Occupational Postexposure Prophylaxis

Introduction

Background

Although exposure prevention remains the primary strategy for reducing occupationally acquired HIV infection, appropriate postexposure management is an important element of workplace safety. In 1990, the Centers for Disease Control and Prevention (CDC) issued a statement that management of occupational exposure to HIV should consider use of zidovudine for postexposure prophylaxis (PEP).[1] The first iteration of the U.S. Public Health Service recommendations advocating the use of PEP dates back to 1996.[2] 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 U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV.[3,4,5,6] Occupational exposures, particularly those known to involve risk for HIV transmission, are urgent medical matters and clinicians should be familiar with updated 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 exposure to other blood borne pathogens (hepatitis B virus or hepatitis C virus) is not addressed in this Topic Review.

Definition of Health Care Worker/Health Care Personnel

For the purposes of initiating PEP, the 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.[3] 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 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.

Estimated Risk for Occupational Acquisition of HIV

In the situation where a health care worker suffers a percutaneous exposure to HIV-infected blood and does not take PEP, the estimated risk for HIV acquisition is approximately 0.2 to 0.3%.[7,8,9] After a mucous membrane exposure, such as eye or mouth contact with blood, the risk is approximately 0.09%.[3] In the United States, from 1985 to 2013, a total of 58 confirmed and 150
possible cases of occupational transmission of HIV had been reported to the CDC; only one of the confirmed cases 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).[10] Of the 58 documented cases of occupationally-acquired HIV, 49 resulted from a percutaneous cut or puncture (Figure 3).[10] Transmission of HIV with blood contact of non-intact skin has been documented in case reports, but most experts consider this risk significantly lower than with a mucous membrane exposure. 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) and a source patient with a diagnosis of terminal AIDS (Table 1).[11] 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.
Rationale for Occupational PEP

When an individual has a percutaneous or mucous membrane exposure to HIV-contaminated blood or fluids, replication of HIV first occurs in the dendritic cells of the skin and mucosa before spreading through lymphatic vessels and developing into systemic infection; the 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. 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. 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. In addition, there are data supporting the use of PEP based on small observational studies among humans and animal transmission models. 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.
Risk Assessment of the Occupational Exposure Event

General Approach

It is important first to determine whether the exposure involving the health care worker actually warrants PEP. In general, this assessment should initially obtain four key items of information: (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.[6] If the exposure is deemed an occupational exposure to a source patient known to be infected with HIV, additional information should be obtained, such as the source patient’s most recent HIV RNA level (also known as viral load), 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.

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 infection. The HIV status of the source patient, if unknown, should be determined to guide appropriate use of PEP.[3] In many health care settings, clinicians have access to FDA-approved rapid HIV tests that can provide a preliminary determination of a source patient’s HIV serostatus within 30 minutes. The FDA-approved rapid HIV antibody tests perform well in detecting persons with chronic HIV infection, but have poor sensitivity in detecting acute or very recent HIV infection. The new rapid fourth-generation Alere Determine HIV-1/2 Ag/Ab test has also shown relatively poor performance in detecting persons with recent infection;[14,15] this contrasts with the relatively high sensitivity of the non-rapid fourth-generation tests Architect HIV-1/2 Ag/Ab Combo test and Bio-Rad GS HIV Comb Ag/Ab EIA, which have approximately 85% sensitivity in detecting recent (acute) HIV infection.[16,17] Any preliminary positive rapid test result requires confirmation with additional HIV testing. If a rapid HIV test is not available, PEP should not be delayed while waiting for the test results. 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 PEP is warranted if HIV testing subsequently shows the source patient is not infected with HIV.

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 4), and thus potentially transmit HIV in the setting of this seroconversion window period (Figure 5).[18] 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 fourth-generation combination antigen-antibody immunoassays, the window period is shortened by approximately 1 week (Figure 6).[18] Accordingly, administering PEP despite a negative HIV antibody test is not recommended, unless the source patient is known to have signs or symptoms that strongly suggest acute HIV infection. In addition, routine use of HIV RNA testing of the source patient is not recommended to determine HIV serostatus 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 7).[3] Blood or visibly bloody fluids are considered the most potentially infectious body fluids. Other body fluids also considered potentially infectious, but 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 amniotic). The risk of transmission from vomitus, feces, urine, nasal
secretions, sputum, sweat and tears is not considered potentially infectious unless they are visibly bloody.[3]

**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 risk of HIV transmission and thus does not warrant further evaluation or postexposure management. For needlestick injuries, additional information should include whether or not 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.

