- to 24-month period to 5.7 per 100 person-years in wives in the circumcision arm and 4.1 per 100 person-years in wives in the control arm.

It appeared that the risk was particularly concentrated among couples who resumed sexual activity more than 5 days before certification of wound healing; of this group, 5 of 18 women (27.8%) became infected, compared with 6 of 63 (9.5%) of those who did not resume sexual activity until 5 or fewer days before certification of healing or after certification. The latter rate was comparable to infection rates in the wives of uncircumcised men (6/68, 8.8%) in the first 6 months of follow-up.

There were no serious adverse events associated with male circumcision in this trial, and the rates of moderate circumcision-associated adverse events were comparable to those reported in HIV-seronegative men (3.1 for each study). Wound healing was slower in this trial of HIV-seropositive men than

in the previous trial in HIV-seronegative men, with 73% of the men in this trial having complete wound healing by 30 days postcircumcision but an 83% healing rate in the same time period in the HIV-seronegative men ($P < .001$). Results of this study suggest that even in relatively healthy HIV-seropositive men, male circumcision is associated with delayed healing and a potential for increased HIV transmission to uninfected female partners, particularly if sexual activity resumes before complete healing.

Auvert (Abstract 2) made a case for widespread implementation of male circumcision in HIV-uninfected men in sub-Saharan Africa. He pointed out that previous modeling exercises suggest that this procedure could avert 2 million to 8 million new HIV infections over 20 years and cost less than the treatment that would be required for those infected.

One of the barriers to widespread implementation is the low number of adequately trained medical practitioners to conduct this surgical procedure. Auvert and colleagues modeled the number and cost of providers if circumcision were made available in the 14 countries in sub-Saharan Africa, where the prevalence of male circumcision is less than 80% and HIV prevalence is greater than 5%. According to this model, 2357 circumcisers would be required in the first 5 years of rollout, and 626 in years 6 through 10. Although cost would be $965 million for the first 5 years, the program would save an estimated $4 billion by year 20 because of reductions in the number of infected persons.

Preexposure Prophylaxis and Microbicides

Several presentations and posters focused on the use of various topical and oral agents, including antiretroviral drugs, to prevent HIV acquisition. Substantial work is being conducted in development of animal models to evaluate the safety of microbicide approaches. Mesquita and colleagues (Abstract 26) presented data from polarized epithelial cell cultures and murine genital tract tissue that may explain results presented at last year's conference that cellulose sulfate, used as a topical microbicide, may be associated with an increased risk of HIV acquisition. In their model, cellulose sulfate caused epithelial disruption and loss of cellular junctions, leading to increased translocation of HIV across the epithelial barrier.

Denton and colleagues (Abstract 558) presented data, also published recently,[1] that humanized mice are susceptible to vaginal HIV infection; they used this model to demonstrate efficacy of systemically administered tenofovir/emtricitabine in protecting against vaginal HIV challenge. Veazey and colleagues (Abstract 560) provided data from nonhuman primate studies suggesting that recombinant RANTES (regulated upon activation, normal T-cell expressed and secreted) analogues may provide protection against simian-HIV (SHIV) acquisition.

An update on oral and topical administration of preexposure prophylaxis (PrEP) was provided by Kashuba (Abstract 95). She noted that although tenofovir and emtricitabine (2 drugs being used in current clinical trials of preexposure prophylaxis) are present in higher concentrations in genital fluid than in the blood, drug levels in the animal challenge models that were most highly protective were 2-$\log_{10}$ copies/mL higher than levels achieved in the genital compartment in standard dosing in women. She urged that additional studies be conducted to define intracellular levels of these agents systemically and in the genital tract in humans.

Karim also presented an overview of microbicides (Abstract 96), noting the shift in the field from broad-spectrum antimicrobial drugs to a greater focus on antiretrovirals. She also noted the shift to different formulations and modes of delivery, including strategies that would unlink the timing of microbicide use from sexual acts.

