Occupational Postexposure Prophylaxis

Introduction

Background

Although exposure prevention remains the primary strategy for reducing occupationally-acquired HIV, appropriate postexposure management is an important element of workplace safety. The first iteration of the U.S. Public Health Service (USPHS) recommendations advocating the use of occupational postexposure prophylaxis (PEP) dates back to 1996. As more data emerged and more antiretroviral medications became available, the occupational PEP guidelines were updated four times (Figure 1), with the most recent of these published as the 2013 USPHS Occupational PEP Guidelines. Occupational exposures, particularly those known to involve risk for HIV transmission, are urgent medical matters and clinicians should be familiar with updated occupational PEP guidelines. In addition, all health care facilities and clinics should have policies and procedures in place to ensure that appropriate mechanisms are available for timely management. Issues related to the management of nonoccupational exposures to HIV are addressed in the Topic Review Nonoccupational Postexposure Prophylaxis. Management of hepatitis B virus or hepatitis C virus is not addressed in this topic review, but recommendations are available from the Centers for Disease Control and Prevention (CDC).

Definition of Health Care Worker/Health Care Personnel

For the purposes of initiating occupational PEP, the 2013 USPHS Occupational PEP Guidelines use the term health care personnel to refer to all paid and unpaid persons working in health care settings who have the potential for exposure to infectious materials, including body substances (blood, tissue, and specific body fluids), contaminated medical supplies and equipment, and contaminated environmental surfaces. Health care personnel (also called health care workers) 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, security, maintenance, and volunteer personnel). In addition, the 2013 USPHS Occupational PEP Guidelines note the same principles of exposure management could be used for similar types of exposures that occur in other occupational settings, such as might occur with public safety officers.

History of Occupational HIV Cases in the United States

In the United States, from 1985 to 2013, a total of 58 confirmed and 150 possible cases of occupational transmission of HIV were reported to the CDC; only one of the confirmed cases has occurred after 1999 and
that case involved a laboratory worker who had a needle puncture wound while working with a live HIV culture (Figure 2).[8] Of the 58 confirmed cases of occupationally-acquired HIV, 49 resulted from a percutaneous cut or puncture, 5 from mucocutaneous exposure, 2 from both percutaneous and mucous membrane exposure, and 2 were unknown.[8]

**Estimated Risk for Occupational Acquisition of HIV**

- **Risk with Percutaneous Exposure**: If a health care worker has a percutaneous exposure to blood from a source person with HIV (and the health care worker does not take PEP), the estimated risk for HIV acquisition is approximately 0.2 to 0.3%.\[9,10,11\]
- **Risk with Mucous Membrane Exposure**: After a mucous membrane exposure to blood from a source with HIV, such as eye or mouth contact with blood, the risk is approximately 0.09%.[2]
- **Risk with Blood Contact of Nonintact Skin**: Transmission of HIV through blood contact of nonintact skin has been documented in case reports, but most experts consider this risk significantly lower than with mucous membrane exposure.
- **Factors Associated with Increased Transmission Risk**: Epidemiological studies have identified several factors associated with increased risk of HIV transmission following an occupational exposure: a larger quantity of blood from the source patient (device visibly contaminated with blood, needle recently used in an artery or vein, larger bore needle, deeper injury).[12] Note that in earlier years of the HIV epidemic, terminal AIDS was considered a surrogate marker for a high plasma HIV RNA level typically seen in late-stage AIDS. In the modern era, a recent source patient plasma HIV RNA level would be considered to have a higher correlation with transmission risk than the stage of HIV disease or CD4 cell count.[12]

<table>
<thead>
<tr>
<th>Risk Factors for HIV Seroconversion in Health Care Workers</th>
<th>Adjusted Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep Injury</td>
<td>15.0</td>
</tr>
<tr>
<td>Visible Blood on Device</td>
<td>6.2</td>
</tr>
<tr>
<td>Terminal Illness in Source Patient</td>
<td>5.6</td>
</tr>
<tr>
<td>Needle in Source Vein/Artery</td>
<td>4.3</td>
</tr>
<tr>
<td>Postexposure Prophylaxis with Zidovudine</td>
<td>0.19</td>
</tr>
</tbody>
</table>

Table 1.
Rationale for Occupational PEP

When an individual has a percutaneous or mucous membrane exposure to blood or potentially infectious fluid from a source person with HIV, replication of HIV first occurs in the dendritic cells of the skin and mucosa before spreading through lymphatic vessels and developing into systemic infection; this delay in spread of HIV is thought to leave a window of opportunity for PEP to prevent establishment of chronic HIV infection.

