



Regulatory Affairs—Summary: Management of Occupational Exposures to HBV, HCV, and HIV

Co-Editor's Note

The *Morbidity and Mortality Weekly Report* recently published (<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5011a1.html>; June 29, 2001) an update on the management of occupational exposures to HBV, HCV, and HIV. Due to the length of the report, we are republishing only a summary of the document, as well as its three appendices. The latter documents provide the specific procedures for the management of exposure to these bloodborne pathogens.

Ira F. Salkin

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

Summary

This report updates and consolidates all previous U.S. Public Health Service recommendations for the management of health care personnel (HCP) who have occupational exposure to blood and other body fluids that might contain hepatitis B virus (HBV), hepatitis C virus (HCV), or human immunodeficiency virus (HIV).

Recommendations for HBV postexposure management include initiation of the hepatitis B vaccine series to any susceptible, unvaccinated person who sustains an occupational blood or body fluid exposure. Postexposure prophylaxis (PEP) with hepatitis B immune globulin (HBIG) and/or hepatitis B vaccine series should be considered for occupational exposures after

evaluation of the hepatitis B surface antigen status of the source and the vaccination and vaccine-response status of the exposed person. Guidance is provided to clinicians and exposed HCP for selecting the appropriate HBV PEP.

Immune globulin and antiviral agents (e.g., interferon with or without ribavirin) are not recommended for PEP of hepatitis C. For HCV postexposure management, the HCV status of the source and the exposed person should be determined, and for HCP exposed to an HCV positive source, follow-up HCV testing should be performed to determine if infection develops.

Recommendations for HIV PEP include a basic 4-week regimen of two drugs (zidovudine [ZDV] and lamivudine [3TC]; 3TC and stavudine [d4T]; or didanosine [ddI] and d4T) for most HIV exposures and an expanded regimen that includes the addition of a third drug for HIV exposures that pose an increased risk for transmission. When the source person's virus is known or suspected to be resistant to one or more of the drugs considered for the PEP regimen, the selection of drugs to which the source person's virus is unlikely to be resistant is recommended.

In addition, this report outlines several special circumstances (e.g., delayed exposure report, unknown source person, pregnancy in the exposed person, resistance of the source virus to antiretroviral agents, or toxicity of the PEP regimen) when consultation with local experts and/or the National Clinicians Postexposure Prophylaxis Hotline ([PEPline] 1-888-448-4911) is advised.

Occupational exposures should be considered urgent medical concerns to ensure timely postexposure management and administration of HBIG, hepatitis B vaccine, and/or HIV PEP.

APPENDIX A

Practice Recommendations for Healthcare Facilities Implementing the U.S. Public Health Service Guidelines for Management of Occupational Exposures to Bloodborne Pathogens

June 29, 2001 / 50(RR11);43-4

Practice Recommendation	Implementation Checklist
Establish a bloodborne pathogen policy.	All institutions where health care personnel (HCP) might experience exposures should have a written policy for management of exposures. The policy should be based on the U.S. Public Health Service (PHS) guidelines. The policy should be reviewed periodically to ensure that it is consistent with PHS recommendations.
Implement management policies.	Health care facilities (HCF) should provide appropriate training to all personnel on the prevention of, and response to, occupational exposures. HCF should establish hepatitis B vaccination programs. HCF should establish exposure-reporting systems. HCF should have personnel who can manage an exposure readily available at all hours of the day. HCF should have ready access to postexposure prophylaxis (PEP) for use by exposed personnel as necessary.
Establish laboratory capacity for bloodborne pathogen testing.	HCF should provide prompt processing of exposed person and source person specimens to guide management of occupational exposures.
Select and use appropriate PEP regimens.	HCF should develop a policy for the selection and use of PEP antiretroviral regimens for HIV exposures within their institution. Hepatitis B vaccine and HBIG should be available for timely administration. HCF should have access to resources with expertise in the selection and use of PEP.
Provide access to counseling for exposed HCP.	HCF should provide counseling for HCP who might need help dealing with the emotional effect of an exposure. HCF should provide medication adherence counseling to assist HCP in completing HIV PEP as necessary.

Monitor for adverse effects of PEP.

HCP taking antiretroviral PEP should be monitored periodically for adverse effects of PEP through baseline testing (every 2 weeks) and clinical evaluation.

Monitor for seroconversion.

HCF should develop a system to encourage exposed HCP to return for follow-up testing.

Exposed HCP should be tested for HCV and HIV.

Monitor exposure management programs.

HCF should develop a system to monitor reporting and management of occupational exposures to ensure timely and appropriate response.

Evaluate 1) exposure reports for completeness and accuracy, 2) access to care (i.e., the time of exposure to the time of evaluation), and 3) laboratory result reporting time.

Review exposures to ensure that HCP exposed to sources not infected with bloodborne pathogens do not receive PEP or that PEP is stopped.

Monitor 1) completion rates of HBV vaccination and HIV PEP and 2) completion of exposure follow-up.

APPENDIX B

Management of Occupational Blood Exposures June 29, 2001 / 50(RR11);45-6

Provide immediate care to the exposure site.

- Wash wounds and skin with soap and water.
- Flush mucous membranes with water.

Determine risk associated with exposure by

- Type of fluid (e.g., blood, visible bloody fluid, other potentially infectious fluid or tissue, and concentrated virus) and
- Type of exposure (i.e., percutaneous injury, mucous membrane or nonintact skin exposure, and bites resulting in blood exposure).

Evaluate exposure source.

- Assess the risk of infection using available information.
- Test known sources for HBsAg, anti-HCV, and HIV antibody (consider using rapid testing).
- For unknown sources, assess risk of exposure to HBV, HCV, or HIV infection.
- Do not test discarded needles or syringes for virus contamination.

Evaluate the exposed person.

- Assess immune status for HBV infection (i.e., by history of hepatitis B vaccination and vaccine response).

Give PEP for exposures posing risk of infection transmission.

- HBV: See Table 3.

- HCV: PEP not recommended.
- HIV: See Table 4 and Table 5.
 - Initiate PEP as soon as possible, preferably within hours of exposure.
 - Offer pregnancy testing to all women of childbearing age not known to be pregnant.
 - Seek expert consultation if viral resistance is suspected.
 - Administer PEP for 4 weeks if tolerated.

Perform follow-up testing and provide counseling.

- Advise exposed persons to seek medical evaluation for any acute illness occurring during follow-up.

HBV exposures

- Perform follow-up anti-HBs testing in persons who receive hepatitis B vaccine.
 - Test for anti-HBs 1 to 2 months after last dose of vaccine.
 - Anti-HBs response to vaccine cannot be ascertained if HBIG was received in the previous 3 to 4 months.

HCV exposures

- Perform baseline and follow-up testing for anti-HCV and alanine amino-transferase (ALT) 4 to 6 months after exposures.
- Perform HCV RNA at 4 to 6 weeks if earlier diagnosis of HCV infection is desired.
- Confirm repeatedly reactive anti-HCV enzyme immunoassays (EIAs) with supplemental tests.

HIV exposures

- Perform HIV-antibody testing for at least 6 months post-exposure (e.g., at baseline, 6 weeks, 3 months, and 6 months).
- Perform HIV antibody testing if illness compatible with an acute retroviral syndrome occurs.
- Advise exposed persons to use precautions to prevent secondary transmission during the follow-up period.
- Evaluate exposed persons taking PEP within 72 hours after exposure and monitor for drug toxicity for at least 2 weeks.

APPENDIX C

Basic and Expanded HIV Postexposure Prophylaxis Regimens
June 29, 2001 / 50(RR11);47-52

BASIC REGIMEN

- Zidovudine (RETROVIR™; ZDV; AZT) + Lamivudine (EPIVIR™; 3TC); available as COMBIVIR™
 - ZDV: 600 mg per day, in two or three divided doses, and
 - 3TC: 150 mg twice daily

Advantages

 - ZDV is associated with decreased risk of HIV transmission in the CDC case-control study of occupational HIV infection.
 - ZDV has been used more than the other drugs for PEP in HCP.
 - Serious toxicity is rare when used for PEP.
 - Side effects are predictable and manageable with antimotility and antiemetic agents.
 - Probably a safe regimen for pregnant HCP.
 - Can be given as a single tablet (COMBIVIR™) twice daily.

Disadvantages

 - Side effects are common and might result in low adherence.
 - Source patient virus might have resistance to this regimen.
 - Potential for delayed toxicity (oncogenic/teratogenic) is unknown.

ALTERNATE BASIC REGIMENS

- **Lamivudine (3TC) + Stavudine (ZERIT™; d4T)**
 - 3TC: 150 mg twice daily, and
 - d4T: 40 mg (if body weight is <60 kg, 30 mg twice daily) twice daily

Advantages

 - Well tolerated in patients with HIV infection, resulting in good adherence
 - Serious toxicity appears to be rare.
 - Twice daily dosing might improve adherence.

Disadvantages

 - Source patient virus might be resistant to this regimen.
 - Potential for delayed toxicity (oncogenic/teratogenic) is unknown.
- **Didanosine (VIDEX™, chewable/dispersable buffered tablet; VIDEX™ EC, delayed-release capsule; ddi) + Stavudine (d4T)**
 - ddi: 400 mg (if body weight is <60 kg, 125 mg twice daily) daily, on an empty stomach
 - d4T: 40 mg (if body weight is <60 kg, 30 mg twice daily) twice daily

Advantages

 - Likely to be effective against HIV strains from source patients who are taking ZDV and 3TC

Disadvantages

 - ddi is difficult to administer and unpalatable.
 - Chewable/dispersable buffered tablet formulation of ddi interferes with absorption of some drugs (e.g., quinolone antibiotics, and indinavir).
 - Serious toxicity (e.g., neuropathy, pancreatitis, or hepatitis) can occur. Fatal and nonfatal pancreatitis has occurred in HIV-positive, treatment-naive patients. Patients taking ddi and d4T should be carefully assessed and closely monitored for pancreatitis, lactic acidosis, and hepatitis.
 - Side effects are common; anticipate diarrhea and low adherence.
 - Potential for delayed toxicity (oncogenic/teratogenic) is unknown.

EXPANDED REGIMEN

Basic regimen plus one of the following:

- **Indinavir (CRIXIVAN™; IDV)**
 - 800 mg every 8 hours, on an empty stomach

Advantage

 - Potent HIV inhibitor

Disadvantages

 - Serious toxicity (e.g., nephrolithiasis) can occur; must take 8 glasses of fluid per day.
 - Hyperbilirubinemia common; must avoid this drug during late pregnancy.
 - Requires acid for absorption and cannot be taken simultaneously with ddi in chewable/dispersable buffered tablet formulation. (Doses must be separated by at least 1 hour.)
 - Concomitant use of astemizole, terfenadine, dihydroergotamine, ergotamine, ergonovine, methylergonovine, rifampin, cisapride, St. John's Wort, lovastatin, simvastatin, pimozide, midazolam, or triazolam is not recommended.
 - Potential for delayed toxicity (oncogenic/teratogenic) is unknown.
- **Nelfinavir (VIRACEPT™; NFV)**
 - 750 mg three times daily, with meals or snack, or
 - 1,250 mg twice daily, with meals or snack

Advantages

 - Potent HIV inhibitor
 - Twice dosing per day might improve adherence.

Disadvantages

- Concomitant use of astemizole, terfenadine, dihydroergotamine, ergotamine, ergonovine, methylergonovine, rifampin, cisapride, St. John's Wort, lovastatin, simvastatin, pimoziide, midazolam, or triazolam is not recommended.
- Might accelerate the clearance of certain drugs, including oral contraceptives (requiring alternative or additional contraceptive measures for women taking these drugs).
- Potential for delayed toxicity (oncogenic/teratogenic) is unknown.

- **Efavirenz (SUSTIVA™; EFV)**

- 600 mg daily, at bedtime

Advantages

- Does not require phosphorylation before activation and might be active earlier than other antiretroviral agents (Note: this might be only a theoretical advantage of no clinical benefit.)
- One dose daily might improve adherence.

Disadvantages

- Drug is associated with rash (early onset) that can be severe and might rarely progress to Stevens-Johnson syndrome.
- Differentiating between early drug-associated rash and acute seroconversion can be difficult and cause extraordinary concern for the exposed person.
- Nervous system side effects (e.g., dizziness, somnolence, insomnia, and/or abnormal dreaming) are common. Severe psychiatric symptoms are possible. (Dosing before bedtime might minimize these side effects.)
- Should not be used during pregnancy because of concerns about teratogenicity.
- Concomitant use of astemizole, cisapride, midazolam, triazolam, ergot derivatives, or St. John's Wort is not recommended because inhibition of the metabolism of these drugs could create the potential for serious and/or life-threatening adverse events (e.g., cardiac arrhythmias, prolonged sedation, or respiratory depression).
- Potential for oncogenic toxicity is unknown.

- **Abacavir (ZIAGEN™; ABC); available as TRIZIVIR™, a combination of ZDV, 3TC, and ABC**

- 300 mg twice daily

Advantages

- Potent HIV inhibitor
- Well tolerated in patients with HIV infection

Disadvantages

- Severe hypersensitivity reactions can occur, usually within the first 6 weeks of treatment.
- Potential for delayed toxicity (oncogenic/teratogenic) is unknown.

ANTIRETROVIRAL AGENTS FOR USE AS PEP ONLY WITH EXPERT CONSULTATION

- **Ritonavir (NORVIR™; RTV)**

Disadvantages

- Difficult to take (requires dose escalation)
- Poor tolerability
- Many drug interactions

- **Saquinavir (FORTOVASE™, soft-gel formulation; SQV)**

Disadvantage

- Bioavailability is relatively poor, even with new formulation.

- **Amprenavir (AGENERASE™; AMP)**

Disadvantages

- Dosage consists of eight large pills taken twice daily
- Many drug interactions

- **Delavirdine (RESCRIPTOR™; DLV)**

Disadvantages

- Drug is associated with a rash (early onset) that can be severe and progress to Stevens-Johnson syndrome.
- Many drug interactions

- **Lopinavir/Ritonavir (KALETRA™)**

- 400/100 mg twice daily

Advantages

- Potent HIV inhibitor
- Well tolerated in patients with HIV infection

Disadvantages

- Concomitant use of flecainide, propafenone, astemizole, terfenadine, dihydroergotamine, ergotamine, ergonovine, methylergonovine, rifampin, cisapride, St. John' Wort, lovastatin, simvastatin, pimozide, midazolam, or triazolam is not recommended because inhibition of the metabolism of these drugs could create the potential for serious and/or life-threatening adverse events (e.g., cardiac arrhythmias, prolonged sedation, or respiratory depression).
- May accelerate the clearance of certain drugs, including oral contraceptives (requiring alternative or additional contraceptive measures for women taking these drugs).
- Potential for delayed toxicity (oncogenic/teratogenic) is unknown.

ANTIRETROVIRAL AGENTS GENERALLY NOT RECOMMENDED FOR USE AS PEP

- **Nevirapine (VIRAMUNE™; NVP)**

- 200 mg daily for 2 weeks, then 200 mg twice daily

Disadvantages

- Associated with severe hepatotoxicity (including at least one case of liver failure requiring liver transplantation in an exposed person taking PEP).
- Associated with rash (early onset) that can be severe and progress to Stevens-Johnson syndrome,
- Differentiating between early drug-associated rash and acute seroconversion can be difficult and cause extraordinary concern for the exposed person.
- Concomitant use of St. John's Wort is not recommended because this might result in suboptimal antiretroviral drug concentrations.