Primary prevention i.e. preventing exposure to Human immunodeficiency virus (HIV) is by far the most effective mechanism of preventing infection in community as well as in occupational settings. However, when exposure does occur, administration of antiretroviral agents for secondary prevention may be required. Although there have been lot of developments about our knowledge on management of occupational exposures but several issues relating to post-exposure prophylaxis still remain resolved. This chapter reviews the current understanding of different aspects of occupation exposure to HIV, its epidemiology, pathogenesis and management.

Recent studies on Pre-exposure prophylaxis have added another exciting dimension to the management of exposure and prevention of HIV. Pre exposure prophylaxis (PrEP) is a novel approach to HIV prevention in which antiretroviral agents are used by an individual prior to potential HIV exposure to reduce the likelihood of infection. PrEP should be distinguished from Post exposure prophylaxis (PEP) in which an individual takes antiretroviral drugs soon after a potential exposure with the goal of reducing the likelihood of infection.

**PATHOGENESIS OF HIV INFECTION**

The exact mechanism of pathogenesis of initial infection has not been firmly established, but the dendritic cells in skin or mucous membrane appear to be the first cell to interact with HIV. Dendritic cells can trap HIV through surface ligands and then transfer virus to susceptible CD4+ T-Lymphocytes.

Theoretically any intervention that can block transfer of HIV from dendritic cells to susceptible CD4+ T-Lymphocytes, can possibly prevent acute infection. Thus based on our understanding of the early events of pathogenesis, the initiation of antiretroviral chemoprophylaxis soon after exposure and body’s cellular immune response may prevent or inhibit systemic HIV infection. The fundamental principle of PEP is actually to limit the proliferation of virus in early stages of infection during a “window of opportunity” during which virus remain localized.

**EXPOSURES PRESENTING A RISK FOR TRANSMISSION**

Most occupational infections have resulted from parenteral or percutaneous exposure to blood from a person known to be infected with HIV. Of the 56 cases reported to CDC, 48 resulted from parenteral exposure and 5 from mucosal exposures and 2 occurred in individuals who sustained both mucous membranes and parenteral exposures; one had an Unknown route of exposure. Other than blood, semen, vaginal secretions, cerebrospinal fluid, synovial, pleural, peritoneal, pericardial and amniotic fluids are potentially infectious for HIV. It should be noted following body secretions are not considered infectious to HIV unless visibly bloody. These secretions are: saliva, sputum, vomitus, tears, sweat, nasal secretions, urine and feces.

The average risk of acquiring HIV infection after different types of occupational exposure is:

<table>
<thead>
<tr>
<th>Exposure Type</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small amount of blood on intact skin</td>
<td>No risk</td>
</tr>
<tr>
<td>Risk with damaged skin/prolonged exposure</td>
<td>1 in 1000</td>
</tr>
<tr>
<td>Exposure on eyes, nose or mouth</td>
<td>1 in 1000</td>
</tr>
<tr>
<td>Needle stick/other sharp injuries</td>
<td>1 in 300</td>
</tr>
</tbody>
</table>

Risk from all “exposures” increases further if exposure involves a large volume of blood or a higher amount of HIV in patients with acute HIV infection or AIDS or patients near death.
Measures to Decrease the Risk of Exposure to HIV

Universal precautions are simple infection control measures that reduce the risk of transmission of blood borne pathogens through exposure to blood or body fluids among patients and health care workers. Under the “universal precaution” principle, blood and body fluids from all persons should be considered as potentially infectious with HIV, regardless of the known or supposed status of the person. Improving the safety of injections is an important component of universal precautions.

Importance of Universal Precautions

Percutaneous or permucosal exposures to blood or body fluids represent a potential source of HIV infection. These include skin-piercing procedures with contaminated objects and exposures of broken skin, open wounds, cuts and mucosal membranes (mouth or eyes) to the blood or body fluid of an infected person.

Although they account for a minority of HIV infections, health care procedures represent a highly preventable source of HIV infection. Among health care associated sources of infection, unsafe injections are of particular concern, accounting for an estimated 3.9% to 7.0% of new infections worldwide.

Health care worker protection is an essential component of any strategy to prevent discrimination against HIV infected patients by health care workers. If health care workers feel they can protect themselves from HIV infection, they can provide better care.

UNIVERSAL PRECAUTIONS

Protective Barriers

Whenever exposure to blood/other potentially infected fluids is anticipated, protective barriers must be used.

Latex gloves must be worn while carrying out any procedure and be decontaminated after each use. Gloves with holes/tears should not be used. Double gloves are not preferred as these are not more protective than single glove and this may be more clumsy also. Heavy-duty rubber gloves should be used for cleaning instruments, handling soiled linen or spills of blood/body fluids. These can be washed and reused.

