

XI. POST-EXPOSURE PROPHYLAXIS (PEP)

TABLE OF CONTENTS

OCCUPATIONAL EXPOSURE TO HIV	XI-1
Risk of Transmission Associated with an Occupational Exposure	XI-1
Efficacy and Timing of PEP	XI-1
Risks and Benefits of PEP	XI-2
PEP Regimens	XI-2
Recommendations for Management of Occupational Exposures to HIV	XI-2
Follow-Up.....	XI-3
PEP FOLLOWING SEXUAL EXPOSURE TO HIV	XI-4
PEP SCENARIOS AND RECOMMENDATIONS	XI-5
Needlestick Involving HIV-Infected Source Patient	XI-5
Exposure Involving a Source Patient Whose HIV Status Is Not Known	XI-6
Exposed Healthcare Worker with a Positive Baseline HIV Test.....	XI-6
Exposure Involving Sexual Assault.....	XI-7
TABLES	
<i>Table 1: Variables that Likely Increase Risk of HIV Transmission in Occupational Exposures</i>	XI-1
<i>Table 2: PEP Management Recommendations: Percutaneous (Needlestick) Exposures</i>	XI-3
<i>Table 3: PEP Management Recommendations: Mucocutaneous or Non-Intact Skin Exposures</i>	XI-3
<i>Table 4: Average Per-Exposure Risk Associated with Exposures to HIV</i>	XI-4
FIGURES	
<i>Figure 1: Recommendations for Antiretroviral Post-exposure Prophylaxis for Non-occupational Exposure to HIV</i>	XI-5

XI. POST-EXPOSURE PROPHYLAXIS

Post-exposure prophylaxis (PEP) refers to the use of antiretroviral agents (ARVs) to reduce the risk of HIV transmission following a potentially infectious exposure to HIV. Typical situations in which PEP may be indicated include occupational exposures involving healthcare personnel or sexual exposures.

OCCUPATIONAL EXPOSURE TO HIV

RISK OF TRANSMISSION ASSOCIATED WITH AN OCCUPATIONAL EXPOSURE

Exposures of healthcare personnel to the body fluids of HIV-infected patients are not uncommon; fortunately, however, transmission of HIV from these exposures is rare. Potentially infectious bodily fluids include blood, spinal fluid, pleural fluid, pus, and amniotic fluid. Urine, sweat, and faeces are not considered infectious unless visibly bloody.

The average risk of transmission associated with a percutaneous (needlestick) injury involving an HIV-infected source patient is estimated to be approximately 0.3%. A retrospective case-control study of healthcare workers who sustained needlestick injuries involving HIV-infected source patients found that the risk of HIV transmission was significantly increased by the following factors: deep injury; visibly bloody needle/device; injury involving a device used in a vein or artery; and end-stage AIDS in the source patient (probably because end-stage AIDS is associated with elevated HIV viral load titres). Other evidence suggests that hollow-bore needles and lack of glove use by the healthcare worker also likely increase the risk of HIV transmission.

Table 1: Variables that Likely Increase Risk of HIV Transmission in Occupational Exposures

PERCUTANEOUS INJURY (e.g. needlestick)	MUCOCUTANEOUS INJURY (e.g. splash to eye, mouth, or broken skin)
<ul style="list-style-type: none">• Deep injury• Visibly bloody needle/device• Needle used in vein or artery• Hollow-bore needle• Source patient with end-stage AIDS• High serum viral load in source patient• Healthcare worker not wearing gloves	<ul style="list-style-type: none">• Large volume of fluid• Prolonged contact with fluid• Source patient with end-stage AIDS• High serum viral load in source patient

HIV can also be transmitted in the occupational setting via splashes of infectious material to nonintact skin or mucous membranes such as the eyes or mouth. The average risk of HIV transmission associated with a mucocutaneous exposure is estimated to be approximately 0.09%, or roughly 1 in 1,000. Similar risk factors likely apply; the risk of transmission may be increased by a high volume of potentially infectious fluid or a high concentration of HIV in the source patient's fluid.

EFFICACY AND TIMING OF PEP

A retrospective case-control study of PEP found that administration of a four-week course of zidovudine (AZT) following an occupational needlestick exposure to an HIV-infected source patient reduced the risk of HIV transmission by approximately 80%. Animal studies suggest that PEP is more effective when initiated within hours, rather than days, following an exposure. However, the exact interval beyond which PEP offers no benefit to humans is unclear. Hence, these guidelines recommend that for occupational exposures that warrant PEP, the medications should be initiated as soon as possible (e.g.

within one to two hours). Initiation of PEP more than thirty-six hours after a significant exposure may be considered, but consultation with an expert HIV clinician is recommended.

