Post Exposure Prophylaxis (PEP)

Occupational exposure

Occupational exposure refers to exposure to potential blood-borne infections (HIV, HBV and HCV) that may occur in healthcare settings during performance of job duties. Post exposure prophylaxis (PEP) refers to comprehensive medical management to minimise the risk of infection among Health Care Personnel (HCP) following potential exposure to blood-borne pathogens (HIV, HBV, HCV). This includes counselling, risk assessment, relevant laboratory investigations based on informed consent of the source and exposed person, first aid and depending on the risk assessment, the provision of short term (four weeks) of antiretroviral drugs, with follow up and support.

Who is at risk?

All Health Care Personnel, including emergency care providers, laboratory personnel, autopsy personnel, hospital employees, interns and medical students, nursing staff and students, physicians, surgeons, dentists, labour and delivery room personnel, laboratory technicians, health facility sanitary staff and clinical waste handlers and health care professionals at all levels. Also at risk are public safety workers, including law enforcement personnel, prison staff, fire-fighters, workers in needle exchange programme and workers in HIV programmes.

What is the risk?

Health Care Personnel are at risk of blood-borne infection transmission through exposure of a percutaneous injury (e.g. needle-stick or cut with a sharp instrument), contact with the mucous membranes of the eye or mouth of an infected person, contact with non-intact skin (particularly when the exposed skin is chapped, abraded, or afflicted with dermatitis or contact with blood or other potentially infectious body fluids.

Any direct contact (i.e., contact without barrier protection) with concentrated virus in a research laboratory or production facility requires clinical evaluation. Transmission of HIV infection from human bites is rarely reported.

The average risk of acquiring HIV infection from different types of occupational exposure is low compared to risk of infection with HBV or HCV. In terms of occupational exposure the important routes are needle stick exposure (0.3% risk for HIV, 9–30% for HBV and 1–10% for HCV) and mucous membrane exposure (0.09% for HIV).

What is infectious and what is not?

Exposure to blood, semen, vaginal secretions, cerebrospinal fluid, synovial, pleural, peritoneal, pericardial fluid, amniotic fluid and other body fluids contaminated with visible blood can lead to infection. Exposure to tears, sweat, saliva, urine and faeces is non-infectious unless these secretions contain visible blood.

Step 1: First aid in management of exposure

For skin — if the skin is broken after a needle-stick or sharp instrument:

- Immediately wash the wound and surrounding skin with water and soap, and rinse. Do not scrub.
- Do not use antiseptics or skin washes (bleach, chlorine, alcohol, betadine).

After a splash of blood or body fluids on unbroken skin:

- Wash the area immediately
- Do not use antiseptics

For the eye:

- Irrigate exposed eye immediately with water or normal saline. Sit in a chair, tilt head back and ask a colleague to gently pour water or normal saline over the eye.
- If wearing contact lens, leave them in place while irrigating, as they form a barrier over the eye and will help protect it. Once the eye is cleaned, remove the contact lens and clean them in the normal manner. This will make them safe to wear again
- Do not use soap or disinfectant on the eye.

For mouth:

- Spit fluid out immediately
- Rinse the mouth thoroughly, using water or saline and spit again. Repeat this process several times
- Do not use soap or disinfectant in the mouth
- Consult the designated physician of the institution for management of the exposure immediately.

Don'ts
• Do not panic
• Do not put pricked finger in mouth
• Do not squeeze wound to bleed it
• Do not use bleach, chlorine, alcohol, betadine, iodine or any antiseptic or detergent

Step 2: Establish eligibility for PEP

The HIV sero-conversion rate of 0.3% after an AEB (for percutaneous exposure) is an average rate. The risk of infection transmission is proportional to the amount of HIV transmitted, which depends on the nature of exposure and the status of the source patient. A baseline rapid HIV testing of exposed and source person must be done for PEP. However, initiation of PEP should not be delayed while waiting for the results of HIV testing of the source of exposure. Informed consent should be obtained before testing of the source as per national HIV testing guidelines.

First PEP dose within 72 hours

A designated person/trained doctor must assess the risk of HIV and HBV transmission following an AEB. This evaluation must be quick so as to start treatment without any delay, ideally within two hours but certainly within 72 hours; PEP is not effective when given more than 72 hours after exposure. The first dose of PEP should be administered within the first 72 hours of exposure. If the risk is insignificant, PEP could be discontinued, if already commenced.

Assessing risk of transmission

Exposure is defined under three categories based on the amount of blood/fluid involved and the entry port. These categories are intended to help in assessing the severity of the exposure but may not cover all possibilities.

