REVIEW ARTICLE

Postexposure Prophylaxis in HIV in India: A Review

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ABSTRACT

The risk of exposure to HIV is high among certain populations like healthcare personnel (HCP), injection drug users (IDUs) and people engaged in unprotected sex. The timely reporting of the needle stick injury or potential exposure to HIV depends on the knowledge and understanding of PEP by the HCP. There is a delay in development of systemic infection after the initial exposure caused by the HIV replication in the dendritic cells of the skin and mucosa before spread through the lymphatic vessels. This window of opportunity can be utilized to block the replication of HIV by providing PEP. The case control study has demonstrated the reduction in acquisition of HIV by 81% after introduction of PEP among HCPs. Hence a comprehensive review on PEP among HCP, particularly with reference to Indian context is presented here.

Keywords: Antiretroviral therapy, Exposure code, Healthcare personnel, HIV, Postexposure prophylaxis, Source code, Tenofovir disoproxil fumarate.

Pediatric Infectious Disease (2019): 10.5005/jp-journals-10081-1209

What is Postexposure Prophylaxis?

Postexposure prophylaxis (PEP) is defined as a comprehensive management for reducing the likelihood of HIV infection after potential exposure, either occupationally or through sexual intercourse, thus categorizing them into occupational and nonoccupational exposure.[1]

Guidelines for PEP to HIV date back to 1990, when PEP was considered for high-risk exposure in occupational setup by the US Centre for Disease Control and Prevention. A case control study demonstrated the prompt initiation of zidovudine in exposed healthcare worker (HCW) reduced the rate of HIV acquisition by 81%. This served as strong evidence for usage of PEP. There are no randomized controlled trials conducted for efficacy of PEP because of ethical concerns.[2]

The comprehensive management for PEP includes first aid/exposure site management, counseling, risk assessment, and assessment of eligibility for PEP, relevant laboratory investigations for both the source and exposed person after obtaining written informed consent. The short-term antiretroviral therapy (ART) is given after risk assessment if eligible for PEP with follow-up and support that also includes maintaining confidentiality.

The scaling up of ART services and longer life span of people living with HIV with the availability of ART for all HIV-positive individuals have increased the risk of exposure "healthcare personnel" (HCP). This increases the need for clinicians to update and be well versed with the guidelines of PEP after accidental exposure.[1]

What is the Rationale for Using PEP?

It can take up to 72 hours, 5 days, and about 8 days for HIV to be detected in regional lymph nodes, blood, and cerebrospinal fluid, respectively. This period provides a window of opportunity to prevent HIV replication and thus prevent acquisition or dissemination of HIV when ART is started early.[3]

What is Considered as Exposure?

As already mentioned, the exposure may be occupational, i.e., those happening when performing job duties or can be nonoccupational, such as unsafe sex/sexual assault.

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How to cite this article: Mahalingam A. Postexposure Prophylaxis in HIV in India: A Review. Pediatr Inf Dis 2019;1(2):52–57.

Source of support: Nil

Conflict of interest: None

The "Exposure" which places the HCP at risk of HIV are as follows:

- A percutaneous injury—any injury with the sharps,
- Contact with
  - Mucous membrane of eye/mouth.
  - Nonintact skin.
  - Intact skin but prolonged exposure with blood or potentially infected body fluids.[1]

Who is "Exposed" and "Source" Person?

"Exposed person" is "the person who is potentially at risk of acquiring HIV infection due to exposure".[1]

"Source person" is "the person either identified or unidentified, who is the possible source of contamination through blood or potentially infectious body fluids". The source can be a patient or a perpetrator in the case of sexual assault.[1]

Who Get PEP from National AIDS Control Program PEP Services?

Those with occupational exposure and victims of sexual assault are provided with PEP. Those with unsafe sexual behavior or high risk of exposure are not given these services.[1]

What is the Risk of Exposure with Different Body Fluids? (Table 1)

Table 1: Exposure risk with different body fluids[1]

At risk	*Not at risk (should not have visible blood)*
Blood	Tears
Semen	Sweat
Vaginal secretions	Urine, feces
Cerebrospinal fluid	Saliva
Synovial, pleural, peritoneal, pericardial fluid	Sputum
Amniotic fluid	Vomitus
Other body fluids contaminated with visible blood	

What is the Risk of Exposure Based on Different Routes?

Transmission of HIV infection after human bites are rare (Table 2).[1]

Table 2: Risk exposure based on different routes[1]

Route of exposure	*Rate of transmission with HIV (%)*
Blood transfusion	90–95
Sexual intercourse	0.1–10
Vaginal	0.05–0.1
Anal	0.065–0.5
Oral	0.005–0.01
Needle stick exposure	0.35
Mucous membrane splash to eye, oronasal	0.09

What are the Practices Increasing the Risk of Occupational Exposure?