RISKS AND BENEFITS OF PEP

Decision-making regarding possible initiation of PEP for a healthcare worker following an occupational exposure can be difficult. Such a decision is best made by an informed healthcare worker who understands the potential risks and benefits associated with four weeks of combination antiretroviral therapy. Hence, extensive counselling of the exposed healthcare worker is recommended. While prompt initiation of PEP following an exposure may significantly reduce the risk of HIV transmission, adverse medication effects are common. Studies suggest that most healthcare workers will experience one or more side effects from PEP such as nausea, headache, fatigue, and gastrointestinal upset. However, these adverse effects can usually be managed with symptomatic treatment or by modification of the PEP regimen in order to allow completion of four weeks of therapy, and adverse reactions typically resolve upon cessation of PEP.

PEP REGIMENS

PEP regimens are typically classified as *basic* or *expanded*. *Basic* regimens consist of two nucleoside reverse transcriptase inhibitors (NRTIs), typically zidovudine (AZT, Retrovir[®]) plus lamivudine (3TC, Epivir[®]); other combinations of NRTIs can be recommended as alternative regimens. An *expanded* regimen consists of a basic regimen plus one or more additional ARV(s) such as nelfinavir (NFV), lopinavir-ritonavir (LPV/r; *Kaletra*), or efavirenz (EFV). Expanded regimens offer the possibility of greater potency, but there is no direct evidence that expanded PEP regimens are more effective in this setting than basic regimens, and expanded regimens typically involve a higher pill burden and more potential for toxicity.

RECOMMENDATIONS FOR MANAGEMENT OF OCCUPATIONAL EXPOSURES TO HIV

Following an occupational exposure to HIV, the exposed area should be immediately decontaminated (e.g. soap and water to percutaneous injury sites; saline rinse for eye exposures). The healthcare worker should be counselled regarding the potential risks and benefits of PEP, and a decision should be made promptly regarding possible initiation of PEP. Because the efficacy of PEP is thought to wane with time, emergency departments or urgent care centres are appropriate facilities to manage exposures and initiation of PEP. Baseline laboratory testing of the healthcare worker, including HIV serology, is also indicated but should not interfere with the initiation of PEP if warranted. The exposure should also be promptly reported to the employee's supervisor.

Decision-making regarding whether to initiate PEP hinges largely upon the severity of the exposure itself and knowledge of the source patient's HIV status. For exposures involving source patients known to be HIV-infected, PEP is generally recommended, consisting of a basic regimen for low-risk exposures and an expanded regimen for higher-risk exposures. Where the HIV status of the source patient is not known, it may be reasonable to initiate PEP if the source patient is strongly suspected to have undiagnosed HIV infection; however, attempts should be made to test the source patient for HIV, and if source patient testing fails to confirm HIV infection, PEP should be discontinued.

Selection of the components of the PEP regimen itself may also depend in part on exposure and source patient characteristics. AZT is generally included in PEP regimens because it has demonstrated efficacy in this setting; however, other agents, such as stavudine (d4T) or tenofovir (TDF) can be substituted if the AZT causes intolerable side effects. 3TC is generally included as well because this agent is generally safe and well-tolerated. If an expanded regimen is indicated, nelfinavir (NFV) is a popular choice because it can be taken twice daily and does not need to be refrigerated. Lopinavir/ritonavir (LPV/r; *Kaletra*) may be more potent than NFV as a third PEP agent, but requires refrigeration and has more potential interactions with other medications. EFV can also be considered in expanded PEP regimens, but not for women who may be pregnant due to its potential for teratogenicity. **NVP should not be included in**

PEP regimens because unacceptably high rates of life-threatening toxicity have been reported in healthcare workers taking NVP-containing PEP regimens.

If antiretroviral drug resistance is suspected in the source patient, the selection of agents for a PEP regimen may need to reflect this possibility by incorporating at least one or more agents to which the source patient’s strain of HIV is likely sensitive. Consultation with an expert HIV clinician is highly recommended if source patient drug resistance is suspected.

Recommendations regarding PEP initiation and regimen selection are summarised in *Table 2* and *Table 3*.

