VIRGINIA
# EPIDEMIOLOGY BULLETIN

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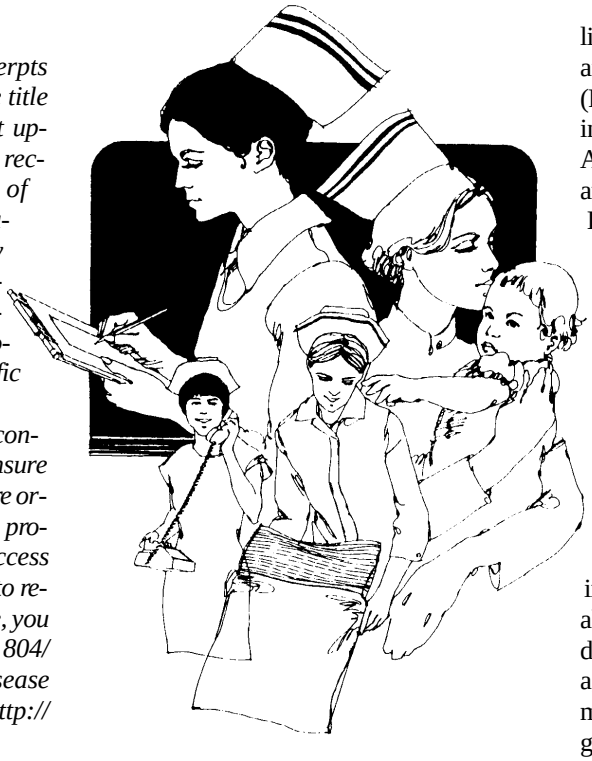
## Public Health Service Guidelines for the Management of Health-Care Worker Exposures to HIV and Recommendations for Postexposure Prophylaxis

### Summary

*The following article includes excerpts from the MMWR article with the above title (1998;47[No. RR-7]:1-33). This report updates and consolidates all previous PHS recommendations for the management of health-care workers who have occupational exposure to blood and other body fluids that may contain human immunodeficiency virus (HIV); it includes recommendations for HIV postexposure prophylaxis (PEP) and discusses the scientific rationale for PEP.*

*Occupational exposures should be considered urgent medical concerns to ensure timely administration of PEP. Health-care organizations should have protocols that promote prompt reporting and facilitate access to postexposure care. If you would like to receive a copy of the entire MMWR article, you may call the Office of Epidemiology at 804/786-6261 or visit the Centers for Disease Control and Prevention web site at http://www.cdc.gov.*



### INTRODUCTION

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. In January 1990, the Centers for Disease Control and Prevention (CDC) issued a statement on the management of HIV exposures that included considerations for zidovudine (ZDV) use for postexposure prophylaxis (PEP). At that time, data were insufficient to assess the efficacy of ZDV as a prophylactic agent in humans or the toxicity of this drug in persons not infected with HIV. Although there are still only limited data to assess safety and efficacy, additional information is now available that is relevant to this issue.

In December 1995, CDC published a brief report of a retrospective case-control study of health-care workers (HCWs) from France, the United Kingdom, and the United States exposed percutaneously to HIV; the study identified risk factors for HIV transmission and documented that the use of ZDV was associated with a decrease in the risk for HIV seroconversion. This information, along with data on ZDV efficacy in preventing perinatal transmission and evidence that PEP prevented or ameliorated retroviral infection in some studies in animals, prompted a Public Health Service (PHS) interagency working group (comprising representatives of CDC, the Food and Drug Administration (FDA), the Health Resources and Services Administration, and the National Institutes of Health), with expert consultation, in June 1996 to issue provisional recommendations for PEP for HCWs after occupational HIV exposure.

Since the provisional recommendations were released, several new antiretroviral drugs have been approved by the FDA, and more information is available about the use and safety of antiretroviral agents in exposed HCWs. This document addresses the management of occupational exposure to HIV, including guidance in assessing and treating exposed HCWs, and updates and replaces all previous PHS guidelines and recommendations for occupational HIV exposure management for HCWs. Included in this document is an algorithm to guide decisions regarding the use of PEP for HIV exposures.

### DEFINITIONS OF HEALTH-CARE WORKERS AND EXPOSURE

In this report, "health-care worker" (HCW) is defined as any person (e.g., an employee, student, contractor, attending clinician, public-safety worker, or volunteer) whose activities involve contact with patients or with blood or other body fluids from patients in a health-care or laboratory setting. An "exposure" that may place an HCW at risk for HIV infection, and therefore requires consideration of PEP, is defined as a percutaneous injury

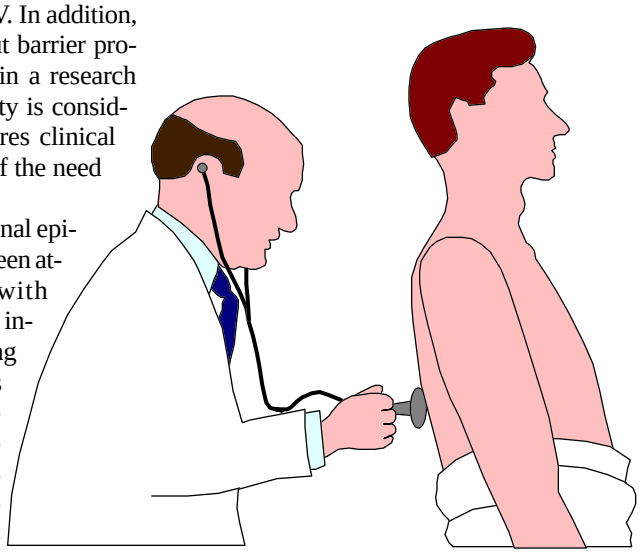
(e.g., a needlestick or cut with a sharp object), contact of mucous membrane or nonintact skin (e.g., when the exposed skin is chapped, abraded, or afflicted with dermatitis), or contact with intact skin when the duration of contact is prolonged (i.e., several minutes or more) or involves an extensive area, with blood, tissue, or other body fluids. Body fluids include a) semen, vaginal secretions, or other body fluids contaminated with visible blood that have been implicated in the transmission of HIV infection; and b) cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids, which have an undetermined risk for transmitting HIV. In addition, any direct contact (i.e., without barrier protection) to concentrated HIV in a research laboratory or production facility is considered an "exposure" that requires clinical evaluation and consideration of the need for PEP.

