Occupational Postexposure Prophylaxis for HIV: The PEPline Perspective

Transmission of HIV through occupational exposure in healthcare personnel is rare. Risk of transmission from an HIV-infected source person is estimated at 0.3% for percutaneous exposures and 0.09% for mucous membrane or nonintact skin exposures, with risk modulated by exposure and source-patient characteristics. Counseling on risk assessment, postexposure prophylaxis (PEP), and baseline and follow-up testing after exposure is provided through PEPline, the National Clinicians’ Post-Exposure Prophylaxis Hotline. PEPline receives approximately 900 calls per month, most from treating clinicians. HIV PEP consists of a 28-day course of a basic or an expanded regimen, depending on the severity or volume of exposure and HIV infection characteristics of the source person. An update to the 2005 US Department of Health PEP drug recommendations is expected in 2011. This article summarizes a lecture given by Ronald H. Goldschmidt, MD, at the 13th Annual Ryan White HIV/AIDS Program Clinical Conference held in August 2010 in Washington, DC.

Healthcare personnel (HCP) have been reported to encounter more than 500,000 bloodborne pathogen exposures annually, about 400,000 of which occur in the hospital (Pan-lilo et al, Infect Control Hosp Epidemiol, 2004). Given the improvement in safety devices and protocols, however, this figure very likely overestimates the current burden of exposure among HCP. Female HCP account for the majority of exposures, consistent with the greater proportion of women in the healthcare field.

Actual HIV transmission to HCP as a result of occupational exposure is rare. Nevertheless, exposure can have an enormous emotional impact. As a survey by the National Clinicians’ Post-Exposure Prophylaxis Hotline (PEPline) revealed, sustaining an exposure was highly stressful and many HCP felt personally responsible for their exposure, most often because of technique problems or not thoroughly following established procedures (Cocohoba JM, Myers JJ, Goldschmidt RH, unpublished data, 2006). Colleagues, treating clinicians, and consultants, including PEPline consultants, were reported as having provided exposed HCP invaluable support for decision making regarding postexposure prophylaxis (PEP). Most HCP who initiated PEP reported experiencing adverse effects with variable severity, and adverse effects played a major role in compounding stress for many HCP. This article summarizes the PEPline approach to risk assessment and counseling for HCP with potential exposures to HIV.

The PEPline Service

Official guidelines for managing exposures and prescribing PEP for occupational exposure to HIV have been published by the US Public Health Service (USPHS) (Centers for Disease Control and Prevention [CDC], MMWR, 2005; CDC, MMWR, 2001); the 2005 report provides updated recommendations for drugs used for PEP and is expected to be further updated online in 2011. The PEPline service is available free of charge at 888-448-4911 (www.nccc.ucsf.edu). The goals for postexposure management are to prevent transmission, avoid unnecessary PEP and PEP toxicity, and provide counseling and follow-up for exposed HCP. PEPline faculty members are HIV-expert physicians and clinical pharmacists. The PEPline is available 24 hours per day; during nonstaffed hours, an answering service pages on-call faculty clinicians, with an average response time of 3 minutes.

The PEPline receives approximately 900 calls per month, of which approximately 760 concern occupational exposures. In 72% of these calls, the caller is a HCP’s treating clinician; the caller is the exposed HCP in 14% of cases and “other” in 14%. Physicians account for 42% of calls, with registered nurses (RNs), nurse practitioners (NPs), physician assistants (PAs), certified nurse midwives (CNMs), and licensed vocational nurses (LVNs) jointly accounting for 45%. The professions of the remainder are categorized as “other” or “unknown.” Most (64%) of the exposed individuals are RNs, NPs, PAs, CNMs, or LVNs; physicians are 16% of exposed HCP, and “other” or “unknown” are 20%. The setting of exposure is a hospital in 26% of cases; an emergency department in 5%; an operating room, labor-and-delivery setting, or other surgical setting in 10%; an outpatient or other medical setting in 20%; and a dental, laboratory, ambulance, or other setting in 38%. The majority (64%) of exposures are percutaneous; other exposures include mucous membrane exposures in 20% and cutaneous exposures in 16%. The exposure substance is blood in 56% of cases, saliva in 16%, and “other” or “unknown” in 28%.

PEPline consultants provide the caller with advice on: (1) assessing the risk associated with the exposure by ascertaining the nature of the injury, the type of substance involved, and source-patient factors; (2) determining whether PEP should be considered; and (3) selecting the PEP regimen. Faculty clinicians also provide advice...
regarding necessary pretreatment laboratory tests, follow-up testing, and follow-up care. In addition, personal counseling and support is given to exposed HCP callers; alternatively, treating-clinician callers are given advice on how to counsel the patient.