Table 2: PEP Management Recommendations: Percutaneous (Needlestick) Exposures

	SOURCE PATIENT FEATURES		
EXPOSURE FEATURES	HIV+, High-Risk*	HIV+, Low-Risk†	Serostatus Unknown‡
HIGH-RISK EXPOSURE§	Recommend three-drug regimen	Recommend two-drug regimen; third drug optional	Consider two-drug regimen if significant possibility that source patient is HIV+
LOW-RISK EXPOSURE**	Recommend two-drug regimen; third drug optional	Recommend two-drug regimen	Consider two-drug regimen if significant possibility that source patient is HIV+

Table 3: PEP Management Recommendations: Mucocutaneous or Non-intact Skin Exposures

	SOURCE PATIENT FEATURES		
EXPOSURE FEATURES	HIV+, High-Risk*	HIV+, Low-Risk†	Serostatus Unknown‡
LARGE VOLUME (E.G. MAJOR SPLASH)	Recommend three-drug regimen	Recommend two-drug regimen; third drug optional	Consider two-drug regimen if significant possibility that source patient is HIV+
SMALL VOLUME (E.G. FEW DROPS)	Recommend two-drug regimen; third drug optional	Consider two-drug regimen	Consider two-drug regimen if significant possibility that source patient is HIV+

FOLLOW-UP

Following a potential exposure to HIV, serologic testing is indicated to screen for HIV transmission. Seroconversion typically occurs within a few weeks of infection, but cases of delayed seroconversion have been documented. HIV antibody screening at six weeks, three months, and six months is suggested. Use of HIV viral load testing to screen for HIV transmission is not recommended except in circumstances

*High-risk features include known high HIV viral load, CD4+ T cell count of <200 cells/mm³, or advanced HIV/AIDS.

†Low-risk features include known low HIV viral load or clinically well on HAART.

‡e.g. known source patient with unknown HIV status, or identity of source patient is unknown.

§e.g. deep injury or injury involving needle that was used in an artery or vein, was visibly bloody, or was hollow-bore.

**None of the high-risk variables apply.

where acute HIV infection is suspected. Though the risk of HIV transmission is low, an occupational exposure can be a psychologically traumatic event for the involved healthcare worker; counselling is often indicated and should be offered. For healthcare workers who initiate PEP, it is reasonable to perform screening laboratory tests for antiretroviral toxicity two weeks after starting PEP, though the efficacy of this strategy in preventing serious PEP-related complications has not been established.

PEP FOLLOWING SEXUAL EXPOSURE TO HIV

The risks of HIV transmission associated with many sexual exposures to HIV are comparable to or exceed those associated with occupational exposures. Furthermore, the risk is probably significantly elevated if the exposure was traumatic (e.g. sexual assault) or if ulcerative lesions were present on either the source or the exposed individual. Many HIV specialists therefore endorse the use of PEP in certain situations following a sexual exposure to HIV, and U.S. Centers for Disease Control and Prevention (CDC) Guidelines have recently endorsed the concept of PEP following non-occupational exposures to HIV that confer a significant risk of transmission.¹ The levels of risk associated with various occupational and sexual exposures to HIV are summarised in *Table 4*.

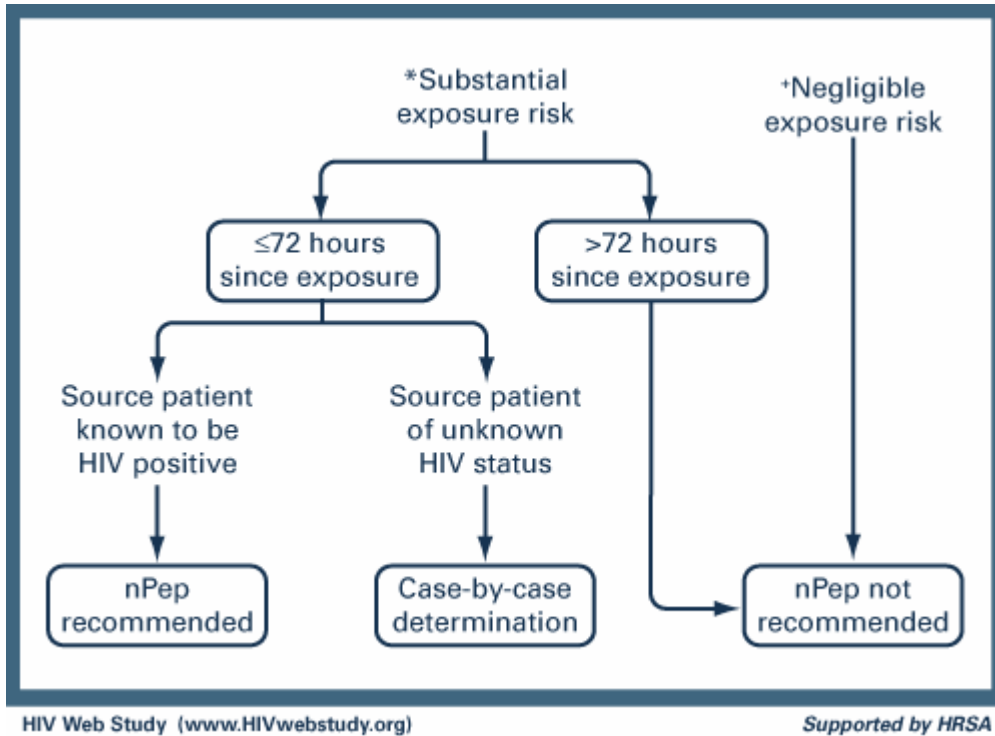
In general, the management of PEP for sexual exposures is extrapolated from the management of occupational exposures, although the difficulty of accurately stratifying risk in such exposures has led the CDC to generally favour the use of expanded three drug regimens over basic two drug regimens. A two-drug NRTI regimen may nevertheless be considered as dictated by clinical circumstances and/or patient preference. Initiation of PEP as soon as possible following an exposure is recommended; many protocols that have been developed for PEP following sexual exposures have used seventy-two hours following the exposure as the upper limit beyond which PEP should not be offered. If initiated, PEP should be continued for twenty-eight days unless the source patient is subsequently discovered to be HIV-uninfected. While concern has been raised that offering PEP for sexual exposures may encourage unsafe sexual behaviour, a study in San Francisco, California, designed to assess this possibility found that risky sexual behaviour decreased, rather than increased, in patients who received PEP and behavioural counselling following sexual exposures to HIV. As it is for occupational PEP, the use of NVP is discouraged, as is the use of EFV in women who are pregnant or anticipate possible imminent pregnancy. In settings where the HIV status of the source patient is not known, case-by-case determination of the appropriateness of PEP is indicated, which may consider factors such as the severity of the exposure itself, prevalence of HIV in the community, and presence/absence of risk factors in the source patient.

Table 4: Estimated Risks of HIV Transmission

EXPOSURE	AVERAGE PER-EPISODE RISK
OCCUPATIONAL	
Percutaneous (blood)	0.3%
Mucocutaneous (blood)	0.09%
SEXUAL	
Receptive Anal Intercourse	1% to 2%
Insertive Anal Intercourse	0.06%
Receptive Vaginal Intercourse	0.1% to 0.2%
Insertive Vaginal Intercourse	0.03% to 0.14%
Receptive Oral (male)	0.06%
Female-Female Orogenital	4 case reports

Figure 1 presents an algorithm adapted from the CDC guidelines for non-occupational exposures to HIV.²

Figure 1: Recommendations for Antiretroviral Post-exposure Prophylaxis for Non-occupational Exposure to HIV



* Substantial risk for HIV exposure is defined in these guidelines as exposure contact of an area of the body known to be associated with acquisition of HIV (vagina, rectum, eye, mouth, or other mucous membrane, non-intact skin, or percutaneous contact) WITH a body substance known to transmit HIV (blood, semen, vaginal secretions, rectal secretions, breast milk, or any body fluid that is visibly contaminated with blood) WHEN the source is known to have HIV infection.

+ Negligible risk is defined in these guidelines as exposure the vagina, rectum, eye, mouth, or other mucous membrane, nonintact skin, intact skin, or percutaneous contact WITH urine, nasal secretions, saliva, sweat, or tears (if not visibly contaminated with blood), REGARDLESS of the known or suspected HIV status of the source.

PEP SCENARIOS AND RECOMMENDATIONS

1. NEEDLESTICK INVOLVING HIV-INFECTED SOURCE PATIENT

A nurse sustains a percutaneous injury (needlestick) to her thumb while transferring a phlebotomy needle she just used to draw blood from an HIV-infected patient who is currently hospitalised for treatment of Pneumocystis jiroveci pneumonia (PCP). The source patient was recently started on antiretroviral therapy, but his CD4+ T cell count and viral load are not immediately available. What steps should be taken, and how should the nurse be counselled regarding HIV PEP?

