Postexposure Prophylaxis: Needles, Sex, and Drugs

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Current rationale for and practice of prophylaxis after occupational, sexual, or injection drug use exposure to HIV-1 were discussed by Julie L. Gerberding, MD, MPH, at the Atlanta course.

Postexposure Prophylaxis for Occupational Exposure

Statistics for the United States through mid-1999 and for other countries through the end of 1997 indicate totals of 97 documented cases and 192 possible cases (ie, seroconversion was not documented) of occupational HIV-1 infection in health care personnel. The majority of these cases (55 documented and 136 possible) have been in the United States, a finding that may reflect the absence of accurate reporting in many other parts of the world. A retrospective study by Cardo and colleagues from the Centers for Disease Control and Prevention (CDC) showed that risk factors for transmission include deep injury, visible blood on the sharp device causing injury, exposure to blood from a source patient with preterminal AIDS, and injury caused by a device that had been inserted in an artery or vein.

A large number of prospective cohort studies have provided convincing evidence that on average, 99.7% of occupational exposures to HIV do not result in infection. Available data suggest that immunologic mechanisms during the first few days after exposure may be the key to determining the final outcome. These findings also provide the rationale for postexposure prophylaxis.

In brief, simian immunodeficiency virus infection models have shown that at 24 hours after inoculation of the vaginal mucosa, virus is largely associated with

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dendritic cells in the mucosal tissue, with no evidence of active replication. At 24 to 48 hours later, virus is found in the germinal centers of the lymph nodes and is undergoing immune processing and active replication. By 5 days, both free and cell-associated virus can be detected in the circulation. Cell-mediated immune response to viral antigens can be detected even in animals that do not subsequently exhibit established infection, suggesting a role for cell-mediated immunity in preventing infection. Similar T-cell responses to specific HIV antigens have been observed in humans with high-risk exposures in whom infection fails to become established. In addition to indicating that immune response may be active in clearing infection, these findings support the biologic plausibility of antiretroviral treatment aiding in the clearance of virus during the early stage after exposure.

Current CDC guidelines for postexposure prophylaxis recommend use of 2 antiretroviral drugs, with the basic regimen consisting of zidovudine 200 mg 3 times a day (or 300 mg bid) and lamivudine 150 mg twice daily (125 mg bid if patient <60 kg). Alternative regimens are often used when the source patient is likely to harbor circulating virus resistant to zidovudine or lamivudine. Selection of these regimens is complicated, but is based on an approach similar to that used for selecting salvage therapy for infected patients. The demonstration of effectiveness of alternative regimens in postexposure prophylaxis is lacking. According to the CDC, use of 3-drug regimens including indinavir 800 mg every 8 hours or nelfinavir 750 mg 3 times a day generally is recommended when a high-risk exposure has occurred, or drug resistance is suspected.

The CDC currently is updating guidelines with the aim of better matching recommended drug regimens to presumed resistance patterns in the source patient. Treatment should be initiated as soon as possible after exposure, with treatment after 72 hours still being recommended for high risk exposures. Treatment should continue for 4 weeks, with laboratory monitoring at baseline and every 2 weeks during treatment. HIV antibody testing should be

performed at baseline, 6 weeks, 3 months, and 6 months after exposure. Testing at 12 months may also be prudent in some circumstances; cases have been observed in which simultaneous exposure to HIV and hepatitis C virus has resulted in symptomatic hepatitis C infection and delayed HIV-seroconversion. HIV viral load testing is recommended if acute symptoms suggestive of HIV infection are present, but is not recommended for routine management due to the possibility of false-positive results.

Information on actual practice of postexposure prophylaxis in occupational exposure is available from the CDC national surveillance system for occupational infections in healthcare personnel. A total of 4154 blood exposures involving 3692 known source patients were reported

between June 1995 and January 1999, with 9% (n=340) involving source patients known to be HIV-seropositive, 57% (n=2087) involving HIV-seronegative source patients, and 1265 involving source patients with unknown HIV serostatus. Of 300 health care workers exposed to HIV-seropositive sources for whom information was available, 173 (58%) initiated postexposure prophylaxis; of 107 whose treatment status was known, 62 (58%) completed the regimen. In comparison, 29% of workers (293/1012) with exposure from HIV-seronegative source patients initiated prophylaxis, with the regimen being completed by 20% (38/186). This information indicates reliance on prophylaxis even in cases in which the exposure does not involve HIV. It also indicates relatively poor adherence of medical personnel to recommended regimens.