A landmark study published in 1997 provided the first convincing evidence that PEP significantly decreased the risk of occupational HIV acquisition following a needlestick injury.\[12\] In this report, investigators performed a case-control study of needlestick injuries involving health care workers and demonstrated that zidovudine PEP, which was typically taken for at least 4 weeks, reduced the risk of seroconversion by 81% if implemented within 4 hours of the exposure.\[12\] This study, along with CDC recommendations, led to the widespread use of antiretroviral therapy for occupational PEP in the late 1990s.

From the year 2000 onward, occupationally-acquired HIV infection in the United States has become exceedingly rare, a finding that indirectly supports the efficacy of PEP.\[8\] In addition, there are data supporting the use of PEP based on small observational studies among humans and animal transmission models.\[13,14,15,16,17,18\] There have been no published randomized control trials that evaluated PEP for occupational exposures to HIV, and due to ethical and logistical reasons, it is unlikely that such studies will be performed in the future. On the basis of available data, there is a strong rationale for using PEP for health care personnel exposed to HIV.\[2\]
Risk Assessment of the Occupational Exposure Event

General Approach

First, it is important to determine whether the exposure involving the health care worker actually warrants PEP. In general, this assessment should include (1) HIV status of the source patient, (2) type of body fluid involved in the exposure, (3) nature of the exposure (percutaneous, mucous membrane, or contact with non-intact skin), and (4) timing of when the exposure occurred.\[5\] If the exposure is deemed an occupational exposure to a source patient known to have HIV, additional information should be obtained, such as the source patient’s most recent plasma HIV RNA level, their current antiretroviral treatment (if any), and any history of HIV drug resistance. Further, as part of the overall exposure evaluation, the risk assessment for transmission of hepatitis B virus or hepatitis C virus should be undertaken.\[6,7\] Even in circumstances where a source patient’s HIV, HBV, and HCV status is unknown (or unobtainable), the health care worker should still be evaluated as soon as possible to facilitate timely baseline testing and discussion of whether PEP should be considered.

Determining HIV Status of Source Patient

The use of PEP applies to situations in which a health care worker has experienced an exposure to blood or body fluids from a source patient with documented or suspected HIV. The HIV status of the source patient, if unknown, should be determined in a timely fashion to guide appropriate use of PEP.\[2\] In many health care settings, clinicians have access to FDA-approved point-of-care HIV tests that can provide a preliminary determination of a source patient’s HIV serostatus within 30 minutes. These tests perform well in detecting persons with chronic HIV but have poor sensitivity in detecting acute or very recent HIV infection. The newer point-of-care HIV-1/2 antigen-antibody test (Alere Determine) has also shown relatively poor performance in detecting persons with very recent HIV infection.\[19,20\] In contrast, the laboratory/instrument-based HIV-1/2 antigen-antibody immunoassays have relatively high sensitivity in detecting recent (acute) HIV infection.\[21,22\] Any preliminary positive point-of-care test result requires confirmation with additional HIV testing. If an immediate result is needed and an HIV point-of-care test is not available, occupational PEP should not be delayed while waiting for the test results.\[2\] In the situation where a source patient’s HIV status is initially unknown and the health care worker starts on antiretroviral PEP, discontinuation of the antiretroviral occupational PEP is warranted if test results subsequently show the source patient does not have HIV.\[2\]

Source Patient in Seroconversion Window Period

Persons with very recent acquisition of HIV can have detectable HIV RNA levels with a negative HIV antibody test result (Figure 3), and thus potentially transmit HIV in the setting of this seroconversion window period (Figure 4).\[23\] Nevertheless, there have been no documented occupational transmissions of HIV related to an exposure involving a source patient with very recent acquisition of HIV who was in the seroconversion window period. In addition, when using newer recommended HIV-1/2 antigen-antibody immunoassays, the window period is shortened by approximately 1 week (Figure 5).\[23\] Accordingly, administering PEP in the setting of a negative HIV antibody test is not recommended, unless the source patient is known to have signs or symptoms that strongly suggest acute HIV. In addition, for source persons of unknown HIV status, routine use of HIV RNA testing for diagnostic purposes is not recommended for decision-making regarding PEP.