Gowns and aprons protect one from splashes of blood or body fluids, e.g. during surgery/delivery. One may wear a waterproof gown or a sterile cloth with a plastic apron underneath. Protective eyewear (swimming goggles) may be used to prevent transmission by splash of fluids to the mucous membrane.

Safe Handling of Sharps

- Careful handling of hollow bore needle is very essential as it may lead to deep injuries
- The needles should never be recapped. In situations where recapping is essential, single hand method should be used
- Needles should never be bent or broken by hand
- Needles should not be left on trolleys and beds and must be disposed off immediately
- Never pass used sharps from one person to another directly
- Use forceps instead of fingers for guiding sutures
- The sharps should be disposed off in a puncture resistant container containing bleach.

Single-use disposable injection equipment for all injections is highly recommended.

Document the quality of the sterilization for all medical equipment used for percutaneous procedures.

Fig. 1: Say no to recapping

Fig. 2: Sharp instrument should be kept in a kidney tray and handed over to surgeon
Disinfect instruments and other contaminated equipment.

Handle properly soiled linen. (Soiled linen should be handled as little as possible. Gloves and leak proof bags should be used if necessary. Cleaning should occur outside patient areas, using detergent and hot water.

ENSURING UNIVERSAL PRECAUTIONS

Understanding of Universal Precautions by HCWs

Health care workers should be educated about occupational risks and should understand the need to use universal precautions with all patients, at all times, regardless of diagnosis. Regular in-service training should be provided for all medical and non-medical personnel in health care settings.

Reduce Unnecessary Procedures

Reduce the supply of unnecessary procedures: Health care workers need to be trained to avoid unnecessary blood transfusions (e.g., using volume replacement solutions), injections (e.g., prescribing oral equivalents), suturing (e.g. episiotomies) and other invasive procedures. Standard treatment guidelines should include the use of oral medications whenever possible.

Make Adequate Supplies Available

Adequate supplies should be made available to comply with basic infection control standards, even in resource constrained settings. Provision of single use, disposable injection equipment matching deliveries of injectable substances, disinfectants and “sharps” containers should be the norm in all health care settings. Attention should also be paid to protective equipment and water supplies.

Use of sterilizable injection equipment should be discouraged, as evidence shows that the adequacy of the sterilization is difficult to ensure.

Institutional guidelines for universal precautions should be in place. The necessary supplies (e.g., oral medications, needles and syringes, sharps containers, disinfectant, antiretrovirals) must be made available. Health care waste management may require the construction of adapted waste treatment options (e.g., incinerators and alternatives to incineration).

Ensure Adherence to Universal Precautions

Although most of the health care workers are aware about universal precautions but they are not followed in usual day to day practice, may be due to inadequate facilities. Sometimes even when the facilities are available, there is a certain degree of inertia and complacency among doctors and other health care workers towards universal precautions. So, concept of universal precautions has to be put to actual use once again, in this era of emerging and re-emerging infections.

Prevention is the mainstay of strategy to avoid occupational exposure to HIV. Universal precautions must be practiced by all the health care workers at all the places, all the times.

RATIONALE FOR ADMINISTERING PEP

Epidemiologic Studies

In a retrospective case-control study by CDC, five factors were identified as being associated with infection following occupational exposure: the depth or severity of exposure, the presence of visible blood on the devise causing injury; the fact that the devise causing injury was in source patient’s vein or arteries; and exposure to blood from a source patient who died within 60 days of exposure. The fifth factor was not “not taking zidovudine as PEP”. This study provided indirect evidence for concept for effectiveness of PEP.

Clinical Studies

All studies which prove that administration of antiretroviral treatment can prevent vertical transmission of HIV provide additional rationale for using these drugs for PEP.

Also studies demonstrating that administration of antiretroviral agents to newborn infants, shortly after birth significantly reduces the risk of infection for newborn, when mother was not given antiretroviral treatment before or during labor. This was the first prospective clinical trial to demonstrate the efficacy of PEP in humans.

Animal Studies

In animal studies using macaques SIV tenofovir model, investigators found that all macaques that received treatment after inoculation for 28 days were protected, whereas only half of macaques treated for 10 days and none treated for 3 days remained infection free. Early initiation of treatment was also highlighted in these studies, whereas 100% of macaques that receives tenofovir within 24 hours of intravenous inoculation of SIV remain uninfected, only 50% of animal that received the first dose of the agent 48 hours following infection and only 25% of animals that received the first dose of
treatment at 72 hours after inoculation remained uninfected. In a study of similar design evaluating prophylaxis following vaginal inoculation of macaques with HIV-2; Otten and coworkers found similar results, with all the animals treated within 48 hours remaining uninfected. Breakthrough infections occurred in animals receiving tenofovir at 72 hours following inoculation.