Data were presented from several clinical trials of PrEP. Analysis of one seroconverter from a PrEP trial in Africa found no evidence of tenofovir resistance mutations in this participant, who reported excellent adherence to study medication (Abstract 570). Baseline data of risk behaviors reported by injection drug users (IDU) (Abstract 568) and MSM (Abstract 569) were also presented, suggesting that risk levels are high in these populations. Efficacy results will be available from 2009 to 2011 from these trials.

Paltiel and colleagues (Abstract 563) modeled the cost-effectiveness and impact of PrEP on a population level, suggesting that this approach could be cost-effective and reduce HIV infection rates if targeted to populations with seroincidence rates in excess of 2% per year, if cost is low, efficacy is very high, or both. Abbas and colleagues (Abstract 564) modeled the emergence and spread of HIV drug resistance if PrEP is used and found that this risk could be minimized by also targeting those at highest risk and using drugs with highest efficacy levels.

Prevention of HIV Transmission Through Breastfeeding

Several oral sessions and abstracts focused on prevention of mother-to-child transmission. Abstracts focused on strategies involving maternal or infant antiretroviral therapy are presented in the review article by Wilkin and colleagues in this issue (pp. 31-60); those presentations focused predominantly on breastfeeding practices are presented here.

Becquet and colleagues (Abstract 46) presented pooled data from Cote d'Ivoire and South African cohorts of 1195 breastfed infants. Infection rates in infants predominantly breastfed were similar to those exclusively breastfed, with one important distinction. The subgroup of infants who were exposed to solid foods at least once during the first 2 months of life had an increased risk of infection (hazard ratio 2.9; 95% CI, 1.1-8.0).

In Bostwana, 1200 HIV-infected pregnant women underwent randomization to either breastfeeding (with infant zidovudine for 6 months) or formula feeding (with infant zidovudine for 1 month). By 24 months of age, 8.3% of infants in the breastfed arm and 10.5% of infants in the formula-fed arm had died. The pattern of mortality was dif-

ferent in the 2 arms; the majority of deaths occurred in the first 3 months in the formula-fed infants, but most deaths in the breastfed arm occurred between 6 and 12 months of age. Independent risk factors for infection in multivariate analysis included infant HIV infection, low birth weight, and lack of a latrine.

Data from the Kisumu Breastfeeding Study (KiBS) (Abstract 645) evaluated the uptake of breastfeeding recommendations among women who opted for exclusive breastfeeding for 6 months after an intensive educational program. Of 504 infants born to these mothers, 21% were mixed-fed before 5 months of age, but only 8% were breastfed beyond 6 months of age in the absence of HIV infection or antiretroviral use. This result suggests substantial progress, although reasons should be explored for departure from World Health Organization recommendations in a minority of women.

Thomas and colleagues (Abstract 646) reported on the success of a safe water system in reducing infant diarrhea in the KiBS study. The safe water system (education, point-of-use water chlorination, and safe water storage vessels) led to significant reductions in infant diarrhea (RR, 0.72; 95% CI, 0.57-0.91), although most of the effect was seen before weaning. Peri-weaning infection rates were quite high both before and after implementation of the safe water system.

Several studies evaluated the properties of breast milk that may contribute to HIV transmission to infants. Semrau and colleagues (Abstract 650) presented data on the effects of mastitis on breast milk HIV RNA level. Among 38 HIV-infected Zambian women with mastitis, HIV RNA level significantly increased from baseline 2.57 $\log_{10}$ copies/mL to 2.9 $\log_{10}$ copies/mL during mastitis, then fell to rates similar to baseline levels after resolution (2.45 $\log_{10}$ copies/mL). There was no statistically significant increase in the breast milk HIV RNA level in the unaffected breast, supporting the recommendation that HIV-infected women with mastitis breastfeed from the unaffected breast. Permar and colleagues (Abstract 652) presented data from rhesus macaques suggesting that although the kinetics of the SIV-specific cellular immune response in breast milk mirrored that seen in blood, the magnitude of the peak response was more than twice as high in breast milk as in the blood, and the duration of the high-level response was longer. Permar also reported that the breast milk HIV RNA level was 1 to 2 $\log_{10}$ copies/mL lower in breast milk than in blood, both at peak and setpoint, suggesting better control of viral replication in the breast milk compartment.

