Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis
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The antiretroviral agents mentioned in the article do not have an approved indication by the FDA for postexposure prophylaxis. The material presented is based on expert review and does not reflect the views of the FDA.
Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis

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Summary

This report updates U.S. Public Health Service recommendations for the management of health-care personnel (HCP) who have occupational exposure to blood and other body fluids that might contain human immunodeficiency virus (HIV). Although the principles of exposure management remain unchanged, recommended HIV postexposure prophylaxis (PEP) regimens have been changed. This report emphasizes adherence to HIV PEP when it is indicated for an exposure, expert consultation in management of exposures, follow-up of exposed workers to improve adherence to PEP, and monitoring for adverse events, including seroconversion. To ensure timely postexposure management and administration of HIV PEP, clinicians should consider occupational exposures as urgent medical concerns.

Introduction

Although preventing exposures to blood and body fluids is the primary means of preventing occupationally acquired human immunodeficiency virus (HIV) infection, appropriate postexposure management is an important element of workplace safety. In 1996, the first U.S. Public Health Service (PHS) recommendations for the use of postexposure prophylaxis (PEP) after occupational exposure to HIV were published; these recommendations have been updated twice (1–3). Since publication of the most recent guidelines in 2001, new antiretroviral agents have been approved by the Food and Drug Administration (FDA), and additional information has become available regarding the use and safety of HIV PEP. In August 2003, CDC convened a meeting of a PHS interagency working group* and consultants to assess use of HIV PEP.

On the basis of this discussion, the PHS working group decided that updated recommendations for the management of occupational exposure to HIV were warranted. This report modifies and expands the list of antiretroviral medications that can be considered for use as PEP. This report also emphasizes prompt management of occupational exposures, selection of tolerable regimens, attention to potential drug interactions involving drugs that could be included in HIV PEP regimens and other medications, consultation with experts for postexposure management strategies (especially determining whether an exposure has actually occurred) and selection of HIV PEP regimens, use of HIV rapid testing, and counseling and follow-up of exposed personnel.

Recommendations on the management of occupational exposures to hepatitis B virus or hepatitis C virus have been published previously (3) and are not included in this report. Recommendations for nonoccupational (e.g., sexual, pediatric, and perinatal) HIV exposures also have been published previously (4–6).

Definition of Health-Care Personnel and Exposure

The definitions of health-care personnel (HCP) and occupational exposures are unchanged from those used in 2001 (3). The term HCP refers to all paid and unpaid persons working in health-care settings who have the potential for exposure to infectious materials (e.g., blood, tissue, and specific body fluids and medical supplies, equipment, or environmental
surfaces contaminated with these substances). HCP might include, but are not limited to, emergency medical service personnel, dental personnel, laboratory personnel, autopsy personnel, nurses, nursing assistants, physicians, technicians, therapists, pharmacists, students and trainees, contractual staff not employed by the health-care facility, and persons not directly involved in patient care but potentially exposed to blood and body fluids (e.g., clerical, dietary, housekeeping, maintenance, and volunteer personnel). The same principles of exposure management could be applied to other workers who have potential for occupational exposure to blood and body fluids in other settings.

An exposure that might place HCP at risk for HIV infection is defined as a percutaneous injury (e.g., a needlestick or cut with a sharp object) or contact of mucous membrane or nonintact skin (e.g., exposed skin that is chapped, abraded, or afflicted with dermatitis) with blood, tissue, or other body fluids that are potentially infectious. In addition to blood and visibly bloody body fluids, semen and vaginal secretions also are considered potentially infectious. Although semen and vaginal secretions have been implicated in the sexual transmission of HIV, they have not been implicated in occupational transmission from patients to HCP. The following fluids also are considered potentially infectious: cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, and amniotic fluid. The risk for transmission of HIV infection from these fluids is unknown; the potential risk to HCP from occupational exposures has not been assessed by epidemiologic studies in health-care settings. Feces, nasal secretions, saliva, sputum, sweat, tears, urine, and vomitus are not considered potentially infectious unless they are visibly bloody; the risk for transmission of HIV infection from these fluids and materials is low (7).

Any direct contact (i.e., contact without barrier protection) to concentrated virus in a research laboratory or production facility requires clinical evaluation. For human bites, clinical evaluation must include the possibility that both the person bitten and the person who inflicted the bite were exposed to bloodborne pathogens. Transmission of HIV infection by this route has been reported rarely, but not after an occupational exposure (8–12).

Risk for Occupational Transmission of HIV

The risks for occupational transmission of HIV have been described; risks vary with the type and severity of exposure (2,3,7). In prospective studies of HCP, the average risk for HIV transmission after a percutaneous exposure to HIV-infected blood has been estimated to be approximately 0.3% (95% confidence interval [CI] = 0.2%–0.5%) (7) and after a mucous membrane exposure, approximately 0.09% (CI = 0.006%–0.5%) (3). Although episodes of HIV transmission after nonintact skin exposure have been documented, the average risk for transmission by this route has not been precisely quantified but is estimated to be less than the risk for mucous membrane exposures. The risk for transmission after exposure to fluids or tissues other than HIV-infected blood also has not been quantified but is probably considerably lower than for blood exposures.

Epidemiologic and laboratory studies suggest that multiple factors might affect the risk for HIV transmission after an occupational exposure (3). In a retrospective case-control study of HCP who had percutaneous exposure to HIV, increased risk for HIV infection was associated with exposure to a larger quantity of blood from the source person as indicated by 1) a device (e.g., a needle) visibly contaminated with the patient’s blood, 2) a procedure that involved a needle being placed directly in a vein or artery, or 3) a deep injury. The risk also was increased for exposure to blood from source persons with terminal illness, possibly reflecting either the higher titer of HIV in blood late in the course of acquired immunodeficiency syndrome (AIDS) or other factors (e.g., the presence of syncytia-inducing strains of HIV). A laboratory study that demonstrated that more blood is transferred by deeper injuries and hollow-bore needles lends further support for the observed variation in risk related to blood quantity (3).

The use of source-person viral load as a surrogate measure of viral titer for assessing transmission risk has not yet been established. Plasma viral load (e.g., HIV RNA) reflects only the level of cell-free virus in the peripheral blood; latently infected cells might transmit infection in the absence of viremia. Although a lower viral load (e.g., <1,500 RNA copies/mL) or one that is below the limits of detection probably indicates a lower titer exposure, it does not rule out the possibility of transmission.

Antiretroviral Agents for PEP

Antiretroviral agents from five classes of drugs are currently available to treat HIV infection (13,14). These include the nucleoside reverse transcriptase inhibitors (NRTIs), nucleotide reverse transcriptase inhibitors (NtRTIs), nonnucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), and a single fusion inhibitor. Only antiretroviral agents approved by FDA for treatment of HIV infection are included in these guidelines. The recommendations in this report provide guidance for two- or more drug PEP regimens on the basis of the level of risk for HIV transmission represented by the exposure (Tables 1 and 2; Appendix).
### TABLE 1. Recommended HIV postexposure prophylaxis (PEP) for percutaneous injuries

<table>
<thead>
<tr>
<th>Exposure type</th>
<th>HIV-positive, class 1*</th>
<th>HIV-positive, class 2†</th>
<th>Source of unknown HIV status‡</th>
<th>Unknown source§</th>
<th>HIV-negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less severe¶</td>
<td>Recommend basic 2-drug PEP</td>
<td>Recommend expanded ≥3-drug PEP</td>
<td>Generally, no PEP warranted; however, consider basic 2-drug PEP** for source with HIV risk factors††</td>
<td>Generally, no PEP warranted; however, consider basic 2-drug PEP** in settings in which exposure to HIV-infected persons is likely</td>
<td>No PEP warranted</td>
</tr>
<tr>
<td>More severe§§</td>
<td>Recommend expanded 3-drug PEP</td>
<td>Recommend expanded ≥3-drug PEP</td>
<td>Generally, no PEP warranted; however, consider basic 2-drug PEP** for source with HIV risk factors††</td>
<td>Generally, no PEP warranted; however, consider basic 2-drug PEP** in settings in which exposure to HIV-infected persons is likely</td>
<td>No PEP warranted</td>
</tr>
</tbody>
</table>

* HIV-positive, class 1 — asymptomatic HIV infection or known low viral load (e.g., <1,500 ribonucleic acid copies/mL). HIV-positive, class 2 — symptomatic HIV infection, acquired immunodeficiency syndrome, acute seroconversion, or known high viral load. If drug resistance is a concern, obtain expert consultation. Initiation of PEP should not be delayed pending expert consultation, and, because expert consultation alone cannot substitute for face-to-face counseling, resources should be available to provide immediate evaluation and follow-up care for all exposures.