Although one nonoccupational episode of HIV transmission has been attributed to contact with blood-contaminated saliva, this incident involved intimate kissing between sexual partners and is not similar to contact with saliva that may occur during the provision of health-care services. Therefore, in the absence of visible blood in the saliva, exposure to saliva from a person infected with HIV is not considered a risk for HIV transmission; also, exposure to tears, sweat, or nonbloody urine or feces does not require postexposure follow-up. [Although exposure to these body substances generally is not considered a risk for occupational HIV transmission, this does not negate the importance of handwashing and appropriate glove use when contacting these body substances. Handwashing and appropriate glove use are part of standard precautions for infection control to prevent transmission of nosocomial and community-acquired pathogens that are required for compliance with the Occupational Safety and Health Administration (OSHA) bloodborne pathogens standard. In addition, postexposure evaluation for hepatitis B (and possibly hepatitis C) should be provided if contact with saliva includes a possible portal of entry (i.e., nonintact skin, mucous membrane, or percutaneous injury).]

Human breast milk has been implicated in perinatal transmission of HIV. However, occupational exposure to human breast milk has not been implicated in HIV transmission to HCWs. Moreover, the contact HCWs may have with human breast milk is quite different from perinatal exposure and does not require postexposure follow-up.

## *RECOMMENDATIONS FOR THE MANAGEMENT OF POTENTIALLY EXPOSED HCWs*

Health-care organizations should make available to their workers a system that includes written protocols for prompt reporting, evaluation, counseling, treatment, and follow-up of occupational exposures that may place HCWs at risk for acquiring any bloodborne infection, including HIV. Employers also are required to establish exposure-control plans, including postexposure follow-up for their employees, and to comply with incident reporting requirements mandated by the OSHA. Access to clinicians who can provide postexposure care should be available during all working hours, including nights and weekends. Antiretroviral agents for PEP should be available for timely administration (i.e., either by providing access to PEP drugs on site or creating links with other facilities or providers to make them available offsite). Persons responsible for providing post-exposure counseling should be familiar with evaluation and treatment protocols and the facility's procedures for obtaining drugs for PEP.



HCWs should be educated to report occupational exposures immediately after they occur, particularly because PEP is most likely to be effective if implemented as soon after the exposure as possible. HCWs who are at risk for occupational exposure to HIV should be taught the principles of postexposure management, including options for PEP as part of job orientation and ongoing job training.

## *Exposure Report*

If an occupational exposure occurs, the circumstances and postexposure management should be recorded in the HCW's confidential medical record (usually on a form the facility designates for this purpose). Relevant information includes:

- date and time of exposure;
- details of the procedure being performed, including where and how the exposure occurred, and if the exposure was related to a sharp device, the type of device and how and when in the course of handling the device the exposure occurred;
- details of the exposure, including the type and amount of fluid or material and the severity of the exposure (e.g., for a percutaneous exposure, depth of injury and whether fluid was injected; or for a skin or mucous- membrane exposure, the estimated volume of material and duration of contact and the condition of the skin [e.g., chapped, abraded, or intact]);
- details about the exposure source (i.e., whether the source material contained HIV or other bloodborne pathogen[s]), and if the source is an HIV-infected person, the stage of disease, history of antiretroviral therapy, and viral load, if known; and
- details about counseling, postexposure management, and follow-up.

## *Exposure Management*

### Treatment of an Exposure Site

Wounds and skin sites that have been in contact with bloody or body fluids should be washed with soap and water; mucous membranes should be flushed with water. There is no evidence that the use of antiseptics for wound care or expressing fluid by squeezing the wound further reduces the risk for HIV transmission. However, the use of antiseptics is not contraindicated. The application of caustic agents (e.g., bleach) or the injection of antiseptics or disinfectants into the wound is not recommended.