Transmission Risks

The overall risk of transmission of HIV from percutaneous exposure is estimated as 0.3% (3 per 1000 exposures) (Bell, Am J Med, 1997). Factors that increase risk of transmission include exposure through a visibly bloody device (odds ratio [OR], 6.2), through a device used in an artery or vein (OR, 4.3), via a deep injury (including intra- and subcutaneous exposure) (OR, 15.0), and from a source individual with more advanced HIV disease (and plasma HIV RNA level > 1500 copies/mL) (OR, 5.6) (Cardo et al, N Engl J Med, 1997). Risk of transmission through mucous membrane exposure is estimated as 0.09% (Ippolito et al, Arch Intern Med, 1993). For HIV transmission, substances or fluids that are considered infectious include blood, tissue, semen, vaginal secretions, and pus, as well as cerebrospinal, amniotic, pericardial, peritoneal, pleural, and synovial fluids. Unless visibly bloody, substances considered noninfectious include urine, feces, nasal secretions, saliva, gastric fluid, sputum, tears, sweat, and vomitus.

Testing and Recommendations for Postexposure Prophylaxis

The PEP decision depends on knowing or assessing the source-patient HIV serostatus. For PEP decisions, rapid HIV antibody testing of the source person can sometimes be performed if the patient is available and no HIV test results are available. Results from rapid tests are considered as accurate as standard test results for making PEP decisions. HIV antibody testing of the exposed HCP should occur pretreatment and at 6 weeks, 3 months, and 6 months postexposure.

The possibility of HIV transmission from a source person during the window period between infection and

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Table 1. HIV Postexposure Prophylaxis (PEP) Recommendations for Percutaneous, Mucous Membrane, and Nonintact Skin Exposures

<table>
<thead>
<tr>
<th>Exposure Type</th>
<th>Infection Status of Source</th>
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<tbody>
<tr>
<td></td>
<td>HIV-Seropositive</td>
</tr>
<tr>
<td>Percutaneous exposure recommendations</td>
<td>Class 1</td>
</tr>
<tr>
<td>Less severe</td>
<td>Basic 2-drug PEP</td>
</tr>
<tr>
<td>More severe</td>
<td>Expanded ≥ 3-drug PEP</td>
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Mucous membrane or nonintact skin exposure recommendations

<table>
<thead>
<tr>
<th>Small volume</th>
<th>Basic 2-drug PEP</th>
<th>Basic 2-drug PEP</th>
<th>Generally, no PEP warranted</th>
<th>Generally, no PEP warranted</th>
<th>No PEP warranted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large volume</td>
<td>Basic 2-drug PEP</td>
<td>Expanded ≥ 3-drug PEP</td>
<td>Generally, no PEP warranted</td>
<td>Consider basic 2-drug PEP for source with HIV risk factors</td>
<td>No PEP warranted</td>
</tr>
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Adapted from Centers for Disease Control and Prevention, MMWR, 2005.
positive HIV antibody test results is a common topic of calls to PEPline. Because most acute HIV infections can be detected by seroconversion within 3 weeks and most cases of acute infection are identifiable by the source person’s history of exposure or presence of a viral syndrome, the likelihood of the source being in an unrecognized infectious window period is extremely small. Additional reassurance can be given by the finding that no cases of occupational transmission involving exposure during the window period have been reported to date in the United States.

Table I provides guidance from the CDC on whether PEP is indicated and if so, whether a basic or expanded regimen is recommended after percutaneous exposure, mucous membrane exposure, or nonintact skin exposure. HIV-seropositive class 1 refers to a source individual with an asymptomatic infection or a plasma HIV RNA level less than 1500 copies/mL, and HIV-seropositive class 2 refers to a source individual who is asymptomatic, has AIDS, has a high viral load, or has acute seroconversion illness. For percutaneous exposures, less severe exposures are those involving, for example, a solid needle or a superficial injury, whereas more severe exposures are those involving, for example, large hollow-bore needles, deep injury, visible blood, or a device used in an artery or vein. For mucous membrane exposures, small volume refers to a few drops, and large volume refers to a major splash. Eye exposures that contact the conjunctiva are thought to carry a risk similar to that of other mucous membrane exposures. Nonintact skin includes any compromised skin integrity, for example, dermatitis, abrasions, and open wounds.

For any percutaneous exposure from an infected source, an expanded PEP regimen is warranted. In cases in which the source is unknown or is of unknown HIV serostatus, PEP is generally not warranted, although a basic regimen should be considered for any exposure to a source with HIV risk factors or in settings in which exposure to HIV-infected persons is likely.

The PEPline receives numerous inquiries about “found needles,” which refer to needles left in garbage cans, parks, or elsewhere in healthcare facilities or public places. There have been 2 apparent cases of transmission in PEP involving found needles in the hospital setting. Thus far, there have been no documented cases of transmission involving found needles in the community. Testing of discarded needles for HIV should not be performed because such a practice results in false-positive and false-negative results.