† For example, deceased source person with no samples available for HIV testing.

‡ For example, a needle from a sharps disposal container.

¶ For example, solid needle or superficial injury.

** The recommendation “consider PEP” indicates that PEP is optional; a decision to initiate PEP should be based on a discussion between the exposed person and the treating clinician regarding the risks versus benefits of PEP.

†† If PEP is offered and administered and the source is later determined to be HIV-negative, PEP should be discontinued.

§§ For example, large-bore hollow needle, deep puncture, visible blood on device, or needle used in patient’s artery or vein.

### TABLE 2. Recommended HIV postexposure prophylaxis (PEP) for mucous membrane exposures and nonintact skin† exposures

<table>
<thead>
<tr>
<th>Exposure type</th>
<th>HIV-positive, class 1*</th>
<th>HIV-positive, class 2†</th>
<th>Source of unknown HIV status‡</th>
<th>Unknown source§</th>
<th>HIV-negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small volume**</td>
<td>Consider basic 2-drug PEP††</td>
<td>Recommend basic 2-drug PEP</td>
<td>Generally, no PEP warranted</td>
<td>Generally, no PEP warranted</td>
<td>No PEP warranted</td>
</tr>
<tr>
<td>Large volume¶¶</td>
<td>Recommend basic 2-drug PEP</td>
<td>Recommend expanded ≥3-drug PEP</td>
<td>Generally, no PEP warranted; however, consider basic 2-drug PEP†† for source with HIV risk factors§§</td>
<td>Generally, no PEP warranted; however, consider basic 2-drug PEP†† in settings in which exposure to HIV-infected persons is likely</td>
<td>No PEP warranted</td>
</tr>
</tbody>
</table>

* For skin exposures, follow-up is indicated only if evidence exists of compromised skin integrity (e.g., dermatitis, abrasion, or open wound).

† HIV-positive, class 1 — asymptomatic HIV infection or known low viral load (e.g., <1,500 ribonucleic acid copies/mL). HIV-positive, class 2 — symptomatic HIV infection, AIDS, acute seroconversion, or known high viral load. If drug resistance is a concern, obtain expert consultation. Initiation of PEP should not be delayed pending expert consultation, and, because expert consultation alone cannot substitute for face-to-face counseling, resources should be available to provide immediate evaluation and follow-up care for all exposures.

‡ For example, deceased source person with no samples available for HIV testing.

† For example, splash from inappropriately disposed blood.

** For example, a few drops.

†† The recommendation “consider PEP” indicates that PEP is optional; a decision to initiate PEP should be based on a discussion between the exposed person and the treating clinician regarding the risks versus benefits of PEP.

§§ If PEP is offered and administered and the source is later determined to be HIV-negative, PEP should be discontinued.

¶¶ For example, a major blood splash.
Toxicity and Drug Interactions of Antiretroviral Agents

Persons receiving PEP should complete a full 4-week regimen (3). However, as a result of toxicity and side effects among HCP, a substantial proportion of HCP have been unable to complete a full 4-week course of HIV PEP (15–20). Because all antiretroviral agents have been associated with side effects (Table 3), the toxicity profile of these agents, including the frequency, severity, duration, and reversibility of side effects, is an important consideration in selection of an HIV PEP regimen. The majority of data concerning adverse events have been reported primarily for persons with established HIV infection receiving prolonged antiretroviral therapy and therefore might not reflect the experience of uninfected persons who take PEP. Anecdotal evidence from clinicians knowledgeable about HIV treatment indicates that antiretroviral agents are tolerated more poorly among HCP taking HIV PEP than among HIV-infected patients on antiretroviral medications.

Side effects have been reported frequently by persons taking antiretroviral agents as PEP (15–23). In multiple instances, a substantial (range: 17%–47%) proportion of HCP taking PEP after occupational exposures to HIV-positive sources did not complete a full 4-week course of therapy because of inability to tolerate the drugs (15–17,19,20). Data from the National Surveillance System for Health Care Workers (NaSH), CDC’s occupational surveillance system for occupational exposures and infections in hospitals, for June 1995–December 2004 indicate that 401 (46.9%) of 921 HCP with at least one follow-up visit after starting PEP experienced one or more symptoms. The symptom reported most frequently was nausea (26.5%), followed by malaise and fatigue (22.8%) (CDC, unpublished data, 2005). Of 503 HCP who stopped HIV PEP prematurely (<28 days), 361 (24.0%) did so because of adverse effects of the drugs. Similar data have been reported from the Italian Registry of Antiretroviral Postexposure Prophylaxis, which includes data primarily on HCP taking PEP but also collects data on those taking PEP after nonoccupational exposures (18). In multivariate analysis, those taking regimens that include PI were more likely to experience PEP-associated side effects and to discontinue PEP prematurely (<28 days). Because side effects are frequent and

### TABLE 3. Primary side effects and toxicities associated with antiretroviral agents used for HIV postexposure prophylaxis, by class and agent

<table>
<thead>
<tr>
<th>Class and agent</th>
<th>Side effect and toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nucleoside reverse transcriptase inhibitors (NRTIs)</strong></td>
<td>Class warning: all NRTIs have the potential to cause lactic acidosis with hepatic steatosis</td>
</tr>
<tr>
<td>Zidovudine (Retrovir®, ZDV, AZT)</td>
<td>Anemia, neutropenia, nausea, headache, insomnia, muscle pain, and weakness</td>
</tr>
<tr>
<td>Lamivudine (Epivir®, 3TC)</td>
<td>Abdominal pain, nausea, diarrhea, rash, and pancreatitis</td>
</tr>
<tr>
<td>Stavudine (Zerit™; d4T)</td>
<td>Peripheral neuropathy, headache, diarrhea, nausea, insomnia, anorexia, pancreatitis, elevated liver function tests (LFTs), anemia, and neutropenia</td>
</tr>
<tr>
<td>Didanosine (Videx®, ddI)</td>
<td>Pancreatitis, lactic acidosis, neuropathy, diarrhea, abdominal pain, and nausea</td>
</tr>
<tr>
<td>Emtricitabine (Emtriva, FTC)</td>
<td>Headache, nausea, vomiting, diarrhea, and rash. Skin discoloration (mild hyperpigmentation on palms and soles), primarily among nonwhites</td>
</tr>
<tr>
<td><strong>Nucleotide analogue reverse transcriptase inhibitor (NtRTI)</strong></td>
<td>Class warning: All NtRTIs have the potential to cause lactic acidosis with hepatic steatosis</td>
</tr>
<tr>
<td>Tenofovir (Viread®, TDF)</td>
<td>Nausea, diarrhea, vomiting, flatulence, and headache</td>
</tr>
<tr>
<td><strong>Nonnucleoside reverse transcriptase inhibitors (NNRTIs)</strong></td>
<td>Rash (including cases of Stevens-Johnson syndrome), insomnia, somnolence, dizziness, trouble concentrating, abnormal dreaming, and teratogenicity</td>
</tr>
<tr>
<td>Efavirenz (Sustiva®, EFV)</td>
<td>Nausea, abdominal pain, nephrolithiasis, and indirect hyperbilirubinemia</td>
</tr>
<tr>
<td><strong>Protease inhibitor</strong></td>
<td>Diarrhea, nausea, abdominal pain, weakness, and rash</td>
</tr>
<tr>
<td>Indinavir (Crixivan®, IDV)</td>
<td>Weakness, diarrhea, nausea, circumoral paresthesia, taste alteration, and elevated cholesterol and triglycerides</td>
</tr>
<tr>
<td>Nefninavir (Viracept®, NFV)</td>
<td>Diarrhea, abdominal pain, nausea, hyperglycemia, and elevated LFTs</td>
</tr>
<tr>
<td>Ritonavir (Norvir®, RTV)</td>
<td>Nausea, diarrhea, rash, circumoral paresthesia, taste alteration, and depression</td>
</tr>
<tr>
<td>Saquinavir (Invirase®, SQV)</td>
<td>Nausea, headache, rash, abdominal pain, diarrhea, vomiting, and indirect hyperbilirubinemia</td>
</tr>
<tr>
<td>Fosamprenavir (Lexiva®, FOSAPV)</td>
<td>Diarrhea, fatigue, headache, nausea, and increased cholesterol and triglycerides</td>
</tr>
<tr>
<td>Atazanavir (Reyataz®, ATV)</td>
<td>Local injection site reactions, bacterial pneumonia, insomnia, depression, peripheral neuropathy, and cough</td>
</tr>
<tr>
<td>Lopinavir/ritonavir (Kaletra®, LPV/RTV)</td>
<td></td>
</tr>
<tr>
<td><strong>Fusion inhibitor</strong></td>
<td></td>
</tr>
<tr>
<td>Enfuvirtide (Fuzeon®, T-20)</td>
<td></td>
</tr>
</tbody>
</table>

particularly because they are cited as a major reason for not completing PEP regimens as prescribed, the selection of regimens should be heavily influenced toward those that are tolerable for short-term use.

