PEP STEPS

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A Quick Guide to Postexposure Prophylaxis in the Health Care Setting

Mountain Plains AIDS Education & Training Center

in consultation with
National Clinicians' Postexposure Prophylaxis (PEP) Hotline

RISK

The risk of exposure to blood and bloodborne pathogens is slightly greater for health care personnel (HCP) than for people who do not work around blood. An exposure to infected blood, tissue, or other potentially infectious body fluids can occur by:

- Percutaneous injury (e.g. a needlestick or cut with a sharp object).

OR

- Contact with mucous membrane or non-intact skin (e.g. skin that is chapped, abraded, or affected by dermatitis).

The risk of infection after an exposure is dependent on a number of variables. After percutaneous injury, the risk of infection varies for specific bloodborne pathogens:

- Hepatitis B virus (HBV):
  - If the source patient is Hepatitis B surface antigen (HBsAg)-positive AND Hepatitis B e antigen (HBeAg)-positive, the risk of Hepatitis B transmission is approximately 37%-62%.
  - If the source patient is HBsAg-positive and HBeAg-negative, the risk of Hepatitis B transmission is approximately 23%-37%.
- If the source patient has Hepatitis C (HCV), the risk of Hepatitis C transmission is approximately 1.8% (range 0%-7%).
- If the source patient has HIV infection, the risk of HIV transmission is approximately 0.3% after a percutaneous exposure, and 0.09% after a mucous membrane exposure.

The risk of infection appears to be higher with:

- Exposure to a larger quantity of blood or other infectious fluid.
- Prolonged or extensive exposure of non-intact skin or mucous membrane to blood or other infectious fluid or concentrated virus in a laboratory setting.
- Exposure to the blood of a patient in an advanced disease stage or with a high viral load.
- A deep percutaneous injury.
- An injury with a hollow-bore, blood-filled needle.

PROTECT

Prevention is primary! HCP should be familiar with Standard Precautions:

- Wash hands frequently and thoroughly before and after patient care.
- Use Personal Protective Equipment (PPE) -- gloves, gowns, boots, shoe covers, eyewear, and masks – as appropriate for the patient care situation.
- Gloves must be worn when any kind of venous or arterial access is being performed.
- Use sharps with caution:
  - Plan ahead – use sharps in a safe environment with a sharps container nearby.
  - Dispose of used sharps in puncture proof receptacles immediately after use.
  - Do not recap needles.
  - Use safety devices if available.

All HCP should receive the HBV vaccine series and consider testing for HBV response one month after completion of the series.

PEP Step 1: Treat Exposure Site

- Use soap and water to wash areas exposed to potentially infectious fluids as soon as possible after exposure.
- Flush exposed mucous membranes with water.
- Flush exposed eyes with water or saline solution.
- Do NOT apply caustic agents, or inject antiseptics or disinfectants into the wound.

PEP Step 2: Report and Document

Report occupational exposures immediately; circumstances of the exposure and postexposure prophylaxis (PEP) management should be recorded in the exposed HCP's confidential medical record. Include:

- Date and time of exposure.
- Details of the incident: where and how the exposure occurred, exposure site(s) on HCP's body; if related to sharp device, the type and brand of device.
- Details of the exposure: type and amount of fluid or material, severity of exposure.

- Details about the exposure source:
  - Whether the source material contained HIV, HBV or HCV.
  - If the source patient is HIV-infected, determine stage of disease, CD4 cell count, HIV viral load, history of antiretroviral therapy, and antiretroviral resistance information.
- Details about the exposed HCP:
  - Hepatitis B vaccination and vaccine-response status.
  - Other medical conditions.
  - Current medications, and drug allergies.
  - Pregnancy or breast-feeding.
- Documentation of counseling, postexposure management and follow-up.

PEP Step 3: Evaluate the Exposure

The exposure should be evaluated for potential to transmit HBV, HCV, or HIV based on the type of body substance involved, the route, and severity of exposure.