**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 U.S. 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 afflicted with dermatitis).[3]
Recommendations for Occupational PEP

Initial Approach Following Exposure Event

It is extremely important that health care workers have an immediate evaluation and consultation following an exposure event that may have involved contact with HIV-contaminated blood or body fluids. 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). 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. If the exposure involves skin (intact or non-intact), the skin should be thoroughly washed with soap and water.

Timing for Initiation of Antiretroviral Therapy

Occupational exposures should be considered an urgent medical issue and addressed immediately. Animal studies have shown that PEP is most effective when started as early as possible after exposure (Figure 8).[12] 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 given (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; in this situation, some experts will consider giving PEP, particularly in cases considered very high risk for HIV acquisition.

Three-Drug Regimens for Occupational PEP

The 2013 Occupational PEP Guidelines recommend the use of three or more antiretroviral medications when PEP is indicated.[3] Prior guidelines utilized a more complicated decision process, whereby either a two-drug (basic) or three-drug (expanded) regimen was chosen based on factors related to the risk of the exposure and the HIV status of the source patient. The new recommendation to use three or more medications for all exposures when PEP is indicated has provided a uniform approach that has simplified the management of occupational PEP. The 2013 Occupational PEP Guidelines note that in certain circumstances, such as difficulty with antiretroviral medication availability, anticipated toxicity, or adherence concerns, a two-drug regimen could be considered if administered with expert consultation. Nevertheless, with the widespread availability of convenient, safe, and well-tolerated antiretroviral medications, most experts would strongly recommend using a three-drug regimen for occupational PEP.

Preferred Regimens for Occupational PEP

The preferred regimen recommended in the 2013 Occupational PEP Guidelines consists of tenofovir DF-emtricitabine plus raltegravir (Table 2).[3] Large-scale studies involving persons with HIV
infection have shown tenofovir DF-emtricitabine plus raltegravir is safe, highly effective, well tolerated, and has minimal drug interactions. The recommended dosing for this regimen is tenofovir DF-emtricitabine once a day and raltegravir twice a day. 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). Since the release of these guidelines, a once daily 1200 mg raltegravir dose (two 600 mg tablets) has been approved by the United States Food and Drug Administration (FDA) for treatment of persons with HIV infection; there are, however, no data with the use of once daily raltegravir for PEP.

**Use of Dolutegravir for Occupational PEP**

Since the release of the 2013 Occupational PEP Guidelines, the integrase inhibitor dolutegravir received FDA approval and has emerged as a first-line antiretroviral medication for initial therapy in persons with HIV infection. Based on the excellent experience with dolutegravir in persons with HIV infection, some experts have substituted dolutegravir for raltegravir for use in occupational PEP. 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. More extensive safety data exists with raltegravir than dolutegravir in pregnancy and in breastfeeding. In addition, on May 18, 2018, an FDA Safety Alert was posted that warned of potential serious neural tube birth defects in infants born to mothers who received dolutegravir at the time of becoming pregnant or early in the first trimester. On May 30, 2018, the HHS Antiretroviral Guideline Panels issued Recommendations Regarding Dolutegravir that address the use of dolutegravir in adults and adolescents with HIV who are pregnant or of child-bearing potential. Note that dolutegravir is also a component of two fixed-dose combinations: dolutegravir-abacavir-lamivudine and dolutegravir-rilpivirine.

**Alternative Regimens for PEP**

Alternative regimens are provided in the 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. 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. Similarly, abacavir should not be used for PEP without expert consultation 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 to develop the hypersensitivity reaction, it may take several days for results to return and thus abacavir is not practical for inclusion in a PEP regimen.

**Duration of Therapy**

The 2013 U.S. Public Health Service Occupational Postexposure Prophylaxis guidelines recommend that health care workers who initiate antiretroviral therapy for PEP should complete a 28-day course. Studies involving macaques have shown that PEP given for 28 days is more effective than 10 days, which is more effective than 3 days. 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 the Source Patient has Undetectable HIV RNA Level**

If the source patient has a recent undetectable HIV RNA level, the risk of transmission in an occupational exposure is likely 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 guidelines recommend that PEP should still be offered.[3]

**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.[22,23] 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.

**Recommended Situations to Obtain Expert Consultation**

The 2013 Occupational PEP Guidelines recommend expert consultation for HIV-related occupational exposures in the following situations:[3]

- 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
- Breastfeeding in the exposed health care worker
- 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 can obtained by calling the National Clinician Consultation Center’s Post-Exposure Prophylaxis PEPline at (888)-448-4911. The hours for PEPline phone consultation are 9 a.m.-9 p.m. EST seven days a week.
Baseline Evaluation and Counseling for Health Care Worker