Relative Risks of Infectious Body Fluids

As part of the evaluation for an occupational exposure to HIV, it is important to determine what type and quantity of body fluid from the source patient is involved in the exposure (Figure 6).\[2\] Blood or visibly bloody fluids are considered the most potentially infectious body fluids. Other body fluids that are also considered potentially infectious, but at lower risk than blood or visibly bloody fluids include semen, vaginal fluids, and fluids found in normally sterile areas of the body (cerebrospinal, synovial, pleural, pericardial, peritoneal, and
Type of Exposure

In the initial evaluation of the health care worker, it is essential to determine if the exposure involved (1) percutaneous injury, (2) mucous membrane exposure, or (3) contact with non-intact skin. The contact of blood or body fluid with intact skin does not confer any risk of HIV transmission and thus does not warrant further evaluation or postexposure management. For needlestick injuries, additional information should include if the skin of the health care worker was punctured, the type and gauge of needle involved, whether the injury sustained was deep or shallow, and if visible blood was present on the needle prior to injury.

Timing of Exposure

As part of the initial evaluation, determination should be made regarding when the exposure took place. Health care workers with an occupational exposure to HIV should immediately seek care, since available data suggest that PEP should be started as soon as possible. Most health care workers promptly seek evaluation after an exposure, but certain circumstances can arise that result in a significant delay. It is particularly important to determine if the delay is longer than 72 hours from the incident, and expert consultation is recommended if that situation arises.

Defining an At-Risk Exposure

For the purposes of initiating PEP, the 2013 USPHS Occupational PEP Guidelines define an at-risk exposure as contact of blood, tissue, or other potentially infectious body fluids from a person with known or suspected HIV via (1) percutaneous injury (e.g. a needlestick or cut with a sharp object), (2) mucous membrane exposure, or (3) contact with non-intact skin (e.g. exposed skin that is chapped, abraded, or affected by significant dermatitis).
Recommended Initial Steps Following An Exposure Event

Initial Approach Following Exposure Event

Occupational exposures should be considered an urgent medical issue and addressed immediately. Thus, it is extremely important that health care workers have an immediate evaluation and consultation following an exposure event that may have involved contact with blood or potentially infectious fluid from a source person with HIV.[2] Prior to any discussions regarding PEP, it is essential to make sure the health care worker has adequately decontaminated the wound or mucous membranes. In addition, one of the goals of the initial evaluation is to make sure the health care worker promptly receives the first doses of antiretroviral medications for PEP, if indicated. All health care facilities should have a plan in place for administering appropriate evaluation and management for a health care worker who has an occupational exposure to a blood-borne pathogen.

Wound Decontamination

All exposure events should prompt an immediate effort to decontaminate the area of the body exposed to potentially infectious fluids. If the wound involved a needlestick injury, wash the area thoroughly with soap and water (if the health care worker was wearing a glove, the glove should be removed prior to washing the wound).[2] The health care workers should not squeeze or “milk” the injury site. For an exposure to a mucous membrane, the health care worker should thoroughly wash and irrigate the area with a large volume of saline.[2] If the exposure involves skin (intact or non-intact), the skin should be thoroughly washed with soap and water.[2]

Timing for Initiation of Antiretroviral Therapy

Occupational exposures should be considered an urgent medical issue and addressed immediately. Thus, health care workers should receive their first dose of antiretroviral medications promptly after the exposure, ideally within 30 to 90 minutes after the exposure event. In some situations, significant delays occur, usually because the health care worker failed to initially consider the exposure event significant enough to seek evaluation. When a delay occurs, but is less than 72 hours, PEP should still be offered (if warranted by the exposure). If the delay extends past 72 hours, PEP is likely to be less effective and expert consultation should be obtained;[2] in this situation, some experts will consider giving PEP, particularly in cases considered very high risk for HIV acquisition. Animal studies have shown that PEP is most effective when started as early as possible after exposure (Figure 7).[14,17]
Recommended Antiretroviral Regimens for Occupational PEP

Preferred Regimens for Occupational PEP

The 2013 USPHS Occupational PEP Guidelines recommend use of three or more antiretroviral medications for occupational PEP, with the preferred regimen consisting of raltegravir 400 mg twice daily plus tenofovir DF-emtricitabine one tablet daily.[2] Of note, these guidelines were published prior to the FDA approval of dolutegravir, which is discussed below. Large-scale studies involving treatment of persons with HIV have shown tenofovir DF-emtricitabine plus raltegravir is safe, highly effective, well tolerated, and has minimal drug interactions.[24] From a practical standpoint, the first doses of antiretroviral PEP should include both tenofovir DF-emtricitabine and raltegravir (the health care workers should NOT take raltegravir alone for the first dose). Although raltegravir once-daily 1,200 mg has been approved for use as a treatment dose in people with HIV, the recommended PEP dosing of raltegravir is 400 mg twice daily.[2]

Table 2. USPHS Guidelines for the Use of Antiretroviral Agents for Occupational Exposures to HIV

<table>
<thead>
<tr>
<th>HIV Postexposure Prophylaxis Regimens</th>
<th>Preferred HIV Postexposure Prophylaxis Regimen</th>
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<tbody>
<tr>
<td></td>
<td>Raltegravir (400 mg twice daily) plus Tenofovir DF-Emtricitabine (300 mg-200 mg [1 tablet] daily)</td>
</tr>
</tbody>
</table>

Alternative HIV Postexposure Prophylaxis Regimens

May combine 1 anchor drug or drug pair from the left column with 1 pair of nucleoside/nucleotide reverse transcriptase inhibitors from the right column; prescribers unfamiliar with these agents/regimens should consult clinicians who are familiar with these agents and their toxicities.