Factors Driving the US HIV Epidemic

One symposium at this year's conference focused on 4 populations at substantial risk for HIV infection and proposed strategies for reducing the epidemic within these populations (Abstracts 53–56). All 4 presenters in the symposium focused on intersecting epidemics (syndemics) of HIV, childhood sexual abuse, substance use, domestic violence, poverty, and social inequalities driving their respective epidemics. All also called for a broadening of research agendas beyond the individual-level interventions to include focus on partners, community, public health infrastructure, and government policy.

Stall and colleagues (Abstract 53) focused on the epidemic in MSM, the only group with continued increasing rates of HIV and AIDS in the United States. They modeled HIV prevalence rates based on data from 20 independent studies of HIV incidence. Among the general MSM population, they estimate that HIV prevalence rates are below 5% in 20-year-old men but rise steadily to 25% in 30-year-old men and 41% in 40-year-old men. Projections for African-American MSM are even worse, with prevalence rates estimated, at 40% by age 30 and 60% by age 40. Stall cites work by Millett that points to lower reported risk among African-American MSM but also lower rates of knowledge of HIV serostatus and lower rates of access to potent antiretroviral therapy. He likened the current focus on individual-level interventions to the era of zidovudine monotherapy and called for prevention regimens that include interventions at the partnership, community, public health, and policy levels.

Adimora (Abstract 54) traced the epidemic in African-American women, where population prevalence rates are 1% in 18- to 39-year-olds and 2.8% in 40- to 49-year-olds according to the National Health and Nutrition Examination Survey. She also pointed to data for African-American women suggesting higher HIV infection rates, even when at comparable levels of risk with white women, and she noted the substantial proportion of women newly diagnosed with HIV who were unaware of partner risk. Adimora traced many of the population-level forces driving these increased infection rates, including factors leading to higher HIV prevalence in African-American men and forces driving concurrency of sexual partnerships.

Rosser (Abstract 55) addressed strategies to reduce HIV transmission from HIV-seropositive persons, arguing that once persons learn of their HIV-serostatus, most substantially reduce or stop risk activities with HIV-seronegative persons. He suggested that the upswing in the use of the Internet to increase the number and efficiency of finding sexual contacts argues for a need to build Internet-based prevention approaches, and he demonstrated one such intervention. Rosser also urged clinicians to provide HIV testing to identify infected persons unaware of their status and to counsel their HIV-seropositive patients about strategies to reduce HIV transmission. He, too, called for structural and environmental interventions to reduce HIV transmission rates in affected communities.

Finally, Vlahov (Abstract 56) addressed the role of recreational drugs in the HIV epidemic. Rates of HIV infection among IDUs have declined substantially since the beginning of the AIDS epidemic, but use of noninjection substances continues to play a major role in sexual transmission. Vlahov addressed the need to intervene on numerous levels and used as an example, evaluation of the Expanded Sy-

ringe Access Demonstration Program in New York. By intervening not only with the IDUs but also with pharmacists and the community, the program was able to improve perceptions of the program itself as well as decrease syringe exchange among IDUs. This type of multitiered intervention program may have a greater likelihood of success than those focusing only on the drug user or the pharmacist.

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A list of all cited abstracts appears on pages 69-77.

Additional Reference

1. **Denton PW,** Estes JD, Sun Z, et al. Antiretroviral pre-exposure prophylaxis prevents vaginal transmission of HIV-1 in humanized BLT mice. *PLoS Med*. 2008;5:e16.

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