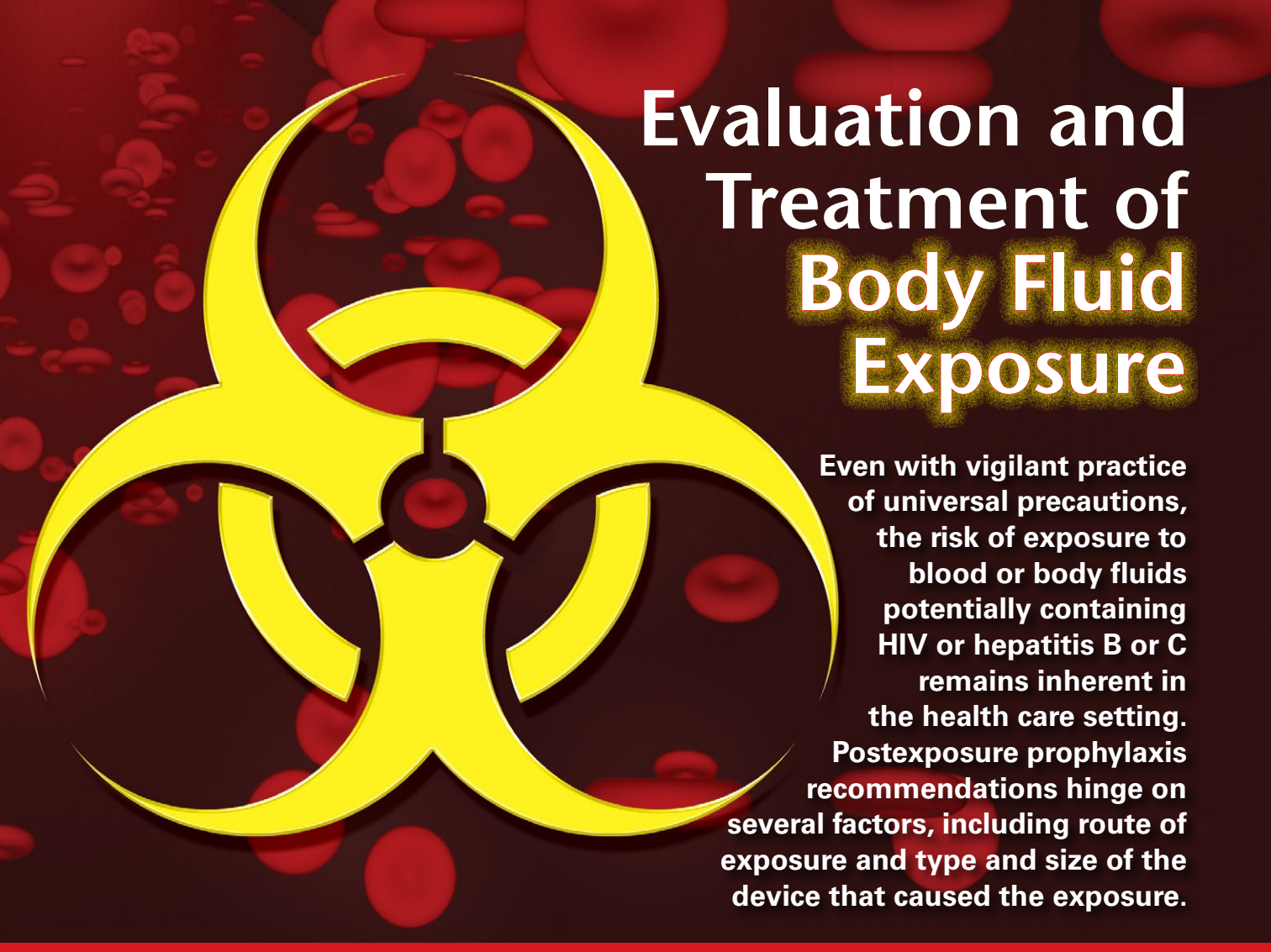

Evaluation and Treatment of Body Fluid Exposure

Even with vigilant practice of universal precautions, the risk of exposure to blood or body fluids potentially containing HIV or hepatitis B or C remains inherent in the health care setting. Postexposure prophylaxis recommendations hinge on several factors, including route of exposure and type and size of the device that caused the exposure.