Significant exposures to any of the following may pose a risk for bloodborne pathogen transmission and require further evaluation:

- Blood
- Semen
- Vaginal secretions
- Cerebrospinal fluid
- Synovial fluid
- Pleural fluid
- Peritoneal fluid
- Pericardial fluid
- Amniotic fluid

Body fluids that do NOT pose a risk of bloodborne pathogen transmission unless visibly contaminated with blood include:

- Urine
- Saliva
- Nonpurulent sputum
- Stool
- Emesis
- Nasal Discharge
- Tears
- Sweat

Factors to consider in assessing the need for follow-up:

- Type of exposure
  - Percutaneous injury
  - Mucous membrane exposure
  - Nonintact skin exposure
  - Bites resulting in blood exposure to either person involved

- Type and amount of fluid/tissue
  - Blood
  - Fluids containing blood
  - Potentially infectious fluid or tissue
  - Direct contact with concentrated virus
- Infection status of source patient
  - If positive for HBsAg, consider testing for presence of HBeAg.
  - If positive for HCV antibody, consider measuring HCV viral load.
  - If positive for HIV antibody, consider obtaining HIV viral load, resistance testing, and evaluating clinical status of patient.
- Susceptibility of exposed HCP
  - Hepatitis B vaccine and vaccine response status
  - HBV, HCV, and HIV status—baseline testing for HbsAb, anti-HCV, and HIV antibody should be completed as early as possible (preferably within 72 hours)

PEP Step 4: Evaluate the Exposure Source

When source patient is known:

- Test patient for HBsAg, HCV antibody and HIV antibody.
  - HIV viral load assessments for routine screening of source patients are NOT recommended.
  - Use a rapid HIV-antibody test.
  - If the source person is NOT infected with a bloodborne pathogen, baseline testing or further follow-up of HCP is not necessary.
  - Follow state regulations related to informed consent and confidentiality.
- For patients who cannot be tested, consider medical diagnoses, clinical symptoms, and history of risk behaviors.

When source patient is NOT known:

- Evaluate the likelihood of high risk exposure:
  - Consider the likelihood of bloodborne pathogen infection among patients in the exposure setting, e.g. what is the community infection rate? Does the clinic/hospital unit care for a large number of HIV-, HBV-, or HCV-infected or at-risk patients?
- Do not test discarded needles for bloodborne pathogens; the reliability of these findings is not known.

PEP Step 5: Disease-Specific PEP Management

Baseline testing of exposed HCPs should be performed for ALL exposures.

HBV Exposures

HBV PEP should be initiated IMMEDIATELY (preferably within 24 hours but within 7 days) according to the following table:

RECOMMENDED PEP FOR EXPOSURE TO HBV

Vaccination status of exposed HCP*	Antibody Response Status		
	Source HBsAg Positive	**Source HBsAg Negative**	**Source unknown or not available for testing**
Unvaccinated	HBIG† x 1 and initiate HBV vaccine series	Initiate HBV vaccine series	Initiate HBV vaccine series
Previously Vaccinated			
Known responder[1]	No treatment	No treatment	No treatment
Known nonresponder[2]	HBIG x 1 and initiate revaccination or HBIG x 2††	No treatment Consider revaccination	If known high risk source, treat as if HBsAg positive
Antibody Response Unknown	Test exposed HCP for anti-HBs** 1. If adequate,[1] no treatment is necessary 2. If inadequate,[2] administer HBIG x 1 and vaccine booster 3. Consider testing HCP for HBsAg	No treatment	Test exposed HCP for anti-HBs** 1. If adequate,[1] no treatment necessary 2. If inadequate,[2] administer vaccine booster and recheck titer in 1-2 months

* Those previously infected with HBV are immune to reinfection and do not require PEP.

† Hepatitis B immune globulin; dose is 0.06 mL/kg intramuscularly within 7 days of exposure.

1 A responder has adequate levels of serum antibody to HBsAg (i.e., anti-HBs ≥ 10 mIU/mL).

2 A nonresponder has inadequate response to vaccination (i.e., anti-HBs < 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. For persons who previously completed a second vaccine series but failed to respond, two doses of HBIG are preferred.

**Antibody to HbsAg

HCV Exposures

At this point, there are no recommendations for HCV PEP. Immune globulin is not effective. Exposed HCP should receive appropriate counseling, testing, and follow up. (See HIV Exposures section below.) For seroconverters, pegylated interferon may be effective if started soon after HCV seroconversion.