Baseline Evaluation

Health care workers who have experienced occupational exposure to HIV should have prompt counseling, baseline laboratory testing, and medical evaluation (Figure 9). It is important to determine if the health care worker has any pre-existing (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. However, the baseline evaluation should not result in a delay of giving the first dose of antiretroviral therapy for PEP. The recommended routine baseline laboratory testing for the health care worker exposed to a known or suspected HIV-positive source should include the following:

- Baseline HIV testing to document HIV status of the health care worker at the time of the exposure
- Complete blood count
- Renal function test
- Hepatic function tests
- Hepatitis B antibody (if indicated)
- Hepatitis C antibody (if indicated)
- Pregnancy test (if indicated)

Evaluation of Management of Other Bloodborne Pathogens

For health care workers exposed to a source patient with HIV infection who has coinfection with hepatitis B virus or hepatitis C virus, additional baseline testing and management considerations are needed. It is beyond the scope of this topic review to address postexposure prophylaxis for hepatitis B and/or hepatitis C. In this situation, we recommend obtaining expert consultation.

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 (i.e., barrier contraception, avoidance of pregnancy and breastfeeding) 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 the risks and benefits of PEP in these settings.
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 psychological counseling 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 or development of acute HIV symptoms during the follow-up period. The schedule for follow-up laboratory testing requires repeat HIV testing of the health care worker at 6 weeks, 12 weeks, and 24 weeks after the occupational exposure. Alternatively, if a fourth-generation combination HIV p24 antigen-HIV antibody test is being utilized (which shortens the window period), the follow-up HIV testing schedule can be modified to 6 weeks and 16 weeks after the exposure.[3] Additional testing should include repeat complete blood counts and renal and liver function tests at 2 weeks after exposure for health care workers who initiate PEP. Further testing may be required in the event of abnormalities or drug toxicities (Figure 10).[3]

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 retroviral syndrome. In the setting of suspected acute HIV infection, it is appropriate to order a fourth-generation HIV antigen-antibody test and an HIV RNA. Based on several case reports of delayed HIV seroconversion in health care workers who also acquired hepatitis C virus from the exposure event, extended follow-up is indicated if the health care worker becomes infected with hepatitis C virus. In this situation, most experts recommend follow-up HIV testing out to 12 months, regardless of the method of HIV testing being used.
Summary Points

- Following an occupational exposure to HIV, PEP is an important element of workplace safety and markedly reduces the risk of HIV acquisition in an exposed health care worker.
- A health care worker who experiences a significant occupational HIV exposure should be evaluated for PEP as soon as possible.
- If PEP is initiated, the regimen should be continued for 28 days.
- Antiretroviral PEP medication regimens should contain 3 (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 recommended regimen for PEP consists of tenofovir DF-emtricitabine plus raltegravir; this recommendation is based on this regimen’s high potency, favorable side effect profile, convenient dosing, and minimal drug interactions. Some experts now use dolutegravir in place of raltegravir due to its greater potency and once-daily dosing.
- Initial evaluation of the exposed person should include both counseling and laboratory studies (baseline HIV testing, blood counts, and renal and hepatic function tests).
- Expert consultation should be sought for all cases involving drug-resistant source virus 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 PEPline at 1-888-448-4911.
- All health care workers who experience an HIV exposure event, regardless of whether they take PEP, should be tested for the presence of HIV antibodies at baseline and following the exposure at 6, 12, and 24 weeks. If, however, a fourth-generation combination HIV p24 antigen-HIV antibody test is utilized for follow-up HIV testing of the health care worker, then follow-up testing can be performed at 6 and 16 weeks.
Citations


References


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

Timeline for Occupational Postexposure Prophylaxis Recommendations

- 1990: CDC suggests consider use of zidovudine for PEP
- 1996: CDC recommends zidovudine for PEP
- 1997: Case control study shows zidovudine PEP reduces HIV transmission risk by 81%
- 1998: CDC recommends risk-based 2-drug (basic) and 3-drug (expanded) regimens for PEP
- 2001: CDC issues guidance for occupational exposures to HIV, HCV, HBV
- 2005: CDC updates basic and expanded regimen options for PEP
- 2013: CDC recommends using 3-drug INSTI-based regimen when PEP indicated
Figure 2 Number of Confirmed Cases of Occupationally-Acquired HIV Infection in United States, 1985-2013

This graphic shows the year-by-year distribution of the 58 cases of occupationally acquired HIV infection in the United States. Most cases occurred between 1985 and 1995 prior to the widespread use of postexposure prophylaxis.