Laura Richey, MD, Abby Tausend, MD, Adam Justice, DO, and Brian Laakaniemi, MD

THE SCENARIO

It's 2 AM and you are the staff physician on duty in the ED. A fourth-year surgery resident presents 20 minutes after sustaining a penetrating needle exposure in the operating room. The source patient is both HIV- and hepatitis C virus (HCV)–positive. The resident asks you what the risk of HIV and HCV seroconversion is and to what extent the risk is reduced by postexposure prophylaxis (PEP).

Unfortunately, exposure to blood or body fluids that may contain fluid-borne pathogens is an all-too-common occurrence in the health care profession today. There are numerous variables in this scenario, including whether the HIV, HCV, and hepatitis B virus (HBV) status of the source is known or can be known; for example, consider a percutaneous exposure from a needle found lying near a sharps container. The type of exposure—percutaneous, mucous membrane, nonintact skin, or intact skin—makes a difference in the PEP recommended. Other factors, such as the type of device, its size, and whether it has a hollow bore or is solid, change the risk, as does the type of body fluid involved. In this article, we summarize current information and describe the accepted standard of practice concerning body fluid–borne exposures to HBV, HCV, and HIV.

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HEPATITIS B VIRUS

The Risk

HBV is the most infectious of the three blood-borne viruses discussed in this article. It can survive and remain infectious on countertops for up to 7 days.[1] HBV

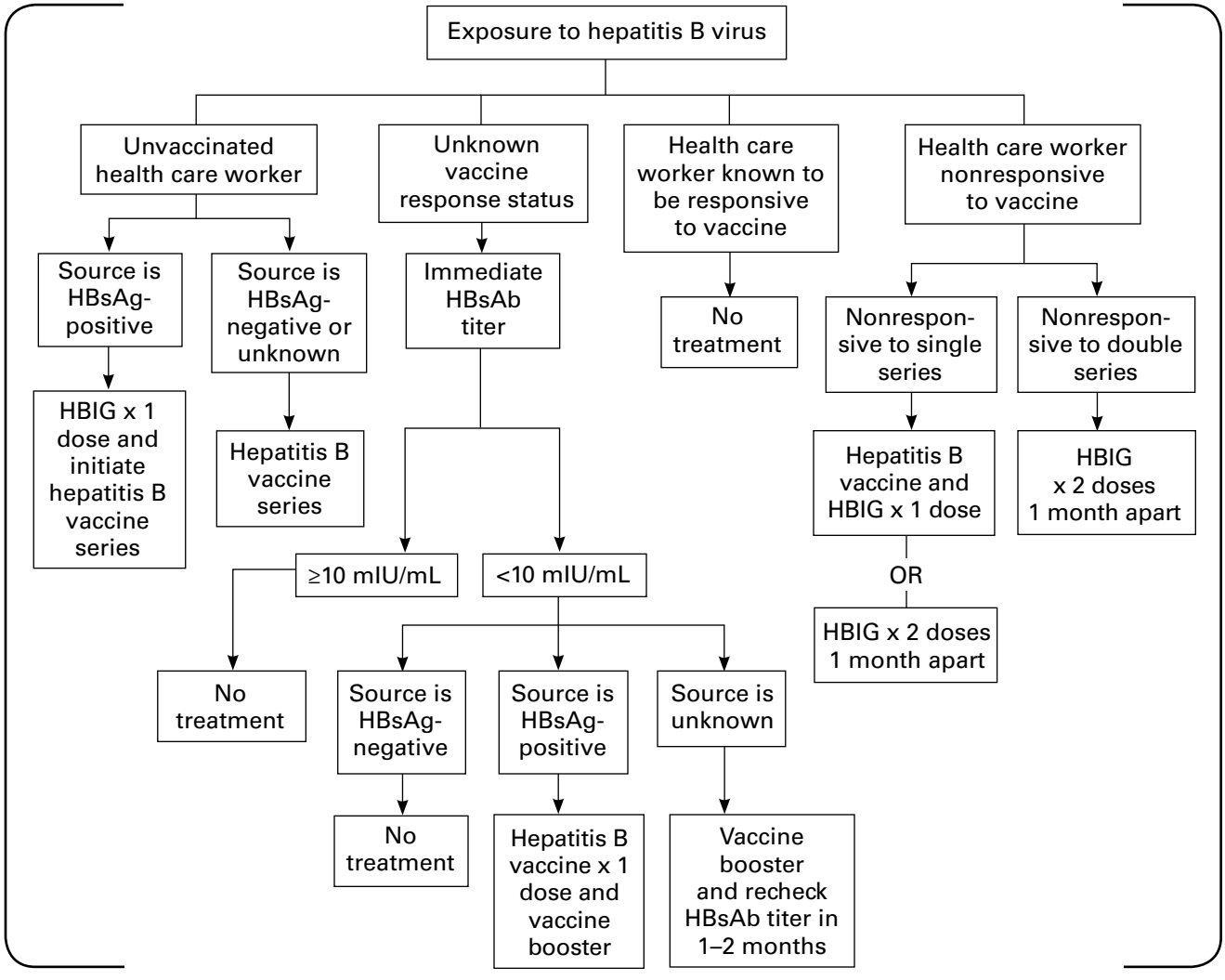
can be transmitted by percutaneous and mucosal exposures, as well as by human bites.[2,3] In unvaccinated individuals, the estimated transmission risk associated with a needlestick injury is between 6% and 30%, depending on the presence or absence of the HBV e antigen (HBeAg) in the serum of the source patient.[4] According to one model, an estimated 66,000 new cases of HBV infection worldwide may have been caused by percutaneous injuries in 2000.[5]