POST-EXPOSURE PROPHYLAXIS (PEP) FOLLOWING NEEDLE STICK INJURY (Flow Chart 1)

Needle Stick Injury

The needle stick injury is defined as a penetrating injury wound from a needle (or other sharp objects like scalpel, broken glass vial etc) that may result in exposure to blood or other body fluids.

Exposure Reporting

First step in managing exposure is to ensure reporting. It should be accurate and prompt. Usually there is underreporting of exposure to blood by health care workers. After reporting of exposure arrangement should be made for follow up care of exposed. Confidentiality of exposed worker must be protected. Proper pre test and post test counseling should be offered to HCW.

Management of Exposure Site

This should be treated as medical emergency and treatment should begin at the earliest possibly, preferably within 2 hours. Exposure site should be decontaminated as soon as possible. Puncture and other cutaneous injuries should be washed with soap and water. Do not try to squeeze the blood out because it can push the blood and inoculum towards systemic circulation. Mucosal exposures involving mouth and nose should be flushed with water. Following an ocular exposure, eyes should be irrigated with clean water, saline or sterile irrigants designed for this purpose.

CLINICAL EVALUATION

Assessment of Exposure and Source Patient

Detailed assessment of exposure incident and thorough evaluation of source patient should be carried out. Medical records of source patient should be reviewed for relevant medical and serological information. If source patient’s status with respect to HIV is not known, the relevant test should be carried with all protocols after pre test and post test counseling. Because of evidence suggesting that early initiation of prophylaxis is important serological testing should be carried out by competent personnel. Rapid testing should be confirmed by enzyme immunoassay as soon as possible.

If results are not immediately available or results are awaited and exposure has occur, the best strategy is to begin prophylaxis immediately and either discontinue or modify regimen when results of test are available.

In case source patient is known to be HIV infected then all information about patient which include time since patient is infected, CD4+ counts, viral load assays and detailed history about past and current antiretroviral therapy should be obtained.

If source patient’s serological status is unknown and can’t be learned, detailed epidemiological assessment of exposure should be made and expert consultation should be taken.

Initial Assessment of Exposed

The detailed history of exposure incident should be obtained. The treating physician should be able to provide detailed supportive counseling to the exposed person about:

1. Risk associated with exposure
2. Epidemiology and transmissibility of HIV
3. Magnitude of risk for occupational infection associated with similar exposure
4. Importance of returning for follow up evaluation and care
5. The planned management programme
6. Importance of adherence to planned regimen
7. Side effects associated with post exposure antiretroviral chemoprophylaxis and strategies use to manage side effects
8. Protocols to protect the confidentiality and medical privacy of exposed personnel.

Baseline evaluation of exposed should be done as soon as after the exposure for HIV by antibody testing and follow up additional testing for HIV antibody should be done at 6 weeks, 12 weeks and 6 months following exposure.

SELECTING A CHEMOPROPHYLAXIS REGIMEN

A number of antiretroviral agents have been used for post exposure prophylaxis. CDC guidelines recommend a “basic” two drug regimes, the preferred regimen are as:

1. Zidovudine plus lamivudine
2. Tenofovir plus lamivudine

Other alternative “basic” two drug regimen recommended are:

1. Stavudine plus lamivudine
2. Didanosine plus lamivudine

For exposure ascertained with an increased risk for exposure i.e. from large bore hollow needle exposure, deep puncture wounds, exposure to needle that had been in artery or vein and exposure to blood from source patients who have symptomatic HIV infection, AIDS, the primary HIV infection or known high viral loads CDC recommends a three drug “expanded” regimen.

The recommended three drug “expanded” regimen consists of a two drug “basic” regimen plus one of the following agents:

1. Lopinavir + ritonavir (preferred)
2. Indinavir ± ritonavir (avoid in late pregnancy)
3. Atazanavir ± ritonavir (must be boosted, if tenofovir used in basic regimen)
4. Saquinavir + ritonavir
5. Nelfinavir
6. Efavirenz (teratogenic; avoid in pregnancy)

A variety of other regimens have been used, particularly in settings in which the source patient for an exposure has extensive antiretroviral experience and in instances in which antiretroviral resistance is known or highly suspected. In those cases prophylaxis should be initiated under expert consultation. There are certain drugs which are not generally recommended for PEP these are: Nevirapine, abacavir, delavirdine and zalcitabine.

