PEP Quick Guide for Occupational Exposures

Updated: December 20, 2013

These CCC post-exposure prophylaxis (PEP) recommendations will help you with urgent decision-making for occupational exposures to HIV and hepatitis B and C. Consultation can be obtained from Occupational Health or Employee Health Services, local experts, or the CCC's PEPline. The PEPline (888-448-4911) is available daily from 9 am – 2 am EST (6 am – 11 pm PST).

For a comprehensive description of HIV post-exposure management, see the 2013 CDC occupational post-exposure prophylaxis guidelines: Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis.

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Initial evaluation: Assessing exposures and testing

What is considered to be a potential exposure to HIV, HBV or HCV?

For transmission of blood borne pathogens (HIV, HBV and HCV) to occur, an exposure must include both of the following:

- **Infectious body fluid:**
  - Blood, semen, vaginal fluids, amniotic fluids, breast milk, cerebrospinal fluid, pericardial fluid, peritoneal fluid, pleural fluid and synovial fluid can transmit HIV, HBV and HCV.
  - Note that saliva, vomitus, urine, feces, sweat, tears and respiratory secretions do not transmit HIV (unless visibly bloody). (See section on Non-Bloody Saliva for potential HBV and HCV transmission.)

- **A portal of entry** (percutaneous, mucous membrane, cutaneous with non-intact skin).

*If these factors are not present, there is no risk of transmission and further evaluation is not required.*

What baseline testing should be performed after an exposure? (If no exposure occurred or SP tests negative, no testing is indicated.)

**Source Person (SP):**

- HIV Ab (rapid HIV Ab testing preferred if accessible)*
- HCV Ab
- HBV surface Ag

*If SP's rapid HIV Ab test is positive, assume this is a true positive and send confirmatory testing, usually with a Western Blot test. See below*.

**Exposed Person (EP):**

- HIV Ab
- HCV Ab
- HBV testing: depends on immunization status. Note that most healthcare and public safety personnel have been immunized against hepatitis B.

**Hepatitis B immunized and responded to vaccination series:** If they know they responded to the vaccination series (a positive titre is >10mIU/mL, but most do not know their titre), they have lifelong immunity and require no further testing or treatment.

**Hepatitis B immunized and unknown whether responded to vaccination series:** If they had the vaccine series but are unaware of their response status, they should have a HBV surface Ab titer (HBsAb) drawn to see if they have a positive titre. Although unnecessary as a baseline test, a HBV surface Ag can be obtained at the same time to avoid a second phlebotomy if the antibody titre result is not positive.

**Hepatitis B un-immunized or uncertain whether immunized:**
- HBV surface Ab titer (HBsAb) + HBV surface Ag (HBsAg)
*Is the rapid HIV test accurate enough to decide on whether to give PEP?

Yes, the rapid HIV test is extremely sensitive and specific and can be used to determine whether to offer PEP. A positive rapid HIV test should be considered a true positive for the purposes of PEP decision-making. A negative rapid test should be considered a true negative. Investigation of whether a source might be in the “window period” is unnecessary for determining whether HIV PEP is indicated unless acute retroviral syndrome is clinically suspected. (See What if the source might be in the "window period" for HIV? below).

Deciding whether to give HIV PEP

What is the time frame for using PEP?

Efficacy is time sensitive: first dose should be given as soon as possible. Optimal time to start PEP is within hours of exposure, rather than days. Do not wait for SP test results (unless results of rapid test will be available within an hour or two) to proceed with a PEP decision and treatment, when indicated. The PEPline considers 72 hours post-exposure as the outer limit of opportunity to initiate PEP; however, a delay of that scale is believed to compromise PEP efficacy. The 72-hour outside limit recommendation is based on animal studies; no human data are available.

Note: PEP should be initiated as soon as possible; if additional information indicates PEP might not be needed, PEP can always be discontinued.

What is the risk of HIV transmission?