In addition, all approved antiretroviral agents might have potentially serious drug interactions when used with certain other drugs, requiring careful evaluation of concomitant medications, including over-the-counter medications and supplements (e.g., herbs), used by an exposed person before prescribing PEP and close monitoring for toxicity of anyone receiving these drugs (24–33) (Tables 3–5). PIs and NNRTIs have the greatest potential for interactions with other drugs. Information regarding potential drug interactions has been published (13,24–33). Additional information is included in the manufacturers’ package inserts. Because of interactions, certain drugs should not be administered concomitantly with PIs or with efavirenz (EFV) (Tables 4 and 5). Consultation with a pharmacist might be considered.

Selection of HIV PEP Regimens

Determining which agents and how many to use or when to alter a PEP regimen is primarily empiric (34). Guidelines for treating HIV infection, a condition typically involving a high total body burden of HIV, recommend use of three or more drugs (13,14); however, the applicability of these recommendations to PEP is unknown. Among HIV-infected patients, combination regimens with three or more antiretroviral agents have proved superior to monotherapy and dual-therapy regimens in reducing HIV viral load, reducing incidence of opportunistic infections and death, and delaying onset of drug resistance (13,14). In theory, a combination of drugs with activity at different stages in the viral replication cycle (e.g., nucleoside analogues with a PI) might offer an additive preventive effect in PEP, particularly for occupational exposures that pose an increased risk for transmission or for transmission of a resistant virus. Although use of a three- (or more) drug regimen might be justified for exposures that pose an increased risk for transmission, whether the potential added toxicity of a third or fourth drug is justified for lower-risk exposures is uncertain, especially in the absence of data supporting increased efficacy of more drugs in the context of occupational PEP. Offering a two-drug regimen is a viable option, primarily because the benefit of completing a full course of this regimen exceeds the benefit of adding the third agent and risking noncompletion (35). In addition, the total body burden of HIV is substantially lower among exposed HCP than among persons with established HIV infection. For these reasons, the recommendations in this report provide guidance for two- and three- (or more) drug PEP regimens on the basis of the level of risk for HIV transmission represented by the exposure (Tables 1 and 2; Appendix).

Resistance to Antiretroviral Agents

Known or suspected resistance of the source virus to antiretroviral agents, particularly those that might be included in a PEP regimen, is a concern for persons making decisions about PEP (36). Drug resistance to all available antiretroviral agents has been reported, and cross-resistance within drug classes is frequent (37). Although occupational transmission of drug-resistant HIV strains has been reported despite PEP

### TABLE 4. Prescription and over-the-counter drugs that should not be administered with protease inhibitors (PIs) because of drug interactions*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimycobacterials: rifampin</td>
<td>Decreases plasma concentrations and area under plasma concentration curve of the majority of PIs by approximately 90%, which might result in loss of therapeutic effect and development of resistance</td>
</tr>
<tr>
<td>Benzodiazepines: midazolam, triazolam</td>
<td>Contraindicated because of potential for serious or life-threatening events (e.g., prolonged or increased sedation or respiratory depression)</td>
</tr>
<tr>
<td>Ergot derivatives: dihydroergotamine, ergotamine, ergonovine, methylergonovine</td>
<td>Contraindicated because of potential for serious or life-threatening events (e.g., acute ergot toxicity characterized by peripheral vasoconstriction and ischemia of the extremities and other tissues)</td>
</tr>
<tr>
<td>Gastrointestinal motility agent: cisapride</td>
<td>Contraindicated because of potential for serious or life-threatening events (e.g., cardiac arrhythmias)</td>
</tr>
<tr>
<td>HMG-CoA reductase inhibitors (“statins“): lovastatin, simvastatin</td>
<td>Potential for serious reactions (e.g., myopathy, including rhabdomyolysis); atorvastatin may be used cautiously, beginning with lowest possible starting dose, and monitoring for adverse events</td>
</tr>
<tr>
<td>Neuroleptic: pimozide</td>
<td>Contraindicated because of potential for serious or life-threatening events (e.g., cardiac arrhythmias)</td>
</tr>
<tr>
<td>Inhaled steroids: fluticasone</td>
<td>Coadministration of fluticasone and ritonavir-boosted protease inhibitors are not recommended unless the potential benefit to the patient outweighs the risk for systemic corticosteroid side effect</td>
</tr>
<tr>
<td>Herbal products: St. John’s wort (hypericum perforatum), garlic</td>
<td>Coadministration might reduce plasma concentrations of protease inhibitors, which might result in loss of therapeutic effect and development of resistance; garlic might lower saquinavir level</td>
</tr>
</tbody>
</table>

* This table does not list all products that should not be administered with PIs (atazanavir, lopinavir/ritonavir, fosamprenavir, indinavir, nelfinavir, saquinavir). Product labels should be consulted for additional information regarding drug interactions.

with combination drug regimens (36,38–40), the effect of exposure to a resistant virus on transmission and transmissibility is not well understood.

Since publication of the previous guidelines, an additional report of an occupational HIV seroconversion despite combination HIV PEP has been published (Table 6) (38), bringing the total number of reports worldwide to six. The exposure was a percutaneous injury sustained by a nurse performing a phlebotomy on a heavily treatment-experienced patient. At the time of the exposure, the source patient was failing treatment with stavudine (d4T), lamivudine (3TC), ritonavir (RTV), and saquinavir (SQV) and had a history of previous treatment with zidovudine (ZDV) and zalcitabine (ddC). Genotypic resistance testing performed within 1 month of the exposure suggested resistance to ZDV and 3TC. Phenotypic testing confirmed resistance to 3TC but demonstrated relative susceptibility to ZDV and d4T. The source virus demonstrated no evidence of resistance to nevirapine (NVP) or other NNRTIs. The initial HIV PEP regimen started within 95 minutes of the exposure was ZDV, 3TC, and indinavir.

**TABLE 5. Prescription and over-the-counter drugs that should not be administered with efavirenz because of drug interactions***

<table>
<thead>
<tr>
<th>Drug</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antifungal: voriconazole</td>
<td>Contraindicated because efavirenz substantially decreases voriconazole plasma concentrations</td>
</tr>
<tr>
<td>Benzodiazepines: midazolam, triazolam</td>
<td>Contraindicated because of potential for serious or life-threatening events (e.g., prolonged or increased sedation or respiratory depression)</td>
</tr>
<tr>
<td>Ergot derivatives: dihydroergotamine, ergotamine, ergonovine, methylergonovine</td>
<td>Contraindicated because of potential for serious or life-threatening events (e.g., acute ergot toxicity characterized by peripheral vasospasm and ischemia of the extremities and other tissues)</td>
</tr>
<tr>
<td>Gastrointestinal motility agent: cisapride</td>
<td>Contraindicated because of potential for serious or life-threatening events (e.g., cardiac arrhythmias)</td>
</tr>
<tr>
<td>Herbal products: St. John’s wort (hypericum perforatum), garlic</td>
<td>Co-administration might reduce plasma concentrations of protease inhibitors, which might result in loss of therapeutic effect and development of resistance</td>
</tr>
</tbody>
</table>

* This table does not list all products that should not be coadministered with efavirenz. Efavirenz product labeling should be consulted for additional information regarding drug interactions.