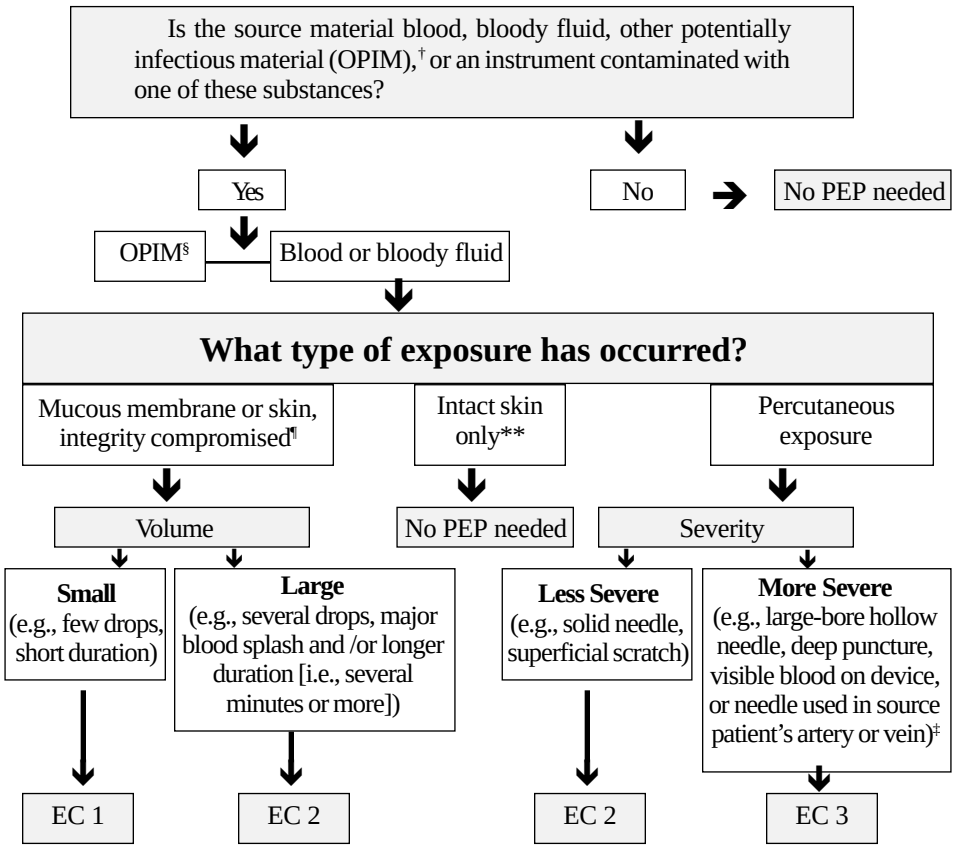
### Assessment of Infection Risk

After an occupational exposure, the source-person and the exposed HCW should be evaluated to determine the need for HIV PEP. Follow-up for hepatitis B virus and hepatitis C virus infections also should be conducted in accordance with previously published CDC recommendations.

**Evaluation of exposure.** The exposure should be evaluated for potential to transmit HIV based on the type of body substance involved and the route and severity of the exposure (Figure 1).

For human bites, the clinical evaluation must consider possible exposure of both the bite re-

**Figure 1. Guidelines for determining the need for HIV postexposure propylaxis (PEP) after an occupational exposure (Step 1 of 3).**




*†Semen or vaginal secretions; cerebrospinal, synovial, pleural, peritoneal, pericardial, or amniotic fluids; or tissue.*

*§Exposures to OPIM must be evaluated on a case-by-case basis. In general, these body substances are considered a low risk for transmission in health-care settings. Any unprotected contact to concentrated HIV in a research laboratory or production facility is considered an occupational exposure that requires clinical evaluation to determine the need for PEP.*

*¶Skin integrity is considered compromised if there is evidence of chapped skin, dermatitis, abrasion, or open wound.*

***Contact with intact skin is not normally considered a risk for HIV transmission. However, if the exposure was to blood, and the circumstances suggest a higher volume exposure (e.g., an extensive area of skin was exposed or there was prolonged contact with blood), the risk for HIV transmission should be considered.*

*‡The combination of these severity factors (e.g., large bore hollow needle and deep puncture) contribute to an elevated risk for transmission if the source person is HIV-positive.*

cipient and the person who inflicted the bite. HIV transmission only rarely has been reported by this route. If a bite results in blood exposure to either person involved, postexposure follow-up, including consideration of PEP should be provided.

**Evaluation and testing of an exposure source.** The person whose blood or body fluids are the source of an occupational exposure should be evaluated for HIV infection (Figure 2). Information available in the medical record at the time of exposure (e.g., laboratory test results, admitting diagnosis, or past medical history) or from the source person may suggest or rule out possible HIV infection. Examples of information to consider when evaluating an exposure source for possible HIV infection include laboratory information (e.g., prior HIV testing results or results of immunologic testing [e.g., CD4+ count]), clinical symptoms (e.g., acute syndrome suggestive of primary HIV infection or undiagnosed immunodeficiency disease), and history of possible HIV exposures (e.g., injecting-drug use, sexual contact with a known HIV-positive partner, unprotected sexual contact with multiple partners [heterosexual and/or homosexual], or receipt of blood or blood products before 1985).

If the source is known to have HIV infection, available information about this person's stage of infection (i.e., asymptomatic or AIDS), CD4+ T-cell count, results of viral load testing, and current and previous antiretroviral therapy, should be gathered for consideration in choosing an appropriate PEP regimen. If this information is not immediately available, initiation of PEP, if indicated, should not be delayed; changes in the PEP regimen can be made after PEP has been started, as appropriate.