<table>
<thead>
<tr>
<th>Route of exposure</th>
<th>Risk of exposure when source person is HIV positive</th>
<th>Factors increasing risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percutaneous</td>
<td>~ 1/300 episodes (0.3%)</td>
<td>hollow bore needles, visibly bloody devices, and deep injury, device used in an artery/vein</td>
</tr>
<tr>
<td>Mucous membrane</td>
<td>~ 1/1000 episodes (0.09%)</td>
<td>large volume</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>&lt; 1/1000 episodes (0.09%)</td>
<td>must involve non-intact skin integrity.</td>
</tr>
</tbody>
</table>

Note: These estimates are from exposures to blood; risk for transmission from infectious fluids other than HIV-infected blood is probably considerably lower than for blood exposures.
Is PEP always recommended if the source person is HIV infected?

PEP is recommended when an exposure to an HIV positive patient has occurred. (See What is considered to be a potential exposure to HIV, HBV or HCV?)

Additional source person information (e.g., the SP’s current or most recent viral load, HIV medications, history of resistance to HIV medications) can be helpful in PEP regimen selection, but initiation of PEP should not be delayed if this information or consultation is not available.

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Is PEP recommended if the source person has an unknown HIV status?

PEP is generally not warranted in cases of unknown status. However, consider PEP for exposures from a source with HIV risk factors. If questions exist, seek expert consultation from Occupational Health, Employee Health, local experts, or the PEPline.

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Is PEP recommended if the source person is unknown (e.g. sharps box injury)?

PEP is generally not warranted in cases of an unknown source person. However, consider PEP in settings where exposure to HIV-infected persons is likely.

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Should PEP be given if it is uncertain whether the exposure constitutes a significant risk?

Yes, if consultation is not available within a few hours, begin PEP and obtain consultation at a later time.

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What if the source person might be in the “window period” for HIV?

If the source patient’s HIV test is negative at the time of the exposure, they are generally considered uninfected and HIV PEP is not recommended.

- The “window period” for HIV Ab seroconversion (after the period between initial HIV infection and the development of detectable HIV antibodies) can cause patient and provider anxiety. The Guidelines state, “To date, no transmission to health care workers from an exposure source during the window period has been detected in the United States.”
Therefore, investigation of whether a source patient might be in the “window period” is unnecessary for determining whether HIV PEP is indicated unless acute retroviral syndrome is clinically suspected, or recent high-risk exposure has occurred.

Clinical suspicion can be implied when a source patient with risk factors has a history of recent (within 1-2 months) exposure (e.g. sexual, injection drug use, etc) and/or a recent illness consistent with possible acute HIV infection. If acute HIV is highly suspected, PEP should be started while confirmation with the source’s HIV RNA PCR viral load is sent.

Is PEP recommended for a patient who was stuck with a sharp device (e.g. needle, razor) from an unknown source outside of a healthcare setting?

This common occurrence falls into the classification of exposure to blood from an unknown SP. A “found needle” is the classic occurrence. No documented cases of HIV transmission from a “found needle” outside of a healthcare setting in the US have occurred. Therefore, the PEPline generally discourages PEP in these cases. Even within healthcare settings, "found needles" have only been implicated in 3 cases of transmission over the past 2 decades.

How should a human bite be managed?

- Human bite exposures can result in exposure to both the biter and the bitten person. The bitten sustains a cutaneous exposure to HIV if blood was present in the mouth of the biter before the bite. The biter sustains a mucous membrane exposure to HIV if blood from the bitten person enters the oral cavity of the biter.
- If the saliva is non-bloody, there is no risk to the exposed for HIV. The risk of HBV and HCV transmission from non-bloody saliva is negligible. However, there are a few reports of HBV and possible HCV transmission, so one may consider further evaluation and treatment. (See section on Exposures to HBV and Exposures to HCV)

HIV PEP: What to give

How to choose a PEP regimen?

Three-drug PEP regimens are now the recommended regimens for all exposures. The new guidelines no longer require assessing the degree of risk for the purpose of choosing a "basic" two-drug regimen vs. an "expanded" three-drug regimen, which was confusing for many treating clinicians. There are some special circumstances, however, in which a two-drug regimen can be used, especially when recommended antiretroviral medications are unavailable or there is concern about potential adherence problems or toxicity. In addition, the Guidelines state, "PEP is not justified for
exposures that pose a negligible risk for transmission." Consultation with an expert can help determine if the exposure poses a "negligible risk" to explore whether alternative approaches, including a modified regimen, are appropriate.