- The most important is recapping needles
- Body fluids being transferred between containers
- Passing or handling needles/sharps after use
- Not disposing needles in puncture proof containers
- Inefficient management of healthcare waste.[1]

How to Manage an Exposed Person Immediately after the Exposure?

Management of exposure site—FIRST AID

- Skin:
  - Immediately wash with soap water and soap and rinse.
  - The cut/pricked finger should not be put into the mouth—a childhood reflex.
  - Scrubbing should not be done.
  - Antiseptics, such as bleach, alcohol, chlorine, bleach should not be used.
- Intact skin:
  - To be washed immediately.
  - Not to use antiseptics.
- Eye:
  - Water/physiological saline are used for irrigation of the eye. If a contact lens is worn, it should not be removed while irrigating as it acts as a barrier. The contact lens can be reused after cleaning it in the normal manner.
  - Soap or disinfectant should not be used on the eye.
- Mouth:
  - It should be spat out immediately.
  - Rinse repeatedly for several times with water or saline and spit out.
  - Soap/disinfectant should not be used.

Consult the physician or the infection control team to manage the exposure immediately.[1]

How to Establish if the Person Needs PEP?

Establish the eligibility of PEP-eligibility assessment

A designated person/trained doctor has to assess the risk of HIV exposure rapidly to decide on the initiation of short-term ART immediately.

The first dose of ART is started within 2 hours, at least within first 72 hours and the risk is evaluated. If the risk is insignificant then the PEP can be discontinued. Postexposure prophylaxis is not effective when given more than 72 hours of exposure.

- Assessing the nature of exposure and risk of transmission (Table 3).

Table 3: Exposure categories[1]

Category of exposure	*Definition*
Mild exposure	Small volume exposure of mucous membrane/ nonintact skin, e.g., erosion of epidermis with low caliber needle, subcutaneous injection with low caliber needle
Moderate exposure	Large volume exposure of mucous membrane/ nonintact skin, e.g., percutaneous superficial exposure with solid needle, needle stick injury penetrating gloves
Severe exposure	Percutaneous exposure with large volume, e.g., accident with high caliber needle (>18 G) contaminated with blood, material previously used intravenously/intra-arterially.

If the discarded sharp contaminated with at risk body fluid beyond 48 hours, the risk of infection by HIV is negligible, unlike Hep B.

- Assessing the HIV status of the source.

The source of the exposed is tested for HIV by rapid test, but PEP is not delayed waiting for the results (Table 4).

Table 4: Source categories[1]

Source HIV status	*Definition of risk of source*
HIV negative	Not HIV infected but consider HBV, HCV
Low risk	HIV positive, clinically asymptomatic
High risk	HIV positive, clinically symptomatic
Unknown	The blood of neither the patient nor his/her blood is available for testing (e.g., the source patient might be unknown when the injury is during medical waste management)
	Here risk assessment is based only upon the type of exposure and HIV prevalence in the area

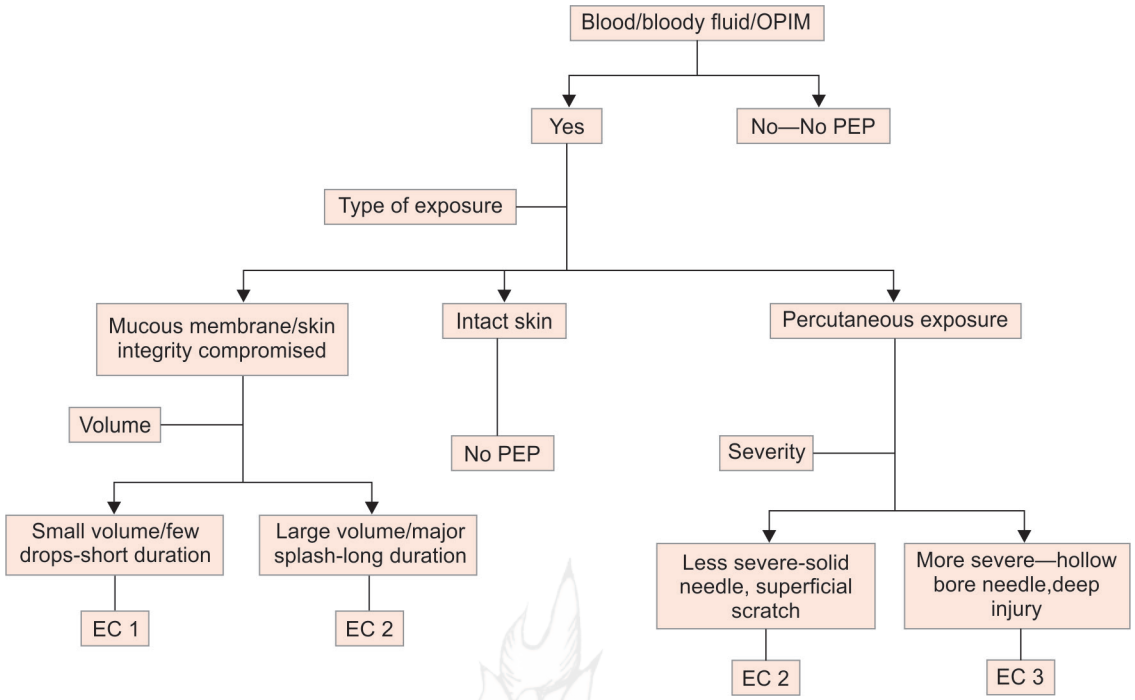
A negative HIV test does not detect the window period and hence does not exclude HIV infection.