ADHERENCE TO PROPHYLAXIS REGIMEN

Adherence to prophylaxis regimen is of utmost importance. All strategies should be undertaken to increase adherence and or to ensure complete adherence. This includes counseling of individual on seriousness of exposure, effectiveness of PEP regimen, need for 100% adherence and regular follow up for management of toxicities if encountered.

Recommended HIV postexposure prophylaxis (PEP) for percutaneous injuries (Table 1).

Duration of Post Exposure Prophylaxis Regimen

The optimal course of treatment is unknown; since it has been observed in clinical and animal studies that 4 weeks of Post exposure treatment appears to provide protection against HIV infection, treatment should probably be taken for 4 weeks.

Follow-up

Serological tests for HIV for exposed person should be done at base line, 6 weeks, 3 months and 6 months with proper pre test and post test counseling. Although viral load or polymerase chain reaction testing is not recommended routinely but they may be considered in special situations (i.e. diagnosis of acute retroviral illness). Person receiving prophylaxis should follow up with the clinician at least once in a week and more frequently if side effects are encountered. He should be advised to refrain from donating blood, semen or organs/tissues and abstain from sexual intercourse. In case sexual intercourse is undertaken by exposed person a latex condom to be used consistently. In addition, women health care personnel should not breast-feed their infants during the follow up period.

Recommended HIV postexposure prophylaxis (PEP) for mucous membrane exposures and nonintact skin exposures (Table 2).

Side Effects/Toxicity

Generally it is presumed since PEP is a short term (4 weeks) course of ARVs, side effects might be less of a problem than long term therapy of HIV infection. Unfortunately this assumption is incorrect. As many as three-fourths of health worker who take post exposure prophylaxis, experience substantive treatment associated side effects. In almost all reported studies at least 50% of individual taking PEP experience side effects. Antiretroviral drugs have a potential to produce substantial toxicity.
Common side-effects of nucleoside/nucleotide analogues used for post exposure prophylaxis include bone marrow suppression, nausea, vomiting, diarrhea, abdominal pain, headache, myalgias, lassitude, malaise and insomnia.

Addition of protease inhibitors to the post exposure prophylaxis regimen is associated with increased in side effects noted for the nucleoside analogues e.g. nausea, vomiting, diarrhea, headache, abdominal pain) as well as anorexia, hyperlipidemia, hyperglycemia and worsening of pre existing diabetes.

As many of common side effects associated with PEP can be anticipated, the clinician who provides post exposure prophylaxis can counsel person taking prophylaxis about these side effects and can manage these toxicities accordingly to ensure completion of desired treatment course.

Tolerability of HIV PEP in Health Care Workers\(^\text{12}\) (Fig. 3).

<table>
<thead>
<tr>
<th>Exposure type</th>
<th>HIV-positive, class 1*</th>
<th>HIV-positive, class 2*</th>
<th>Source of unknown HIV status</th>
<th>Unknown source(^\text{5})</th>
<th>HIV-negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less severe(^\text{6})</td>
<td>Recommend basic 2-drug PEP</td>
<td>Recommend expanded ≥ 3-drug PEP</td>
<td>Generally, no PEP warranted: however, consider basic 2-drug PEP** for source with HIV risk factors(^\text{11})</td>
<td>Generally, no PEP warranted: however, consider basic 2-drug PEP** in setting in which exposure to HIV-infected persons is likely</td>
<td>No PEP warranted</td>
</tr>
<tr>
<td>More severe(^\text{55})</td>
<td>Recommend expanded 3-drug PEP</td>
<td>Recommend expanded ≥ 3-drug PEP</td>
<td>Generally, no PEP warranted: however, consider basic 2-drug PEP** for source with HIV risk factors(^\text{11})</td>
<td>Generally, no PEP warranted: however, consider basic 2-drug PEP** in setting in which exposure to HIV-infected persons is likely</td>
<td>No PEP warranted</td>
</tr>
</tbody>
</table>

* HIV-positive, class 1—asymptomatic HIV infection or known low viral load (e.g. < 1,500 ribonucleic acid copies/mL). HIV-positive, class 2—symptomatic HIV infection, acquired immunodeficiency syndrome, acute seroconversion, or known high viral load. If drug resistance is a concern, obtain expert consultation. Initiation of PEP should not be delayed pending expert consultation, and because expert consultation alone cannot substitute for face-to-face counseling, resources should be available to provide immediate evaluation and follow-up care for all exposures.

\(^\text{1}\) For example, deceased source person with no samples available for HIV testing.

\(^\text{2}\) For example, a needle from a sharps disposal container.