**TABLE 6. Reported instances of failure of combination drug postexposure prophylaxis (PEP) to prevent HIV-infection among health-care personnel exposed to HIV-infected blood through percutaneous injury**

<table>
<thead>
<tr>
<th>Year of incidence</th>
<th>Device</th>
<th>PEP regimen*</th>
<th>Time to first dose (hrs)</th>
<th>No. of days to onset of retroviral illness</th>
<th>No. of days to document seroconversion†</th>
<th>HIV-infection status</th>
<th>Source-patient</th>
<th>Virus resistant to antiretrovirals‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>1992†</td>
<td>Biopsy needle</td>
<td>ZDV, ddl</td>
<td>0.5</td>
<td>23</td>
<td>23</td>
<td>AIDS</td>
<td>Terminally ill</td>
<td>Unknown</td>
</tr>
<tr>
<td>1996**</td>
<td>Hollow-bore needle</td>
<td>ZDV, ddl‡</td>
<td>1.5</td>
<td>45</td>
<td>97</td>
<td>Asymptomatic HIV infection</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>1997***</td>
<td>Large or hollow-bore needle</td>
<td>ZDV, 3TC, IDV§§</td>
<td>1.5</td>
<td>40</td>
<td>55</td>
<td>AIDS</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>1998¶¶</td>
<td>Hollow-bore needle</td>
<td>ZDV, 3TC, ddl, IDV</td>
<td>0.7</td>
<td>70</td>
<td>83</td>
<td>AIDS</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>1999***</td>
<td>Unknown sharp</td>
<td>d4T, IDV</td>
<td>2.0</td>
<td>42</td>
<td>100</td>
<td>AIDS</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>2001†††</td>
<td>Phlebotomy needle</td>
<td>ZDV, 3TC, IDV</td>
<td>1.6</td>
<td>24</td>
<td>−90</td>
<td>AIDS</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* ZDV = zidovudine; ddl = didanosine; 3TC = lamivudine; IDV = indinavir; d4T = stavudine; and NVP = nevirapine.
† By enzyme immunoassay for HIV-1 antibody and Western blot.
‡ By genotypic or phenotypic resistance testing.
††† ZDV and 3TC taken for 1 dose and then changed to ddl, d4T, and NVP; ddl was discontinued after 3 days as a result of severe vomiting.
‡‡‡ ZDV, 3TC, and IDV initially and then changed after first dose to d4T, ddl, and NVP; then ddl discontinued after 8 days; and d4T and NVP taken for 4 weeks.
The worker was referred to a hospital where the regimen was changed within 6 hours of the exposure to didanosine (ddI), d4T, and NVP because of concerns regarding possible drug resistance to certain or all of the components of the initial PEP regimen. The exposed worker stopped ddI after 8 days because of symptoms but continued to take d4T and NVP, stopping at day 24 because of a generalized macular pruritic rash and mild thrombocytopenia. Seroconversion was documented at 3 months. Sequencing of viruses from the source and exposed worker demonstrated their close relatedness. Virus from the worker demonstrated the same resistance patterns as those in the source patient. In addition, the worker’s virus had a mutation suggesting resistance to the NNRTI class (38).

Empiric decisions regarding the presence of antiretroviral drug resistance are often difficult because patients frequently take more than one antiretroviral agent. Resistance should be suspected in a source patient when clinical progression of disease or a persistently increasing viral load or decline in CD4+ T-cell count occurs despite therapy, or when no virologic response to therapy occurs. However, resistance testing of the source virus at the time of an exposure is impractical because the results will not be available in time to influence the choice of the initial PEP regimen. No data suggest that modification of a PEP regimen after resistance testing results become available (usually 1–2 weeks) improves efficacy of PEP (41).

### Antiretroviral Drugs During Pregnancy

Data regarding the potential effects of antiretroviral drugs on the developing fetus or neonate are limited (3). Carcinogenicity and mutagenicity are evident in certain in vitro screening tests for ZDV and all other FDA-licensed NRTIs. The relevance of animal data to humans is unknown; however, because teratogenic effects were reported among primates at drug exposures similar to those representing human therapeutic exposure, pregnant women should not use efavirenz (EFV). Indinavir (IDV) is associated with infrequent side effects in adults (i.e., hyperbilirubinemia and renal stones) that could be problematic for a newborn. Because the half-life of IDV in adults is short, these concerns might be relevant only if the drug is administered shortly before delivery. Other concerns regarding use of PEP during pregnancy have been raised by reports of mitochondrial dysfunction leading to neurologic disease and death among uninfected children whose mothers had taken antiretroviral drugs to prevent perinatal HIV transmission and of fatal and nonfatal lactic acidosis in pregnant women treated throughout gestation with a combination of d4T and ddI (3).

### Management of Occupational Exposure by Emergency Physicians

Although PHS guidelines for the management of occupational exposures to HIV were first published in 1985 (42), HCP often are not familiar with these guidelines. Focus groups conducted among emergency department (ED) physicians in 2002 indicated that of 71 participants, >95% had not read the 2001 guidelines before being invited to participate (43). All physicians participating in these focus groups had managed occupational exposures to blood or body fluids. They cited three challenges in exposure management most frequently: evaluation of an unknown source patient or a source patient who refused testing, inexperience in managing occupational HIV exposures, and counseling of exposed workers in busy EDs.

### Occupational HIV Exposure Management and PEP Use in U.S. Hospitals

Analysis of NaSH data for June 1995–December 2004 provides information regarding the management of occupational exposure to HIV in a convenience sample of 95 U.S. hospitals. These data indicate improved adherence to PHS recommendations concerning use of HIV PEP after occupational exposures. A total of 28,010 exposures to blood and body fluids were reported by these hospitals (CDC, unpublished data, 2005). For all 25,510 exposures with known sources, 1,350 (5.3%) were to HIV-positive sources, 15,301 (60.0%) to HIV-negative sources, and 8,859 (34.7%) to sources of unknown HIV status. Of 1,350 HCP exposed to a known HIV-positive source, 788 (58.4%) started PEP, and 317 (49%) of 647 for whom follow-up information was available took PEP for >21 days. The overall median duration of HIV PEP after exposure to an HIV-positive source was 27 days, increasing from 10 days in 1995 to 26.5 days in 2004; the overall median duration of HIV PEP after exposure to an HIV-negative source was 2 days, decreasing from 7.5 days in 1995 to 1 day in 2004. The use of rapid HIV tests for evaluation of source patients has increased; during 1995–1997, none of 25 NaSH facilities used rapid HIV tests, whereas in 2004, a total of 21 (84%) did (CDC, unpublished data, 2005). Rapid HIV tests could result in decreased use of PEP and spare personnel both undue anxiety and adverse effects of antiretroviral PEP (44–47). The annual median time to initiation of PEP was consistent (2 hours). Of 1,350 HCP with exposures to HIV-positive sources, 909 (67.1%) had at least one follow-up serologic test recorded, but only 289 (31.8%) had tests recorded at 4–6 months (CDC, unpublished data, 2005).
In 1996, of 24 HCP taking PEP after exposure to HIV-positive sources, 10 (42%) took a three-drug PEP regimen compared with 30 (76.9%) of 39 in 2004 (CDC, unpublished data, 2005). After 227 HIV exposures for which only a two-drug PEP regimen was recommended (i.e., the exposure was to mucous membranes or skin or was a superficial percutaneous injury and the source person did not have end-stage AIDS or acute HIV illness), 104 (45.8%) HCP initiated a three-drug HIV PEP regimen. The National Clinicians’ Post-Exposure Prophylaxis Hotline (PEPline)\(^1\) reports similar findings. PEPline staff recommended changing or discontinuing PEP regimens for 45 (38%) of 118 exposures involving source patients with known viral load or CD4 cell count concerning which they were consulted during April 2002–March 2003 (48; R. Goldschmidt, PEPline, personal communication, 2004). For 14 (11.9%) HCP, the recommendation was to decrease the number of drugs in the PEP regimens; for 22 (18.7%) HCP, the recommendation was to increase the number of drugs; and for nine (7.6%), the recommendation was to change the PEP regimen, keeping the same number of drugs.

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### Recommendations for the Management of HCP Potentially Exposed to HIV

Exposure prevention remains the primary strategy for reducing occupational bloodborne pathogen infections. However, occupational exposures will continue to occur, and PEP will remain an important element of exposure management.

#### HIV PEP

The recommendations provided in this report (Tables 1 and 2; Appendix) apply to situations in which HCP have been exposed to a source person who either has or is considered likely to have HIV infection. These recommendations are based on the risk for HIV infection after different types of exposure and on limited data regarding efficacy and toxicity of PEP. If PEP is offered and taken and the source is later determined to be HIV-negative, PEP should be discontinued. Although concerns have been expressed regarding HIV-negative sources being in the window period for seroconversion, no case of transmission involving an exposure source during the window period has been reported in the United States (39). Rapid HIV testing of source patients can facilitate making timely decisions regarding use of HIV PEP after occupational exposures to sources of unknown HIV status. Because the majority of occupational HIV exposures do not result in transmission of HIV, potential toxicity must be considered when prescribing PEP. Because of the complexity of selecting HIV PEP regimens, when possible, these recommendations should be implemented in consultation with persons having expertise in antiretroviral therapy and HIV transmission. Reevaluation of exposed HCP should be strongly encouraged within 72 hours postexposure, especially as additional information about the exposure or source person becomes available.