- Assessing the exposed individual.

Assessed for preexisting HIV infection. If the person is HIV positive, then he/she should not receive PEP.

- The decision for need for PEP for HIV depends on exposure code and source code[1] (Flowcharts 1 and 2).

Flowchart 1: HIV exposure codes[1]



OPIM, Other potentially infected material

Flowchart 2: HIV source codes (Table 5)[1]

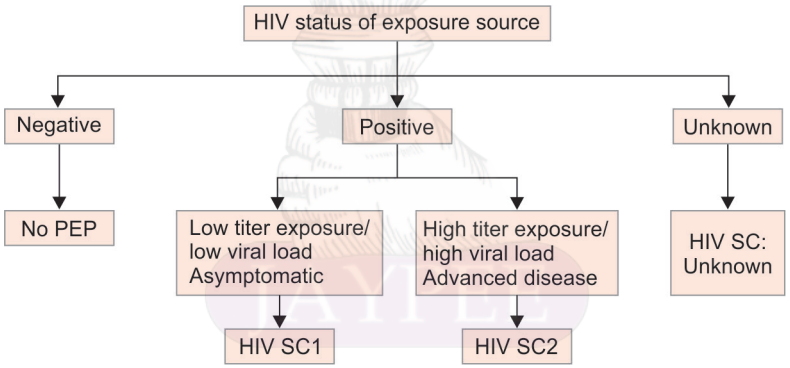


Table 5: NACO recommendations of PEP for HCP based on source and exposure codes[1]

Exposure code	*Source code*	*PEP recommendation*	*Duration*
1	1	Not recommended	–
1	2	Recommended	28 days
2	1	Recommended	28 days
2	2	Recommended	28 days
3	1 or 2	Recommended	28 days
2 or 3	Unknown	Recommended in population with high HIV prevalence and based on risk categorization	28 days

What are the Prerequisites before Starting PEP in an Eligible Exposed Individual?

Counseling for PEP

Information should be given regarding what is PEP, its risk and benefits, understand what is window period, baseline test, drugs that are used, and their adverse effects. It should be made clear that PEP is not mandatory. Also, counseling should be given on safe sexual practices until baseline and 3-month HIV tests are negative. Adequate counseling should be given on adherence and follow-up protocol. It should also be informed to the exposed person that PEP reduce the risk of transmission substantially, but a small risk of transmission exits in spite of prompt completion of prescribed PEP.

Adherence information is essential with psychological support. More than 95%, adherence is important to maximize

efficacy of medication in PEP. Enhanced adherence counseling is recommended for those initiated on PEP.

The decision to start PEP should not be delayed by HIV testing/assessment of the source patient.[1,3]

How to Choose the Regimen for PEP?

Postexposure prophylaxis has to be started as soon as possible, preferably within 2 hours. There is little benefit if started after 72 hours of exposure. This recommendation is based on very low-quality evidence based on animal studies and best practices, hence for the benefit of HCW, PEP can be initiated after 72 hours if HCW presents late.[4]

Never delay the start of PEP by debating over the regimen. The available three-drug regimen can be started and then opinion can be sought regarding the regimen (Table 6).[1]

Table 6: Drug regimens for PEP

Dosages and drugs	*Recommendations*	*Alternate*
PEP for adults		
TDF 300 mg + 3TC 300 mg	1 tab (FDC) OD in morning/night	
Lopinavir 200 mg + ritonavir 50 mg	2 tab (FDC) BD	Efavirenz 600 mg 1 tab OD
PEP for pediatric age group		
AZT + 3TC	As per weight band	ABC if AZT is contraindicated
Lopinavir + ritonavir	As per weight band	Efavirenz in >3 years/>10 kg