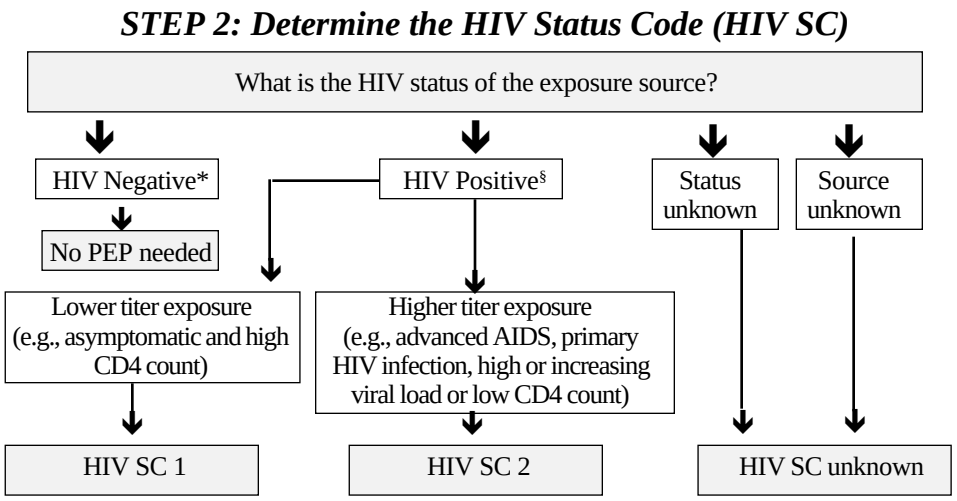
If the HIV serostatus of the source person is unknown, the source person should be informed of the incident and, if consent is obtained, tested for serologic evidence of HIV infection. If consent cannot be obtained (e.g., patient is unconscious), procedures should be followed for testing source persons according to applicable state and local laws. Confidentiality of the source person should be maintained at all times.

HIV-antibody testing of an exposure source should be performed as soon as possible. Hospitals, clinics, and other sites that manage exposed HCWs should consult their laboratories regarding the most appropriate test to use to expedite these results. An FDA-approved rapid HIV-antibody test kit should be considered for use in this situation, particularly if testing by enzyme immunoassay (EIA) cannot be completed within 24-48 hours. Repeatedly reactive results by EIA or rapid HIV-antibody tests are considered highly suggestive of infection, whereas a negative result is an excellent indicator of the absence of HIV antibody. Confirmation of a reactive result by Western blot or immunofluorescent antibody is not necessary for making initial decisions about postexposure management but should be done to complete the testing process.

If the source is HIV seronegative and has no clinical evidence of acquired immunodeficiency syndrome (AIDS) or symptoms of HIV infection, no further testing of the source is indicated. It is unclear whether follow-up testing of a source who is HIV negative at the time of exposure, but recently (i.e., within the last 3-6 months) engaged in behaviors that pose a risk for HIV transmission, is useful in postexposure management of HCWs; HCWs who become infected generally seroconvert before repeat testing of a source would normally be performed.

If the exposure source is unknown, information about where and under what circumstances the exposure occurred should be assessed epidemiologically for risk for transmission of HIV. Certain situations, as well as the type of exposure, may suggest an increased or decreased risk; an important consideration is the prevalence of HIV in the population group (i.e., institution or community) from which the contaminated source material is derived. For example, an exposure that occurs in a geographic area where injecting-drug use is prevalent would be considered epidemiologically to have a higher risk for transmission than one that occurs in a nursing home for the elderly where no known HIV-infected residents are

**Figure 2. Guidelines for determining the need for HIV postexposure propylaxis (PEP) after an occupational exposure (Step 2 of 3).**




**A source is considered negative for HIV infection if there is laboratory documentation of a negative HIV antibody, HIV polymerase chain reaction, or HIV p24 antigen test result from a specimen collected at or near the time of exposure and there is no clinical evidence of recent retroviral-like illness.*
*§A source is considered infected with HIV (HIV positive) if there has been a positive laboratory result for HIV antibody, HIV polymerase chain reaction, or HIV p24 antigen or physician-diagnosed AIDS.*

present. In addition, exposure to a blood-filled hollow needle or visibly bloody device suggests a higher-risk exposure than exposure to a needle that was most likely used for giving an injection. Decisions regarding appropriate management should be individualized based on the risk assessment.

HIV testing of needles or other sharp instruments associated with an exposure, regardless of whether the source is known or unknown, is not recommended. The reliability and interpretation of findings in such circumstances are unknown.

## *Clinical Evaluation and Baseline Testing of Exposed HCWs*

Exposed HCWs should be evaluated for susceptibility to bloodborne pathogen infections. Baseline testing (i.e., testing to establish serostatus at the time of exposure) for HIV antibody should be performed. If the source person is seronegative for HIV, baseline testing or further follow-up of the HCW is normally not necessary. If the source person has recently engaged in behaviors that are associated with a risk for HIV transmission, baseline and follow-up HIV-antibody testing (e.g., 3 and/or 6 months postexposure) of the HCW should be considered. Serologic testing should be made available to all HCWs who are concerned that they may have been exposed to HIV.

For purposes of considering HIV PEP, the evaluation also should include information about medications the HCW may be taking and any current or underlying medical conditions or circumstances (i.e., pregnancy, breast feeding, or renal or hepatic disease) that may influence drug selection. Pregnancy testing should be offered to all nonpregnant women of childbearing age whose pregnancy status is unknown.

## *HIV PEP*

The following recommendations apply to situations where an HCW has had an exposure to a source person with HIV or where information suggests that there is a likelihood that the source person is HIV-infected. These recommendations are based on the risk for HIV infection after different types of exposure and limited data regarding efficacy and toxicity of PEP. Because most occupational HIV exposures do not result in the transmission of HIV, 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.

### Explaining PEP to HCWs

Recommendations for chemoprophylaxis should be explained to HCWs who have sustained occupational HIV exposures (Figure 3). For exposures for which PEP is considered appropriate, HCWs should be informed that a) knowledge about the efficacy and toxicity of drugs used for PEP are limited; b) only ZDV has been shown to prevent HIV transmission in humans; c) there are no data to address whether adding other antiretroviral drugs provides any additional benefit for PEP but experts recommend combination drug regimens because of increased potency and concerns about drug-resistant virus; d) data regarding toxicity of antiretroviral drugs in persons without HIV infection or in pregnant women are limited for ZDV and not known regarding other antiretroviral drugs; and e) any or all drugs for PEP may be declined by the HCW. HCWs who have HIV occupational exposures for which PEP is not recommended should be informed that the potential side effects and toxicity of taking PEP outweigh the negligible risk of transmission posed by the type of exposure.