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There are some practical approaches used at the PEPline that are helpful in managing most exposures:

- When the source person’s HIV serostatus is not known, risk factors (when known) need to be considered, but the decision whether to recommend PEP needs to be made despite the incomplete source information. The decision should not be delayed pending receipt of laboratory results or additional history data, unless the results of a rapid HIV test or additional patient history are expected within a few hours.

- The determination about whether to recommend PEP is made by the treating clinician, but the decision to take PEP is made by the exposed HCP after hearing the assessment of risk of the specific exposure and the benefits and risks of PEP. For the HCP, deciding whether to take PEP is a highly personal decision in most cases.

- Initiating PEP, when indicated, should never be delayed. There has been misunderstanding of the current guidelines that (correctly) state that PEP should not be initiated past 72 hours. This does not mean, however, that there is a 72-hour window to initiate PEP, only that there is no evidence of efficacy when initiated past 72 hours.

- When PEP is indicated but the HCP is undecided about whether to take PEP (which often occurs in the emotionally charged postexposure state), the PEPline service encourages the HCP to initiate PEP immediately and reconsider the longer term decision the next day. The reasoning is that PEP can always be discontinued, but once the chance to initiate PEP as early as possible is missed, it cannot be retrieved. This message can be reassuring to exposed HCP and allows time for test results to be obtained and for HCP to reconsider whether they want to continue treatment on the basis of additional risk assessment or test results. Conversely, delaying initiation of PEP and then realizing hours later that the opportunity to take early PEP has been missed can be emotionally (and possibly clinically) devastating.

Selection of Postexposure Prophylaxis Regimen

PEP is administered for 28 days. The duration of treatment is not based on controlled studies, although some animal evidence indicates that shorter duration PEP is not as effective. Similarly, there are no comparative studies of the various drugs used for PEP, so recommendations are based on presumed efficacy and known tolerability. The recommended basic regimens for HIV PEP (CDC, MMWR, 2005) are tenofovir plus emtricitabine or zidovudine plus lamivudine. Tenofovir-containing regimens are generally better tolerated in PEP but should not be used when renal insufficiency is present. The recommended expanded regimen, if warranted, is formed by adding ritonavir-boosted (r/r) lopinavir to either of the 2-drug regimens. Once-daily darunavir/r is considered better tolerated than lopinavir/r. Alternatives for constructing the expanded regimen in cases of resistance, drug interactions, or intolerance include darunavir/r, atazanavir/r, or raltegravir. The expanded drug regimens are associated with more toxicity and less adherence than the basic
regimens. New York state guidelines (available at http://www.ceiwidget.com/online/) recommend that PEP always consist of 3 nucleoside analogue transcriptase inhibitors: either fixed-dose zidovudine/lamivudine plus tenofovir or fixed-dose tenofovir/emtricitabine plus zidovudine.

Newer drugs might have some advantages and likely will replace some of the currently recommended drug regimens. A recent survey showed that PEPline recommendations differed from USPHS guidelines recommendations in 14% of cases. Predictors for recommendations outside of the guidelines regimens included the following source-person characteristics: current use of specific antiretroviral drugs, prior antiretroviral drug exposure, antiretroviral drug resistance, and clinical status. Alternatives for the expanded regimen recommended by PEPline faculty in this 14% of cases included darunavir/r in 36% of cases, raltegravir in 31%, atazanavir/r in 18%, and maraviroc in 6% (Hensic and Dong, CROI, 2011).

Overtreatment in cases of occupational exposure to HIV is common. As long as the HCP is aware of the risks and benefits of PEP, initiating basic PEP even when there is minimal risk from the exposure or prescribing expanded regimens as a precaution when a basic regimen might suffice can be reassuring to the exposed HCP that everything possible has been done. Such overtreatment actually constitutes a conservative approach from the perspective of the treating clinician as well, ensuring the best chance that transmission does not occur. This approach seems to be working, as no new cases of transmission via occupational exposures have been reported in more than 5 years and few serious toxicities from PEP have been reported. In addition to use of PEP, other factors contribute to the reduced risk of occupational exposure and transmission of HIV, including improvement in safety devices, better safety habits among HCP, better institutional adherence to safety procedures, the presence of fewer HIV-infected patients in the hospital setting, and reduced viral load in the infected population as the result of effective treatment.

Lecture presented by Dr Goldschmidt in August 2010. First draft prepared from transcripts by Matthew Stenger. Reviewed and edited by Dr Goldschmidt in December 2010.

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Suggested Reading


Hensic L, Dong B. Non-guideline post-exposure prophylaxis regimens for occupational percutaneous exposures to HIV+ source patients. [Abstract.] Accepted for presentation at the 18th Conference on Retroviruses and Opportunistic Infections (CROI). February 27-March 2, 2011; Boston, MA.