The phlebotomist should immediately wash the injured region with soap and water, and then seek evaluation for initiation of PEP. An aggressive three-drug PEP regimen is recommended because the exposure was high-risk (involving a hollow-bore needle used in the source patient's vein) and the source patient is also high-risk (advanced HIV disease as evidenced by his PCP); note that either of these high-

risk conditions alone would be sufficient to warrant an expanded PEP regimen. A regimen of AZT plus 3TC plus NFV or lopinavir/ritonavir (LPV/r) would be reasonable. These medications should be initiated as soon as possible, and continued for four weeks. A baseline HIV test and a pregnancy test are also indicated, but may be performed after initiation of PEP. Counselling and psychological support should be offered. She should be monitored clinically for adverse effects of the medications; if available, laboratory monitoring after two weeks of therapy may also be helpful but is not mandatory. An anti-diarrhoeal agent may be recommended to counteract this common side effect of the protease inhibitor (PI) in her regimen. Changes to her PEP regimen may be made for intolerable side effects (e.g. substitution of d4T for AZT). She should be tested for HIV infection by standard serology (ELISA with confirmatory Western blot if the ELISA is positive) periodically, e.g. at six weeks, three months, and six months following the exposure. She should not be tested for HIV using the viral load assay unless she develops signs and symptoms suggestive of primary (acute) HIV infection.

2. EXPOSURE INVOLVING A SOURCE PATIENT WHOSE HIV STATUS IS NOT KNOWN

A dentist is splashed in the eye with bloody saliva from a patient whose HIV status is not known, but is from a region where the HIV prevalence is high. What steps should be taken, and is PEP recommended for the dentist?

The dentist should rinse his/her eye immediately and thoroughly with a sterile rinse. A decision should be made promptly about possible administration of PEP. Initiation of a two-drug PEP regimen (e.g. AZT plus 3TC) would be reasonable given that the prevalence of HIV in the local population is high, but it would also be reasonable for the dentist to decline PEP given that the risk of HIV transmission in this situation is low, the source patient is not known to be HIV-infected, and PEP is often associated with adverse effects. The decision regarding possible initiation of PEP should not be deferred until HIV testing of the source patient can be performed, because PEP is most effective when initiated promptly. However, if rapid HIV testing is available, and the source patient consents to immediate testing, the decision regarding initiation of PEP can be based on the results of this rapid test.

Testing of the source patient should be attempted even if rapid HIV testing is not available. If the source patient tests negative for HIV infection, PEP for the dentist should be stopped. If PEP has been initiated and the source patient tests positive for HIV, or refuses to be tested, PEP should be continued for four weeks. Counselling and psychological support should be offered to the dentist, and baseline and follow-up HIV serology testing should be performed, e.g. at six weeks, three months, and six months following the exposure. If testing of the source patient reveals previously undiagnosed HIV infection, the source patient should be offered counselling and referred to an HIV/AIDS treatment centre for further management.

The dentist should also be tested for HIV at baseline as soon as possible, though this testing does not need to be performed before PEP is initiated.

3. EXPOSED HEALTHCARE WORKER WITH A POSITIVE BASELINE HIV TEST

A nursing assistant sustains a needlestick injury while disposing of a phlebotomy needle; it is not clear who the source patient is. After counselling, she elects to receive PEP, and a two-drug regimen is initiated. Three days later, her baseline HIV serology test reveals previously undiagnosed HIV infection. How should she be managed?

PEP should be discontinued. She should be offered counselling and promptly referred to an HIV/AIDS treatment centre for further management.

4. EXPOSURE INVOLVING SEXUAL ASSAULT

A woman reports being sexually assaulted (vaginal penetration) approximately twenty-four hours previously by a male acquaintance that is HIV-infected. Physical examination reveals perineal bruising and a shallow vaginal laceration. What recommendations should be made regarding HIV PEP?

This sexual assault, involving traumatic vaginal penetration by an HIV-infected source, involves a risk of HIV transmission comparable to (and perhaps higher than) that of a needlestick exposure. Hence, many expert HIV clinicians as well as recently published CDC guidelines³ would endorse initiation of an expanded PEP regimen in this scenario. As with an occupational exposure, the exposed patient should be offered counselling and psychological support as well as baseline and follow-up HIV testing. Other concerns such as the potential for pregnancy, prophylaxis against other sexually transmitted infections (STIs), and collection of evidence for possible legal action should also be addressed. If she initiates PEP, monitoring for antiretroviral toxicity should be performed.

¹ Smith DK, Grohskopf LA, Black RJ, et al. Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States: recommendations from the U.S. Department of Health and Human Services. *MMWR* [serial on the Internet] 2005;54(RR02):1-20. Available at <http://www.aidsinfo.nih.gov/Guidelines>

² Ibid.

³ Ibid.