Figure 3 Route of Exposure for Occupationally-Acquired HIV Infection in United States, 1985-2013

Most cases of occupational HIV infection in the United States have resulted from a percutaneous puncture or cut.

Figure 4 Timing of HIV RNA and HIV Antibodies following HIV Acquisition
Figure 5 HIV Seroconversion Window

Seroconversion Window Period = Time Between Infection and Detectable HIV Antibodies
Figure 6 Timing of Positivity of Various Laboratory Tests Following HIV Acquisition

### Figure 7 Relative Risk of Body Fluids Involved in Occupational Exposure to HIV


<table>
<thead>
<tr>
<th>Category of Infectivity</th>
<th>Fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infectious Fluids</strong></td>
<td>• Blood</td>
</tr>
<tr>
<td></td>
<td>• Visibly bloody body fluids</td>
</tr>
<tr>
<td><strong>Potentially Infectious Body Fluids</strong></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><strong>Not Considered Infectious (Unless Visibly Bloody)</strong></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>
In this study, investigators inoculated 24 macaques with simian immunodeficiency virus (SIV) and then instituted various postexposure prophylaxis regimens with tenofovir, which is (R)-9-(2-phosphonylmethoxypropyl).


<table>
<thead>
<tr>
<th>SIV Inoculation</th>
<th>Start PEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Hour</td>
<td>0</td>
</tr>
</tbody>
</table>

**Study Features**
- N = 24 macaques
- Randomized to 6 treatment arms
- SIV inoculated intravenously
- SIV dose 10x 50% infective dose
- PEP started at 24, 48, or 72 hours
- PEP duration: 3, 10, or 28 days
- PEP regimen: Tenofovir (PMPA) SQ
- Analyzed for antibody and viremia

Tenofovir (PMPA) = (R)-9-(2-phosphonylmethoxypropyl) adenine
Figure 8 (Image Series) - Tenofovir for Postexposure Prophylaxis following SIV-1 Inoculation of Macaques

Image 8B: SIV Transmission Based on Timing of Initiation and Duration of PEP

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 9 Initial Counseling and Laboratory Studies for Persons with Occupational Exposure to HIV**


<table>
<thead>
<tr>
<th>Initial Counseling and Laboratory Studies for Persons with Occupational Exposure to HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Counseling (at the time of exposure and at follow-up appointments)</strong></td>
</tr>
<tr>
<td>Exposed healthcare provider should be advised 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 6–12 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><strong>Counseling when Postexposure Prophylaxis Prescribed</strong></td>
</tr>
<tr>
<td>For exposures for which postexposure prophylaxis is prescribed, healthcare 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 10 Follow-Up Counseling and Laboratory Studies for Persons with Occupational Exposure to HIV


<table>
<thead>
<tr>
<th>Follow-Up Counseling and Monitoring for Occupational Postexposure Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Early Reevaluation after Exposure (within 72 hours)</strong></td>
</tr>
<tr>
<td>Regardless of whether a healthcare provider is taking postexposure prophylaxis, reevaluation of exposed healthcare 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>

<table>
<thead>
<tr>
<th>Follow-up Testing and Appointments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up testing at a minimum should include the following:</td>
</tr>
<tr>
<td>□ HIV testing at 6 weeks, 12 weeks, and 6 months after exposure; alternatively, if the clinician is certain that a fourth-generation combination HIV p24 antigen–HIV antibody test 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 healthcare provider at face-to-face appointments.</td>
</tr>
<tr>
<td>□ Complete blood counts (2 weeks after exposure; further testing may be indicated if abnormalities are detected)</td>
</tr>
<tr>
<td>□ Renal and hepatic function tests (2 weeks after exposure; further testing may be indicated if abnormalities are detected)</td>
</tr>
</tbody>
</table>
Table 1.

<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 PO 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 physicians familiar with the agents and their toxicities. The alternatives regimens are listed in order of preference; however, other alternatives may be reasonable based on patient and clinician preference.

<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 antiretrovirals are needed: Elvitegravir-cobicistat-tenofovir DF-emtricitabine

**Alternative Antiretroviral Agents for Use as PEP Only with Expert Consultation**

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

**Antiretroviral Agents Generally Not Recommended for Use as PEP**

- Didanosine
- Nelfinavir
- Tipranavir

**Antiretroviral Agents Contraindicated as PEP**

- Nevirapine

Note. For consultation or assistance with HIV PEP, contact the National Clinicians’ 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:
