

## NEW GUIDELINES FOR PROPHYLAXIS FOLLOWING OCCUPATIONAL EXPOSURE TO HIV

**S**TANDARD INFECTION control precautions remain the most reliable means of preventing occupationally acquired HIV infection. Needlestick and other occupational exposures have not been eliminated, however. The merits of postexposure chemoprophylaxis (PEP) after occupational exposure to HIV have been a topic of debate since the 1980s, but only recently has enough evidence accumulated to justify specific recommendations. Data are still limited regarding the efficacy and toxicity of PEP and the risk of HIV infection after different types of exposure, but the Centers for Disease Control and Prevention (CDC) has released new guidelines<sup>1</sup> that recommend PEP after some kinds of occupational exposures. These provisional recommendations are summarized here. Interested readers are referred to the complete report.\*

PEP is expensive and may cause potentially serious side effects, although existing data suggest that—given the recommended four-week regimen—the latter risk is relatively low, even for gravidae. In every exposure incident, the likelihood of transmission must be considered when weighing the risks and benefits of PEP. For a more extensive discussion, the complete CDC report should be consulted.

### TRANSMISSION RISKS

The average risk for HIV infection from all types of reported percutaneous exposures to HIV-infected blood has been estimated as 3/1000.<sup>2</sup> Important variables include the volume of blood involved and the level of viremia. In a recent case-control study,<sup>3</sup> increased risk was associated with:

- deep injury;
- visible blood on the offending device;

- injury from a device previously placed in a vein or artery (e.g., a phlebotomy needle); and
- exposure to blood from a patient who died of AIDS within 60 days of the exposure (and therefore presumably had a high titer of HIV).

The risks after mucous membrane or skin exposures to HIV-contaminated blood were typically less—0.1% and <0.1%, respectively.<sup>4</sup> Even controlling for these variables, however, the risk of infection was significantly lower among persons given zidovudine (ZDV, *née* AZT).

### CDC RECOMMENDATIONS

*N.B.: These recommendations were not developed to address non-occupational (e.g., sexual) exposures.*

#### When to Offer Prophylaxis

Chemoprophylaxis should be *recommended* to workers after occupational exposures associated with the highest risk for HIV transmission. For exposures with a lower, but non-negligible risk, PEP should be *offered*, balancing the lower risk against the use of drugs having uncertain efficacy and toxicity. For exposures with negligible risk, PEP is not justified (see table). Exposed workers should be informed that a) knowledge about the efficacy and toxicity of PEP is limited; b) for agents other than ZDV, data are limited regarding toxicity in persons without HIV infection or who are pregnant. Accordingly, any exposed worker has the right to decline PEP in whole or in part.

#### What to Use

At present, ZDV should be considered for all PEP regimens. It is the only agent for which data support the efficacy of PEP in the clinical setting. Lamivudine (3TC) should usually be added to ZDV for increased antiretroviral activity and for activity against many ZDV-resistant strains. A protease inhibitor should be added for exposures with the highest risk for HIV transmission (see table). Indinavir (IDV) is currently recommended

because it appears to be more potent, has fewer drug interactions, and may have fewer short-term adverse effects.

Protease inhibitors may be considered for lower risk exposures to a probable ZDV-resistant strain,<sup>†</sup> although it is uncertain whether the potential additional toxicity of a third drug outweighs the benefit for lower risk exposures. For exposures to HIV strains resistant to both ZDV and 3TC or to any protease inhibitor, or if these drugs are contraindicated or poorly tolerated, the optimal PEP regimen is uncertain; expert consultation is advised.

#### Timing is Critical

PEP should be initiated promptly, preferably within 1-2 hours after the exposure. Animal studies suggest that PEP is probably not effective when started after more than 24-36 hours,<sup>4,5</sup> but the interval after which there is no benefit from PEP for humans is undefined. Initiating therapy after intervals of a week or more may be considered for the highest risk exposures; even if infection is not prevented, early treatment may be beneficial. The optimal duration of PEP is unknown. Assuming the drugs are tolerated, four weeks is the recommended interval.

#### When HIV Status is Unknown

If the source individual's HIV status is unknown, decisions about PEP should be based on the exposure risk and the likelihood of HIV infection in the known or presumed source. Remember that PEP should be initiated within hours of exposure—long before any new serological test results would be available. Decisions about PEP can be discontinued or modified as additional information becomes available.

<sup>†</sup> An HIV strain is more likely to be resistant to a specific antiretroviral agent if it derives from a patient exposed to the agent for a prolonged period of time (e.g., >6-12 months). In general, resistance develops more readily in persons with more advanced HIV infection (e.g., CD4+ T-lymphocyte count <200 cells/μl), reflecting the increasing rate of viral replication during later stages of the infection.

\* The complete report, published in the MMWR, is available without charge from the National AIDS Clearinghouse (800/458-5231) or can be downloaded as a .pdf file from the WWW (<http://www.cdc.gov>) or by anonymous ftp (<ftp://ftp.cdc.gov>); look for MM4522.pdf amongst the MMWRs).

**Recommended Regimens by Type of Exposure and Source**

Type of exposure	Source material*	Antiretroviral prophylaxis†	Antiretroviral regimen§
Percutaneous	Blood¶		
	Highest risk	Recommend	ZDV plus 3TC plus IDV
	Increased risk	Recommend	ZDV plus 3TC, ± IDV**
	No increased risk	Offer	ZDV plus 3TC
Mucous membrane	Fluid containing visible blood, other potentially infectious fluid††, or tissue	Offer	ZDV plus 3TC
	Other body fluid (e.g., urine)	Not offer	
	Blood	Offer	ZDV plus 3TC, ± IDV**
	Fluid containing visible blood, other potentially infectious fluid††, or tissue	Offer	ZDV, ± 3TC
Skin, increased risk§§	Other body fluid (e.g., urine)	Not offer	
	Blood	Offer	ZDV plus 3TC, ± IDV**
	Fluid containing visible blood, other potentially infectious fluid††, or tissue	Offer	ZDV, ± 3TC
	Other body fluid (e.g., urine)	Not offer	

\* Any exposure to concentrated HIV (e.g., in a research laboratory or production facility) is treated as percutaneous exposure to blood with highest risk.

† *Recommend*—Postexposure prophylaxis (PEP) should be recommended to the exposed worker with counseling (see text). *Offer*—PEP should be offered to the exposed worker with counseling (see text). *Not offer*—PEP should not be offered because these are not occupational exposures to HIV (1).

§ Regimens: zidovudine (ZDV), 200 mg three times a day; lamivudine (3TC), 150 mg two times a day; indinavir (IDV), 800 mg three times a day (if IDV is not available, saquinavir may be used, 600 mg three times a day). Prophylaxis is given for 4 weeks. For full prescribing information, see package inserts.

¶ *Highest risk*—BOTH larger volume of blood (e.g., deep injury with large diameter hollow needle previously in source patient's vein or artery, especially involving an injection of source-patient's blood) AND blood containing a high titer of HIV (e.g., source with acute retroviral illness or end-stage AIDS; viral load measurement may be considered, but its use in relation to PEP has not been evaluated). *Increased risk*—EITHER exposure to larger volume of blood OR blood with a high titer of HIV. *No increased risk*—NEITHER exposure to larger volume of blood NOR blood with a high titer of HIV (e.g., solid suture needle injury from source patient with asymptomatic HIV infection).

\*\* Possible toxicity of additional drug may not be warranted (see text).

†† Includes semen; vaginal secretions; cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids.

§§ For skin, risk is increased for exposures involving a high titer of HIV, prolonged contact, an extensive area, or an area in which skin integrity is visibly compromised. For skin exposures without increased risk, the risk for drug toxicity outweighs the benefit of PEP. (from ref. 1)

Existing Health Division rules<sup>6</sup> govern procedures for determining the HIV status of source individuals following occupational exposure to body fluids.

**Postexposure Testing**

Workers with occupational exposures to HIV should receive follow-up counseling and medical evaluation, including

HIV-antibody tests at baseline and periodically for at least 6 months post-exposure (e.g., 6 weeks, 12 weeks, and 6 months), and should observe precautions to prevent possible secondary transmission.<sup>7</sup>

If PEP is used, drug-toxicity monitoring should include a complete blood

count and renal and hepatic chemical function tests at baseline and 2 weeks after starting PEP. If subjective or objective toxicity is noted, dose reduction or drug substitution should be considered with expert consultation, and further diagnostic studies may be indicated. Health-care workers who become infected with HIV should receive appropriate medical care.

Beginning July 15, 1996, health-care providers in the United States are encouraged to enroll all workers who receive PEP in an anonymous registry being developed by CDC, Glaxo Wellcome Inc., and Merck & Co., Inc., to assess toxicity. For more information, contact the registry (888/737-4448). Unusual or severe toxicity from antiretroviral drugs should be reported to the manufacturer and/or the FDA (800/332-1088). These recommendations for PEP will be reconsidered as additional information becomes available.

**REFERENCES**

1. CDC. Update: Provisional Public Health Service Recommendations for Chemoprophylaxis after Occupational exposure to HIV. MMWR 1996; 45:468-472.
2. Tokars JI, Marcus R, Culver DH, et al. Surveillance of HIV infection and zidovudine use among health care workers after occupational exposure to HIV-infected blood. Ann Intern Med 1993;118:913-9
3. CDC. Case-control study of HIV seroconversion in health-care workers after percutaneous exposure to HIV-infected blood — France, United Kingdom, and United States, January 1988-August 1994. MMWR 1995;44:929-33.
4. Gerberding JL. Management of occupational exposures to blood-borne viruses. N Engl J Med 1995;332:444-51.
5. CDC. Public Health Service statement on management of occupational exposure to human immunodeficiency virus, including considerations regarding zidovudine postexposure use. MMWR 1990;39(no. RR-1).
6. OAR 333-12-260 through OAR 333-12-269.
7. Niu MT, Stein DS, Schnittmann SM. Primary human immunodeficiency virus type 1 infection: review of pathogenesis and early treatment interventions in humans and animal retrovirus infections. J Infect Dis 1993;168:1490-1501.