HIV Exposures

- HIV PEP should be started IMMEDIATELY. If the delay lasts more than 24-36 hours, seek expert consultation. PEP should continue for 28 days. Typical choices for PEP are:
  - A basic 2-drug regimen, appropriate for lower risk exposures.
  - An expanded ≥ 3-drug regimen, for exposures that pose an increased risk for transmission.

- If questions about the extent of risk remain after the incident, starting the basic 2 or expanded 3-drug PEP is better than delaying administration.

- If information on the source is unknown, and the decision to start PEP is made (based on risk factors, exposure type, etc.), PEP should not be delayed; changes can be made as needed after PEP has been started. The exposed HCP should be reevaluated within 72 hours as additional information about the source is obtained. If source patient is found to be HIV-negative, PEP should be discontinued.

- If PEP is initiated, obtain baseline CBC, creatinine, and liver enzyme tests (AST, ALT, alkaline phosphatase, total bilirubin).

Drug Selection

- For all HCP exposures to known or suspected HIV-infected sources, PEP regimen should be initiated promptly and continued for 28 days. HCP are often unable to complete PEP regimens due to side effects. Providing appropriate education about options for symptom management can improve adherence to the PEP regimen.

- Drug selection decisions should be made based in part on information about the source patient including antiretroviral therapy; response to therapy including HIV viral load, CD4 cell count, current disease stage; and any data on HIV resistance testing. Delays in getting information should NOT delay initiation of PEP; modifications can be made later as needed.

- Typical regimens include the basic regimen plus a protease inhibitor. Additional medications are rarely used. If using an expanded regimen, check for potential drug interactions with other medications the exposed HCP may be taking.

- When initiating an expanded regimen, expert consultation is recommended.

Refer to PEP Tables

HIV PEP FOR PERCUTANEOUS INJURIES

EXPOSURE TYPE	Infectious Status of Source				
	HIV-Infected Class 1	**HIV-Infected Class 2**	**Source of Unknown HIV Status**	**Unknown Source**	**HIV-Negative**
	e.g., Asymptomatic HIV infection or known low HIV viral load (e.g. < 1,500 RNA copies/mL)	e.g., Symptomatic HIV infection, AIDS, acute seroconversion, or known high HIV viral load*	e.g., Source patient refuses testing or is unavailable	e.g., Needle from sharps container	
Less Severe - Solid needle - Superficial injury	Recommend basic 2-drug PEP	Recommend expanded ≥ 3-drug PEP	Generally no PEP warranted; Consider basic 2-drug PEP[1] for source with HIV risk factors[2]	Generally no PEP warranted; Consider basic 2-drug PEP[1] in settings where exposure to HIV-infected persons is likely[3]	No PEP warranted
More Severe - Large-bore, hollow needle - Deep puncture - Visible blood on device - Needle used in artery or vein	Recommend expanded 3-drug PEP	Recommend expanded ≥ 3-drug PEP	Generally no PEP warranted; Consider basic 2-drug PEP[1] for source with HIV risk factors[2]	Generally no PEP warranted; Consider basic 2-drug PEP[1] in settings where exposure to HIV-infected persons is likely[3]	No PEP warranted

[1]The designation "consider PEP" indicates that PEP is optional and should be based on an individualized decision between the exposed person and the treating clinician.
[2]If PEP is initiated and the source is later determined to be HIV-negative, PEP should be discontinued.
[3]e.g. healthcare setting. No exposures reported to date in non-health care settings.

*Seek expert consultation if drug resistance is a concern. Initiation of PEP should NOT be delayed pending expert consultation.

HIV PEP FOR MUCOUS MEMBRANE AND NONINTACT SKIN EXPOSURES

EXPOSURE TYPE	Infectious Status of Source				
	HIV-Infected Class 1	**HIV-Infected Class 2**	**Source of Unknown HIV Status**	**Unknown Source**	**HIV-Negative**
	e.g., Asymptomatic HIV infection or known low HIV viral load (e.g. < 1,500 RNA copies/mL)	e.g., Symptomatic HIV infection, AIDS, acute seroconversion, or known high HIV viral load*	e.g., Source patient refuses testing or is unavailable	e.g., Blood spill or bloody equipment that cannot be traced to a patient	
Small Volume - A few drops	Consider basic 2-drug PEP[1]	Recommend basic 2-drug PEP	Generally no PEP warranted	Generally no PEP warranted	No PEP warranted
Large Volume - Large blood splash	Recommend basic 2-drug PEP	Recommend expanded ≥ 3-drug PEP	Generally no PEP warranted; Consider basic 2-drug PEP[1] for source with HIV risk factors[2]	Generally no PEP warranted; Consider basic 2-drug PEP[1] in settings where exposure to HIV-infected persons is likely	No PEP warranted

[1]The designation "consider PEP" indicates that PEP is optional and should be based on an individualized decision between the exposed person and the treating clinician.
[2]If PEP is initiated and the source is later determined to be HIV-negative, PEP should be discontinued.

*Seek expert consultation if drug resistance is a concern. Initiation of PEP should NOT be delayed pending expert consultation.

HIV PEP POST-EXPOSURE REGIMENS

	Preferred	Alternatives**	Agents Not Recommended
Basic Regimen: (2-drug)	• Zidovudine (AZT) 300 mg twice daily + lamivudine (3TC) 150 mg twice daily or emtricitabine (FTC) 200 mg once daily* • Tenofovir (TDF) 300 mg once daily + lamivudine (3TC) 300 mg once daily or emtricitabine (FTC) 200 mg once daily#	• Stavudine (d4T) + lamivudine (3TC) or emtricitabine (FTC) • Didanosine (ddI) + lamivudine (3TC) or emtricitabine (FTC)	• nevirapine (NVP) • delavirdine (DLV) • abacavir (ABC) • zalcitabine (ddC) • didanosine (ddI) + stavudine (d4T)
Expanded Regimens* (3-drug)**	• Basic regimen + lopinavir-ritonavir (LPV/r) 400/100 mg twice daily	• Basic + atazanavir-ritonavir (ATV/RTV) • Basic + fosamprenavir-ritonavir (FPV/RTV) • Basic + indinavir-ritonavir (IDV/RTV) • Basic + saquinavir/ritonavir (SQV/RTV) • Basic + nelfinavir (NFV/RTV) • Basic + efavirenz (EFV)¶	

* Less well tolerated than tenofovir-containing regimen, available as Combivir (ZDV + 3TC) one tablet twice daily.

Well tolerated, available as Truvada (TDF + FTC) once daily.

** For dosing of alternative regimens, see DHHS PEP guidelines at http://aidsinfo.nih.gov

¶ Efavirenz is Pregnancy Category D.

*** Enfuvirtide (T-20) should only be used with expert consultation.

PEP Step 6: Follow Up

Hepatitis-exposed HCP

➤ HBV exposure follow-up testing and counseling:

- Test for anti-HBs 1-2 months after last dose of vaccine; Anti-HBs cannot be ascertained if HBIG given within 6-8 weeks.
- Advise exposed HCP to refrain from donating blood, plasma, organs, tissue, or semen and use risk reduction methods including latex barriers during sex, not sharing injection equipment, and abstaining from risk behaviors.
- Offer mental health counseling as needed.

➤ HCV exposure follow-up testing and counseling:

- Repeat test for anti-HCV and ALT at least 4-6 months post exposure; confirm repeatedly positive anti-HCV EIA results with supplemental tests.

  -AND-
- Test for HCV RNA at 4-6 weeks for earlier diagnosis. (Caution must be used due to occurrence of false positive results.)
- During follow-up period, refrain from donating blood, plasma, organs, tissue, or semen.
- Guidelines do not recommend changes in sexual activity, pregnancy, breastfeeding, or professional activities.
- Offer mental health counseling as needed.

HIV-exposed HCP

➤ HIV exposure follow-up testing:

- Repeat HIV-antibody testing at 6 weeks, 3 months, and 6 months post exposure.
- If illness compatible with acute retroviral syndrome occurs, perform HIV viral load.
- Extended follow-up (12 months) is recommended for HCP who become infected with HCV following an exposure to a source co-infected with HIV and HCV.