**PREFERRED HIV 3-DRUG PEP REGIMEN:**

Truvada™ 1 PO Once Daily

[Tenofovir DF (Viread®; TDF) 300mg + emtricitabine (Emtriva™; FTC) 200mg]  

**PLUS**

Raltegravir (Isentress®; RAL) 400mg PO Twice Daily

**ALTERNATIVE REGIMENS**

May combine one drug or drug pair from the left column with one pair of nucleoside/nucleotide reverse transcriptase inhibitors from the right column.

| Raltegravir (Isentress®; RAL) | Tenofovir DF (Viread®; TDF) + emtricitabine (Emtriva™; FTC); available as Truvada™ |
| Darunavir (Prezista®; DRV) + ritonavir (Norvir®; RTV) | Tenofovir DF (Viread®; TDF) + lamivudine (Epivir®; 3TC) |
| Etravirine (Intelence®; ETR) | Zidovudine (Retrovir™; ZDV; AZT) + lamivudine (Epivir®; 3TC); available as Combivir® |
| Rilpivirine (Edurant™; RPV) | Zidovudine (Retrovir™; ZDV; AZT) + emtricitabine (Emtriva™; FTC) |
| Atazanavir (Reyataz®; ATV) + ritonavir (Norvir®; RTV) | |
| Lopinavir/ritonavir (Kaletra®; LPV/RTV) | |

*The alternative regimens are listed in order of preference. Others may be reasonable based upon patient and clinician preference.

**ANTIRETROVIRAL AGENTS FOR USE AS PEP ONLY WITH EXPERT CONSULTATION:** Abacavir (Ziagen®; ABC), Efavirenz (Sustiva®; EFV), Enfuvirtide (Fuzeon®; T20), Fosamprenavir (Lexiva®; FOSAPV), Maraviroc (Selzentry®; MVC), Saquinavir (Invirase®; SQV), Stavudine (Zerit®; d4T)

**ANTIRETROVIRAL AGENTS GENERALLY NOT RECOMMENDED FOR USE AS PEP:** Didanosine (Videx EC®; ddI), Nelfinavir (Viracept®; NFV), Tipranavir (Aptivus®; TPV)

**ANTIRETROVIRAL AGENTS CONTRAINDICATED AS PEP:** Nevirapine (Viramune®; NVP)
## ARV drug dosing and toxicity monitoring

<table>
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<th>HIV meds</th>
<th>Adult Dosing</th>
<th>Combination Form</th>
<th>Toxicity monitoring</th>
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</thead>
<tbody>
<tr>
<td>Tenofovir®</td>
<td>300 mg po daily</td>
<td></td>
<td>BUN, Creatinine, LFTs</td>
</tr>
<tr>
<td>Emtricitabine®</td>
<td>200 mg po daily</td>
<td>Truvada™</td>
<td>Rash</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>400 mg po BID</td>
<td></td>
<td>Nausea, headache</td>
</tr>
<tr>
<td>Zidovudine*</td>
<td>300 mg po BID</td>
<td>Combi®</td>
<td>CBC, LFTs</td>
</tr>
<tr>
<td>Lamivudine*</td>
<td>150 mg po BID</td>
<td></td>
<td>Rash</td>
</tr>
<tr>
<td>Lopinavir/ritonavir®</td>
<td>2 tabs po BID</td>
<td>Kaletra ®</td>
<td>GI toxicity, especially diarrhea. LFTs</td>
</tr>
<tr>
<td>(200/50 mg)</td>
<td></td>
<td></td>
<td>*Note: Lopinavir/ritonavir has many drug-drug interactions with common medications; use with caution.</td>
</tr>
</tbody>
</table>

* Zidovudine + Lamivudine: generic co-formulation available.

**How long is PEP given?**

PEP is **given for 28 days**. If source person testing is negative for HIV, PEP can be stopped before 28 days.