Evaluation and Treatment

Figure 1 demonstrates an algorithmic approach to risk assessment and treatment in a health care worker who has been exposed to HBV. Since 1991, the Occupational Safety and Health Administration (OSHA) has required that all health care workers in whom exposure to blood is reasonably anticipated be offered the hepatitis B vaccine.[6] The vaccine series has been shown to be safe and effective in preventing the transmission of HBV.[6] A 95% decline in the incidence of HBV infection among health care workers between 1983 and 1995 has been documented.[7] Unfortunately, one survey revealed that even with the OSHA guidelines in place, only 75% of health care workers have been vaccinated against hepatitis B.[8]

Within 1 to 2 months of completing the primary vaccine series, health care workers should be tested for HBV surface antibody (HBsAb). The CDC now

FIGURE 1. Risk Assessment and Treatment in Exposure to Hepatitis B Virus



HBsAg = hepatitis B surface antigen; HBIG = hepatitis B immune globulin; HBsAb = hepatitis B surface antibody.

believes that successful vaccination with the hepatitis B vaccine (as documented by an HBsAb titer ≥10 mIU/mL) confers lifetime protection against HBV infection.[9]

Health care workers who have an HBsAb titer below 10 mIU/mL should be tested for HBV surface antigen (HBsAg). If results are positive, these workers should be referred to a specialist for further evaluation. If it is determined that the workers do not have HBV, they should receive a second series of the hepatitis B vaccine and then have their HBsAb titer reassessed. If the HBsAb level remains below 10 mIU/mL, the workers should be considered nonresponsive to the vaccine and should be counseled to receive hepatitis B immune globulin (HBIG) in the event of any subsequent exposures to hepatitis B. The decision to offer PEP is based on several factors, including the route of exposure, HBsAg status of the source patient, and vaccination status of the exposed individual (ie, documented vaccine response vs vaccine nonresponse vs unvaccinated).

In all unvaccinated health care workers, any exposure should lead to the initiation of the hepatitis B vaccine series, regardless of the source's status. If the source is known to have HBsAg, then the exposed health care worker should receive a single dose of HBIG. In health care workers who have a known vaccine response, no further testing or treatment is needed. Those who have not responded to a single series of the vaccine should receive either the hepatitis B vaccine and a single dose of HBIG or simply two doses of HBIG 1 month apart. Those who do not respond to two series of hepatitis B vaccine should receive two doses of HBIG 1 month apart. HBIG should be administered as soon as possible after exposure, preferably within 24 hours.[6]

Exposed health care workers with an unknown vaccine response status should have their HBsAb titer measured immediately upon exposure. If the titer is greater than 10 mIU/mL, no further treatment is necessary. If the titer is less than 10 mIU/mL and the source is known to be HBsAg-positive, then one dose of HBIG and a vaccine booster should be given. If the titer is less than 10 mIU/mL and the source is unknown, then a vaccine booster should be given and the HBsAb titer of the health care worker should be rechecked in 1 to 2 months.[6] The above recommendations are derived from prospective research involving the perinatal transmission of HBV, where the risk of transmission of HBV to the infant was reduced 85% to 95% by the administration of the hepatitis B vaccine and HBIG.[10]

HEPATITIS C VIRUS

The Risk

HCV transmission from an occupational exposure is an uncommon event. Although HCV RNA can be found in blood, saliva, menstrual fluid, semen, urine, spinal fluid, and ascitic fluid, transmission from body fluids other than blood has not yet been documented.[11] The CDC reports an average 1.8% incidence of HCV seroconversion after a percutaneous exposure.[6] The rate of seroconversion varies from 0% to 10%[12] in different case report studies. Only a few case reports document HCV transmission from mucous membrane exposure.[11] There have been no documented cases of HCV transmission in health care professionals from exposure of intact or nonintact skin to HCV-contaminated blood.[6]

Evaluation and Treatment

There are no studies that support the use of PEP for HCV; therefore, prophylactic therapy cannot be recommended. There are two reasonable approaches for follow-up of the health care worker who has sustained a percutaneous exposure to HCV: watchful waiting and early aggressive treatment.[11] Figure 2 outlines both approaches.