<table>
<thead>
<tr>
<th>Anchor Drug</th>
<th>Nucleoside Reverse Transcriptase Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raltegravir</td>
<td>Tenofovir DF-emtricitabine</td>
</tr>
<tr>
<td>Darunavir + ritonavir</td>
<td>Tenofovir DF + lamivudine</td>
</tr>
<tr>
<td>Etravirine</td>
<td>Zidovudine-lamivudine</td>
</tr>
<tr>
<td>Rilpivirine</td>
<td>Zidovudine + emtricitabine</td>
</tr>
<tr>
<td>Atazanavir + ritonavir</td>
<td></td>
</tr>
<tr>
<td>Lopinavir-ritonavir</td>
<td></td>
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</tbody>
</table>

The following alternative is a complete fixed-dose combination regimen, and no additional antiretroviral medications are needed:

Elvitegravir-cobicistat-tenofovir DF-emtricitabine

Alternative Agents for Use as PEP Only with Expert Consultation

- Abacavir
- Efavirenz
- Enfuvirtide
- Fosamprenavir
- Maraviroc
- Saquinavir
- Stavudine

Agents Generally Not Recommended for Use as PEP

- Didanosine
- Nelfinavir
- Tipranavir

Agents Contraindicated as PEP

- Nevirapine

Note. For consultation or assistance with HIV PEP, contact the National Clinician Consultation Center’s Post-Exposure Hotline at telephone number 888-448-4911 or visit its website at [http://nccc.ucsf.edu/](http://nccc.ucsf.edu/)

The alternatives regimens are listed in order of preference; however, other alternatives may be reasonable based on patient and clinician preference.

Use of Dolutegravir for Occupational PEP
Since the release of the 2013 USPHS Occupational PEP Guidelines, the integrase strand transfer inhibitor dolutegravir received FDA approval and has emerged as a first-line antiretroviral medication as a component of the antiretroviral regimen for initial therapy in persons with HIV.\[25\] Based on the excellent experience with dolutegravir in persons with HIV, many experts have substituted dolutegravir for raltegravir for use in occupational PEP. In addition, the CDC Nonoccupational PEP Guidelines, which were released after the approval of dolutegravir, include dolutegravir as a component of a preferred regimen for nonoccupational PEP.\[26\] Further, dolutegravir is dosed once daily, has a higher genetic barrier to resistance than raltegravir, and is active against some HIV isolates that have resistance to raltegravir.\[27\]

**Alternative Regimens for Occupational PEP**

Alternative regimens are provided in the 2013 USPHS Occupational PEP Guidelines if concern exists that the source patient has drug resistance to any agent of the preferred regimen, as well as for circumstances, such as in a rural area, when a site may only have access to alternative medications until preferred medications can be obtained through ordering.\[2\] Certain medications should be avoided in selecting alternative regimens for PEP. For example, the medication nevirapine should never be used in the provision of PEP due to the potential risk of fatal hepatotoxicity and serious skin reactions.\[28\] Similarly, abacavir should not be used for PEP because of the risk of developing a potentially fatal abacavir hypersensitivity reaction. Although HLA-B*5701 testing can be performed and predict those at risk of developing the hypersensitivity reaction, it may take several days for results to return. It is possible, however, that a switch to abacavir while taking a PEP regimen could be indicated, assuming HLA-B*5701 testing is negative and there is a strong reason to consider a medication switch, such as intolerance to tenofovir DF.

**Use of Tenofovir alafenamide-Emtricitabine for Occupational PEP**

Since the release of the 2013 USPHS Occupational PEP Guidelines, the medication tenofovir alafenamide-emtricitabine has received FDA approval (2016) and has emerged as a component of multiple first-line antiretroviral regimens for initial therapy in persons with established HIV, as well as for some indications for HIV preexposure prophylaxis.\[25\] At this time, however, tenofovir alafenamide-emtricitabine (or any fixed-dose combination containing tenofovir alafenamide-emtricitabine) is not recommended for routine use for occupational PEP, based on very little data regarding its use for occupational PEP. Further, tenofovir DF and tenofovir alafenamide should not be viewed as interchangeable, since the tissue distribution and kinetics of these two medications are very different. The key circumstance that would warrant consideration for the use of tenofovir alafenamide-emtricitabine for occupational PEP would be when initiating occupational PEP in a person with known renal disease who has an estimated creatinine clearance between 30 and 60 mL/min (given the established association between tenofovir DF and renal toxicity).

