

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 ¹ | HIV+, Low-Risk ² | Serostatus Unknown ³ |
| HIGH-RISK EXPOSURE⁴ | 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 EXPOSURE⁵ | 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+ |

¹High-risk features include known high HIV viral load, CD4+ T cell count of <200 cells/mm³, or advanced HIV/AIDS.

²Low-risk features include known low HIV viral load or clinically well on HAART.

³e.g. known source patient with unknown HIV status, or identity of source patient is unknown.

⁴e.g. deep injury or injury involving needle that was used in an artery or vein, was visibly bloody, or was hollow-bore.

⁵None of the high-risk variables apply.