VIRGINIA
EPIDEMIOLOGY BULLETIN

Randolph L. Gordon, M.D., M.P.H., Commissioner
Grayson B. Miller, Jr., M.D., Epidemiologist

Elizabeth Eustis Turf, Ph.D., Editor
Vickie L. O'Dell, Layout Editor

October 1996

Volume 96, Number 10

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

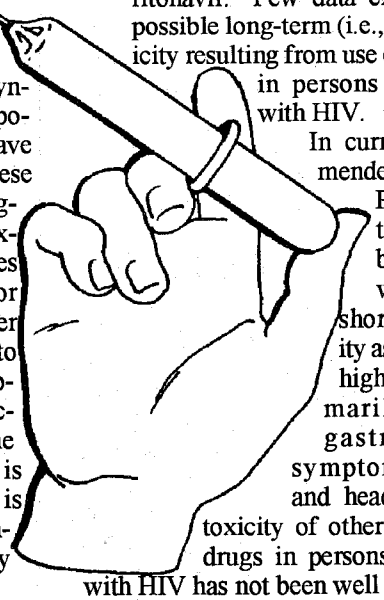
The following article is reprinted from the June 7, 1996, MMWR and provides Public Health Service recommendations for HIV-postexposure prophylaxis. As stated in the title, these recommendations are only provisional and do not provide solutions for every problem. Exposures in which the risk for HIV transmission is unidentified should be handled on a case-by-case basis in consultation with an expert.

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 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 This Issue:

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.

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

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 fluids (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.

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.

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 indicated. 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.

References

1. 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-l).

2. 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.

3. 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.

4. Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. N Engl J Med 1994;331:1173-80.

5. Sperling RS, Shapiro DE, Coombs R, et al. Maternal plasma HIV-1 RNA and the success of zidovudine in the prevention of mother-child transmission [Abstract no. LB1]. In: Program and abstracts of the 3rd conference on retroviruses and opportunistic infections. Alexandria, Virginia: Infectious Diseases Society of America, 1996.

6. 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;168:1490-501.

7. Gerberding JL. Management of occupational exposures to blood-borne viruses. N Engl J Med 1995;332:444-51.

8. Anonymous. New drugs for HIV infection. The Medical Letter on Drugs and Therapeutics 1996;38:35-7.

9. Connor E, Sperling R, Shapiro D, et al. Long term effect of zidovudine exposure among uninfected infants born to HIV-infected mothers in pediatric AIDS Clinical Trials Group protocol 076. In: Abstracts of the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy. Washington, DC: American Society for Microbiology, 1995;205.

10. Kinloch-de Loes S, Hirschel BJ, Hoen B, et al. A controlled trial of zidovudine in primary human immunodeficiency virus infection. N Engl J Med 1995;333:408-13.

Videoconference: Surveillance of Vaccine-Preventable Diseases

The Centers for Disease Control and Prevention (CDC) will present a Public Health Training Network Satellite Videoconference on "Surveillance of Vaccine-Preventable Diseases," December 5, 1996, 12:00 Noon - 3:30 PM EST. This live, interactive satellite videoconference will provide guidelines for vaccine-preventable disease (VPD) surveillance, case investigation, and outbreak control. The 3.5 hour broadcast will feature a question and answer session in which participants nationwide can address questions to the course instructors on toll free telephone lines. A comprehensive manual for VPD surveillance will be included with the training course.

Target audiences include nurses, physicians, epidemiologists, sanitarians, infection control practitioners, laboratorians, disease reporters, and others who are interested in surveillance and reporting of VPDs. Continuing Education Credit will be offered for a variety of professions, based on 3.5 hours of instruction.

For more information or to register at a site nearest you, please call the Virginia Department of Health, Division of Immunization at 1-800-568-1929. There is no cost for registration and course materials.