**Duration of Therapy**

The 2013 USPHS Occupational PEP Guidelines recommend that health care workers who initiate antiretroviral therapy for PEP should complete a 28-day course.\[2\] Older studies involving macaques have shown that PEP given for 28 days is more effective than 10 days, which is more effective than 3 days.\[14\] The pervading theory is that, in most instances, PEP aborts a very early and limited HIV infection, rather than truly preventing any cell in the body from becoming infected with HIV. Thus, prompt initiation of PEP is important to minimize the tissue involvement, and continuing therapy for 28 days is important to control HIV replication while allowing sufficient time for localized immune responses to clear out a very limited HIV infection.

**Use of PEP if Source Person has Undetectable HIV RNA Level**

If the source patient has a recent undetectable HIV RNA level, the risk of transmission from an occupational exposure is likely to be significantly reduced. Nevertheless, undetectable plasma HIV RNA in the source patient does not eliminate the possibility that transmission of HIV could occur, especially with a needlestick injury. Plasma viral load measurements reflect only the level of cell-free virus in the peripheral blood, not the
persistence of HIV in latently infected cells present in whole blood. Thus, even when the source patient with HIV infection has an undetectable plasma HIV RNA level, the 2013 USPHS Occupational PEP Guidelines recommend that PEP should still be offered.[2]

Health Care Worker is Pregnant or Has Childbearing Potential

For pregnant people who require occupational PEP, expert consultation is advised. The preferred regimen, raltegravir plus tenofovir DF-emtricitabine, is considered safe during pregnancy and for persons who become pregnant while taking this regimen.[29] The use of dolutegravir plus tenofovir DF-emtricitabine is also considered safe in pregnancy and for persons of childbearing potential.[29] One of the alternative recommended anchor medications—darunavir boosted with ritonavir—can cause significant drug interactions with oral contraceptives.[29]

Choice of PEP Regimen with Known or Suspected HIV Drug Resistance

Rare cases of documented PEP failure have occurred due to transmission of drug-resistant HIV from the source patient.[30,31] In the case of known or suspected resistance in the source virus to antiretroviral medications, expert consultation is strongly advised. If access to an expert is not immediately available, initiation of standard PEP should take place without delay; the regimen can be adjusted after initiation as additional information or advice from an expert becomes available.
Obtaining Expert Consultation for Occupational PEP

The 2013 USPHS Occupational PEP Guidelines recommend expert clinical consultation for HIV-related occupational exposures in the following situations:[2]

- Delay of greater than 72 hours from exposure to evaluation
- Unknown source (e.g., needle in sharps disposal container or laundry, source patient declines HIV testing)
- Known or suspected antiretroviral drug resistance of the source virus
- Known or suspected pregnancy in the exposed health care worker
- The exposed health care worker is breastfeeding
- Serious medical illness in the exposed health care worker
- Development of toxicity of the initial PEP regimen

Expert Consultation: National Clinician Consultation Center PEPline

Expert consultation for health care professionals can be obtained by calling the National Clinician Consultation Center’s Post-Exposure Prophylaxis PEPline at (888)-448-4911. See the website for hours of operation.
Baseline Evaluation and Counseling for Health Care Worker

Baseline Evaluation

Health care workers who have experienced an occupational exposure to HIV should have prompt counseling, baseline laboratory testing, and medical evaluation.\(^2\) It is important to determine if the health care worker has any preexisting (or significant risk of) renal disease since PEP antiretroviral therapy, specifically tenofovir DF, carries potential nephrotoxicity and requires dose adjustment if renal dysfunction is present, or consideration of alternative PEP medications. The first dose of PEP should be administered as soon as possible and can be given while the individual is undergoing baseline evaluation. It is important the baseline evaluation should not result in a delay in the health care worker receiving their first dose of antiretroviral therapy for PEP. The recommended routine counseling and baseline laboratory testing for the health care worker exposed to a known or suspected source with HIV should include the following (Figure 8):\(^2,7\)

Evaluation of Management of Other Bloodborne Pathogens

For health care workers exposed to a source patient with HIV who has coinfection with HBV and/or HCV, additional baseline testing and management considerations are needed. It is beyond the scope of this topic review to address postexposure prophylaxis for exposures to HBV and/or HCV. In this situation, we recommend using existing CDC guidelines and, if needed, obtaining expert consultation.\(^6,7\)