### Factors in Selection of a PEP Regimen

Selection of the PEP regimen should consider the comparative risk represented by the exposure and information about the exposure source, including history of and response to antiretroviral therapy based on clinical response, CD4+ T-lymphocyte counts, viral load measurements, and current disease stage. Most HIV exposures will warrant only a two-drug regimen, using two nucleoside analogue reverse transcriptase inhibitors (NRTIs), usually ZDV and lamivudine (3TC). The addition of a third drug, usually a protesae inhibitor (PI) (i.e., idinavir [IDV] or nelfinavir [NEL]), should be considered for exposures that pose an increased risk for transmission or where resistance to the other drugs used for PEP is known or suspected.

### Timing of PEP Initiation

PEP should be initiated as soon as possible. The interval within which PEP should be started for optimal efficacy is not known. Animal studies have demonstrated the importance of starting PEP within hours after an exposure. To assure timely access to PEP an occupational exposure should be regarded as an urgent medical concern and PEP started as soon as possible after the exposure (i.e., within a few hours rather than days). If there is a question about which antiretroviral drugs to use, or whether to use two or three drugs, it is probably better to start ZDV and 3TC immediately than to delay PEP administration. Although animal studies suggest that PEP probably is not effective when started later than 24-36 hours postexposure, the interval after which there is no benefit from PEP for humans is undefined. Therefore, if appropriate for the exposure, PEP should be started even when the interval since exposure exceeds 36 hours. Initiating therapy after a longer interval (e.g., 1-2 weeks) may be considered for exposures that represent an increased risk for transmission; even if infection is not prevented, early treatment of acute HIV

infection may be beneficial. The optimal duration of PEP is unknown. Because 4 weeks of ZDV appeared protective in HCWs, PEP probably should be administered for 4 weeks, if tolerated.

### PEP if Serostatus of Source Person is Unknown

If the source person's HIV serostatus is unknown at the time of exposure (including when the source is HIV negative but may have had a recent HIV exposure), use of PEP should be decided on a case-by-case basis, after considering the type of exposure and the clinical and/or epidemiologic likelihood of HIV infection in the source. If these considerations suggest a possibility for HIV transmission and HIV testing of the source is pending, it is reasonable to initiate a two-drug PEP regimen until laboratory results have been obtained and later modify or discontinue the regimen accordingly.

### PEP for Pregnant HCWs

If the HCW is pregnant, the evaluation of risk and need for PEP should be approached as with any other HCW who has had an HIV exposure. However, the decision to use any antiretroviral drug during pregnancy should involve discussion between the woman and her health-care provider regarding the potential benefits and potential risks to her and her fetus.

## *Follow-up of HCWs Exposed to HIV*

### Postexposure Testing

HCWs with occupational exposure to HIV should receive follow-up counseling, postexposure testing, and medical evaluation regardless of whether they receive PEP. HIV-antibody testing should be performed for at least 6 months postexposure (e.g., at 6 weeks, 12 weeks, and 6 months). It is unclear whether an extended follow-up period (e.g., 12 months) is indicated in certain circumstances. Although rare instances of delayed HIV seroconversion have been reported, the infrequency of this occurrence does not warrant adding to HCWs' anxiety by routinely extending the duration of postexposure follow-up. Circumstances for which extending the duration of follow-up have been suggested include the use of highly potent antiretroviral regimens (i.e., more than two drugs) because of theoretical concerns that HIV seroconversion could be delayed, or simultaneous exposure to hepatitis C virus. Data are insufficient for making a general recommendation in these situations. However, this should not preclude a decision to extend follow-up in an individual situation based on the clinical judgment of the HCW's health-care provider. HIV testing should be performed on any HCW who has an illness that is compatible with an acute retroviral syndrome, regardless of the interval since exposure. HIV-antibody testing using EIA should be used to monitor for seroconversion. The routine use of direct virus assays, (e.g., HIV p24 antigen EIA or polymerase chain reaction for HIV RNA) to detect infection in exposed HCWs generally is not recommended. Although direct virus assays may detect HIV infection a few days earlier than EIA, the infrequency of HCW seroconversion and increased costs of these tests do not warrant their routine use in this setting. Also, HIV RNA is approved for use in established HIV infection; its reliability in detecting very early infection has not been determined.

### Monitoring and Management of PEP Toxicity

If PEP is used, drug-toxicity monitoring should be performed at baseline and again 2 weeks after starting PEP. Clinical judgment, based on medical conditions that may exist in the HCW and any toxicity associated with drugs included in the PEP regimen, should determine the scope of testing. Minimally these should include a complete blood count and renal and hepatic chemical function tests. Monitoring for evidence of hyperglycemia should be included for HCWs whose regimen includes any PI; if the HCW is receiving IDV, monitoring for crystalluria, hematuria, hemolytic anemia, and hepatitis also should be included. If toxicity is noted, modification of the regimen should be considered after expert consultation; further diagnostic studies may be indicated.

HCWs who fail to complete the recommended regimen often do so because of the side effects they experience (e.g., nausea and diarrhea). These symptoms often can be managed without changing the regimen by prescribing antimotility and antiemetic agents or other medications that target the specific symptoms. In other situations, modifying the dose interval (i.e., administering a lower dose of drug more frequently throughout the day, as recommended by the manufacturer), may help promote adherence to the regimen.