**How to monitor and manage side effects of PEP?**

Side effects can be a limiting factor in PEP adherence. Side effects are generally self-limited but sometimes can last the duration of the 28-day PEP course. Gastrointestinal side effects (nausea, vomiting, diarrhea) are most common. Headache, fatigue, insomnia and gastrointestinal upset are other side effects. Antiemetic and antidiarrheal medications can be prescribed to help with PEP adherence. If side effects are severe, consider changing to a different regimen. Toxicities are rare with the current preferred PEP regimens, are generally not life-threatening and are reversible.

The most important side effect of the preferred regimen, tenofovir + emtricitabine (Truvada™) plus raltegravir, is renal toxicity from tenofovir. This regimen should be used with caution in patients with impaired renal function.

**Lab monitoring for drug toxicity:** Test CBC, renal and hepatic function tests at baseline and two weeks after starting PEP.
What are common drug-drug interactions between PEP and the exposed person’s medications?

- The following drugs should NOT be co-administered with lopinavir/ritonavir (Kaletra); lovastatin, pitavastatin, simvastatin, rifampin, rifapentine, cisapride, pimozide, midazolam, triazolam, dihydroergotamine, ergonovine, ergotamine, methylergonovine, St. John's wort, alfuzosin, salmeterol and sildenafil.
- Other Common medications may have interactions with PEP regimens and require dosing adjustments. See (see Table 14 of the CDC Adult ARV Guidelines). Contact a local expert or the PEPline the next day for further consultation regarding evaluation or management of drug-drug interactions.

Pregnancy and Breastfeeding

How should exposures to a pregnant patient be managed?

Pregnancy is not a contraindication to HIV PEP. Zidovudine has been well studied over 20 years and does not appear to be associated with birth defects or significant toxicities in the infant when given for a short time to the mother. There is considerable experience with zidovudine+lamivudine and lopinavir+ritonavir in HIV positive women. The Pregnancy Registry has not shown increased prevalence of birth defects compared with baseline population incidence. The risk, however, is considered higher in the first trimester as compared with later in pregnancy. Most antiretroviral drugs are category B or C. Decision making should weigh the benefits of PEP to the mother and fetus against the unknown effects to the fetus.

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How should an exposed woman who is breastfeeding be managed?

Both the HIV virus and antiretroviral medications can be found in breast milk. Some guidelines recommend avoiding breastfeeding for up to 6 months post exposure to prevent potential exposure of the infant to HIV should transmission to the mother occur and/or to avoid potential PEP drug toxicities. Because there are significant benefits from breastfeeding and HIV is rarely transmitted to the exposed person (particularly when PEP is used), the PEPline advises discussing potential risks with the exposed woman and leaving the decision up to the breastfeeding mother. As most transmissions are diagnosed by 6 weeks and almost all transmissions are detected by 3 months, the option to pump and discard breast milk initially and later reinitiate breastfeeding may be a reasonable choice.

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## Exposures to HBV and HCV

### How are exposures to HBV managed?

#### Recommendations for Post Exposure Prophylaxis After Exposure to HBV

<table>
<thead>
<tr>
<th>Vaccination and antibody response status of exposed person****</th>
<th>Source HBsAg* positive</th>
<th>Source HBsAg* negative</th>
<th>Source unknown or not available for testing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unvaccinated:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>HBIG# x 1 and initiate HBV vaccine series immediately</td>
<td>Initiate HBV vaccine series</td>
<td>Initiate HBV vaccine series If known high risk source, may treat as if source were HBsAg positive</td>
</tr>
<tr>
<td><strong>Previously vaccinated:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Known responder**</td>
<td>No treatment</td>
<td>No treatment</td>
<td>No treatment</td>
</tr>
<tr>
<td>Known nonresponder@@</td>
<td>HBIG x 1 and initiate revaccination or HBIG x 2 with second dose separated from first by 4 wks***</td>
<td>No treatment</td>
<td>If known high risk source, treat as if source were HBsAg positive</td>
</tr>
<tr>
<td>Antibody response unknown</td>
<td>Test exposed person for HBsAb 1. If adequate**, no treatment necessary 2. If inadequate@@, administer HBIG x 1 and vaccine booster, recheck HBsAb ## titer in 3-4 months. If titer is still inadequate for immunity, complete full second series of vaccinations.</td>
<td>No treatment</td>
<td>Test exposed person for HBsAb 1. If adequate**, no treatment necessary 2. If inadequate@@, administer vaccine booster and recheck HBsAb titer in 1-2 months. If titer is still inadequate for immunity, complete full second series of vaccinations.</td>
</tr>
</tbody>
</table>