Initial Counseling

Health care workers who receive PEP should be informed of possible drug interactions, drug toxicities and side effects, the need for high levels of adherence with the PEP regimen, the importance of completing the entire 28-day postexposure course, and the importance of follow-up testing. Health care workers should be advised to use preventative measures (e.g. barrier contraception) to prevent secondary transmission of HIV, especially in the initial 6 to 12 weeks following the exposure. From a practical standpoint, this counseling should not delay the patient receiving their first doses of antiretroviral medications for PEP. Management of pregnant or breastfeeding health care workers who require PEP should involve expert consultation for counseling regarding the risks and benefits of PEP in these settings, concerns regarding potential transmission of HIV, and as well as unique considerations for monitoring during the postexposure surveillance period. In addition, the guidelines note that for health care providers who seek to completely eliminate any risk of HIV transmission to their infant, the health care provider may want to consider stopping breastfeeding.
Follow-Up of Health Care Worker After Exposure Event

Early Reevaluation

Early reevaluation of the exposed health care worker within 72 hours of exposure is strongly recommended, both to assess tolerance with the antiretroviral medications and to consider any new information about the source patient that may be available. Providing exposed health care personnel with counseling and education should be considered an essential component of management.

Follow-Up Laboratory Testing

Regardless of whether a health care worker is taking PEP, reevaluation within 72 hours is recommended. If PEP is used, the health care worker should be advised about the importance of completing the prescribed regimen and should undergo close monitoring for any drug toxicities, side effects, or development of acute HIV symptoms during the follow-up period. When using HIV-1/2 antigen-antibody immunoassay as the HIV test, follow-up HIV testing should take place 6 weeks and 16 weeks after the exposure.[2] If HIV antibody testing alone is used, the repeat HIV testing should occur at 6 weeks, 12 weeks, and 24 weeks after the occupational exposure.[2] Some experts also perform testing for complete blood counts and renal and hepatic aminotransferase levels at 2 weeks after the health care worker initiates PEP, but this is infrequently done in the current era, given the excellent safety profile of the medications used for PEP. Further testing may be required in the event of abnormalities or drug toxicities (Figure 9).[2]

Indications for HIV RNA Testing or Extended Follow-Up

Routine use of HIV RNA testing of an exposed health care worker for follow-up after occupational exposure to HIV is not recommended, except in the scenario where the exposed health care worker manifests signs or symptoms suggestive of acute HIV. In the setting of suspected acute HIV infection, it is appropriate to order an HIV-1/2 antigen-antibody immunoassay and an HIV RNA. Based on several case reports of delayed HIV seroconversion in health care workers who also acquired HCV from the exposure event, extended follow-up is indicated if the health care worker becomes infected with HCV. In this situation, most experts recommend follow-up HIV testing out to 12 months, regardless of the method of HIV testing being used.[2,32]
Summary Points

- Following an occupational exposure to HIV, PEP is an important element of workplace safety and use of PEP markedly reduces the risk of HIV acquisition in an exposed health care worker.
- Occupational exposures to blood or potentially infectious bodily fluids should be considered an urgent medical issue and addressed immediately.
- Antiretroviral PEP medication regimens should contain three (or more) antiretroviral drugs for all occupational exposures to HIV; the number of medications should no longer be based on the risk of the individual exposure.
- The USPHS-recommended regimen for occupational PEP consists of a 28-day course of tenofovir DF-entricitabine plus raltegravir; this recommendation is based on this regimen’s high potency, favorable side effect profile, convenient dosing, and minimal drug interactions.
- Many experts recommend use of dolutegravir in place of raltegravir due to its once-daily dosing, greater potency, and higher genetic barrier to resistance.
- Regimens that contain tenofovir alafenamide-entricitabine are not currently recommended for occupational PEP based on paucity of data for use as occupational PEP.
- If occupational PEP is indicated, the antiretroviral regimen should be started as soon as possible. If a health care worker presents 72 (or more) hours after exposure, expert consultation should be sought.
- Initial evaluation of the exposed person should include both counseling and laboratory studies (baseline HIV testing, complete blood counts, renal and hepatic function tests, and pregnancy testing if pregnancy is possible).
- Expert consultation should be sought for all cases involving drug-resistant HIV in the source patient and for situations that fall outside the scope of the guidelines. Expert consultation can be obtained by calling the National Clinician Consultation Center’s Post-Exposure Prophylaxis PEP line at 888-448-4911.
- All health care workers who experience an HIV exposure event, regardless of whether they take PEP, should undergo baseline testing with an HIV-1/2 antigen-antibody immunoassay and this test should be repeated 6 and 12 weeks following the exposure.
Citations