#### Timing and Duration of PEP

PEP should be initiated as soon as possible, preferably within hours rather than days of exposure. If a question exists concerning which antiretroviral drugs to use, or whether to use a basic or expanded regimen, the basic regimen should be started immediately rather than delay PEP administration. The optimal duration of PEP is unknown. Because 4 weeks of ZDV appeared protective in occupational and animal studies, PEP should be administered for 4 weeks, if tolerated (49–52).

#### Recommendations for the Selection of Drugs for HIV PEP

The selection of a drug regimen for HIV PEP must balance the risk for infection against the potential toxicities of the agent(s) used. Because PEP is potentially toxic, its use is not justified for exposures that pose a negligible risk for transmission (Tables 1 and 2). The initial HIV PEP regimens recommended in these guidelines should be viewed as suggestions that can be changed if additional information is obtained concerning the source of the occupational exposure (e.g., possible treatment history or antiretroviral drug resistance) or if expert consultation is provided. Given the complexity of choosing and administering HIV PEP, whenever possible, consultation with an infectious diseases consultant or another physician who has experience with antiretroviral agents is recommended, but it should not delay timely initiation of PEP.

Consideration should be given to the comparative risk represented by the exposure and information regarding the exposure source, including history of and response to antiretroviral therapy based on clinical response, CD4+ T-cell counts, viral load measurements, and current disease stage. When the source person’s virus is known or suspected to be resistant to one or more of the drugs considered for the PEP regimen, the selection of drugs to which the source person’s virus is unlikely to be resistant is recommended; expert consultation is advised. If this information is not immediately available, initiation of PEP, if indicated, should not be delayed; changes

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\(^1\) Administered by staff members from the University of California at San Francisco and San Francisco General Hospital; supported by the Health Resources and Services Administration Ryan White CARE Act and AIDS Education and Training Centers, and by CDC.
in the regimen can be made after PEP has started, as appropriate. For HCP who initiate PEP, re-evaluation of the exposed person should occur within 72 hours postexposure, especially if additional information about the exposure or source person becomes available.

PHS continues to recommend stratification of HIV PEP regimens based on the severity of exposure and other considerations (e.g., concern for antiretroviral drug resistance in the exposure source). The majority of HIV exposures will warrant a two-drug regimen, using two NRTIs or one NRTI and one NNRTI (Tables 1 and 2; Appendix). Combinations that can be considered for PEP include ZDV and 3TC or emtricitabine (FTC); d4T and 3TC or FTC; and tenofovir (TDF) and 3TC or FTC. In the previous PHS guidelines, a combination of d4T and ddI was considered one of the first-choice PEP regimens; however, this regimen is no longer recommended because of concerns about toxicity (especially neuropathy and pancreatitis) and the availability of more tolerable alternative regimens (3).

The addition of a third (or even a fourth) drug should be considered for exposures that pose an increased risk for transmission or that involve a source in whom antiretroviral drug resistance is likely. The addition of a third drug for PEP after a high-risk exposure is based on demonstrated effectiveness in reducing viral burden in HIV-infected persons. However, no definitive data exist that demonstrate increased efficacy of three- compared with two-drug HIV PEP regimens. Previously, IDV, nelfinavir (NFV), EFV, or abacavir (ABC) were recommended as first-choice agents for inclusion in an expanded PEP regimen (3).

PHS now recommends that expanded PEP regimens be PI-based. The PI preferred for use in expanded PEP regimens is lopinavir/ritonavir (LPV/RTV). Other PIs acceptable for use in expanded PEP regimens include atazanavir, fosamprenavir, RTV-boosted IDV, RTV-boosted SQV, or NFV (Appendix). Although side effects are common with NNRTIs, EFV may be considered for expanded PEP regimens, especially when resistance to PIs in the source person’s virus is known or suspected. Caution is advised when EFV is used in women of childbearing age because of the risk of teratogenicity.

Drugs that may be considered as alternatives to the expanded regimens, with warnings about side effects and other adverse events, are EFV or PIs as noted in the Appendix in combination with ddl and either 3TC or FTC. The fusion inhibitor enfuvirtide (T20) has theoretic benefits for use in PEP because its activity occurs before viral-host cell integration; however, it is not recommended for routine HIV PEP because of the mode of administration (subcutaneous injection twice daily). Furthermore, use of T20 has the potential for production of anti-T20 antibodies that cross react with HIV gp41. This could result in a false-positive, enzyme immunoassay (EIA) HIV antibody test among HIV-uninfected patients. A confirmatory Western blot test would be expected to be negative in such cases. T20 should only be used with expert consultation.

Antiviral drugs not recommended for use as PEP, primarily because of the higher risk for potentially serious or life-threatening adverse events, include ABC, delavirdine, ddC, and, as noted previously, the combination of ddI and d4T. NVP should not be included in PEP regimens except with expert consultation because of serious reported side effects, including hepatotoxicity (with one instance of fulminant liver failure requiring liver transplantation), rhabdomyolysis, and hypersensitivity syndrome (53–55).

Because of the complexity of selection of HIV PEP regimens, consultation with persons having expertise in antiretroviral therapy and HIV transmission is strongly recommended. Certain institutions have required consultation with a hospital epidemiologist or infectious diseases consultant when HIV PEP use is under consideration. This can be especially important in management of a pregnant or breastfeeding worker or a worker who has been exposed to a heavily treatment-experienced source (Box 1).

Resources for consultation are available from the following sources:

- PEPline at http://www.ucsf.edu/hivcntr/Hotlines/PEPline; telephone 888-448-4911;
- HIV Antiretroviral Pregnancy Registry at http://www.apregistry.com/index.htm; Address: Research Park, 1011 Ashes Drive, Wilmington, NC 28405, Telephone: 800-258-4263; Fax: 800-800-1052; E-mail: registry@nc.crl.com;
- FDA (for reporting unusual or severe toxicity to antiretroviral agents) at http://www.fda.gov/medwatch; telephone: 800-332-1088; address: MedWatch, HF-2, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857;
- CDC (for reporting HIV infections in HCP and failures of PEP) at telephone 800-893-0485; and

**Follow-Up of Exposed HCP**

**Postexposure Testing**

HCP with occupational exposure to HIV should receive follow-up counseling, postexposure testing, and medical evaluation regardless of whether they receive PEP. HIV-antibody
BOX 1. Situations for which expert consultation* for HIV postexposure prophylaxis (PEP) is advised

- Delayed (i.e., later than 24–36 hours) exposure report
  - Interval after which lack of benefit from PEP undefined
- Unknown source (e.g., needle in sharps disposal container or laundry)
  - Use of PEP to be decided on a case-by-case basis
  - Consider severity of exposure and epidemiologic likelihood of HIV exposure
  - Do not test needles or other sharp instruments for HCV
- Known or suspected pregnancy in the exposed person
  - Use of optimal PEP regimens not precluded
  - PEP not denied solely on basis of pregnancy
- Breastfeeding in the exposed person
  - Use of optimal PEP regimens not precluded
  - PEP not denied solely on basis of breastfeeding
- Resistance of the source virus to antiretroviral agents
  - Influence of drug resistance on transmission risk unknown
  - If source person’s virus is known or suspected to be resistant to one or more of the drugs considered for PEP, selection of drugs to which the source person’s virus is unlikely to be resistant recommended
  - Resistance testing of the source person’s virus at the time of the exposure not recommended
  - Initiation of PEP not to be delayed while awaiting any results of resistance testing
- Toxicity of the initial PEP regimen
  - Adverse symptoms (e.g., nausea and diarrhea) common with PEP
  - Symptoms often manageable without changing PEP regimen by prescribing antimotility or antiemetic agents
  - In other situations, modifying the dose interval (i.e., taking drugs after meals or administering a lower dose of drug more frequently throughout the day, as recommended by the manufacturer) might help alleviate symptoms when they occur

* Either with local experts or by contacting the National Clinicians’ Post-Exposure Prophylaxis Hotline (PEPline), telephone 888-448-4911.