In the first approach (watchful waiting), polymerase chain reaction testing for HCV RNA is performed every 2 weeks, and those health care workers who develop viremia are then monitored for spontaneous resolution of the viremia for an additional 2 to 4 months. If it does not resolve, only those with an elevated serum alanine aminotransferase (ALT) level are then treated with antiviral medication. The premise of this strategy is that 15% to 20% of acute HCV infections spontaneously resolve, and patients in whom the infection resolves would be spared the toxicities and harsh side effects of antiviral treatment.[12] Some authorities also believe that the antiviral medications may be more efficacious in the setting of an active host immune response, as manifested by symptoms and an elevated ALT level.[13]

The second approach (early aggressive treatment) is to monitor HCV RNA every 2 weeks and initiate aggressive therapy as soon as there is evidence of an acute HCV infection. A study that adopted this

strategy reported outcomes in 44 patients with acute hepatitis C and elevated ALT levels who were treated with interferon alfa-2b.[14] Forty-three of the study participants were found to be HCV RNA–negative and to have normal ALT levels 24 weeks after termination of treatment. Fourteen of these patients were infected by needlestick injuries. There is no consensus as to which strategy is most effective.

HUMAN IMMUNODEFICIENCY VIRUS

The Risk

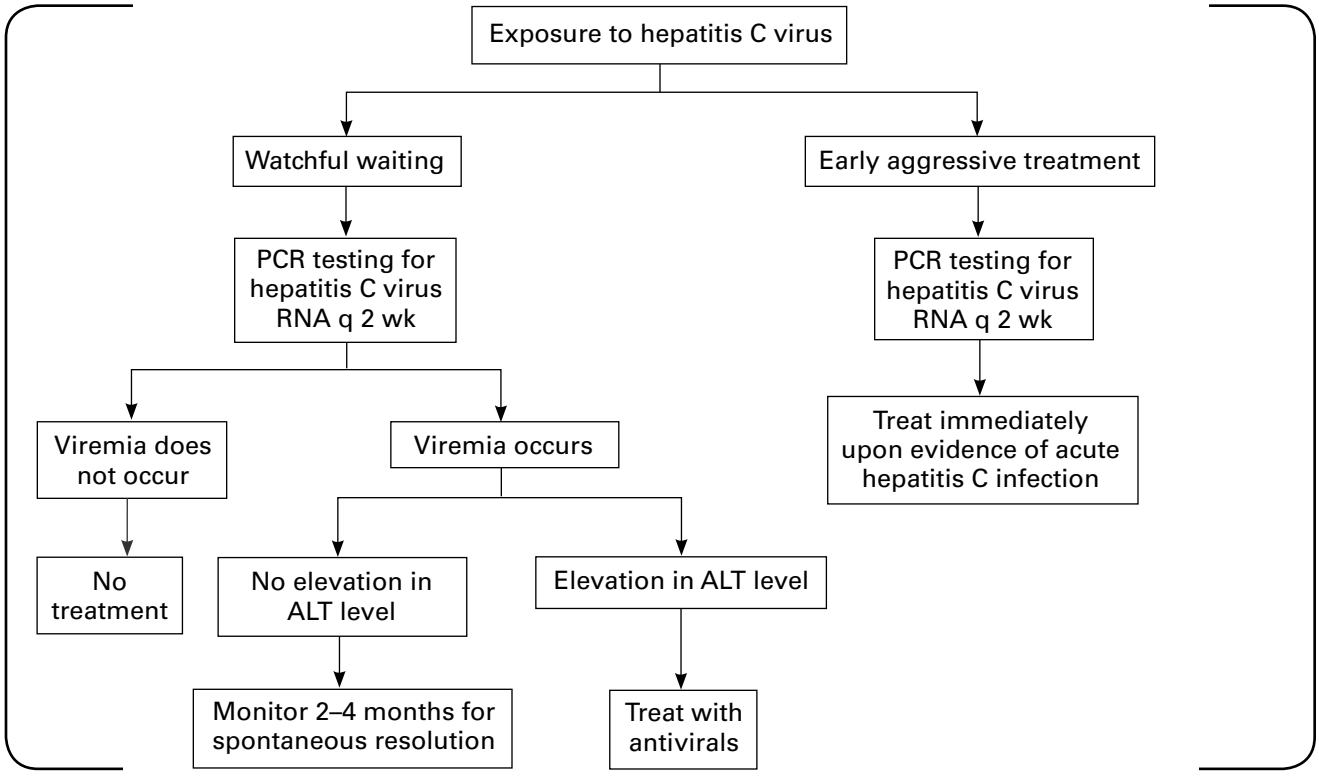
The three routes of exposure that convey risk for HIV transmission are percutaneous injury, exposure of mucous membranes, and exposure of nonintact skin, which includes abrasions and eczematous lesions. Intact skin is an effective barrier against HIV infection, and contact of intact skin with blood or other potentially contaminated fluids is not considered an exposure.[6]