### Counseling and Education

Although HIV infection following an occupational exposure occurs infrequently, the emotional impact of the exposure often is substantial. In addition, HCWs are given seemingly conflicting information. Although HCWs are told that there is a low risk for HIV transmission, a 4-week regimen of PEP is recommended and they are asked to commit to be-

**Figure 3. Guidelines for determining the need for HIV postexposure propylaxis (PEP) after an occupational exposure (Step 3 of 3).**

***STEP 3: Determine the PEP Recommendation***

| EC | HIV SC | PEP Recommendation |
|---|---|---|
| 1 | 1 | **PEP may not be warranted**. Exposure type does not pose a known high risk for HIV transmission. Whether the risk for drug toxicity outweighs the benefit of PEP should be decided by the exposed HCW and treating clinician. |
| 1 | 2 | **Consider basic regimen.*** Exposure type poses a negligible risk for HIV transmission. A high HIV titer in the source may justify consideration of PEP. Whether the risk for drug toxicity outweighs the benefit of PEP should be decided by the exposed HCW and treating clinician. |
| 2 | 1 | **Recommend basic regimen**. Most HIV exposures are in this category; no increased risk for HIV transmission has been observed but use of PEP is appropriate. |
| 2 | 2 | **Recommend expanded regimen.*** Exposure type represents an increased HIV transmission risk. |
| 3 | 1 or 2 | **Recommend expanded regimen.** Exposure type represents an increased HIV transmission risk. |
| Unknown | | If the source or, in the case of an unknown source, the setting where the exposure occurred suggests a possible risk for HIV exposure and the EC is 2 or 3, consider PEP basic regimen. |

**See Table 1, page 7.*

| First-Line Drugs for HIV Postexposure Prophylaxis (PEP)* | | | |
|---|---|---|---|
| **Drug** | **Dosage** | **Primary Toxicities/ Side Effects** | **Comments** |
| **Nucleoside Reverse Transcriptase Inhibitors** | | | |
| **Zidovudine** (RETROVIR®; ZDV, AZT) | 600 mg every day in divided doses (e.g., 300 mg twice a day, 200 mg three times a day, or 100 mg every four hours). | Neutropenia, anemia, nausea, fatigue, malaise, headache, insomnia, and asthenia. | Caution should be used if co-administered with bone marrow suppressive drugs or cytotoxic therapy. |
| **Lamivudine** (EPIVIR™; 3TC) | 150 mg twice a day. | Headache, abdominal pain, diarrhea, and in rare cases, pancreatitis. Toxicity of ZDV and 3TC when used in combination is approximately equal to that of ZDV alone. | |
| **ZDV plus 3TC** (COMBIVIR™) | 1 tablet twice a day; each tablet contains 300 mg ZDV and 150 mg 3TC. | See above for ZDV and 3TC. | Caution should be used if co-administered with bone marrow suppressive drugs or cytotoxic therapy. |
| **Protease Inhibitors (PIs)§†** | | | |
| **Indinavir** (CRIXIVAN®; IDV) | 800 mg every 8 hours on an empty stomach (i.e., without food or with a light meal). | Nephrolithiasis, crystalluria, hematuria, nausea, headache, indirect hyperbilirubinemia, elevated liver function tests, and hyperglycemia/diabetes. | Incidence of nephrolithiasis may be reduced by consuming large quantities of water (i.e., drinking six 8 oz glasses of water [total 48 oz] throughout the day). |
| **Nelfinavir** (VIRACEPT™) | 750 mg three times a day (with meals or a light snack). | Diarrhea and hyperglycemia/diabetes. | Diarrhea usually can be controlled with over-the-counter antidiarrheal drugs (e.g., loperamide).<br>If oral contraceptives are being used, alternative or additional contraceptive measures should be used while taking nelfinavir. |

**Information included in these recommendations may not represent Food and Drug Administration (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.*
*§It is recommended that consultation with experts in the treatment of HIV infection and disease be sought when considering the inclusion of PIs or the use of alternative agents in PEP regimens.*
*†No PI should be co-administered with terfenadine (Seldane®), astemizole (Hismanal®), cisapride (Propulsid®), triazolam, and midazolam. Rifampin should not be administered with PIs. Cytochrome P450 metabolism inhibitors like ketoconazole may increase PI plasma concentrations; dose reduction of the PI is only indicated for indinavir. Ergot alkaloid preparations should not be used in combination with PIs. If rifabutin is used concomitantly, rifabutin dose should be reduced because of inhibition of rifabutin metabolism; with concomitant indinavir or nelfinavir use, reduce rifabutin dose by 50%. Serum levels of PIs may be increased when multiple PIs are used in combination.*

havioral measures (i.e., sexual abstinence or condom use) to prevent secondary transmission, all of which influence their lives for several weeks to months. Therefore, access to persons who are knowledgeable about occupational HIV transmission and who can deal with the many concerns an HIV exposure may raise for the HCW is an important element of postexposure management.

HIV-exposed HCWs should be advised to use the following measures to prevent secondary transmission during the follow-up period, especially during the first 6-12 weeks after the exposure when most HIV-infected persons are expected to seroconvert: use sexual abstinence or condoms to prevent sexual transmission and to avoid pregnancy; and refrain from donating blood, plasma, organs, tissue, or semen. If the exposed HCW is breastfeeding, she should be counseled about the risk for HIV transmission through breast milk, and discontinuation of breastfeeding should be considered, especially following high-risk exposures. If the HCW chooses to receive PEP, temporary discontinuation of breastfeeding while she is taking PEP should be considered to avoid exposing the infant to these agents. NRTIs are known to pass into breast milk; it is not known whether this also is true for PIs.