testing by enzyme immunoassay should be used to monitor HCP for seroconversion for >6 months after occupational HIV exposure. After baseline testing at the time of exposure, follow-up testing could be performed at 6 weeks, 12 weeks, and 6 months after exposure. Extended HIV follow-up (e.g., for 12 months) is recommended for HCP who become infected with HCV after exposure to a source coinfected with HIV and HCV. Whether extended follow-up is indicated in other circumstances (e.g., exposure to a source co-infected with HIV and HCV in the absence of HCV seroconversion or for exposed persons with a medical history suggesting an impaired ability to mount an antibody response to acute infection) is unclear. Although rare instances of delayed HIV seroconversion have been reported (56,57), the infrequency of this occurrence does not warrant adding to exposed persons’ anxiety by routinely extending the duration of postexposure follow-up. However, this should not preclude a decision to extend follow-up in a particular situation based on the clinical judgment of the exposed person’s health-care provider. The routine use of direct virus assays (e.g., HIV p24 antigen EIA or tests for HIV ribonucleic acid) to detect infection among exposed HCP usually is not recommended (58). Despite the ability of direct virus assays to detect HIV infection a few days earlier than EIA, the infrequency of occupational seroconversion and increased costs of these tests do not warrant their routine use in this setting. In addition, the relatively high rate of false-positive results of these tests in this setting could lead to unnecessary anxiety or treatment (59,60). Nevertheless, HIV testing should be performed on any exposed person who has an illness compatible with an acute retroviral syndrome, regardless of the interval since exposure. A person in whom HIV infection is identified should be referred for medical management to a specialist with expertise in HIV treatment and counseling. Health-care providers caring for persons with occupationally acquired HIV infection can report these cases to CDC at telephone 800-893-0485 or to their state health departments.

Monitoring and Management of PEP Toxicity

If PEP is used, HCP should be monitored for drug toxicity by testing at baseline and again 2 weeks after starting PEP. The scope of testing should be based on medical conditions in the exposed person and the toxicity of drugs included in the PEP regimen. Minimally, laboratory monitoring for toxicity should include a complete blood count and renal and hepatic function tests. Monitoring for evidence of hyperglycemia should be included for HCP whose regimens include any PI; if the exposed person 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 might be indicated.

Exposed HCP 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 drugs that should not be taken with PEP, side effects of prescribed drugs, measures to minimize side effects, and methods of clinical monitoring for toxicity.
during the follow-up period. HCP should be advised that evaluation of certain symptoms (e.g., rash, fever, back or abdominal pain, pain on urination or blood in the urine, or symptoms of hyperglycemia (e.g., increased thirst or frequent urination) should not be delayed.

HCP often fail to complete the recommended regimen often because they experience side effects (e.g., nausea or diarrhea). These symptoms often can be managed with antimotility and antiemetic agents or other medications that target specific symptoms without changing the regimen. 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) might facilitate adherence to the regimen. Serious adverse events should be reported to FDA’s MedWatch program.

Although recommendations for follow-up testing, monitoring, and counseling of exposed HCP are unchanged from those published previously (3), greater emphasis is needed on improving follow-up care provided to exposed HCP (Box 2). This might result in increased adherence to HIV PEP regimens, better management of associated symptoms with ancillary medications or regimen changes, improved detection of serious adverse effects, and serologic testing among a larger proportion of exposed personnel to determine if infection is transmitted after occupational exposures. Closer follow-up should in turn reassure HCP who become anxious after these events (61,62). The psychologic impact on HCP of needlesticks or exposure to blood or body fluid should not be underestimated. Providing HCP with psychologic counseling should be an essential component of the management and care of exposed HCP.

**Reevaluation and Updating of HIV PEP Guidelines**

As new antiretroviral agents for treatment of HIV infection and additional information concerning early HIV infection and prevention of HIV transmission become available, the PHS Interagency Working Group will assess the need to update these guidelines. Updates will be published periodically as appropriate.

**References**


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**BOX 2. Follow-up of health-care personnel (HCP) exposed to known or suspected HIV-positive sources**

- Exposed HCP should be advised to use precautions (e.g., avoid blood or tissue donations, breastfeeding, or pregnancy) to prevent secondary transmission, especially during the first 6–12 weeks postexposure.
- For exposures for which PEP is prescribed, HCP should be informed regarding
  - possible drug toxicities and the need for monitoring,
  - possible drug interactions, and
  - the need for adherence to PEP regimens.
- Consider reevaluation of exposed HCP 72 hours postexposure, especially after additional information about the exposure or source person becomes available.

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5 Defined by FDA as follows: “Any adverse drug experience occurring at any dose that results in any of the following outcomes: death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition” (63).


APPENDIX

Basic and Expanded HIV Postexposure Prophylaxis Regimens

BASIC REGIMEN

• **Zidovudine** *(Retrovir™; ZDV; AZT) + lamivudine (Epivir®; 3TC); available as Combivir™*

  **Preferred dosing**
  - ZDV: 300 mg twice daily or 200 mg three times daily, with food; total: 600 mg daily
  - 3TC: 300 mg once daily or 150 mg twice daily
  - Combivir: one tablet twice daily

  **Dosage forms**
  - ZDV: 100 mg capsule, 300 mg tablet
  - 3TC: 150 or 300 mg tablet
  - Combivir: tablet, 300 mg ZDV + 150 mg 3TC

  **Advantages**
  - ZDV associated with decreased risk for HIV transmission
  - ZDV used more often than other drugs for PEP for health-care personnel (HCP)
  - Serious toxicity rare when used for PEP

  **Disadvantages**
  - Side effects predictable and manageable with antimotility and antiemetic agents
  - Can be used by pregnant HCP
  - Can be given as a single tablet (COMBIVIR™) twice daily

  **Side effects (especially nausea and fatigue) common and might result in low adherence**
  - Source-patient virus resistance to this regimen possible
  - Potential for delayed toxicity (oncogenic/teratogenic) unknown

• **Zidovudine** *(Retrovir®; ZDV; AZT) + emtricitabine (Emtriva™; FTC)*

  **Preferred dosing**
  - ZDV: 300 mg twice daily or 200 mg three times daily, with food; total: 600 mg/day, in 2–3 divided doses
  - FTC: 200 mg (one capsule) once daily

  **Disadvantages**
  - Side effects predictable and manageable with antimotility and antiemetic agents
  - Can be used by pregnant HCP
  - Can be given as a single tablet (COMBIVIR™) twice daily

  **Side effects (especially nausea and fatigue) common and might result in low adherence**
  - Source-patient virus resistance to this regimen possible
  - Potential for delayed toxicity (oncogenic/teratogenic) unknown

  **Zidovudine** *(Retrovir®; ZDV; AZT) + emtricitabine (Emtriva™; FTC)*
**Dosage forms**
- ZDV: see above
- FTC: 200 mg capsule
**FTC general comments**
- Nucleoside analogue; same structure as 3TC, except fluoride residue at position 5 on pyrimidine ring
- Same resistance and safety profile as 3TC
- No apparent advantage over 3TC; tolerability and virologic response rates appear better than regimens containing ddi + d4T

**Advantages**
- ZDV: see above.
- FTC
  - Convenient (once daily)
  - Well tolerated
  - Long intracellular half-life (~40 hours)

**Disadvantages**
- ZDV: see above.
- FTC
  - Rash perhaps more frequent than with 3TC
  - No long-term experience with this drug
  - Cross resistance to 3TC
  - Hyperpigmentation among non-Caucasians with long-term use: 3%

**Tenofovir DF (Viread®; TDF) + lamivudine (Epivir®; 3TC)**

**Preferred dosing**
- TDF: 300 mg once daily
- 3TC: 300 mg once daily or 150 mg twice daily

**Dosage forms**
- TDF: 300 mg tablet
- 3TC: see above

**Advantages**
- 3TC: see above
- TDF
  - Convenient dosing (single pill once daily)
  - Resistance profile activity against certain thymidine analogue mutations
  - Well tolerated

**Disadvantages**
- TDF
  - Same class warnings as nucleoside reverse transcriptase inhibitors (NRTIs)
  - Drug interactions
  - Increased TDF concentrations among persons taking atazanavir and lopinavir/ritonavir; need to monitor patients for TDF-associated toxicities
  - Preferred dosage of atazanavir if used with TDF: 300 mg + ritonavir 100 mg once daily + TDF 300 mg once daily

**Alternate Basic Regimens**

**• Lamivudine (Epivir®; 3TC) + stavudine (Zerit®; d4T)**

**Preferred dosing**
- 3TC: 300 mg once daily or 150 mg twice daily
- d4T: 40 mg twice daily (can use lower doses of 20–30 mg twice daily if toxicity occurs; equally effective but less toxic among HIV-infected patients with peripheral neuropathy); 30 mg twice daily if body weight is <60 kg