The average risk estimate for HIV transmission by the percutaneous route is generally quoted as 0.3%.[6] Mucous membrane and nonintact skin exposure conversion rates are quoted as 0.09% and less than 0.09%, respectively.[6] Prospective studies in the 1980s by Henderson et al and Ippolito et al helped establish these estimates.[15,16]

The following characteristics are associated with an increased risk of seroconversion after percutaneous exposures: deep injury, visible blood on the device, procedures involving placement of a needle in the source patient's blood vessel, and a terminal HIV-related illness in the source patient.[17] The risk of seroconversion after mucous membrane or nonintact skin exposure is increased if the exposure involves large volumes of blood or if the source's viral load is high.

Body fluids that pose a risk of HIV transmission include amniotic, cerebrospinal, pericardial, peritoneal, pleural, and synovial fluids; vaginal secretions; semen; breast milk; saliva (in association with dental work); and exudates from burns or skin lesions. Exposure to unfixed human tissues and organs also conveys risk. Fluids that are not considered infectious unless they contain blood include feces, nasal secretions, saliva, sputum, sweat, tears, urine, and vomitus.[6]

FIGURE 2. Risk Assessment and Treatment in Exposure to Hepatitis C Virus[a]



PCR = polymerase chain reaction; RNA = ribonucleic acid; ALT = alanine aminotransferase.
[a]Either approach is considered reasonable.

Evaluation and Treatment

Needlesticks and cuts should be immediately washed with soap and water. Splashes to the nose, mouth, or skin should be flushed with water. Eye splashes should be irrigated with clean water, saline, or sterile irrigants. There is no evidence that antiseptics or squeezing the wound will reduce the transmission of HIV.[18]

A risk assessment should be rapidly performed (Figure 3), as PEP for an HIV exposure is most likely to be efficacious if it is commenced within 1 hour of the exposure. This risk assessment should consider the type or route of exposure, the type and amount of body fluid involved, the disease status of the source patient, and the susceptibility of the exposed individual.

If the HIV status of the source patient is unknown, a rapid HIV test may help in determining the need for PEP. One study found that use of a rapid HIV antibody test significantly reduced the amount of unnecessary PEP given to exposed health care workers, resulting in both cost savings and a reduction in repetitive thoughts of the exposure on the part of the workers.[19] Initiation of PEP should not be significantly delayed while the source patient's disease status is determined.