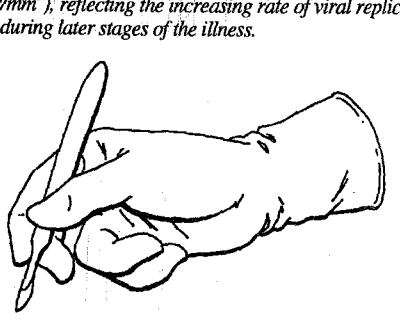
*MMWR. 1996. Vol. 45, No. 22:468-472.

†*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.*

‡*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.*



Cases of Selected Notifiable Diseases Reported in Virginia.*

Disease	Total Cases Reported, September 1996						Total Cases Reported Statewide, January through September		
		Regions							
	State	NW	N	SW	C	E	This Yr	Last Yr	5 Yr Avg
AIDS	104	2	32	9	38	23	904	988	842
Campylobacteriosis	106	30	15	19	23	19	610	488	516
Giardiasis	56	9	19	8	12	8	265	197	239
Gonorrhea	928	17	98	131	279	403	7099	8188	10282
Hepatitis A	24	2	4	2	2	14	134	157	121
Hepatitis B	14	2	2	2	2	6	110	89	121
Hepatitis NANB	2	0	2	0	0	0	12	14	23
HIV Infection	42	0	8	11	9	14	772	917	995
Influenza	0	0	0	0	0	0	373	929	720
Legionellosis	0	0	0	0	0	0	13	18	12
Lyme Disease	10	1	6	1	1	1	40	47	85
Measles	1	0	0	0	1	0	3	0	10
Meningitis, Aseptic	36	2	10	6	0	18	142	554	291
Meningitis, Bacterial†	4	2	1	0	0	1	57	100	83
Meningococcal Infections	6	3	0	0	2	1	47	51	44
Mumps	0	0	0	0	0	0	12	20	36
Pertussis	16	14	0	0	0	2	55	15	24
Rabies in Animals	57	17	10	9	12	9	448	319	273
Rocky Mountain Spotted Fever	19	2	6	3	5	3	46	24	16
Rubella	0	0	0	0	0	0	2	0	0
Salmonellosis	154	18	34	33	42	27	876	865	830
Shigellosis	91	11	52	10	2	16	507	237	360
Syphilis, Early‡	57	0	1	3	15	38	660	930	1055
Tuberculosis	29	3	17	2	3	4	234	208	256

Localities Reporting Animal Rabies: Accomack 1 raccoon; Albemarle 1 dog; Alexandria 1 bat; Augusta 2 cats, 1 skunk; Bath 1 raccoon; Bedford 1 raccoon, 1 skunk; Buckingham 1 skunk; Chesterfield 1 fox, 3 raccoons; Culpeper 1 raccoon; Fairfax 1 fox, 5 raccoons; Fauquier 1 raccoon; Franklin County 1 skunk; Grayson 2 raccoons; Hanover 1 raccoon; Henrico 1 raccoon; James City 1 mink; King George 1 raccoon; King William 1 skunk; Loudoun 1 cat, 2 raccoons; Lunenburg 1 raccoon; Mecklenburg 1 raccoon; Northampton 5 raccoons; Pittsylvania 1 raccoon, 1 skunk; Powhatan 1 raccoon; Richmond City 1 raccoon; Rockbridge 2 raccoons; Rockingham 1 fox; Smyth 1 bat; Spotsylvania 1 fox, 1 raccoon, 1 skunk; Stafford 2 raccoons; Sussex 1 raccoon; Tazewell 1 raccoon; Virginia Beach 1 raccoon; Warren 1 raccoon.
Occupational Illnesses: Asbestosis 25; Carpal Tunnel Syndrome 1; Lead Poisoning 4; Pneumoconiosis 11.
*Data for 1996 are provisional.
†Other than meningococcal.
‡Includes primary, secondary, and early latent.

Published monthly by the
VIRGINIA DEPARTMENT OF HEALTH
Office of Epidemiology
P.O. Box 2448
Richmond, Virginia 23218

Telephone: (804) 786-6261

Bulk Rate
U.S. POSTAGE
PAID
Richmond, Va.
Permit No. 591