**Dosage forms**
- 3TC: see above
- d4T: 15, 20, 30, and 40 mg tablet

**Advantages**
- 3TC: see above
- d4T: gastrointestinal (GI) side effects rare

**Disadvantages**
- Possibility that source-patient virus is resistant to this regimen
- Potential for delayed toxicity (oncogenic/teratogenic) unknown
Emtricitabine (Emtriva™; FTC) + stavudine (Zerit®; d4T)

Preferred dosing
- FTC: 200 mg daily
- d4T: 40 mg twice daily (can use lower doses of 20–30 mg twice daily if toxicity occurs; equally effective but less toxic among HIV-infected patients who developed peripheral neuropathy); if body weight is <60 kg, 30 mg twice daily

Dosage forms
- FTC: see above
- d4T: see above

Advantages
- 3TC and FTC: see above; d4T’s GI side effects rare

Disadvantages
- Potential that source-patient virus is resistant to this regimen
- Unknown potential for delayed toxicity (oncogenic/teratogenic) unknown

Lamivudine (Epivir®; 3TC) + didanosine (Videx®; ddI)

Preferred dosing
- 3TC: 300 mg once daily or 150 mg twice daily
- ddI: Videx® chewable/dispersible buffered tablets can be administered on an empty stomach as either 200 mg twice daily or 400 mg once daily. Patients must take at least two of the appropriate strength tablets at each dose to provide adequate buffering and prevent gastric acid degradation of ddI. Because of the need for adequate buffering, the 200-mg strength tablet should be used only as a component of a once-daily regimen. The dose is either 200 mg twice daily or 400 mg once daily for patients weighing >60 kg and 125 mg twice daily or 250 mg once daily for patients weighing >60 kg.

Dosage forms
- 3TC: 150 or 300 mg tablets
- ddI: 25, 50, 100, 150, or 200 mg buffered white tablets

Advantages
- ddI: once daily dosing option
- 3TC: see above

Disadvantages
- Tolerability: diarrhea more common with buffered preparation than with enteric-coated preparation
- Associated with toxicity: peripheral neuropathy, pancreatitis, and lactic acidosis
- Must be taken on empty stomach except with TDF
- Drug interactions
- FTC: see above

PREFERRED EXPANDED REGIMEN
Basic regimen plus:
- Lopinavir/ritonavir (Kaletra®; LPV/RTV)

Preferred dosing
- LPV/RTV: 400/100 mg = 3 capsules twice daily with food

Dosage form
- LPV/RTV: 133/33 mg capsules

Advantages
- Potent HIV protease inhibitor
- Generally well-tolerated

Disadvantages
- Potential for serious or life-threatening drug interactions (see Table 4)
- Might accelerate clearance of certain drugs, including oral contraceptives (requiring alternative or additional contraceptive measures for women taking these drugs)
- Can cause severe hyperlipidemia, especially hypertriglyceridemia
- GI (e.g., diarrhea) events common

ALTERNATE EXPANDED REGIMENS
Basic regimen plus one of the following:
- Atazanavir (Reyataz®; ATV) + ritonavir (Norvir®; RTV)

Preferred dosing
- ATV: 400 mg once daily, unless used in combination with TDF, in which case ATV should be boosted with RTV, preferred dosing of ATV 300 mg + RTV: 100 mg once daily
Dosage forms
- ATV: 100, 150, and 200 mg capsules
- RTV: 100 mg capsule

Advantages
- Potent HIV protease inhibitor
- Convenient dosing – once daily
- Generally well tolerated

Disadvantages
- Hyperbilirubinemia and jaundice common
- Potential for serious or life-threatening drug interactions (see Table 4)
- Avoid coadministration with proton pump inhibitors
- Separate antacids and buffered medications by 2 hours and H2-receptor antagonists by 12 hours to avoid decreasing ATV levels
- Caution should be used with ATV and products known to induce PR prolongation (e.g., diltiazem)

• Fosamprenavir (Lexiva®, FOSAPV) + ritonavir (Norvir®, RTV)

Preferred dosing
- FOSAPV: 1400 mg twice daily (without RTV)
- FOSAPV: 1400 mg once daily + RTV 200 mg once daily
- FOSAPV: 700 mg twice daily + RTV 100 mg twice daily

Dosage form
- FOSAPV: 700 mg tablets
- RTV: 100 mg capsule

Advantages
- Once daily dosing when given with ritonavir

Disadvantages
- Tolerability: GI side effects common
- Multiple drug interactions. Oral contraceptives decrease fosamprenavir concentrations
- Incidence of rash in healthy volunteers, especially when used with low doses of ritonavir. Differentiating between early drug-associated rash and acute seroconversion can be difficult and cause extraordinary concern for the exposed person

• Indinavir (Crixivan®, IDV) + ritonavir (Norvir®, RTV)

Preferred dosing
- IDV 800 mg + RTV 100 mg twice daily without regard to food

Alternative dosing
- IDV: 800 mg every 8 hours, on an empty stomach

Dosage forms
- IDV: 200 mg, 333, and 400 mg capsule
- RTV: 100 mg capsule

Advantages
- Potent HIV inhibitor

Disadvantages
- Potential for serious or life-threatening drug interactions (see Table 4)
- Serious toxicity (e.g., nephrolithiasis) possible; consumption of 8 glasses of fluid/day required
- Hyperbilirubinemia common; must avoid this drug during late pregnancy
- Requires acid for absorption and cannot be taken simultaneously with ddl, chewable/dispersible buffered tablet formulation (doses must be separated by ≥1 hour)

• Saquinavir (Invirase®, SQV) + ritonavir (Norvir®, RTV)

Preferred dosing
- SQV: 1,000 mg (given as Invirase) + RTV 100 mg, twice daily
- SQV: five capsules twice daily + RTV: one capsule twice daily

Dosage forms
- SQV (Invirase): 200 mg capsule
- RTV: 100 mg capsule

Advantages
- Generally well-tolerated, although GI events common

Disadvantages
- Potential for serious or life-threatening drug interactions (see Table 4)
- Substantial pill burden

• Nelfinavir (Viracept®, NFV)

Preferred dosing
- NFV: 1,250 mg (2 x 625 mg or 5 x 250 mg tablets), twice daily with a meal

Dosage forms
- NFV: 250 or 625 mg tablet

Advantages
- Generally well-tolerated

Disadvantages
- Diarrhea or other GI events common
- Potential for serious and/or life-threatening drug interactions (see Table 4)

• Efavirenz (Sustiva®, EFV)

Preferred dosing
- EFV: 600 mg daily, at bedtime

Dosage forms
- EFV: 50, 100, 200 capsules
- EFV: 600 mg tablet
Advantages
— Does not require phosphorylation before activation and might be active earlier than other antiretroviral agents (a theoretic advantage of no demonstrated clinical benefit)
— Once daily dosing

Disadvantages
— Drug associated with rash (early onset) that can be severe and might rarely progress to Stevens-Johnson syndrome
— Differentiating between early drug-associated rash and acute seroconversion can be difficult and cause extraordinary concern for the exposed person
— Central nervous system side effects (e.g., dizziness, somnolence, insomnia, or abnormal dreaming) common; severe psychiatric symptoms possible (dosing before bedtime might minimize these side effects)
— Teratogen; should not be used during pregnancy
— Potential for serious or life-threatening drug interactions (see Table 5)

ANTIRETROVIRAL AGENTS GENERALLY NOT RECOMMENDED FOR USE AS PEP
• Nevirapine (Viramune®; NVP)

Disadvantages
— Associated with severe hepatotoxicity (including at least one case of liver failure requiring liver transplantation in an exposed person taking PEP)
— Associated with rash (early onset) that can be severe and progress to Stevens-Johnson syndrome
— Differentiating between early drug-associated rash and acute seroconversion can be difficult and cause extraordinary concern for the exposed person
— Drug interactions: can lower effectiveness of certain antiretroviral agents and other commonly used medicines

• Delavirdine (Rescriptor®; Dlv)

Disadvantages
— Drug associated with rash (early onset) that can be severe and progress to Stevens-Johnson syndrome
— Multiple drug interactions

• Abacavir (Ziagen®; ABC)

Disadvantages
— Severe hypersensitivity reactions can occur, usually within the first 6 weeks
— Differentiating between early drug-associated rash/hypersensitivity and acute seroconversion can be difficult