\(^\text{3}\) For example, solid needle or superficial injury.

\(^\text{4}\) The recommendation “consider PEP” indicates that PEP is optional; a decision to initiate PEP should be based on a discussion between the exposed person and the treating clinician regarding the risks versus benefits of PEP.

\(^\text{5}\) If PEP is offered and administered and the source is later determined to be HIV-negative, PEP should be discontinued.

\(^\text{6}\) For example, large-bore hollow needle, deep puncture, visible blood and device, or needle used in patient's artery or vein.

(Source: CDC prevention recommendations for PEP for mucous membranes and nonintact skin exposures to HIV)\(^\text{10}\)

**Advisability of Expert Consultation**

It is seen in many instances that PEP is frequently advised by clinicians who are not very familiar with all the aspects of this subject. A properly trained experienced consultant is often best suited to probe whether an exposure had occurred or not, then to select number of agents to be administered, and to help tailor a regimen specifically for unique situation. If one prescribes a multiple-drug regimen so toxic that individual cannot take it, the purpose of prophylaxis is defeated. There are some special cases which should be particularly managed by an expert only e.g. management of exposure if source patient has experience with antiretroviral agents\(^\text{11}\); management of exposure if reporting was delayed; and management of exposure in a pregnancy\(^\text{1}\).

In developed countries there are 24 hours operating telephone PEP help lines which offer consultations and advise by experts about all the issues relating to post
exposure prophylaxis. There is dire need of such help line for effective and timely management of post exposure prophylaxis to HIV occurring among health care workers in our country also.

### Table 2: Recommended HIV postexposure prophylaxis (PEP) for mucous membrane exposures and nonintact skin* exposures

<table>
<thead>
<tr>
<th>Exposure type</th>
<th>HIV-positive, class 1†</th>
<th>HIV-positive, class 2†</th>
<th>Source of unknown HIV status§</th>
<th>Unknown source§§</th>
<th>HIV-negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small volume**</td>
<td>Consider basic 2-drug PEP††</td>
<td>Recommend basic 2-drug PEP</td>
<td>Generally, no PEP warranted§§</td>
<td>Generally, no PEP warranted</td>
<td>No PEP warranted</td>
</tr>
<tr>
<td>Large volume¶¶</td>
<td>Recommend basic 2-drug PEP</td>
<td>Recommend expanded ≥ 3-drug PEP</td>
<td>Generally, no PEP warranted: however, consider basic 2-drug PEP†† for source with HIV risk factors§§</td>
<td>Generally, no PEP warranted: however, consider basic 2-drug PEP†† in settings in which exposure to HIV-infected persons is likely</td>
<td>No PEP warranted</td>
</tr>
</tbody>
</table>

* For skin exposures, follow-up is indicated only if evidence exists of compromised skin integrity (e.g. dermatitis, abrasion, or open wound).
† HIV-positive, class 1—asymptomatic HIV infection or known low viral load (e.g., < 1,500 ribonucleic acid copies/mL), HIV-positive, class 2—symptomatic HIV infection, AIDS, acute seroconversion, or known high viral load. If drug resistance is a concern, obtain expert consultation. Initiation of PEP should not be delayed pending expert consultation, and because expert consultation alone cannot substitute for face-to-face counseling, resources should be available to provide immediate evaluation and follow-up care for all exposures.
§ For example, deceased source person with no samples available for HIV testing.
† For example, splash from inappropriately disposed blood.
** For example, a few drops.
†† The recommendation “consider PEP” indicates that PEP is optional; a decision to initiate PEP should be based on a discussion between the exposed person and the treating clinician regarding the risks versus benefits of PEP.
§§ If PEP is offered and administered and the source is later determined to be HIV-negative, PEP should be discontinued.
¶¶ For example, a major blood splash

( Source: CDC prevention recommendations for PEP for mucous membranes and nonintact skin exposures to HIV)

### Pre-Exposure Prophylaxis (PrEP)

Studies to evaluate the safety and/or efficacy of Pre-exposure prophylaxis in various risk population in sub-Saharan, Southeast Asia and United States are currently being planned or are going on. Trials are going on for use of tenofovir and other drugs in Pre exposure prophylaxis regimes and results are encouraging. PrEP is also evaluated for its application in health care settings.

Whether or not HIV PrEP will come to play a significant role in HIV prevention, it will largely depend on the outcome of current and future studies evaluating the safety and effectiveness of PrEP as a HIV prevention strategy. It will also rest on how acceptable such strategy if effective, is to programme planners, care providers and the public. As with all interventions, a careful risk benefit analysis would be required to determine in which context such an approach is warranted.

### REFERENCES