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[U.S. Public Health Service] -

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Figures

**Figure 1 Timeline for Occupational Postexposure Prophylaxis Recommendations in the United States**

Abbreviations: CDC = Centers for Disease Control and Prevention; PEP = postexposure prophylaxis; INSTI= integrase strand transfer inhibitor

Illustration by David H. Spach, MD
Figure 2 Confirmed Cases of Occupationally-Acquired HIV in the United States, 1985-2013

This graphic shows the year-by-year distribution of the 58 confirmed cases of occupationally-acquired HIV in the United States.

Figure 3 Timing of HIV RNA and HIV Antibodies following HIV Acquisition

![Graph showing the timing of HIV RNA and HIV Antibodies following HIV Acquisition.](image)
Figure 4 HIV Seroconversion Window

The HIV seroconversion window period is the time between HIV acquisition and detectable antibodies against HIV.
**Figure 5 Timing of Positivity for HIV Diagnostic Tests**

This graphic illustrates the approximate time from HIV infection to test positivity.

### Figure 6 Relative Risk of Body Fluids Involved in Occupational Exposure to HIV

Note: although semen and vaginal secretions are known to be infectious for HIV in sexual exposures, they have not been implicated in transmissions in the occupational setting.


<table>
<thead>
<tr>
<th>Category of Infectivity</th>
<th>Fluid</th>
</tr>
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<tbody>
<tr>
<td>Infectious Fluids</td>
<td>• Blood</td>
</tr>
<tr>
<td></td>
<td>• Visibly bloody body fluids</td>
</tr>
<tr>
<td>Potentially Infectious Body Fluids</td>
<td>• Semen and vaginal secretions</td>
</tr>
<tr>
<td></td>
<td>• Cerebrospinal fluid</td>
</tr>
<tr>
<td></td>
<td>• Synovial fluid</td>
</tr>
<tr>
<td></td>
<td>• Pleural fluid</td>
</tr>
<tr>
<td></td>
<td>• Peritoneal fluid</td>
</tr>
<tr>
<td></td>
<td>• Pericardial fluid</td>
</tr>
<tr>
<td></td>
<td>• Amniotic fluid</td>
</tr>
<tr>
<td>Not Considered Infectious (Unless Visibly Bloody)</td>
<td>• Saliva, vomitus, and feces</td>
</tr>
<tr>
<td></td>
<td>• Nasal secretions and sputum</td>
</tr>
<tr>
<td></td>
<td>• Sweat and tears</td>
</tr>
<tr>
<td></td>
<td>• Urine</td>
</tr>
</tbody>
</table>
Abbreviations: SIV = simian immunodeficiency virus; PEP = postexposure prophylaxis; TFV = tenofovir

In this study, investigators inoculated 24 macaques with simian immunodeficiency virus (SIV) and then instituted various postexposure prophylaxis regimens with tenofovir (PMPA), which is (R)-9-(2-phosphonomethoxypropyl)adenine.

Among animals that received placebo, all became infected with simian immunodeficiency virus (SIV). The most effective tenofovir prevention regimen consisted of early initiation of tenofovir (at 24 hours) and long duration of postexposure prophylaxis (28 days).

### Figure 8 Initial Counseling and Laboratory Studies for Persons with Occupational Exposure to Blood or Potentially Infectious Body Fluids


<table>
<thead>
<tr>
<th><strong>Initial Counseling and Laboratory Studies for Persons with Occupational Exposure to HIV</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Counseling (at the time of exposure and at follow-up appointments)</strong></td>
</tr>
<tr>
<td>Advise health care provider to use precautions (e.g. use of barrier contraception and avoidance of blood or tissue donations, pregnancy, and, if possible, breast-feeding) to prevent secondary transmission, especially during the first 6 to 12 weeks after exposure.</td>
</tr>
<tr>
<td><strong>Baseline Laboratory Studies</strong></td>
</tr>
<tr>
<td>☐ HIV testing</td>
</tr>
<tr>
<td>☐ Complete blood counts</td>
</tr>
<tr>
<td>☐ Renal and hepatic function tests</td>
</tr>
<tr>
<td>☐ Serologic testing for HBV and/or HCV (if indicated)</td>
</tr>
<tr>
<td>☐ Pregnancy test (if indicated)</td>
</tr>
<tr>
<td><strong>Counseling when Postexposure Prophylaxis Prescribed</strong></td>
</tr>
<tr>
<td>For exposures for which postexposure prophylaxis is prescribed, health care provider should be informed regarding the following:</td>
</tr>
<tr>
<td>• Possible drug toxicities (e.g. rash and hypersensitivity reactions that could imitate acute HIV seroconversion and the need for monitoring)</td>
</tr>
<tr>
<td>• Possible drug interactions</td>
</tr>
<tr>
<td>• The need for adherence to postexposure prophylaxis regimens</td>
</tr>
</tbody>
</table>
### Figure 9 Follow-Up Counseling and Laboratory Studies for Persons with Occupational Exposure to HIV


