Child Labor — Continued

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Notice to Readers

Update: Provisional Public Health Service Recommendations For Chemoprophylaxis After Occupational Exposure to HIV

Although preventing blood exposures is the primary means of preventing occupationally acquired human immunodeficiency virus (HIV) infection, appropriate postexposure management is an important element of workplace safety (*1*). Information suggesting that zidovudine (ZDV) postexposure prophylaxis (PEP) may reduce the risk for HIV transmission after occupational exposure to HIV-infected blood (*2*) prompted a Public Health Service (PHS) interagency working group*, with expert consultation†, to update a previous PHS statement on management of occupational exposure to HIV with the following findings and recommendations on PEP (*1*).§

Background

Although failures of ZDV PEP have occurred (*3*), ZDV PEP was associated with a decrease of approximately 79% in the risk for HIV seroconversion after percutaneous exposure to HIV-infected blood in a case-control study among health-care workers (*2*). In a prospective trial in which ZDV was administered to HIV-infected pregnant women and their infants, a direct effect of ZDV prophylaxis on the fetus and/or infant may have contributed to the observed 67% reduction in perinatal HIV transmission (*4*); the protective effect of ZDV was only partly explained by reduction of the HIV titer

*The interagency working group comprised representatives of CDC, the Food and Drug Administration (FDA), the Health Resources and Services Administration, and the National Institutes of Health. Information included in these recommendations may not represent FDA approval or approved labeling for the particular products or indications in question. Specifically, the terms "safe" and "effective" may not be synonymous with the FDA-defined legal standards for product approval.

†CDC and the National Foundation for Infectious Diseases cosponsored a workshop, HIV Post-Exposure Management for Health Care Workers, on March 4–5, 1996; proceedings of the workshop will be published in the *American Journal of Medicine*.

§Single copies of this report will be available free until June 7, 1997, from the CDC National AIDS Clearinghouse, P.O. Box 6003, Rockville, MD 20849-6003; telephone (800) 458-5231 or (301) 217-0023.

Occupational Exposure to HIV — Continued

in maternal blood (*5*). PEP also prevented or ameliorated retroviral infection in some studies in animals (*6,7*).

The average risk for HIV infection from all types of reported percutaneous exposures to HIV-infected blood is 0.3% (*3*). In the case-control study (*2*), risk was increased for exposures involving 1) a deep injury to the health-care worker, 2) visible blood on the device causing the injury, 3) a device previously placed in the source-patient's vein or artery (e.g., a needle used for phlebotomy), or 4) a source-patient who died as a result of acquired immunodeficiency syndrome (AIDS) within 60 days postexposure (and therefore was presumed to have a high titer of HIV) (*2*). Identification of these risk factors in the case-control study suggests that the risk for HIV infection exceeds 0.3% for percutaneous exposures involving a larger blood volume and/or higher HIV titer in blood. The risks after mucous membrane and skin exposures to HIV-infected blood (on average, approximately 0.1% and <0.1%, respectively [*7*]) probably also depend on volume of blood and titer of HIV. The risk is probably higher for skin contact that is prolonged, involves an area that is extensive or in which skin integrity is visibly compromised, and/or involves a higher HIV titer.

Although information about the potency and toxicity of antiretroviral drugs is available from studies of HIV-infected patients, it is uncertain to what extent this information can be applied to uninfected persons receiving PEP. In HIV-infected patients, combination therapy with the nucleosides ZDV and lamivudine (3TC) has greater antiretroviral activity than ZDV alone and is active against many ZDV-resistant HIV strains without significantly increased toxicity (*8*). Adding a protease inhibitor provides even greater increases in antiretroviral activity; among protease inhibitors, indinavir (IDV) is more potent than saquinavir at currently recommended doses and appears to have fewer drug interactions and short-term adverse effects than ritonavir (*8*). Few data exist to assess possible long-term (i.e., delayed) toxicity resulting from use of these drugs in persons not infected with HIV.

