CHAPTER

100

Post Exposure Prophylaxis in HIV

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Management of Exposures to HIV and Post Exposure Prophylaxis

Although preventing exposures to blood is the primary means of preventing occupationally acquired HIV infection, appropriate post exposure management is an important element of workplace safety. In January 1990, CDC issued a statement on the management of HIV exposures that included considerations for zidovudine (ZDV) use for post exposure prophylaxis (PEP). At that time, data were insufficient to assess the efficacy of ZDV. Although there are still only limited data to assess safety and efficacy, additional information is now available that is relevant to this issue and newer modifications have been released.

Who needs? In whom PEP indicated?

Health-care worker (HCW) is defined as any person (e.g., an employee, student, attending clinician, public-safety worker, or volunteer) whose activities involve contact with patients or with blood or other body fluids from patients in a health-care or laboratory setting. An "**exposure**" that may place an HCW at risk for HIV infection and therefore requires consideration of PEP is defined as a percutaneous injury (e.g., a needle stick or cut with a sharp object), contact of mucous membrane or nonintact skin (e.g., when the exposed skin is abraded, or afflicted with dermatitis), or contact with intact skin when the duration of contact is prolonged (i.e, several minutes or more) or involves an extensive area, with blood, tissue, or other body fluids. Body fluids include a) semen, vaginal secretions, or other body fluids contaminated with visible blood and b) cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids. In the absence of visible blood in the saliva, exposure to saliva from a person infected with HIV is not considered risk for transmission; also, exposure to tears, sweat, or non-bloody urine or feces does not require postexposure follow-up. Human breast milk has been implicated in perinatal transmission of HIV. However, occupational exposure to human breast milk has not been implicated in HIV transmission to HCWs.

Is there a risk at all ? What is the risk?

Prospective studies of HCWs have estimated that the average risk for HIV transmission after a percutaneous exposure to HIV-infected blood is approximately 0.3% and after a mucous membrane exposure is 0.09%. Although episodes of HIV transmission after skin exposure have been documented, the risk for transmission by this route has not been precisely quantified because

no HCW enrolled in prospective studies have seroconverted after an isolated skin exposure. The risk for transmission is less than the risk for mucous membrane exposures.

Epidemiologic and laboratory studies suggest that several factors affect the risk for HIV transmission. The one retrospective case-control study of HCWs who had percutaneous exposure to HIV found that the risk for HIV transmission was increased with exposure to a larger quantity of blood from the source patient as indicated by

a. a device visibly contaminated with the patient's blood,
b. a procedure that involved a needle placed directly in a vein or artery, or
c. a deep injury.

The risk also was increased for exposure to blood from source patients with terminal illness, possibly reflecting either the higher titer of HIV in blood late in the course of AIDS. The risk for HIV transmission from exposures that involve a larger volume of blood, particularly when the source patient's viral load is probably high, exceeds the average risk of 0.3%.

According to CDC, of those healthcare personnel for whom case investigations were completed from 1981-2006, 57 had documented seroconversion to HIV following occupational exposures (see table for occupations). The routes of exposure resulting in infection were: 48 percutaneous (puncture/cut injury); five, mucocutaneous (mucous membrane and/or skin); two, both percutaneous and mucocutaneous; and two were of unknown route. Forty-nine healthcare personnel were exposed to HIV-infected blood; three to concentrated virus in a laboratory; one to visibly bloody fluid; and four to an unspecified fluid. Majority were nurses and lab. staff, Ub personnel followed by non surgical doctors and residents.

There have been reports in the literature on occupational hazards of HIV in developing countries. One study evaluated occupational exposure to HIV in healthcare workers in South Africa. Thirteen per cent of the staff reported injuries with HIV positive patients. Registrars in training were the highest risk group (60%). Of the injuries, 94% were percutaneous and 65% occurred during emergency surgery. The commonest place of injury was the operating theater (46%) and the commonest procedure associated with accidental exposure was cesarean section (57%). Fifty-one per cent were not wearing eye protection during procedures and although 83% initiated post-exposure prophylaxis (PEP), 48% discontinued treatment due to side effects of the drugs. Occupational exposure to HIV is common in the developing world.

On the basis of, for example, a surgeon sustaining three percutaneous injuries over 12 months and not taking PEP after each, the annual risks ranged from 1 in 2,000,000 for urological/renal surgeons to 1 in 200,000 for those performing general surgery/ ENT/gynecological procedures. The administration of PEP after each injury would reduce these rates to 1 in 10,000,000 and 1 in 1,000,000 respectively.

When should we watch? Time for seroconversion

81% experienced a syndrome compatible with primary HIV infection a median of 25 days after exposure. In a recent analysis, the median interval from exposure to seroconversion was 46 days (mean: 65 days); an estimated 95% seroconverted within 6 months after the exposure. These data suggest that the time course of HIV seroconversion in HCWs is similar to that in other persons who have acquired HIV through non occupational modes of transmission.

How does it work ?