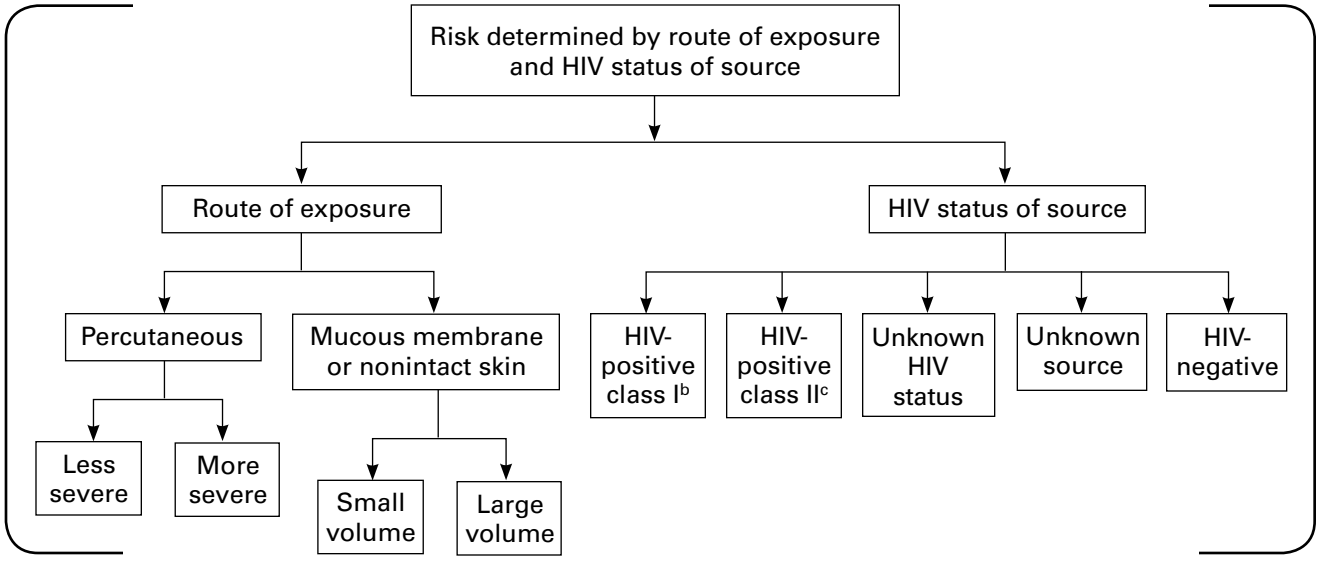
When the HIV status of the source cannot be determined, epidemiologic factors may help determine the risk for HIV transmission. A stick from a needle found near a sharps disposal bin in a ward with patients known to be HIV infected obviously carries a higher risk of HIV transmission than does a needlestick sustained in a nursing home with no known HIV-infected patients.

Animal models suggest that HIV can be detected in regional lymph nodes 48 to 72 hours following exposure, and that HIV becomes disseminated widely enough to be detectable in the blood after 5 days.[20] This delay in systemic spread provides a "window of opportunity" during which postexposure antiretroviral medication may be of benefit.[21]

A 1997 retrospective case-control study of health care workers with percutaneous occupational HIV exposures suggested that the use of zidovudine was associated with a significant decrease in the risk of HIV transmission.[17] The risk of HIV seroconversion in health care workers who received postexposure zidovudine prophylaxis was decreased by about 80%, compared to the risk in those who did not receive PEP. Prospective, randomized, controlled studies would be required to further delineate the effectiveness of PEP; however, such studies would be unethical.

In animal models, PEP has been shown to work best when given within hours of the initial exposure. These models also demonstrate that PEP confers

FIGURE 3. Risk Assessment in Exposure to HIV[a]



[a]See Tables 1 and 2 for more specific information regarding risk assessment and treatment recommendations.
[b]Asymptomatic HIV infection or known low viral load.
[c]HIV infection, AIDS, acute seroconversion, or known high viral load.

no benefit when started more than 24 to 36 hours after the exposure.[21,22] The exact time frame after which PEP has no benefit in humans is unknown. Therefore, it is recommended that PEP be initiated within 24 hours of the exposure, but it is most likely to be effective if started within hours of the exposure. However, according to the CDC, starting PEP after longer postexposure periods (eg, 1 week) can be considered for those exposures that represent an increased risk of transmission.[6]

Currently, combination therapy is recommended for PEP, despite a lack of direct evidence to support its use. This recommendation is based on the success of combination therapy, compared to monotherapy, in both the treatment of individuals with HIV infection and the prevention of perinatal transmission of the virus.[23] There have been at least six reported cases of health care workers contracting HIV despite having received combination therapy for PEP.[24]

Choosing the proper medications for HIV PEP can be a daunting task for clinicians who do not specialize in infectious disease. Selection of the most appropriate drugs for a PEP regimen requires consideration of many factors. These include the severity of the exposure, the disease status of the source patient, and the toxicities or side effects of the drugs under consideration. For this reason, we recommend using a protocol established by your hospital's infection control or pharmacy and therapeutics committee. Consultation with an infectious disease or HIV specialist should be obtained whenever possible. Other resources are listed on page 14.