In currently recommended doses, ZDV PEP usually is tolerated well by health-care workers; short-term toxicity associated with higher doses primarily includes gastrointestinal symptoms, fatigue, and headache (*3,7*). The toxicity of other antiretroviral drugs in persons not infected with HIV has not been well characterized. In HIV-infected adults, 3TC can cause gastrointestinal symptoms and, in rare instances, pancreatitis. IDV toxicity includes gastrointestinal symptoms and, usually after prolonged use, mild hyperbilirubinemia (10%) and kidney stones (4%); the latter may be limited by drinking at least 48 oz (1.5 L) of fluid per 24-hour period (*8*). During the first 4 weeks of IDV therapy, the reported incidence of kidney stones was 0.8% (Merck Research Laboratories, unpublished data, 1996). As stated in the package insert, the concurrent use of IDV and certain other drugs, including some nonsedating antihistamines, is contraindicated. Based on limited data, ZDV use in the second and third trimesters of pregnancy and early infancy was not associated with serious adverse effects in mothers or infants (*4,9*); data are limited regarding the safety of ZDV during the first trimester of pregnancy or of other antiretroviral agents during pregnancy. Although 3TC has been associated with pancreatitis in HIV-infected children (*8*), whether 3TC causes fetal toxicity is unknown.

Occupational Exposure to HIV — Continued

Recommendations

The following recommendations are provisional because they are based on limited data regarding efficacy and toxicity of PEP and risk for HIV infection after different types of exposure. Because most occupational exposures to HIV do not result in infection transmission, potential toxicity must be carefully considered when prescribing PEP. When possible, these recommendations should be implemented in consultation with persons having expertise in antiretroviral therapy and HIV transmission. Changes in drug regimens may be appropriate, based on factors such as the probable antiretroviral drug resistance profile of HIV from the source patient; local availability of drugs; and medical conditions, concurrent drug therapy, and drug toxicity in the exposed worker. These recommendations were not developed to address nonoccupational (e.g., sexual) exposures.

1. Chemoprophylaxis should be recommended to exposed workers after occupational exposures associated with the highest risk for HIV transmission. For exposures with a lower, but nonnegligible 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 (Table 1). 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; and c) any or all drugs for PEP may be declined by the exposed worker.
2. At present, ZDV should be considered for all PEP regimens because ZDV is the only agent for which data support the efficacy of PEP in the clinical setting. 3TC should usually be added to ZDV for increased antiretroviral activity and activity against many ZDV-resistant strains. A protease inhibitor (preferably IDV because of the characteristics summarized in this report) should be added for exposures with the highest risk for HIV transmission (Table 1). Adding a protease inhibitor also may be considered for lower risk exposures if ZDV-resistant strains are likely, although it is uncertain whether the potential additional toxicity of a third drug is justified for lower risk exposures. For HIV strains resistant to both ZDV and 3TC or resistant to a protease inhibitor, or if these drugs are contraindicated or poorly tolerated, the optimal PEP regimen is uncertain; expert consultation is advised¶.
3. PEP should be initiated promptly, preferably within 1–2 hours postexposure. Although animal studies suggest that PEP probably is not effective when started later than 24–36 hours postexposure (*6,7*), the interval after which there is no benefit from PEP for humans is undefined. Initiating therapy after a longer interval (e.g., 1–2 weeks) may be considered for the highest risk exposures; even if infection is not prevented, early treatment of acute HIV infection may be beneficial (*10*). The optimal duration of PEP is unknown; because 4 weeks of ZDV appeared protective (*2*), PEP should probably be administered for 4 weeks, if tolerated.
4. If the source patient or the patient's HIV status is unknown, initiating PEP should be decided on a case-by-case basis, based on the exposure risk and likelihood of HIV infection in known or possible source patients. If additional information becomes available, decisions about PEP can be modified.

¶An HIV strain is more likely to be resistant to a specific antiretroviral agent if it is derived from a patient who has been exposed to the agent for a prolonged period of time (e.g., 6–12 months or longer). In general, resistance develops more readily in persons with more advanced HIV infection (e.g., CD4+ T-lymphocyte count of <200 cells/mm^3), reflecting the increasing rate of viral replication during later stages of the illness.