There is no need to modify an HCW's patient-care responsibilities to prevent transmission to patients based solely on an HIV exposure. If HIV seroconversion is detected, the HCW should be evaluated according to published recommendations for HIV-infected HCWs.

Exposed HCWs should be advised to seek medical evaluation for any acute illness that occurs during the follow-up period. Such an illness, particularly if characterized by fever, rash, myalgia, fatigue, malaise, or lymphadenopathy, may be indicative of acute HIV infection but also may be due to a drug reaction or another medical condition.

Exposed HCWs who choose to take PEP should be advised of the importance of completing the prescribed regimen. Information should be provided about potential drug interactions and the drugs that should not be taken with PEP, the side effects of the drugs that have been prescribed, measures to minimize these effects, and the methods of clinical monitoring for toxicity during the follow-up period. They should be advised that the evaluation of certain symptoms should not

### *Virginia Resources*

The Virginia Department of Health funds four Regional AIDS Resource and Consultation Centers, whose mission is to provide education and consultation to health care providers in Virginia. Additional materials and specific educational programs targeting occupational exposure and postexposure prophylaxis may be obtained by calling:

Central Regional HIV/AIDS Center 800/525-7605
Eastern Regional HIV/AIDS Center 800/999-8385
Northern Regional HIV/AIDS Center 800/828-4927
Western Regional HHIV/AIDS Center 800/421-1102 Charlottesville
800/950-4056 Roanoke

| Table 1. Basic and Expanded Postexposure Prophylaxis Regimens | | |
|---|---|---|
| **Regimen Category** | **Application** | **Drug Regimen** |
| **Basic** | Occupational HIV exposures for which there is a recognized transmission risk.* | 4 weeks (28 days) of both zidovudine 600 mg every day in divided doses (i.e., 300 mg twice a day, 200 mg three times a day, or 100 mg every 4 hours) and lamivudine 150 mg twice a day. |
| **Expanded** | Occupational HIV exposures that pose an increased risk for transmission (e.g., larger volume of blood and/or higher virus titer in blood).* | Basic regimen plus either indinavir 800 mg every 8 hours or nelfinavir 750 mg three times a day.† |

**See Figure 3, page 5.*
*†Indinavir should be taken on an empty stomach (i.e., without food or with a light meal) and with increased fluid consumption (i.e., drinking six 8 oz glasses of water throughout the day); nelfinavir should be taken with meals.*

be delayed (e.g., back or abdominal pain, pain on urination or blood in the urine, or symptoms of hyperglycemia [i.e., increased thirst and/or frequent urination]).

## *RECOMMENDATIONS FOR THE SELECTION OF DRUGS FOR PEP*

The selection of a drug regimen for HIV PEP must strive to balance the risk for infection against the potential toxicity of the agent(s) used. Because PEP is potentially toxic, its use is not justified for exposures that pose a negligible risk for transmission. Also, there is insufficient evidence to recommend a highly active regimen for all HIV exposures. Therefore, two regimens for PEP are provided (Table 1): a "basic" two-drug regimen that should be appropriate for most HIV exposures and an "expanded" three-drug regimen that should be used for exposures that pose an increased risk for transmission or where resistance to one or more antiretroviral agents is known or suspected.

### *Situations That Require Special Consideration*

#### Resistance of the Source Virus to Antiretroviral Drugs

It is unknown whether drug resistance influences transmission risk; however, transmission of drug-resistant HIV has been reported and is therefore a theoretical concern when choosing PEP regimens. If the source person's virus is known or suspected to be resistant to one or more of the drugs included in the PEP regimen, the selection of drugs to which the source person's virus is unlikely to be resistant is recommended. If the resistance is to one class of antiretroviral drugs, the addition to the basic PEP regimen of a drug from another class might be considered (e.g., addition of a PI when a source patient has not been treated with a PI but has virus resistant to one or more NRTIs). It is strongly recommended that PEP be started regardless of the resistance status in the source virus; if resistance is known or suspected, a third or fourth drug may be added to the regimen until consultation with a clinical expert in the treatment of HIV infection or disease can be obtained.

#### Known or Suspected Pregnancy in the HCW

Pregnancy should not preclude the use of optimal PEP regimens, and PEP should not be denied to an HCW solely on the basis of pregnancy. However, as discussed previously, an occupationally exposed pregnant HCW must be provided with full information about what is known and not known regarding the potential benefits and risks associated with use of the antiretroviral drugs to her and her fetus for her to make an informed decision regarding the use of PEP. The choice of antiretroviral drugs to use for PEP in pregnant HCWs is complicated by the potential need to alter dosing because of physiologic changes associated with pregnancy and the potential for short- or long-term effects on the fetus and newborn. Thus, considerations that should be discussed with a pregnant HCW include the potential risk for HIV transmission based on the type of exposure; the stage of pregnancy (the first trimester being the period of maximal organogenesis and risk for teratogenesis); and what is known about the pharmacokinetics, safety, and tolerability of the drug or combination of drugs in pregnancy.

## *POSTEXPOSURE REGISTRIES*

Health-care providers in the United States are encouraged to enroll HCWs who receive PEP in a confidential registry developed by CDC, Glaxo Wellcome Inc., and Merck & Co., Inc., to assess toxicity (Table 2). Unusual or serious and unexpected toxicity from antiretroviral drugs should be reported to the manufacturer and/or FDA.