The core tenet of PEP selection is risk stratification. Lower-risk exposures are treated with a "ba-

TABLE 1. Recommended HIV Postexposure Prophylaxis (PEP) for Percutaneous Injuries

	Infection Status of Source				
Exposure Type	**HIV-Positive (Class 1)[a]**	**HIV-Positive (Class 2)[b]**	**Unknown HIV Status[c]**	**Unknown Source[d]**	**HIV-Negative**
Less severe (eg, solid needle, superficial injury)	Basic 2-drug PEP	Expanded ≥3-drug PEP	Generally, no PEP, but consider basic 2-drug PEP if source has HIV risk factors[e,f]	Generally, no PEP, but consider basic 2-drug PEP if exposure to HIV-infected persons is likely[e,f]	No PEP
More severe (eg, large-bore hollow needle, deep puncture, visible blood on device, needle used in patient's blood vessel)	Expanded 3-drug PEP	Expanded ≥3-drug PEP	Generally, no PEP, but consider basic 2-drug PEP if source has HIV risk factors[e,f]	Generally, no PEP, but consider basic 2-drug PEP if exposure to HIV-infected persons is likely[e,f]	No PEP

[a]Asymptomatic HIV infection or known low viral load.
[b]Symptomatic HIV infection, AIDS, acute seroconversion, or known high viral load. If drug resistance is a concern, obtain expert consultation, but do not delay PEP pending consultation.
[c]For example, source is deceased and testing is not possible.
[d]For example, needle from a sharps container.
[e]Recommendation to consider PEP indicates PEP is optional; discussion of risks/benefits should take place between the exposed person and the treating clinician.
[f]If PEP is given, discontinue if the source is later determined to be HIV-negative.

Adapted from Centers for Disease Control and Prevention.[24]

sic" two-drug regimen, while higher-risk exposures are treated with an "expanded" protocol involving three and, occasionally, four drugs. There are several branches in the risk assessment tree, the first of which divides the exposure mechanism into two limbs: percutaneous exposures and mucous membrane or nonintact skin exposures. Each of these limbs is further divided into two categories: less severe versus more severe for percutaneous exposures, and small volume versus large volume for mucous membrane and nonintact skin exposures. Once the exposure type and severity have been determined, the next branch point in the risk assessment is based on the HIV status of the source, which is classified into one of five categories: HIV-positive class 1, HIV-positive class 2, source of unknown HIV status, unknown source, and source negative for HIV. There are PEP recommendations for each of these five categories (Tables 1 [page 11] and 2).[24]

There are five primary classes of antiretroviral medications: reverse transcriptase inhibitors, protease inhibitors, fusion inhibitors, integrase inhibitors, and entry inhibitors (Tables 3 and 4). These antiretrovirals are classified by the stage of the HIV life cycle they affect. The reverse transcriptase inhibitors may be further divided into three subclasses: nucleoside reverse transcriptase inhibitors (NRTIs), nonnucleoside reverse transcriptase inhibitors (NNRTIs), and nucleotide analog reverse transcriptase inhibitors (NtRTIs).

Basic PEP regimens may combine two NRTIs or an NRTI plus an NtRTI. The expanded drug protocol generally adds a protease inhibitor to one of the basic regimens; however, protease inhibitors tend to increase side effects. The use of fusion inhibitors is not standard practice at this time, but may be suggested in consultation with an infectious disease specialist. Both basic and expanded protocols should be continued for 28 days. Table 4 lists some of the more common drugs in each of the different classes.

Postexposure Follow-up

The exposed health care worker should have a base-

TABLE 2. Recommended HIV Postexposure Prophylaxis (PEP) for Mucous Membrane Exposures and Nonintact Skin Exposures[a]

	Infection Status of Source				
Exposure Type	**HIV-Positive (Class 1)[b]**	**HIV-Positive (Class 2)[c]**	**Unknown HIV Status[d]**	**Unknown Source[e]**	**HIV-Negative**
Small volume (eg, a few drops)	Consider basic 2-drug PEP[f]	Basic 2-drug PEP	Generally, no PEP[g]	Generally, no PEP	No PEP
Large volume (eg, a major blood splash)	Basic 2-drug PEP	Expanded ≥3-drug PEP	Generally, no PEP, but consider basic 2-drug PEP if source has HIV risk factors[f,g]	Generally, no PEP, but consider basic 2-drug PEP if exposure to HIV-infected persons is likely[f]	No PEP

[a]Follow-up for skin exposure is warranted only in cases of compromised skin integrity (eg, open wound, dermatitis).
[b]Asymptomatic HIV infection or known low viral load.
[c]Symptomatic HIV infection, AIDS, acute seroconversion, or known high viral load. If drug resistance is a concern, obtain expert consultation, but do not delay PEP pending consultation.
[d]For example, source is deceased and testing is not possible.
[e]For example, splash from inappropriately disposed blood.
[f]Recommendation to consider PEP indicates PEP is optional; discussion of risks/benefits should take place between the exposed person and the treating clinician.
[g]If PEP is given, discontinue if the source is later determined to be HIV-negative.