Postexposure Prophylaxis for Sexual or Injection Drug Use Exposure

The potential role of postexposure prophylaxis in HIV exposure through sexual contact or needle sharing by injection drug users is controversial. What should a clinician do in the case of a patient presenting within a short time after such exposure? Should treatment be offered on the basis of risk of exposure? The per-episode risk of infection following sexual exposure is difficult to define, although epidemiologic studies suggest many factors that may increase risk of transmission (Table 1). Data primarily based on modeling have indicated probabilities of infection of 0.8% to 3.2% per episode of receptive anal intercourse and of 0.05% to 0.15% per episode of receptive vaginal intercourse. By comparison, the estimated risk following a percutaneous occupational exposure is 0.32% and that following sharing of a needle is 0.67%. In other words, the per-episode transmission risk for occupational, sexual, and injection drug exposures to HIV appear similar, varying within a single order of magnitude.

A potential scheme for offering treatment, used in San Francisco and some other locales, is based on the risk assessed at the time of presentation. Treatment is offered for anal and vaginal exposures, and for oral receptive sexual exposures involving mucosal contact with semen. However, thresholds for treatment differ among the clinicians and programs offering postexposure prophylaxis.

The rationale for postexposure prophylaxis in cases of sexual or needle exposure is similar to that in cases of occupational exposure: efficacy of prophylactic therapy is biologically plausible, the per-episode transmission risk is low but not zero, and current treatments appear to be reasonably safe. At present, however, there are no data on effectiveness of prophylaxis following sexual or injection drug use (IDU) exposure, whereas there is at least some evidence of effectiveness in cases of occupational exposure. Occupational exposure prophylaxis has been endorsed by authoritative bodies (the Occupational Safety and Health Administration, the US Public Health Service) but there has been limited endorsement of prophylaxis for sexual or IDU exposure by the International AIDS Society–USA and others.

The other issues surrounding use of prophylaxis for community exposures to HIV include its cost, its feasibility, particularly with regard to adherence, and most importantly, its public health impact. The public health impact of post-exposure prophylaxis for occupational exposures is

> CDC surveillance data indicate that the prophylaxis regimen was completed by 58% of health care workers with exposure to a source patient known to have HIV infection

small, given that such exposure accounts for a very small fraction of incident HIV infection. In theory, programs for prophylaxis for sexual or IDU exposure could have a great public health impact. However, it is not clear if such programs would be beneficial or harmful. In the pessimistic view, the existence of such programs may result in disinhibition of risk behavior (Figure 1), resulting in increased exposure and incidence of infection. In addition, if prophylaxis is ineffective, the risk for emergence of drug-resistant virus increases. In the optimistic view, the incidence of infection would be decreased by the effectiveness of prevention counseling in decreasing risk behavior, the effectiveness of prophylaxis in preventing established infection, and the detection of undiagnosed infections among persons presenting for treatment. A number of projects supported by the CDC and National Institutes of Health are designed to evaluate program feasibility and assess the magnitude of these potential risks and benefits.

An ongoing postexposure prophylaxis program in San Francisco is designed as a postexposure prevention program that (1) focuses on risk avoidance counseling, (2) clearly conveys the message that postexposure prophylaxis is a back-up measure at best, and (3) devotes considerable resources to the monitoring of adherence and behavioral outcomes, as well as of treatment and virologic outcomes. The criteria for administration of postexposure prevention in the program include an eligible HIV exposure or high-risk exposure within the past 72 hours, negative baseline HIV-antibody test, and patient commitment to adherence to the drug treatment

Table **1.** Factors That May Increase Risk of HIV Infection During Sex

HIV-Infected Partner	High plasma viral load
	High viral load in semen/vagina
	Menses at time of exposure
	Inflammatory genital exposure
	Lack of circumcision
Uninfected Partner	Genetic susceptibility
	Genital ulcer disease
	Inflammatory genital disease
	Lack of circumcision
	Cervical ectopy
Characteristics of the Sexual Act	Trauma (eg, fisting)
	Douching prior to anal or vaginal sex
	Increased duration or intensity of intercourse
Viral Characteristics	Macrophage tropism
	Nonsyncytium-inducing phenotype