Occupational Exposure to HIV — Continued

5. 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 postexposure (e.g., 6 weeks, 12 weeks, and 6 months), and should observe precautions to prevent possible secondary transmission (*1*). 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 indi-

TABLE 1. Provisional Public Health Service recommendations for chemoprophylaxis after occupational exposure to HIV, by type of exposure and source material — 1996

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
	Fluid containing visible blood, other potentially infectious fluid††, or tissue	Offer	ZDV plus 3TC
	Other body fluid (e.g., urine)	Not offer	
Mucous membrane	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	
Skin, increased risk§§	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.

Occupational Exposure to HIV — Continued

cated. Health-care workers who become infected with HIV should receive appropriate medical care.

6. 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 (telephone [888] 737-4448 [(888) PEP-4HIV]). Unusual or severe toxicity from antiretroviral drugs should be reported to the manufacturer and/or the Food and Drug Administration (telephone [800] 332-1088). Updated information about HIV PEP will be available beginning in early 1997 from the Internet at CDC's home page (http://www.cdc.gov); CDC's fax information service, telephone (404) 332-4565 (Hospital Infections Program directory); the National AIDS Clearinghouse, telephone (800) 458-5231; and the HIV/AIDS Treatment Information Service, telephone (800) 448-0440.

Reported by: Center for Drug Evaluation and Research, Food and Drug Administration. AIDS Program Office, Health Resources and Svcs Administration. National Institute of Allergy and Infectious Diseases, Warren H. Magnuson Clinical Center, National Institutes of Health. National Center for HIV, STD, and TB Prevention (proposed); National Institute for Occupational Safety and Health; and National Center for Infectious Diseases, CDC.

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MORBIDITY AND MORTALITY WEEKLY REPORT

Scopolamine Poisoning among Heroin Users — New York City, Newark, Philadelphia, and Baltimore, 1995 and 1996

Heroin is mixed ("cut") frequently with other substances primarily to increase its weight for retail sale (e.g., mannitol and starch) and to add pharmacologic effects (e.g., dextromethorphan and lidocaine). During 1995 and 1996, health departments and poison-control centers in New York City (NYC); Newark, New Jersey; Philadelphia; and Baltimore reported at least 325 cases of drug overdoses requiring medical treatment in persons who had used "street drugs" sold as heroin that probably also contained scopolamine, an anticholinergic drug. This report summarizes the clinical and epidemiologic features of these cases, which represent a new type of drug overdose.

New York City

On March 16, 1995, eight persons were treated in the emergency department (ED) of a Bronx hospital for acute onset of agitation and hallucinations approximately 1 hour after "snorting" heroin. On physical examination, all these persons had clinical manifestations of anticholinergic toxicity (i.e., tachycardia, mild hypertension, dilated pupils, dry skin and mucous membranes, and diminished or absent bowel sounds); five had urinary retention. All were initially lethargic and became agitated and combative after emergency medical service (EMS) personnel treated them with parenteral naloxone, which is routinely used for suspected heroin overdose to reverse the toxic effects of opioids (e.g., coma and respiratory depression). All patients received diazepam or lorazepam for sedation, and signs and symptoms resolved during the next 12–24 hours.

During March 17–April 5, 1995, a total of 10 persons who reported using heroin presented with similar clinical findings to hospital EDs in the Bronx and Manhattan. Seven patients reported having used heroin with the street names "Point on Point" or "Sting." Specimens of "Sting" heroin obtained from two patients on April 5 and analyzed by gas chromatography-mass spectrophotometry (GC–MS) by the Bureau of Laboratories, New York City Department of Health (NYCDOH), contained heroin and scopolamine. The GC–MS patterns of the scopolamine suggested it was synthetic rather than derived from a plant source. As a result of this finding, these patients were treated for suspected scopolamine poisoning with physostigmine (an antidote for anticholinergic toxicity). While receiving physostigmine intravenously for 5–10 minutes, their paranoia, hallucinations, and agitation resolved (*1*).

During March 17–April 10, 1995, NYCDOH issued press releases warning of scopolamine-adulterated heroin sold under the street names "Point on Point" and