Information about primary HIV infection indicates that systemic infection does not occur immediately, leaving a brief "**window of opportunity**" during which post exposure anti retro viral intervention may modify viral replication. In a primate model of simian immunodeficiency virus (SIV) infection, infection of dendritic-like cells occurred at the site of inoculation

during the first 24 hours following mucosal exposure to cell-free virus. During the subsequent 24-48 hours, migration of these cells to regional lymph nodes occurred, and virus was detectable in the peripheral blood within 5 days. HIV replication is rapid (generation time: 2.5 days) and results in bursts of up to 5,000 viral particles from each replicating cell.

Which all drugs ?

Several antiretroviral agents are available for the treatment of HIV disease. These include the nucleoside analog reverse transcriptase inhibitors (NRTIs), nonnuceloside reverse transcriptase inhibitors (NNRTIs), and protease inhibitors (PIs). Among these drugs, ZDV is the only agent shown to prevent HIV transmission in humans. There are no data to directly support the addition of other antiretroviral drugs. However, in HIV-infected patients, combination regimens have proved superior to monotherapy regimens in reducing HIV viral load. Thus, theoretically a combination of drugs with activity at different stages in the viral replication cycle (e.g., NRTIs with a PI) could offer an additive preventive effect in PEP, particularly for occupational exposures that pose an increased risk for transmission. Guidelines for the treatment of early HIV infection recommend the use of three drugs (two NRTIs and a PI); however, the applicability of these recommendations to PEP remains unknown. In addition, the routine use of three drugs for all occupational HIV exposures may not be needed. Although the use of a highly potent regimen can be justified for exposures that pose an increased risk for transmission, it is uncertain whether the potential additional toxicity of a third drug is justified for lower-risk exposures. 3TC (Lamivudine) was recommended as a second agent for PEP based on greater antiretroviral activity of the ZDV/3TC combination and its activity against many ZDV-resistant HIV strains without substantially increased toxicity. The present options available include

1. Zidovudine (ZDV)-600 mg in divided doses (300 mg/twice a day for 4 weeks) + Lamivudine (3TC) – 150 mg twice a day for 4 weeks.
2. Zidovudine (as above) Plus Emtricitabine 200 mg capsule once each day.
3. Tenofovir (TDF) 300 mg once daily plus Lamivudine (3TC) 300 mg once daily or 150 mg twice daily.

The addition of a PI as a third drug is based on the site of activity in the replication cycle and demonstrated effectiveness in reducing viral burden. The NNRTIs have not been included in these recommended regimens for PEP. However, concerns about side effects and the availability of alternative agents argue against routinely using this class of drugs for initial PEP.

Many other combinations using other NRTIs, PIs and boosted PIs and even fusion inhibitors are being evaluated.

Are they safe ?

An important goal of PEP is to encourage and facilitate compliance with a 4-week PEP regimen. Therefore, the toxicity profile including the frequency, severity, duration, and reversibility of side effects, is a relevant consideration. All anti retroviral agents have been associated with side effects. However, studies of adverse events have been reported primarily for persons with advanced disease (and longer treatment courses) and therefore may not reflect the experience of persons with less advanced disease or those who are uninfected. Side effects associated with many of the NRTIs are chiefly gastrointestinal and in general the incidence has not been greater when these agents are used in combination. Common symptoms included nausea, vomiting, malaise or fatigue, headache, or insomnia. Mild decrease in hemoglobin and absolute neutrophil count also were observed. All side effects were reversed when PEP was discontinued.

What to do in case ?

Treatment of an Exposure Site: Wounds and skin sites that have been in contact with blood

or body fluids should be washed with soap and water; mucous membranes should be flushed with water. There is no evidence that the use of antiseptics for wound care or expressing fluid by squeezing the wound further reduces the risk for HIV transmission. However, the use of antiseptics is not contraindicated. The application of caustic agents (e.g., bleach) or disinfectants into the wound is not recommended.

Assessment of Infection Risk: After an occupational exposure, the source-person and the exposed HCW should be evaluated to determine the need for HIV PEP. Follow-up for hepatitis B and C virus infections also should be conducted.

Evaluation of exposure: The exposure should be evaluated for potential to transmit HIV based on the type of body substance involved and the route and severity of the exposure. Exposures to blood, fluid containing visible blood, or other potentially infectious fluid (including semen; vaginal secretions; and cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids) or tissue through a percutaneous injury (i.e., needlestick or other sharps-related event) or through contact with a mucous membrane are situations that pose a risk for bloodborne transmission and require further evaluation

For skin exposures, follow-up is indicated if it involves direct contact with a body fluid listed above and there is evidence of compromised skin integrity (e.g., dermatitis, abrasion, or open wound). However, if the contact is prolonged or involves a large area of intact skin, postexposure follow-up may be considered on a case-by-case basis or if requested by the HCW.