PESSIMISTIC VIEW: INCREASED HIV INCIDENCE
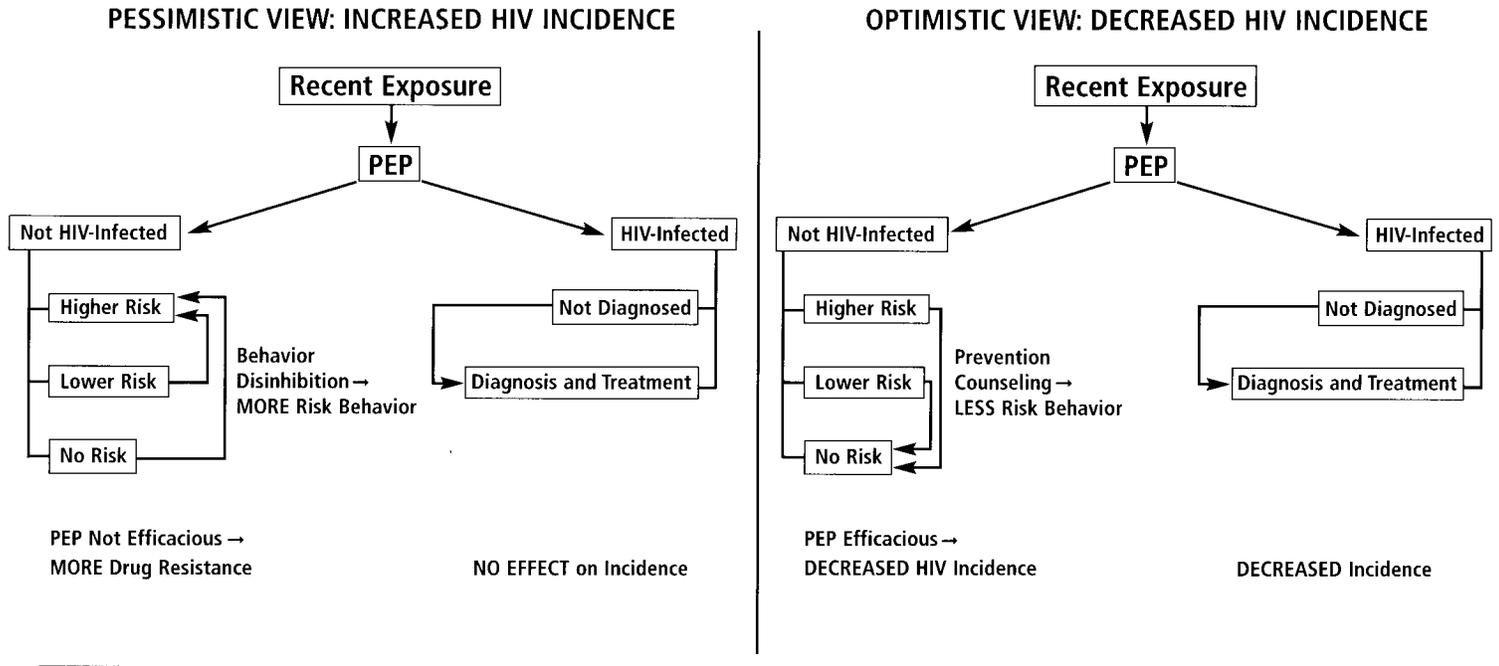
OPTIMISTIC VIEW: DECREASED HIV INCIDENCE

Figure **1.** Pessimistic (left) and optimistic (right) views of impact of postexposure prophylaxis (PEP) and prevention programs.

and to follow-up. Convenient program access sites are employed, and personnel are experienced in risk counseling, as well as treatment, monitoring, and adherence counseling. Preliminary data from the program indicate that more than 80% of the exposures for which treatment was offered were sexual exposures. Most patients received 2-drug regimens; only 3% received a protease inhibitor. Thus far, more than 70% of patients have completed the recommended 4 weeks of therapy without changing treatment, an adherence rate equivalent to or somewhat better than that observed among health care workers.

Information from this and other ongoing projects can be expected to provide important insights into the feasibility and potential public health impact of postexposure prevention programs. A focus on risk prevention and behavior modification is a critical element in the success of such programs.

Suggested Reading

Bamberger JD, Waldo CR, Gerberding JL, et al. Postexposure prophylaxis for human immunodeficiency virus (HIV) infection following sexual assault. Am J Med. 1999;106(3):323-326.

Bell DM. Occupational risk of human immunodeficiency virus infection in healthcare workers: an overview. Am J Med. 1997;102(5B):9-15.

Cardo DM, Culver DH, Ciesielski CA, et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. Centers for Diseases Control and

Prevention Needlestick Surveillance Group. N Engl J Med. 1997;337(21):1485-1490.

Centers for Disease Control and Prevention. Public health service guidelines for the management of health-care worker exposures to HIV and recommendations for post-exposure prophylaxis. MMWR Morb Mortal Wkly Rep. 1998;47:1-33.

Clerici M, Levin JM, Kessler HA. HIV-specific T-helper activity in seronegative health care workers exposed to contaminated blood. JAMA. 1994;271:42-46.

Gerberding, JL. HIV exposure risk assessment and prophylactic treatment. In: Sande MA, Volberding P, eds. The Medical Management of AIDS. Philadelphia, Pa: W. B. Saunders Co; 1999.

Katz MH, Gerberding JL. Care of persons with recent sexual exposure to HIV. Ann Intern Med. 1998;128:306-312.