Adapted from Centers for Disease Control and Prevention.[24]

line test for HIV performed at the time of exposure and periodically thereafter for 6 months. The CDC recommends HIV testing at 6 weeks, 12 weeks, and 6 months, regardless of whether PEP was given. In addition, HIV testing should be repeated at 12 months in workers whose exposure to a patient coinfected with HCV resulted in HCV seroconversion. HIV testing should be performed at any time in an HIV-exposed worker who develops an acute viral syndrome, because fever, rash, and lymphadenopathy may be evidence of a primary HIV infection.[24] All exposed workers should be evaluated 1 week after exposure to review all test results and to be screened for medication compliance and adverse effects caused by PEP. At 2 weeks, laboratory testing may be required to monitor for toxicity, with the specific testing requirements determined by the particular drug regimen being used. Further testing for PEP toxicity will

TABLE 3. Classification of Antiretroviral Drugs

Reverse transcriptase inhibitors

- Nucleoside reverse transcriptase inhibitors (NRTIs)
- Nonnucleoside reverse transcriptase inhibitors (NNRTIs)
- Nucleotide analog reverse transcriptase inhibitors (NtRTIs)

Protease inhibitors

Fusion inhibitors

Integrase inhibitors

Entry inhibitors

TABLE 4. Common Antiretrovirals

Generic Name (Brand Name)	
Nucleoside/Nucleotide Reverse Transcriptase Inhibitors	***Protease Inhibitors***
Lamivudine (Epivir, Heptovir)	Tipranavir (Aptivus)
Stavudine (Zerit)	Indinavir (Crixivan)
Didanosine (Videx)	Saquinavir (Invirase, Fortovase)
Emtricitabine (Emtriva)	Lopinavir + ritonavir (Kaletra, Aluvia)
Abacavir (Ziagen)	Fosamprenavir (Lexiva, Telzir)
Zidovudine (Retrovir)	Ritonavir (Norvir)
Tenofovir (Viread)	Darunavir (Prezista)
	Atazanavir (Reyataz)
Nonnucleoside Reverse Transcriptase Inhibitors	Nelfinavir (Viracept)
Efavirenz (Sustiva, Stocrin)	***Fusion Inhibitor***
Etravirine (Intelence)	Enfuvirtide (Fuzeon)
Nevirapine (Viramune)	***Integrase Inhibitor***
Delavirdine (Rescriptor)	Raltegravir (Isentress)
	Entry Inhibitor
	Maraviroc (Selzentry)

Combination Antiretrovirals	
Lamivudine + zidovudine (Combivir)	Tenofovir + efavirenz + emtricitabine (Atripla)
Lamivudine + abacavir (Epzicom, Kivexa)	Tenofovir + emtricitabine (Truvada)
Lamivudine + zidovudine + abacavir (Trizivir)	

Resources

- PEPline
  http://www.nccc.ucsf.edu/about_nccc/pepline or
  1-888-448-4911
- CDC National Hotline
  1-800-CDC-INFO (232-4636)
- CDC Division of Healthcare Quality Promotion
  http://www.cdc.gov/ncidod/dhqp/index.html or
  1-800-893-0485
- CDC National Institute for Occupational Safety and Health (NIOSH)
  www.cdc.gov/niosh

be dictated by these initial studies.

Finally, health care workers should be counseled about expected adverse events associated with PEP and the strategies in place for managing them. Exposed workers should also be reminded that PEP is not 100% effective in preventing HIV seroconversion and that they should report any febrile illness to their employee health department for further evaluation. All postexposure patients should be counseled about the possibility of secondary transmission of HIV, especially during the first 3 months following exposure. Secondary transmission can occur through blood or tissue donation, pregnancy, breastfeeding, and sexual contact.

The best defense against exposure to blood- or body fluid–borne pathogens is to always practice universal precautions. Unfortunately, strict adherence to universal precautions will not prevent all needlesticks, and exposures will continue to occur in the health care setting. Health care workers need to be well informed not only of the risks of transmission of blood-borne pathogens but also of the available treatment options and appropriate follow-up required after an exposure. □

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