Categories of exposure	
Category	**Definition and example**
Mild exposure	mucous membrane/non-intact skin with small volumes E.g.: a superficial wound (erosion of the epidermis) with a plain or low calibre needle, or contact with the eyes or mucous membranes, subcutaneous injections following small-bore needles.
Moderate exposure	mucous membrane/non intact skin with large volumes **OR** percutaneous superficial exposure with solid needle E.g. : a cut or needle stick injury penetrating gloves
Severe exposure	percutaneous with large volume e.g.: an accident with a high calibre needle (>18 G) visibly contaminated with blood; a deep wound (haemorrhagic wound and/or very painful); transmission of a significant volume of blood; an accident with material that has previously been used intravenously or intra-arterially.
The wearing of gloves during any of these accidents constitutes a protective factor. ***Note:*** In case of an AEB with material such as discarded sharps/needles, contaminated for over 48 hours, the risk of infection is negligible for HIV, but still remains significant for HBV. HBV survives longer than HIV outside the body.	

Assess exposed individual

The exposed individual should have confidential counselling and assessment by an experienced physician. Exposed individuals who are known or discovered to be HIV positive should not receive PEP. They should be offered counselling and information on prevention of transmission and referred to clinical and laboratory assessment to determine eligibility for antiretroviral therapy (ART). Besides the medical assessment, counselling exposed HCP is essential to allay fear and start PEP.

Step 3: Counselling for PEP

Exposed persons (clients) should receive appropriate information about what PEP is about and the risk and benefits of PEP in order to provide informed consent for taking PEP. It should be clear that PEP is not mandatory.

Psychological support

Many people feel anxious after exposure. Every exposed person needs to be informed about the risks, and the measures that can be taken. This will help to relieve part of the anxiety. Some clients may require further specialised psychological support.

Document exposure

Documentation of exposure is essential. Special leave from work should be considered initially for a period of two weeks. Subsequently, it can be extended based on the assessment of the exposed person's mental state,

side effects and requirements.

Practical application in the clinical settings

- For prophylactic treatment the exposed person must sign consent form.
- Informed consent also means that if the exposed person has been advised PEP, but refuses to start it, this needs to be recorded. This document should be kept by the designated officer for PEP.
- An information sheet covering the PEP and the biological follow-up after any AEB must be given to the person under treatment. However, this sheet cannot replace verbal explanations.

Step 4: Prescribe PEP

Deciding on PEP regimen

There are two types of regimens:

- Basic regimen: 2-drug combination
- Expanded regimen: 3-drug combination

The decision to initiate the type of regimen depends on the type of exposure and HIV serostatus of the source person.

HIV PEP Evaluation			
Exposure	Status of Source		
	HIV+ and Asymptomatic	**HIV+ and Clinically symptomatic**	**HIV status unknown**
Mild	Consider 2-drug PEP	Start 2- drug PEP	Usually no PEP or consider 2-drug PEP
Moderate	Start 2-drug PEP	Start 3- drug PEP	Usually no PEP or consider 2-drug PEP
Severe	Start 3-drug PEP	Start 3- drug PEP	Usually no PEP or consider 2-drug PEP

- In the case of a high risk exposure from a source patient who has been exposed to or is taking antiretroviral medications, consult an expert to choose the PEP regimen, as the risk of drug resistance is high. Refer/consult expert physician. Start 2-drug regimen first.

Seek expert opinion in case of

- Delay in reporting exposure (> 72 hours).
- Unknown source
- Known or suspected pregnancy, but initiate PEP
- Breastfeeding mothers, but initiate PEP
- Source patient is on ART
- Major toxicity of PEP regimen.

Step 5: HIV chemoprophylaxis

Because post-exposure prophylaxis (PEP) has its greatest effect if begun within two hours of exposure, it is essential to act immediately. The prophylaxis needs to be continued for four weeks. Exposure must be immediately reported to designated authority and therapy administered. Never delay start of therapy due to debate over regimen. Begin with basic 2-drug regimen, and once expert advice is obtained, change as required.