According to the World Health Organization and National AIDS Control Organization recommendation, tenofovir disoproxil fumarate (TDF) + lamivudine (3TC) is the preferred backbone in adults and adolescents but for children <10 years, ZDV + 3TC is the backbone that has to be used.[3] TDF + 3TC is better than regimens with zidovudine (ZDV) because of fewer newer infections and discontinuation due to adverse events.[5] Though TDF can cause bone toxicity in children, these adverse events need not be considered because in PEP, TDF is used for short-term. TDF is also approved by the US Food and Drug Administration for children aged ≥2 years but TDF is not available in pediatric formulation.[6] Among people with chronic HBV infection, TDF can cause hepatic flare after PEP discontinuation and this has to be monitored.[7,8]

Though efavirenz (EFV) is widely available and inexpensive, it is associated with early neuropsychiatric events in HIV-negative individuals who may have anxiety regarding their HIV exposure and the rate of adherence is poor when used in PEP. Since EFV is widely used as first-line ART in the country, the chances of EFV-resistant virus are high. Hence, the recommended third drug is lopinavir/ritonavir.[2]

Lopinavir/ritonavir is the third drug which is recommended in all age groups.[4] Integrase inhibitors, such as raltegravir have better adherence and completion rates and is preferred among well-resourced countries but it is more expensive with limited availability in resource-limited settings.[5]

The first dose is initiated as per the above guidelines in a case of highly treatment-experienced sources. Centres of Excellence/antiretroviral therapy plus center gives the expert opinion regarding the appropriate regimen for these exposures.

The PEP must be taken for 4 weeks. Drugs of PEP have a shelf life of 1–1.5 years. Easy availability and continuous accessibility for PEP drugs should be ensured for the HCW in emergency department, labor room, and ICU.[1]

What are the Lab Investigations (Flowchart 3) Recommended before Initiation of PEP?

HIV, HCV, and anti-HbS have to be tested within 6 days of exposure to know the baseline status. The positive predictive of HIV RNA testing by PCR is poor during PEP and hence not recommended.[1]

How to Follow-up an Exposed Person?

Follow-up is required to monitor infections and psychological support even in those exposed persons not on PEP.

Clinical Monitoring

- For acute seroconversion illness.
  - Appearance of signs, such as acute fever, generalized lymphadenopathy, cutaneous eruptions, pharyngitis, nonspecific flu, ulcers of mouth, and genital area. They appear in 50–70% of exposed individuals within 3–6 weeks after exposure.
  - A referral to ART center is done if suspected.
- Avoid.
  - Blood donation.
  - Breastfeeding for 6–12 weeks after exposure.[9]
  - Unprotected sexual relations/pregnancy.

Secondary transmission has to be prevented, especially during first 3 months after exposure.

- To use precautions.
- Condoms protection
- Adherence and adverse drug reaction counseling, monitoring with laboratory tests.
- Laboratory follow-up.
  - HIV test after PEP at 3 months and 6 months. Very few cases seroconvert after 6 months (Table 7).[1]