#### Follow-Up Counseling and Monitoring for Occupational Postexposure Prophylaxis

<table>
<thead>
<tr>
<th>Early Reevaluation after Exposure (within 72 hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regardless of whether a health care provider is taking postexposure prophylaxis, reevaluation of exposed health care provider within 72 hours after exposure is strongly recommended, as additional information about the exposure or source person may be available.</td>
</tr>
</tbody>
</table>

#### Follow-up Testing and Appointments

Follow-up testing at a minimum should include the following:

- HIV testing at 6 weeks, 12 weeks, and 6 months after exposure; alternatively, if the clinician is certain that an HIV-1/2 antigen–antibody immunoassay is being utilized, then HIV testing could be performed at baseline, 6 weeks after exposure, and 4 months after exposure. HIV testing results should preferably be given to the exposed health care provider at face-to-face appointments.

- Complete blood counts (2 weeks after exposure; further testing may be indicated if abnormalities are detected)

- Renal and hepatic function tests (2 weeks after exposure; further testing may be indicated if abnormalities are detected)
**Table 1.**

**Risk Factors for HIV Seroconversion in Health Care Workers**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Adjusted Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep Injury</td>
<td>15.0</td>
</tr>
<tr>
<td>Visible Blood on Device</td>
<td>6.2</td>
</tr>
<tr>
<td>Terminal Illness in Source Patient</td>
<td>5.6</td>
</tr>
<tr>
<td>Needle in Source Vein/Artery</td>
<td>4.3</td>
</tr>
<tr>
<td>Postexposure Prophylaxis with Zidovudine</td>
<td>0.19</td>
</tr>
</tbody>
</table>

Source:

Table 2. *USPS Guidelines for the Use of Antiretroviral Agents for Occupational Exposures to HIV*

### HIV Postexposure Prophylaxis Regimens

#### Preferred HIV Postexposure Prophylaxis Regimen
- Raltegravir (400 mg twice daily) plus Tenofovir DF-Emtricitabine (300 mg-200 mg [1 tablet] daily)

#### Alternative HIV Postexposure Prophylaxis Regimens
May combine 1 anchor drug or drug pair from the left column with 1 pair of nucleoside/nucleotide reverse transcriptase inhibitors from the right column; prescribers unfamiliar with these agents/regimens should consult clinicians who are familiar with these agents and their toxicities

<table>
<thead>
<tr>
<th>Anchor Drug</th>
<th>Nucleoside Reverse Transcriptase Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raltegravir</td>
<td>• Tenofovir DF-emtricitabine</td>
</tr>
<tr>
<td>Darunavir + ritonavir</td>
<td>• Tenofovir DF + lamivudine</td>
</tr>
<tr>
<td>Etravirine</td>
<td>• Zidovudine-lamivudine</td>
</tr>
<tr>
<td>Rilpivirine</td>
<td>• Zidovudine + emtricitabine</td>
</tr>
<tr>
<td>Atazanavir + ritonavir</td>
<td></td>
</tr>
<tr>
<td>Lopinavir-ritonavir</td>
<td></td>
</tr>
</tbody>
</table>

The following alternative is a complete fixed-dose combination regimen, and no additional antiretroviral medications are needed:
- Elvitegravir-cobicistat-tenofovir DF-emtricitabine

#### Alternative Agents for Use as PEP Only with Expert Consultation
- Abacavir
- Efavirenz
- Enfuvirtide
- Fosamprenavir
- Maraviroc
- Saquinavir
- Stavudine

#### Agents Generally Not Recommended for Use as PEP
- Didanosine
- Nelfinavir
- Tipranavir

#### Agents Contraindicated as PEP
- Nevirapine

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Note. For consultation or assistance with HIV PEP, contact the National Clinician Consultation Center’s Post-Exposure Prophylaxis Hotline at telephone number 888-448-4911 or visit its website at [http://nccc.ucsf.edu/](http://nccc.ucsf.edu/)

The alternatives regimens are listed in order of preference; however, other alternatives may be reasonable based on patient and clinician preference.

Source: