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New guidelines for occupational exposure to blood-borne viruses

ABSTRACT

The US Public Health Service recently updated its guidelines for managing health care workers exposed to blood or other body fluids that might contain blood-borne viruses. The update addresses, among other things, timely administration of hepatitis B immune globulin and hepatitis B vaccine, appropriate testing for hepatitis C exposure, and new information on prophylaxis after exposure to human immunodeficiency virus (HIV).

KEY POINTS

All health care workers who may come into contact with body fluids should be vaccinated against hepatitis B.

The risk of hepatitis B transmission is related primarily to the degree of contact with blood or body fluid and the hepatitis B e antigen (HBeAg) status of the source person.

The average risk of seroconversion after a percutaneous injury involving blood infected with hepatitis C virus is approximately 1.8%.

All health care workers taking HIV postexposure prophylaxis should be monitored for drug toxicity by testing at baseline and at 2 weeks after beginning the regimen.

Hospitals should set up programs to prevent exposure to blood-borne viruses and to manage cases of exposure should these occur.

YOU WERE IN A HURRY, weren't paying attention, and stuck yourself with the needle used to give a shot.

Or you were splashed in the face with amniotic fluid. Or you notice a hole in your examination glove after performing a procedure.

Are you at risk of acquiring hepatitis B, hepatitis C, or human immunodeficiency virus (HIV)? And what should you do?

The best way to avoid transmission of blood-borne viruses in the workplace is to avoid exposure to blood and body fluids. Hospitals and medical offices have safety programs, and we do our best to be careful. Nevertheless, exposures still occur, and when they do it may be time for postexposure testing, and in some cases, prophylaxis.

The US Public Health Service recently updated its guidelines for managing exposures to body fluids that may contain hepatitis B virus, hepatitis C virus, or human immunodeficiency virus (HIV).¹ The new guidelines include specific recommendations on the management of occupational exposure to hepatitis B virus and hepatitis C virus. In addition, several developments warranted some rethinking of postexposure prophylaxis against HIV:

- New antiretroviral agents have been approved for treating HIV infection
- New data exist about the safety of HIV postexposure prophylaxis
- Drug-resistant HIV strains have emerged
- Unnecessary use of HIV postexposure prophylaxis has been reported.^{2,3}

The updated guidelines provide a single, comprehensive document for clinicians who manage occupational exposures to blood-borne viruses. In this review, we summarize the

This paper discusses treatments that are experimental or are not approved by the US Food and Drug Administration for the use under discussion.

most important features of the updated guidelines. For a comprehensive understanding, clinicians should consult the document itself, available online at www.cdc.gov/mmwr/pre-view/mmwrhtml/rr5011a1.htm.

■ DEFINITION OF EXPOSURE

An exposure that may place health care personnel at risk for hepatitis B, hepatitis C, or HIV infections is defined as:

- A percutaneous injury, eg, a needle-stick or cut with a sharp object (or “sharp”) that may be contaminated with blood or other body fluid; or
- Contact of a mucous membrane or non-intact skin with blood, tissue, or other body fluids that are potentially infectious, eg, semen, vaginal secretions, and cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids.^{4,5} (Feces, nasal secretions, saliva, sputum, sweat, tears, urine, and vomitus are not considered to carry hepatitis B, hepatitis C, or HIV unless they contain visible blood.)

In the case of human bites, the clinical evaluation must consider possible exposure of both the person bitten and the person who inflicted the bite.

■ THE RISKS OF OCCUPATIONAL TRANSMISSION

Common routes of transmission of hepatitis B virus

The risk of hepatitis B transmission is related primarily to the degree of contact with blood or body fluid and the hepatitis B e antigen (HBeAg) status of the source person.

In studies of health care personnel who sustained percutaneous injuries from needles contaminated with blood containing hepatitis B, the risk of developing serologic evidence of hepatitis B infection if the blood was positive for both hepatitis B surface antigen (HBsAg) and HBeAg was 37% to 62%. By comparison, if the blood was negative for HBsAg and HBeAg, the risk was 23% to 37%.⁶

Although percutaneous injury is one of the most efficient modes of hepatitis B transmission, these exposures account for only a minority of hepatitis B infections among

health care workers. This is probably because we have a higher number of mucocutaneous exposures that could introduce the virus into nonintact skin or mucosal surfaces, and the hepatitis B virus can survive in dried blood for at least 1 week.⁷

Programs and regulations aimed at vaccinating health care workers have been effective in reducing the incidence of this infection by 95% from 1983 to 1995.⁸

Common routes of transmission of hepatitis C virus

In contrast, percutaneous injury is the most common mode of occupational transmission of hepatitis C virus. The average risk of seroconversion after a percutaneous injury involving blood infected with hepatitis C virus is approximately 1.8%.^{9,10}

Unlike hepatitis B, hepatitis C virus is very rarely transmitted via exposure to mucous membrane or nonintact skin. Environmental contamination does not appear to be a major risk for transmission, except in the hemodialysis setting.¹¹

Common routes of transmission of HIV

Based on prospective studies of health care workers, the risk of HIV transmission after percutaneous exposure to HIV-infected blood is estimated at approximately 0.3%,¹² and after mucous membrane exposure, approximately 0.09%.¹³ There have been reports of HIV transmission after exposure to nonintact skin, but the average risk is estimated to be lower than for exposure to mucous membranes.¹⁴

In a retrospective case-control study of health care workers who had percutaneous exposures to HIV, the risk of infection was higher in those exposed to a larger quantity of blood (eg, if the injury was deep or involved a sharp visibly contaminated with blood, a needle used in a vein or artery, or a hollow-bore needle) and in those exposed to a source patient with a terminal illness, possibly reflecting a higher titer of HIV in blood or other viral characteristics (eg, syncytia-inducing strains).¹⁵ A lower viral load (< 1,500 RNA copies/mL) may indicate a lower titer exposure but does not eliminate the risk of transmission.

**Hepatitis B
can survive in
dry blood
for 1 week**



■ VACCINATION AGAINST HEPATITIS B INFECTION

The Public Health Service recommends that any person who performs tasks involving contact with blood, blood-contaminated body fluids, other body fluids, or sharps should be vaccinated against hepatitis B, and the response should be documented.^{16,17} In addition, unvaccinated, susceptible workers exposed to any blood or body fluid should receive the hepatitis B vaccine series.

■ MANAGING EXPOSURES

First, wounds and exposed skin should be washed with soap and water, and mucous membranes should be flushed with water. The exposure should be evaluated for the potential to transmit hepatitis B virus, hepatitis C virus, and HIV, based on the type of body substance involved and the route and severity of the exposure.

Evaluate the source of the exposure

The person whose blood or body fluid is the source of an occupational exposure should be evaluated as soon as possible for infection with these viruses.

Consult your laboratories about the most appropriate test to use to get this information quickly. A rapid HIV antibody test kit, approved by the US Food and Drug Administration, should be considered for use in this situation, particularly if enzyme immunoassay testing cannot be completed within 24 to 48 hours of the exposure.

Initial assessment of risk to the exposed worker

If the source person is not infected with any blood-borne pathogen, then baseline testing of the worker and follow-up for seroconversion are not necessary.

However, any exposed worker who has not had the hepatitis B vaccine and is susceptible should be vaccinated.

If the person who is the source of the exposure cannot be tested, available data (eg, medical diagnoses, symptoms, history of risk behaviors) should be used to assess the risk for

infection with hepatitis B, hepatitis C, or HIV.

Document the event. In the worker's confidential medical record, the clinician in charge of the case should document details of how the exposure occurred and of how it was managed, adhering to state and federal (eg, Occupational Safety and Health Administration) reporting requirements.

■ EXPOSURE TO HEPATITIS B VIRUS

After a percutaneous or permucosal exposure to HBsAg-positive blood or body fluids, appropriate prophylaxis should be given.

If hepatitis B immune globulin is warranted (TABLE 1), it should be given as soon as possible, since its effectiveness beyond 7 days after exposure is unknown.

If hepatitis B vaccination is indicated, it should be given in the deltoid muscle as soon as possible. It can be given at the same time as immune globulin, but at a different site.

If the worker is in the process of vaccination at the time of the exposure, the vaccination series should continue as scheduled, and hepatitis B immune globulin should be administered, if indicated.

■ EXPOSURE TO HEPATITIS C VIRUS

Immune globulin and antiviral agents are not recommended as prophylaxis in health care workers exposed to blood positive for hepatitis C virus. Nonetheless, the exposed worker should be followed up to determine if hepatitis C infection has been transmitted: the worker should be tested for anti-hepatitis C antibodies and for serum alanine aminotransferase level elevations at 4 to 6 months.

If earlier diagnosis of hepatitis C infection is desired, testing for hepatitis C viral RNA at 4 to 6 weeks can be considered. Any positive anti-HCV enzyme immunoassay should be confirmed with recombinant immunoblot assay (RIBA) or polymerase chain reaction (PCR) testing.¹⁸

An exposed worker who develops a positive response on any of these tests should be referred for medical management to a specialist knowledgeable in this area.

Percutaneous injury is the most common route of hepatitis C transmission in workers

TABLE 1

Recommended postexposure prophylaxis against hepatitis B virus

VACCINATION STATUS OF EXPOSED WORKER*	HEPATITIS B STATUS OF SOURCE		
	POSITIVE FOR HEPATITIS B SURFACE ANTIGEN	NEGATIVE FOR HEPATITIS B SURFACE ANTIGEN	UNKNOWN OR NOT AVAILABLE FOR TESTING
Unvaccinated	Give one dose of hepatitis B immune globulin, 0.06 mL/kg intramuscularly, and initiate hepatitis A B vaccine series	Initiate hepatitis B vaccine series	Initiate hepatitis B vaccine series
Previously vaccinated			
Known responder [†]	No treatment	No treatment	No treatment
Known nonresponder [‡]	Give one dose of hepatitis B immune globulin and initiate revaccination OR Give two doses of immune globulin [§]	No treatment	If source is known to be high-risk, treat as if source were positive for hepatitis B surface antigen
Antibody response unknown	Test exposed worker for antibody to hepatitis B surface antigen If response is adequate, [†] no treatment is necessary If response is inadequate [§] give one dose of immune globulin and vaccine booster	No treatment	Test exposed worker for antibody to hepatitis B surface antigen If response is adequate, [†] no treatment is necessary If response is inadequate, administer vaccine booster and recheck titer in 1 to 2 months

*People previously infected with hepatitis B virus are immune to reinfection and do not require postexposure prophylaxis

[†]Serum levels of antibody to hepatitis B surface antigen are 10 mIU/mL or higher

[‡]Serum levels of antibody to hepatitis B surface antigen are below 10 mIU/mL

[§]The option of giving one dose of hepatitis B immune globulin and restarting the vaccine series is preferred for nonresponders who have not completed a second three-dose vaccine series. For those who previously completed a second vaccine series but failed to respond, two doses of immune globulin are preferred

FROM THE CENTERS FOR DISEASE CONTROL AND PREVENTION. UPDATED US PUBLIC HEALTH SERVICE GUIDELINES FOR THE MANAGEMENT OF OCCUPATIONAL EXPOSURES TO HBV, HCV, AND HIV AND RECOMMENDATIONS FOR POSTEXPOSURE PROPHYLAXIS. MMWR 2001; 50 (NO. RR-11).

■ EXPOSURE TO HIV

Most occupational exposures to HIV do not result in HIV transmission, and since HIV post-exposure prophylaxis has a number of potential toxicities, one must weigh the risk that HIV was transmitted against the potential ill effects of postexposure prophylactic treatment. Whenever possible, the Public Health Service recommendations should be implemented in consultation with clinicians who have expertise in HIV antiretroviral therapy (TABLE 2, TABLE 3).

Timing of antiretroviral therapy

Animal studies demonstrate that antiretrovi-

ral therapy is less effective if started more than 24 to 36 hours after the exposure.^{19,20} If indicated, antiretroviral prophylaxis should be started as soon as possible, because its efficacy decreases with time.

The optimal duration of HIV prophylactic treatment is undefined, but because 4 weeks of zidovudine appeared protective in animal studies, the Public Health Service recommends a 28-day course, if tolerated.²¹

Reevaluate at 72 hours

All exposed workers who start the regimen should be reevaluated within 72 hours of the exposure event. If the source person's HIV sta-

**TABLE 2****Recommended HIV postexposure prophylaxis for percutaneous injuries**

TYPE OF EXPOSURE	HIV STATUS OF SOURCE				
	POSITIVE, CLASS 1*	POSITIVE, CLASS 2†	UNKNOWN‡	UNKNOWN SOURCE: EG, NEEDLE FROM A SHARPS DISPOSAL CONTAINER	NEGATIVE
Less severe (eg, solid needle, superficial injury)	Two-drug regimen	Three-drug regimen	Generally, none warranted Two-drug regimen can be given if source has HIV risk factors; if source is later found to be HIV-negative, stop treatment	Generally, none warranted, but a two-drug regimen can be given if the source person is likely to have been HIV-positive	None warranted
More severe (eg, large-bore hollow needle, deep puncture, visible blood on device, needle used in patient's artery or vein)	Three-drug regimen	Three-drug regimen	Generally, none warranted Two-drug regimen can be given if source has HIV risk factors; if source is later found to be HIV-negative, stop treatment	Generally, none warranted, but a two-drug regimen can be given if the source person is likely to have been HIV-positive	None warranted

*Class 1: asymptomatic HIV infection or known low viral load (< 1,500 RNA copies/mL); if drug resistance is a concern, obtain expert consultation, but do not delay starting postexposure prophylaxis

†Class 2: symptomatic HIV infection, acquired immunodeficiency syndrome, acute seroconversion, or known high viral load; if drug resistance is a concern, obtain expert consultation, but do not delay starting postexposure prophylaxis

‡For example, if source is deceased, and no samples are available for HIV testing

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tus was unknown at the time of exposure but is now known to be negative, then HIV prophylaxis can be stopped at this time.

Two-drug or three-drug regimen?

In most cases, HIV exposure warrants a two-drug regimen of two nucleoside analogues:

- Zidovudine and lamivudine
- Lamivudine and stavudine
- Stavudine and didanosine.

Exposures that pose an increased risk of HIV transmission may warrant a three-drug regimen, consisting of one of the above regimens plus indinavir, nelfinavir, efavirenz, or abacavir (TABLE 4).

Potential adverse effects of HIV postexposure prophylaxis

Once HIV postexposure prophylaxis is pre-

scribed, management has three main objectives:

- To monitor carefully for signs and symptoms that could herald serious toxicity or acute seroconversion
- To manage side effects
- To complete the 4-week regimen.

Registry data indicate that almost half of all exposed health care workers develop adverse symptoms while on HIV prophylaxis, and that approximately one third stop the treatment because of side effects.^{1,22} Not surprisingly, many who stop were taking a three-drug regimen, suggesting that clinicians should balance the exposure risk with the probability of completing the regimen.

Nucleoside reverse transcriptase inhibitors such as zidovudine, lamivudine, stavudine, and didanosine can cause nausea

TABLE 3

Recommended HIV postexposure prophylaxis for mucous membrane exposures and nonintact skin exposures*

TYPE OF EXPOSURE	HIV STATUS OF SOURCE		UNKNOWN [§]	UNKNOWN SOURCE: EG, NEEDLE FROM A SHARPS DISPOSAL CONTAINER	NEGATIVE
	POSITIVE, CLASS 1†	POSITIVE, CLASS 2‡			
Small volume (a few drops)	Two-drug regimen	Two-drug regimen	Generally, none warranted Two-drug regimen can be given if source has HIV risk factors; if source is later found to be HIV-negative, stop treatment	Generally, none warranted Two-drug regimen can be given if the source person is likely to have been HIV-positive	None warranted
Large volume (major blood splash)	Two-drug regimen	Three-drug regimen	Generally, none warranted Two-drug regimen can be given if source has HIV risk factors; if source is later found to be HIV-negative, stop treatment	Generally, none warranted Two-drug regimen can be given if the source person is likely to have been HIV-positive	None warranted

*For skin exposures, follow-up is indicated only if there is evidence of compromised skin integrity, such as dermatitis, abrasion, open wound

†Class 1: asymptomatic HIV infection or known low viral load (<1,500 RNA copies/mL); if drug resistance is a concern, obtain expert consultation, but do not delay starting postexposure prophylaxis

‡Class 2: symptomatic HIV infection, acquired immunodeficiency syndrome, acute seroconversion, or known high viral load; if drug resistance is a concern, obtain expert consultation, but do not delay starting postexposure prophylaxis

§For example, splash from inappropriately disposed blood

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and diarrhea, which often can be managed with antimotility agents or antiemetics or by modifying the dosing interval. Before modifying the dosing, however, the manufacturer's recommendations should be checked. Abacavir has been linked to hypersensitivity reactions, and its potential for delayed toxicity (oncogenic or teratogenic) is unknown.

Protease inhibitors such as indinavir and nelfinavir have been linked to hyperglycemia, new-onset diabetes mellitus, and dyslipidemia.^{23,24} Patients taking these drugs should be tested for hyperglycemia. Indinavir has been associated with nephrolithiasis, but this may be limited by drinking 1.5 L of fluid per day.²⁵

Nonnucleoside reverse transcriptase inhibitors (eg, efavirenz) have been associated with severe skin reactions, including Stevens-Johnson syndrome. Efavirenz is associated with central nervous system side effects such as dizziness, insomnia, and abnormal dreaming. Nevirapine, another drug in this category, is not recommended for occupational postexposure prophylaxis against HIV because of serious adverse events attributed to its use for this indication, including two reports of fulminant hepatitis.^{26,27}

Monitoring for adverse effects

All health care workers taking HIV postexposure prophylaxis should be monitored for drug toxicity by testing at baseline and at 2 weeks



after beginning the regimen. At a minimum, testing should include complete blood cell counts and renal and hepatic function tests. If indinavir is taken, one should also monitor for crystalluria, hematuria, hemolytic anemia, and hepatitis. Again, patients taking protease inhibitors should be tested for hyperglycemia. The exposed worker's medical history may suggest the need for other testing.

Managing toxicity: Consult and counsel

Once toxicity is suspected, clinicians should seek expert consultation to determine if additional studies are needed and whether an alteration of the regimen is warranted. Just as important, exposed workers who take HIV postexposure prophylaxis should be counseled about the common side effects of the drugs prescribed and the necessity of seeking medical evaluation at once if certain symptoms develop, such as rash, fever, back pain, abdominal pain, pain on urination, hematuria, or symptoms of hyperglycemia. They also should receive instruction about potential drug interactions and drugs to avoid while on HIV postexposure prophylaxis.

HIV antibody testing

Regardless of whether they take HIV prophylaxis or not, all health care workers with occupational exposure to HIV should have a baseline HIV antibody test by enzyme immunoassay and should receive counseling and follow-up. HIV antibody testing should be performed for at least 6 months after exposure (eg, at 6 weeks, 12 weeks, and 6 months).

Extended follow-up (eg, at 12 months) is recommended for those who become infected with hepatitis C virus after an occupational exposure to a source coinfecting with hepatitis C and HIV. It is unknown whether workers need extended follow-up if they are exposed to hepatitis C and HIV but do not develop hepatitis C seroconversion.

Managing emotional stress

HIV exposure can generate great emotional distress.^{28,29} To make matters worse, exposed workers are presented with a paradox: the probability of acquiring HIV is low even in "higher-risk" exposures, yet they are told to

TABLE 4

Examples of basic and expanded regimens for prophylaxis after exposure to HIV

BASIC TWO-DRUG REGIMENS

Zidovudine 600 mg/day in two or three divided doses, plus
Lamivudine 150 mg twice a day

Lamivudine 150 mg twice a day, plus
Stavudine 40 mg twice a day
(if weight is < 60 kg, use 30 mg twice a day)

Didanosine 400 mg daily
(if weight is < 60 kg, use 125 mg twice a day), plus
Stavudine 40 mg twice a day
(if weight is < 60 kg, use 30 mg twice a day)

EXPANDED (THREE-DRUG) REGIMENS

One of the basic two-drug regimens above, plus one of the following:

Indinavir 800 mg every 8 hours on an empty stomach

Nelfinavir 750 mg three times a day with meals or snacks
or 1,250 mg twice a day with meals or snacks

Efavirenz 600 mg daily at bedtime

Abacavir 300 mg twice a day

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adhere to a 4-week drug regimen and to modify their behavior (ie, abstain from intercourse or use condoms; refrain from donating blood, plasma, organs, or semen; and consider stopping breastfeeding) to avoid secondary transmission.³⁰ Therefore, it is important to have access to experts who are knowledgeable about occupational HIV transmission and who can deal with the many concerns an HIV exposure generates.

■ OTHER ISSUES IN OCCUPATIONAL EXPOSURE

Health care workers exposed to blood-borne viruses may continue their patient-care duties.

Clinicians managing occupational exposures to blood-borne pathogens have a number of resources to consult for assistance (TABLE 5) in addition to local experts.

TABLE 5

Resources for managing occupational exposure to blood-borne viruses

National Clinicians' Postexposure Prophylaxis Hotline (PEpline)

www.ucsf.edu/hivcntr/resources/pep/index.html

(888) 448-4911

Run by the clinical staff of the University of California San Francisco-San Francisco General Hospital, and supported by the US Health Resources and Services Administration, the Ryan White CARE Act, the AIDS Education and Training Centers, and the Centers for Disease Control and Prevention

Hepatitis Information Hotline

www.cdc.gov/hepatitis

(888) 443-7232

Reporting to Centers for Disease Control and Prevention

(800) 893-0485

To report occupationally acquired HIV infections and failure of postexposure prophylaxis

Antiretroviral Pregnancy Registry

www.apregistry.com

(800) 258-4263

(800) 800-1052 (fax)

US Food and Drug Administration

www.fda.gov/medwatch

(800) 332-1088

To report unusual or severe toxicity to antiretroviral agents

HIV/AIDS Treatment Information Service

www.aidsinfo.nih.gov/

Needlestick!

www.needlestick.mednet.ucla.edu/

An interactive website funded by the Centers for Disease Control and Prevention; guides the health care provider in acquiring relevant data and selecting appropriate laboratory tests and treatments; once the case is complete, the health care provider may print case-specific aftercare instructions to be given to the exposed worker and included in the medical record

Consult an HIV expert in cases of occupational exposure

Primary prevention is principal goal

Primary prevention of exposure to blood-borne pathogens is essential. Many percutaneous injuries may be prevented by using safer work practices, discarding used needles in the appropriate sharps disposal containers, and using

medical devices with features engineered to prevent sharps injury. In addition, health care facilities must promote and facilitate percutaneous injury reporting by workers, and data on percutaneous injuries should be analyzed periodically to identify areas for intervention. 

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