Flowchart 3: Lab investigations

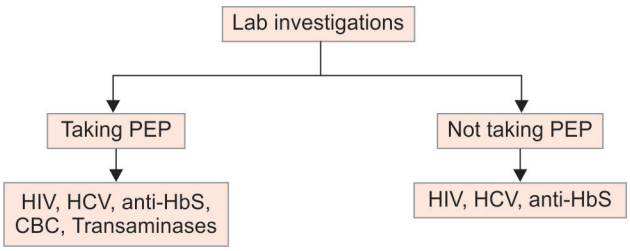
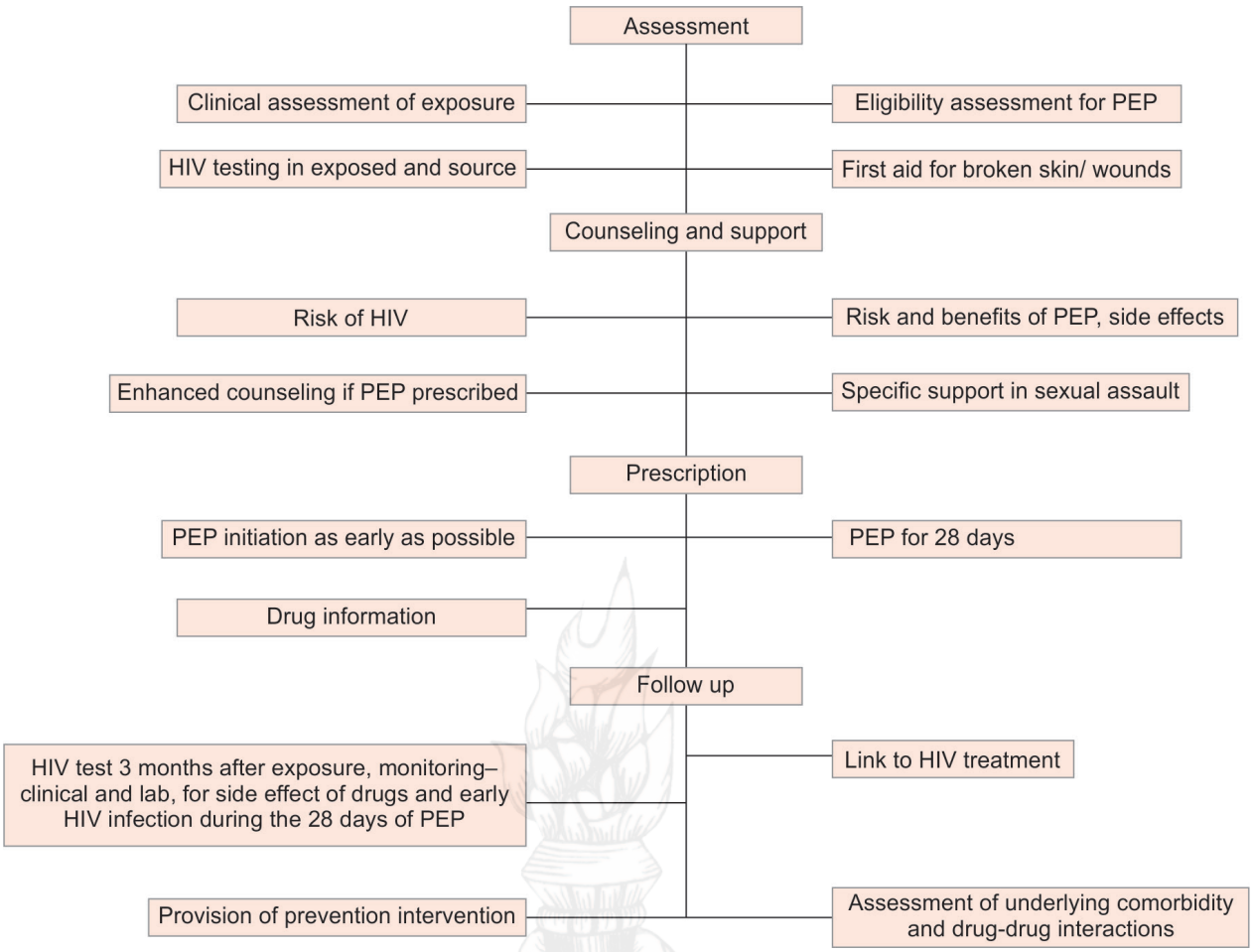


Table 7: Minimum lab follow up in an individual on PEP regime for HIV[1]

Timings	*Tests*
Weeks 2 and 4	CBC (for those on AZT)
Week 6	HIV-Ab
Week 12	HIV-Ab
Week 24	HIV-Ab

Flowchart 4: Summary of care pathway for PEP



What are the factors which Influence the Efficacy of PEP?

Postexposure prophylaxis is not 100% effective in preventing the acquisition of HIV. The factors that influence the effectiveness are:

- Time of starting PEP.
- Adherence and completion to PEP regime.
- Drug resistance in the source.
- Penetration of drugs into tissue compartments.
- Type of exposure.[3]

Is the PEP Same for a Pregnant HCW?

It is similar to the PEP provided for other exposed HCW. The potential benefits and adverse effects of ART for both mother and fetus has to be discussed in detail with the woman and informed decision has been taken regarding the initiation of postexposure treatment in pregnancy. Certain drugs, such as EFV, stavudine, didanosine, and indinavir have to be avoided during pregnancy because of their teratogenic potential. They may cause lactic acidosis or hyperbilirubinemia in newborns. A three drug regimen consisting of integrase inhibitors with nucleoside reverse transcriptase inhibitors, and a nonnucleoside inhibitor of reverse transcriptase or protease inhibitor is usually preferred. The recommended PEP regimen is emtricitabine with tenofovir, which can be taken as a single tablet (the first generic fixed-dose combination of emtricitabine (200 mg) and tenofovir alafenamide (25 mg)–Tafero–em was launched in India in February 2018) once a day supplemented with raltegravir 400 mg two times daily.[9,10]

Care pathway for PEP is summarized in Flowchart 4.

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