• Zalcitabine (Hivid®; ddC)

Disadvantages
— Three times a day dosing
— Tolerability
— Weakest antiretroviral agent

ANTIRETROVIRAL AGENT FOR USE AS PEP ONLY WITH EXPERT CONSULTATION
• Enfuvirtide (Fuzeon™; T20)

Preferred dosing
— T20: 90 mg (1 ml) twice daily by subcutaneous injection

Dosage forms
— T20: Single-dose vial, reconstituted to 90 mg/ml

Advantages
— New class
— Unique viral target; to block cell entry
— Prevalence of resistance low

Disadvantages
— Twice-daily injection
— Safety profile: local injection site reactions
— Never studied among antiretroviral-naïve or HIV-negative patients
— False-positive EIA HIV antibody tests might result from formation of anti-T20 antibodies that cross-react with anti-gp41 antibodies

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Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis

INSTRUCTIONS

By Internet
1. Read this MMWR (Vol. 54, RR-9), which contains the correct answers to the questions beginning on the next page.
2. Go to the MMWR Continuing Education Internet site at http://www.cdc.gov/mmwr/cme/conted.html.
3. Select which exam you want to take and select whether you want to register for CME, CEU, or CNE credit.
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7. Immediately print your Certificate of Completion for your records.

By Mail or Fax
1. Read this MMWR (Vol. 54, RR-9), which contains the correct answers to the questions beginning on the next page.
2. Complete all registration information on the response form, including your name, mailing address, phone number, and e-mail address, if available.
3. Indicate whether you are registering for CME, CEU, or CNE credit.
4. Select your answers to the questions, and mark the corresponding letters on the response form. To receive continuing education credit, you must answer all of the questions. Questions with more than one correct answer will instruct you to "Indicate all that apply."
5. Sign and date the response form or a photocopy of the form and send no later than September 30, 2007, to Fax: 770-488-8555  Mail: MMWR CE Credit
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6. Your Certificate of Completion will be mailed to you within 30 days.
Goal and Objectives

This report provides recommendations regarding clinical practice for managing occupational exposures to HIV in health-care settings, including appropriate use of HIV postexposure prophylaxis (PEP). The goal of this report is to provide recommendations for guiding clinical practice in managing PEP for health-care personnel (HCP) with occupational exposure to HIV. Upon completion of this educational activity, the reader should be able to a) describe occupational exposures for which exposure management is appropriate; b) describe the appropriate selection of HIV PEP; c) describe the appropriate use of HIV PEP; d) describe the follow-up evaluation of exposed HCP; e) describe the follow-up counseling of exposed HCP; and f) list situations for which expert consultation in the management of occupational exposures is recommended.

To receive continuing education credit, please answer all of the following questions.

1. Contact with which body fluid(s) poses a risk for HIV transmission in health-care settings? (Indicate all that apply.)
   A. Blood.
   B. Urine.
   C. Sweat.
   D. Amniotic fluid.
   E. A and D.
   F. B and C.

2. What is the recommended duration of HIV PEP for occupational exposures to HIV? (Choose the one correct answer.)
   A. 7 days.
   B. 14 days.
   C. 21 days.
   D. 28 days.
   E. 2 months.

3. What is the recommended time to initiation of HIV PEP after exposure when PEP is indicated? (Choose the one correct answer.)
   A. 2 days.
   B. 24–48 hours.
   C. As soon as possible (preferably within hours).

4. Follow-up after occupational exposures to HIV should include which of the following? (Choose the one correct answer.)
   A. Serologic follow-up for HIV infection.
   B. Monitoring for adverse effects of HIV postexposure prophylaxis if taken.
   C. Monitoring for acute seroconversion illness.
   D. Counseling on adherence with HIV PEP and the emotional stress of dealing with exposures.
   E. All of the above.

5. The potential for interactions with other medications is greatest for which of the antiretroviral drug classes recommended for HIV postexposure prophylaxis? (Choose the one correct answer.)
   A. Reverse transcriptase inhibitors (nucleoside analogues).
   B. Nonnucleoside reverse transcriptase inhibitors.
   C. Protease inhibitors.
   D. A and B.
   E. B and C.
   F. A and C.

6. Which antiretrovirals are not currently recommended for use by pregnant HCP? (Indicate all that apply.)
   A. Efavirenz.
   B. Zidovudine.
   C. Nelfinavir.
   D. Tenofovir.

7. Resistance testing of the source-patient after an exposure should always be performed to help in selection of HIV postexposure prophylaxis regimens.
   A. True.
   B. False.

8. Adverse effects of antiretroviral HIV postexposure prophylaxis are uncommonly reported by HCP.
   A. True.
   B. False.

9. Which types of exposure pose a risk for HIV transmission in health-care settings? (Indicate all that apply.)
   A. Intact skin exposure to blood.
   B. Mucous membrane splash of urine.
   C. Needlestick injury after phlebotomy.
   D. Splash of blood on abraded skin.
   E. C and D.
   F. A and B.

10. A 12-month serologic follow-up after an occupational exposure to HIV is recommended in which situation(s)? (Indicate all that apply.)
    A. Any percutaneous exposure to an HIV-infected source.
    B. If the exposed worker takes HIV postexposure prophylaxis.
    C. If the exposure source is coinfected with HIV and HCV and becomes HCV-infected.
    D. None of the above.

11. Which best describes your professional activities:
    A. Physician.
    B. Nurse.
    C. Health educator.
    D. Office staff.
    E. Other.

12. I plan to use these recommendations as the basis for …(Indicate all that apply.)
    A. health education materials.
    B. insurance reimbursement policies.
    C. local practice guidelines.
    D. public policy.
    E. other.

13. Overall, the length of the journal article was…
    A. much too long.
    B. a little too long.
    C. just right.
    D. a little too short.
    E. much too short.

14. After reading this report, I am confident I can describe occupational exposures for which exposure management is appropriate.
    A. Strongly agree.
    B. Agree.
    C. Undecided.
    D. Disagree.
    E. Strongly disagree.
15. After reading this report, I am confident I can describe the appropriate selection of HIV PEP.
   A. Strongly agree.
   B. Agree.
   C. Undecided.
   D. Disagree.
   E. Strongly disagree.

16. After reading this report, I am confident I can describe the appropriate use of HIV PEP.
   A. Strongly agree.
   B. Agree.
   C. Undecided.
   D. Disagree.
   E. Strongly disagree.

17. After reading this report, I am confident I can describe the follow-up evaluation of exposed HCP.
   A. Strongly agree.
   B. Agree.
   C. Undecided.
   D. Disagree.
   E. Strongly disagree.

18. After reading this report, I am confident I can describe the follow-up counseling of exposed HCP.
   A. Strongly agree.
   B. Agree.
   C. Undecided.
   D. Disagree.
   E. Strongly disagree.

19. After reading this report, I am confident I can list situations for which expert consultation in the management of occupational exposures is recommended.
   A. Strongly agree.
   B. Agree.
   C. Undecided.
   D. Disagree.
   E. Strongly disagree.

20. The learning outcomes (objectives) were relevant to the goal of this report.
   A. Strongly agree.
   B. Agree.
   C. Undecided.
   D. Disagree.
   E. Strongly disagree.

21. The instructional strategies used in this report (text, tables, boxes, and appendix) helped me learn the material.
   A. Strongly agree.
   B. Agree.
   C. Undecided.
   D. Disagree.
   E. Strongly disagree.

22. The content was appropriate given the stated objectives of the report.
   A. Strongly agree.
   B. Agree.
   C. Undecided.
   D. Disagree.
   E. Strongly disagree.

(Continued on pg CE-4)
Correct answers for questions 1–10.

23. The content expert(s) demonstrated expertise in the subject matter.
A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

24. Overall, the quality of the journal article was excellent.
A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

25. These recommendations will improve the quality of my practice.
A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

26. The availability of continuing education credit influenced my decision to read this report.
A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

27. The MMWR format was conducive to learning this content.
A. Strongly agree.
B. Agree.
C. Undecided.
D. Disagree.
E. Strongly disagree.

28. Do you feel this course was commercially biased? (Indicate yes or no; if yes, please explain in the space provided.)
A. Yes.
B. No.

29. How did you learn about the continuing education activity?
A. Internet.
B. Advertisement (e.g., fact sheet, MMWR cover, newsletter, or journal).
C. Coworker/supervisor.
D. Conference presentation.
E. MMWR subscription.
F. Other.
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