Health-care providers also should report instances of prenatal exposure to antiretroviral agents to the Antiretroviral Pregnancy Registry. The registry is an epidemiologic project to collect observational, nonexperimental data on antiretroviral drug exposure during pregnancy to assess potential teratogenicity.

A protocol has been developed to evaluate HIV seroconversion in an HCW who received PEP. These events can be reported to CDC, telephone (404) 639-6425.

| Table 2. HIV Postexposure Prophylaxis Resources and Registries | |
|---|---|
| **Resource or Registry** | **Contact Information** |
| HIV Postexposure Prophylaxis Registry (for reporting HCWs who receive PEP) | Telephone: (888)737-4448<br>Write: 1410 Commonwealth Drive<br>Suite 215<br>Wilmington, NC 28405 |
| Food and Drug Administration (for reporting unusual or severe toxicity to antiretroviral agents) | Telephone: (800)332-1088 |
| Antiretroviral Pregnancy Registry (for reporting pregnant women who receive PEP) | Telephone: (800)258-4263<br>(800)722-9292, ext 39437<br>Fax: (800)800-1052<br>Write: 1410 Commonwealth Drive<br>Suite 215<br>Wilmington, NC 28405 |
| CDC (for reporting HIV seroconversions in HCWs who receive PEP) | Telephone: (404)639-6425 |
| National Clinicians' Postexposure Hotline (for obtaining information about postexposure management of HCWs) | Telephone: (888)448-4911 |

## Cases of Selected Notifiable Diseases Reported in Virginia*

| Disease | Total Cases Reported, February 1998 | | | | | | Total Cases Reported Statewide, January through February | | |
|---|---|---|---|---|---|---|---|---|---|
| | State | Regions | | | | | This Year | Last Year | 5 Yr Avg |
| | | NW | N | SW | C | E | | | |
| **AIDS** | 64 | 6 | 16 | 4 | 22 | 16 | 99 | 186 | 175 |
| **Campylobacteriosis** | 47 | 18 | 6 | 17 | 4 | 2 | 64 | 32 | 47 |
| **Giardiasis** | 27 | 3 | 9 | 9 | 4 | 2 | 46 | 50 | 35 |
| **Gonorrhea** | 519 | 25 | 63 | 35 | 106 | 290 | 1068 | 1544 | 1620 |
| **Hepatitis A** | 15 | 1 | 4 | 2 | 3 | 5 | 25 | 24 | 23 |
| **Hepatitis B** | 7 | 0 | 1 | 4 | 0 | 2 | 10 | 11 | 15 |
| **Hepatitis NANB** | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 2 |
| **HIV Infection** | 78 | 3 | 38 | 2 | 21 | 14 | 120 | 166 | 125 |
| **Influenza** | 64 | 26 | 8 | 21 | 3 | 6 | 470 | 355 | 426 |
| **Legionellosis** | 2 | 2 | 0 | 0 | 0 | 0 | 4 | 0 | 1 |
| **Lyme Disease** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 |
| **Measles** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Meningitis, Aseptic** | 12 | 0 | 3 | 3 | 0 | 6 | 15 | 21 | 21 |
| **Meningitis, Bacterial†** | 4 | 1 | 0 | 2 | 0 | 1 | 8 | 9 | 10 |
| **Meningococcal Infections** | 5 | 0 | 0 | 0 | 1 | 4 | 9 | 9 | 9 |
| **Mumps** | 2 | 0 | 1 | 0 | 0 | 1 | 2 | 1 | 4 |
| **Pertussis** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 3 |
| **Rabies in Animals** | 49 | 12 | 18 | 8 | 7 | 4 | 83 | 64 | 54 |
| **Rocky Mountain Spotted Fever** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Rubella** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Salmonellosis** | 42 | 2 | 8 | 8 | 14 | 10 | 83 | 89 | 110 |
| **Shigellosis** | 9 | 1 | 6 | 1 | 0 | 1 | 17 | 61 | 51 |
| **Syphilis, Early‡** | 35 | 0 | 2 | 9 | 13 | 11 | 96 | 102 | 159 |
| **Tuberculosis** | 24 | 1 | 9 | 4 | 3 | 7 | 30 | 86 | 36 |

*Localities Reporting Animal Rabies This Month:* Accomack 1 raccoon; Albemarle 1 raccoon; Amherst 2 skunks; Appomattox 1 raccoon; Bedford 1 raccoon; Clarke 1 fox, 1 raccoon; Essex 1 skunk; Fairfax 1 bat, 3 foxes, 6 raccoons, 2 skunks; Floyd 1 skunk; Frederick 1 raccoon; Goochland 1 raccoon; Greensville 1 skunk; Halifax 2 raccoons; Hanover 1 bat; Loudoun 1 cat, 1 fox, 2 raccoons, 1 skunk; Nelson 2 raccoons; Newport News 1 raccoon; Patrick 1 raccoon; Pittsylvania 1 raccoon, 1 skunk; Powhatan 1 raccoon; Prince William 1 raccoon; Rockingham 1 cow; Spotsylvania 3 raccoons; Stafford 2 raccoons; Sussex 1 dog; York 1 raccoon.

*Occupational Illnesses:* Asbestosis 18; Carpal Tunnel Syndrome 47; Hearing Loss 12; Lead Poisoning 4; Pneumoconiosis 12.

*Data for 1998 are provisional. †Other than meningococcal. ‡Includes primary, secondary, and early latent.

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