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* Hepatitis B surface antigen  
** A responder is a person with documented adequate levels of HBsAb (> or = 10 mIU/mL)  
*** The option of giving one dose of HBIG and reinitiating the vaccine series is preferred for nonresponders who have not completed a second 3-dose vaccine series. Two doses of HBIG are preferred for persons who have previously completed a second vaccine series but failed to respond.  
**** Persons who have previously been infected with HBV are not at risk of re-infection and do not require postexposure prophylaxis  
# Hepatitis B immune globulin (dose: 0.06 mL/kg intramuscularly)  
** Hepatitis B surface antibody  
@@ A nonresponder is a person with inadequate levels of HBsAb (<10 mIU/mL)  
## Hepatitis B surface antibody  
Adapted from MMWR 2001;50 (No. RR-11) and other sources

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How soon do hepatitis B vaccine and HBIG need to be given?

In general, if hepatitis B vaccine and/or HBIG are required, the sooner they are administered the better. It is best to give hepatitis B vaccine within 3 days; giving hepatitis B vaccine after that timeframe is better than not giving it. HBIG is best given within 24 hours, but can be given up to 7 days for occupational exposures (14 days for sexual exposures).

How are exposures to HCV managed?

- The risk of transmission of HCV attributed to needlestick exposure is about 1 in 50 (1.8%) when the source patient is infected. There is no post-exposure prophylaxis available for HCV.
- Direct viral testing with HCV RNA PCR viral load at 6 weeks, before HCV Ab seroconversion has occurred, allows for early identification of transmission and subsequent referral for early evaluation and potential HCV treatment. The rate of spontaneous clearance of HCV infection is about 25% in otherwise healthy people. However, early diagnosis and treatment may increase HCV clearance to 90% or greater.

Follow-up Testing

What follow-up testing should be performed?

Source Person: The SP does not need follow-up testing.
Exposed Person: Standard follow-up for an EP should include the following:

HIV
- If SP is HIV positive, check HIV Ab at 6 weeks, and a 4th generation Ag/Ab test or HIV RNA test at 3-4 months. If these tests are not available, standard antibody testing should be performed at 3 and 6 months. Extended testing to 12 months is only indicated for HCP who actually became infected with HCV after exposure to an HCV-HIV co-infected source. Symptoms of acute HIV should prompt immediate evaluation.
- If SP cannot be tested for HIV or SP is unknown, testing should be as above.
- If SP tests negative for HIV, no follow-up HIV testing is recommended for the EP.

HBV
- Serologic follow-up testing for HBV exposures is only required for persons who do not have baseline positive HBV surface Ab. See How are Exposures to HBV managed?

HCV
- If SP is HCV positive, obtain HCV RNA PCR viral load at 6 weeks and HCV Ab at 3-4 mo. - to synchronize with HIV testing – and at 24 weeks. Note: Guidelines (2001) suggest HCV antibody at 12 and 24 weeks. Symptoms of acute hepatitis should prompt immediate evaluation.
- If SP has unknown HCV status, check HCV Ab at 12 and 24 weeks. Symptoms of acute hepatitis should prompt immediate evaluation.
- If SP is HCV negative, no follow-up testing is recommended for EP.
Guidance for Exposed Persons

What do I do if I am the exposed individual?

Exposure to HIV, HBV, and HCV requires immediate evaluation by a medical professional (e.g., emergency room, urgent care, Occupational/Employee Health service, personal physician). Report your exposure to your supervisor immediately.

The material on this website is intended for educational purposes for healthcare providers only. It is not intended as a substitute for professional medical care or advice, nor to replace a healthcare professionals' clinical judgment regarding their individual patient care.