- If PEP is given, HCP should be monitored for drug toxicity. CBC, creatinine, and liver enzyme tests (AST, ALT, alkaline phosphatase, total bilirubin) should be repeated at 2 weeks.
  - For those receiving a protease inhibitor, monitor for hyperglycemia.
  - If receiving indinavir (IDV) or tenofovir (TDF), tests should include urinalysis.

➤ Counseling after HIV exposure:

- Advise exposed HCP to refrain from donating blood, plasma, organs, tissue, or semen; to avoid breastfeeding; to use methods to prevent pregnancy; and to use risk reduction methods including latex barriers during sex, not sharing injection equipment, and abstaining from risk behaviors.
- Offer mental health counseling as needed.
- Counsel HCP about the signs and symptoms of acute retroviral syndrome (flu-like syndrome), and the need to come in for additional testing at the onset of symptoms.
- If PEP is given, advise regarding the importance of adherence and potential side effects and how to minimize these. Inform regarding any possible drug interactions or toxicities and the importance of monitoring for these.

Special Considerations

Expert consultation in providing HIV PEP is advised in the following situations: (For expert consultation resources see back cover.)

➤ Delayed exposure report (> than 24-36 hours post exposure)

- The interval after which there is no benefit from PEP is undefined.

➤ Unknown source (e.g. needle in sharps container)

- Decide use of PEP on a case-by-case basis.
- Consider the severity of the exposure and epidemiological likelihood of HIV exposure.
- Do not test needles or other sharp instruments for HIV.

➤ **Known or suspected pregnancy of HCP**

- Does not preclude the use of optimal PEP regimens.
- Do not deny PEP solely on the basis of pregnancy.
- While most drugs used in HIV therapy have been safe in pregnancy, assess for new information. There are recommendations against using efavirenz (pregnancy category D), as well as the combination of didanosine (ddI) and stavudine (d4T) in pregnant women.

➤ **Resistance of the source virus to antiretroviral agents**

- Influence of drug resistance on transmission risk is unknown.
- If the source patient's virus is known or suspected to be resistant to one or more of the drugs considered for the standard PEP regimen, select alternate drugs.
- Resistance testing of the source patient's virus at the time of exposure is not recommended.
- Do not delay initiation of PEP while waiting for resistance testing results.

➤ **Toxicity of the initial PEP regimen**

- Adverse symptoms such as nausea, diarrhea, fatigue and headaches are common with PEP.
- Symptoms often can be managed without changing the PEP regimen by taking the PEP regimen with meals, prescribing antiemetic, antimotility and/or analgesic agents.
- Consultation should be obtained when side effects are difficult to manage:
  - Modification of dose intervals (e.g., administering a lower dose of drug more frequently), might help alleviate symptoms.

➤ **Expanded Regimen**

- The use of nevirapine has been associated with severe toxicity in HCP. Nevirapine should only be considered if no other options exist for expanded regimen and should always be prescribed with expert consultation.
- Seek expert consultation when considering dual protease inhibitor, efavirenz, or abacavir therapy

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PEP RESOURCES

National Clinicians' Post-exposure Prophylaxis Hotline (PEPline)	1-888-448-4911 www.ucsf.edu/hivcntr/Hotlines/PEPline.html
Mountain Plains E-mail Clinical Consultation Service for HIV Infection	hivconsultation@UCHSC.edu
Centers for Disease Control and Prevention (CDC) Report occupationally acquired HIV infections and failures of PEP	1-800-893-0485
HIV Antiretroviral Pregnancy Registry	1-800-258-4263 www.apregistry.com
Food and Drug Administration Report unusual or severe toxicity to antiretroviral agents	1-800-332-1088 www.fda.gov/medwatch
AIDS*info*	http://aidsinfo.nih.gov
Needlestick!	www.needlestick.mednet.ucla.edu
Hepatitis Hotline	1-888-443-7232 www.cdc.gov/hepatitis
National HIV Telephone Consultation Service	1-800-933-3413
HIVdent	http://www.hivdent.org

This pocket guide is based on U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV (2005) and Recommendations for Postexposure Prophylaxis and the U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis (2001). Available at: www.aidsinfo.nih.gov

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