Dosage of drugs for PEP		
Medication	**2-drug regimen**	**3-drug regimen**
Zidovudine (AZT)	300 mg twice a day	300 mg twice a day
Stavudine (d4T)	30 mg twice a day	30 mg twice a day
Lamivudine (3TC)	150 mg twice a day	150 mg twice a day

Protease Inhibitors	**1st choice** Lopinavir/ritonavir (LPV/r) 400/100 mg twice a day or 800/200 mg once daily with meals **2nd choice** Nelfinavir (NLF) 1250 mg twice a day or 750 mg three times a day with empty stomach **3rd choice** Indinavir (IND) 800 mg every 8 hours and drink 8–10 glasses (1.5 litres) of water daily
Note: If protease inhibitor is not available and the 3rd drug is indicated, one can consider using Efavirenz (EFV 600 mg once daily). Monitoring should be instituted for side effects of this drug eg CNS toxicity such as nightmares, insomnia etc. * Fixed Dose Combination (FDC) are preferred, if available. Ritonavir requires refrigeration.	

PEP regimens to be prescribed by Health Centres		
	Preferred	**Alternative**
2-drug regimen (basic PEP regimen)	Zidovudine (AZT) + Lamivudine (3TC)	Stavudine (d4T) + Lamivudine (3TC)
3-drug regimen (consult expert opinion for starting 3 drug eg LPV/r, NLF or IND regimen)		
Not recommended	ddI + d4T combination NNRTI such as Nevirapine should not be used in PEP	
More information on alternative schedules is available in the latest update USPHS guidelines issued 30 September 2005. (http://www. cdc.gov/mmwr/preview/mmwrhtml/rr5409a1.htm)		

Selection of PEP regimen when the source patient is on ART

The physician should consider the comparative risk represented by the exposure taking in view exposure source's history of and response to antiretroviral therapy based on clinical response, CD4 cell counts, viral load measurements (if available), and current disease stage (WHO clinical staging and history). If the source person's virus is known or suspected to be resistant to one or more drugs considered for the PEP regimen, exposed person needs to be given alternate PEP drug regimen, and referred for expert opinion.

Changes in the PEP regimen can be made after PEP has been started. Re-evaluation of the exposed person should be considered within 72 hours post-exposure, especially as additional information about the exposure or source person becomes available.

ARV drugs during pregnancy

Data regarding the potential effects of antiretroviral drugs on the developing foetus or neonate are limited. There is a clear contraindication for Efavirenz (first 3 months of pregnancy) and Indinavir (pre natal).

For a female HCP considering PEP, a pregnancy test is recommended in case of a doubt. Pregnant HCP are recommended to begin the basic 2-drug regimen, and if a third drug is needed, Nelfinavir is the drug of choice.

Side-effects and adherence to PEP

Studies have indicated more side effects, most commonly nausea and fatigue, among HCP taking PEP than PLHAs taking ART. These side-effects occur mainly at the beginning of the treatment and include nausea, diarrhoea, muscular pain and headache. The person taking the treatment should be informed that these may occur and should be dissuaded from stopping the treatment as most side-effects are mild and transient, though possibly uncomfortable. Anaemia and/or leucopenia and/or thrombocytopenia may occur during the month of treatment.

Adherence information and psychological support are essential. More than 95% adherence is important in order to maximise the efficacy of the medication in PEP. Side effects can be reduced through medications. A complete blood count and liver function tests (transaminases) may be performed at the beginning of treatment (as baseline) and after 4 weeks.

Step 6: Follow-up of an exposed person
Whether or not post-exposure prophylaxis is started, a follow up is needed to monitor for possible infections and to provide psychological support.

Clinical follow-up
In the weeks following an AEB, the exposed person must be monitored for the eventual appearance of signs indicating an HIV seroconversion: acute fever, generalized lymphadenopathy, cutaneous eruption, pharyngitis, non-specific flu symptoms and ulcers of the mouth or genital area. These symptoms appear in 50%-70% of individuals with an HIV primary (acute) infection and almost always within 3 to 6 weeks after exposure. When a primary (acute) infection is suspected, referral to an ART centre or for expert opinion should be arranged rapidly.
An exposed person should be advised to use precautions (e.g., avoid blood or tissue donations, breastfeeding, unprotected sexual relations or pregnancy) to prevent secondary transmission, especially during the first 6–12 weeks following exposure. Condom use is essential.
Drug adherence and side effect counselling should be provided and reinforced at every follow-up visit. Psychological support and mental health counselling is often required.

Laboratory follow-up
Exposed persons should have post-PEP HIV tests. HIV-test at 3 months and again at 6 months is recommended. If the test at 6 months is negative, no further testing is recommended.

(Refer *Antiretroviral Therapy Guidelines for HIV-infected Adults and Adolescents including Post-exposure Prophylaxis, May 2007, NACO, Ministry of Health and Family Welfare, Government of India* for details on exposure prevention and essential information to be provided to exposed person.)