Evaluation and testing of an exposure source: The person whose blood or body fluids are the source of exposure should be evaluated for HIV infection. Information available in the medical record at the time of exposure (e.g., laboratory test results, admitting diagnosis, or past medical history) or from the source person may suggest or rule out possible HIV infection. Examples of information to consider when evaluating an exposure source for possible HIV infection include laboratory information (e.g., prior HIV testing results or results of immunologic testing {e.g., CD4+ count}), clinical symptoms (e.g., acute syndrome of primary HIV infection or undiagnosed immunodeficiency disease), and history of possible HIV exposures (e.g., injecting-drug use, unprotected sexual contact with multiple partners (heterosexual and/or homosexual), or receipt of blood or blood products.

If the source is known to have HIV infection, available information about this person's stage of infection (i.e., asymptomatic or AIDS), CD4+ T-cell count, results of viral load testing, and current and previous antiretroviral therapy, should be gathered for consideration in choosing an appropriate PEP regimen. If this information is not immediately available, and if PEP is indicated then start treatment and change regimen when appropriate.

If the HIV serostatus of the source person is unknown, the source person should be informed of the incident and with consent, tested for serologic evidence of HIV infection. Confidentiality of the source person should be maintained at all times. HIV-antibody testing of an exposure source should be performed as soon as possible. Hospitals, clinics, and other sites that manage exposed HCWs should consult their laboratories regarding the most appropriate test to expedite these results. Repeatedly reactive results by EIA (spot) or rapid HIV-antibody tests are considered highly suggestive of infection, whereas a negative result is an excellent indicator of the absence of HIV antibody. Confirmation of result by Western blot or immunofluorescent antibody is not necessary for making initial decisions about postexposure management. If the source is HIV seronegative and has no evidence of acquired immunodeficiency syndrome (AIDS) or symptoms of HIV infection, no further testing of the source is indicated. The use of source-person viral load as a surrogate measure of viral titer for assessing transmission risk has not yet been established. Plasma viral load (e.g., HIV RNA) reflects only

the level of cell-free virus in the peripheral blood; latently infected cells might transmit infection in the absence of viremia. Although a lower viral load (e.g., < 1,500 RNA copies/mL) or one that is below the limits of detection probably indicates a lower titer exposure, it does not rule out the possibility of transmission.

HIV testing of needles or other sharp instruments associated with an exposure is not recommended.

PEP must be done under expert centres/ personnel only in cases of delayed exposure reporting, unknown source, known or suspected pregnancy, breast feeding, resistance of the source virus to ARV drugs and in cases of hypersensitivity or drug reactions to first line drugs.

How to evaluate Exposed HCWs ?

Exposed HCWs should be evaluated for susceptibility to bloodborne pathogen infections. Baseline testing (i.e., testing to establish serostatus at the time of exposure) for HIV antibody should be performed. If the source person is seronegative for HIV, baseline testing or further follow-up of the HCW normally is not necessary. Serologic testing should be made available to all HCWs who are concerned that they may have been exposed to HIV.

How to explain?

Recommendations for chemoprophylaxis should be explained to HCWs who have sustained occupational HIV exposures. For exposures for which PEP is considered appropriate, HCWs should be informed that a) knowledge about the efficacy and toxicity of drugs used for PEP are limited; b) only ZDV has been shown to prevent HIV transmission in humans; c) there are no data to address whether adding other antiretroviral drugs provides any additional benefit for PEP, but experts recommend combination drug regimens because of increased potency and concerns about drug-resistant virus; d) data regarding toxicity of antiretroviral drugs in persons without HIV infection are limited for ZDV and not known regarding other antiretroviral drugs; and e) any or all drugs for PEP may be declined by the HCW. HCWs who have occupational exposures for which PEP is not recommended should be informed that the potential side effects and toxicity of taking PEP outweigh the negligible risk of transmission posed by the type of exposure.

How fast should we act ?

PEP should be initiated as soon as possible. The interval within which PEP should be started for optimal efficacy is not known. Animal studies have demonstrated the importance of starting PEP within hours after an exposure. To assure timely access to PEP, an occupational exposure should be regarded as an urgent medical concern and PEP started as soon as possible after the exposure (i.e., within a few hours rather than days. The optimal duration of PEP is unknown. Because 4 weeks of ZDV appeared protective in HCWs , PEP probably should be administered for 4 weeks, if tolerated.

How to follow up ?

HCWs with occupational exposure to HIV should receive follow-up counseling, postexposure testing, and medical evaluation regardless of whether they receive PEP. HIV-antibody testing should be performed for at least 6 months postexposure (e.g., at 6 weeks, 12 weeks, and 6 months). Exposed HCWs should be advised to seek medical evaluation for any acute illness that occurs during the follow-up period. Such an illness, particularly if characterized by fever, rash, myalgia, fatigue, malaise, or lymphadenopathy, may be indicative of acute HIV infection but also may be due to a drug reaction or another medical condition.

Exposed HCWs who choose to take PEP should be advised of the importance of completing the prescribed regimen.

Is it cost effective?

Assuming that 35% of exposures were to HIV-positive sources, the zidovudine regimen prevented 53 HIV seroconversions per 100,000 exposures,

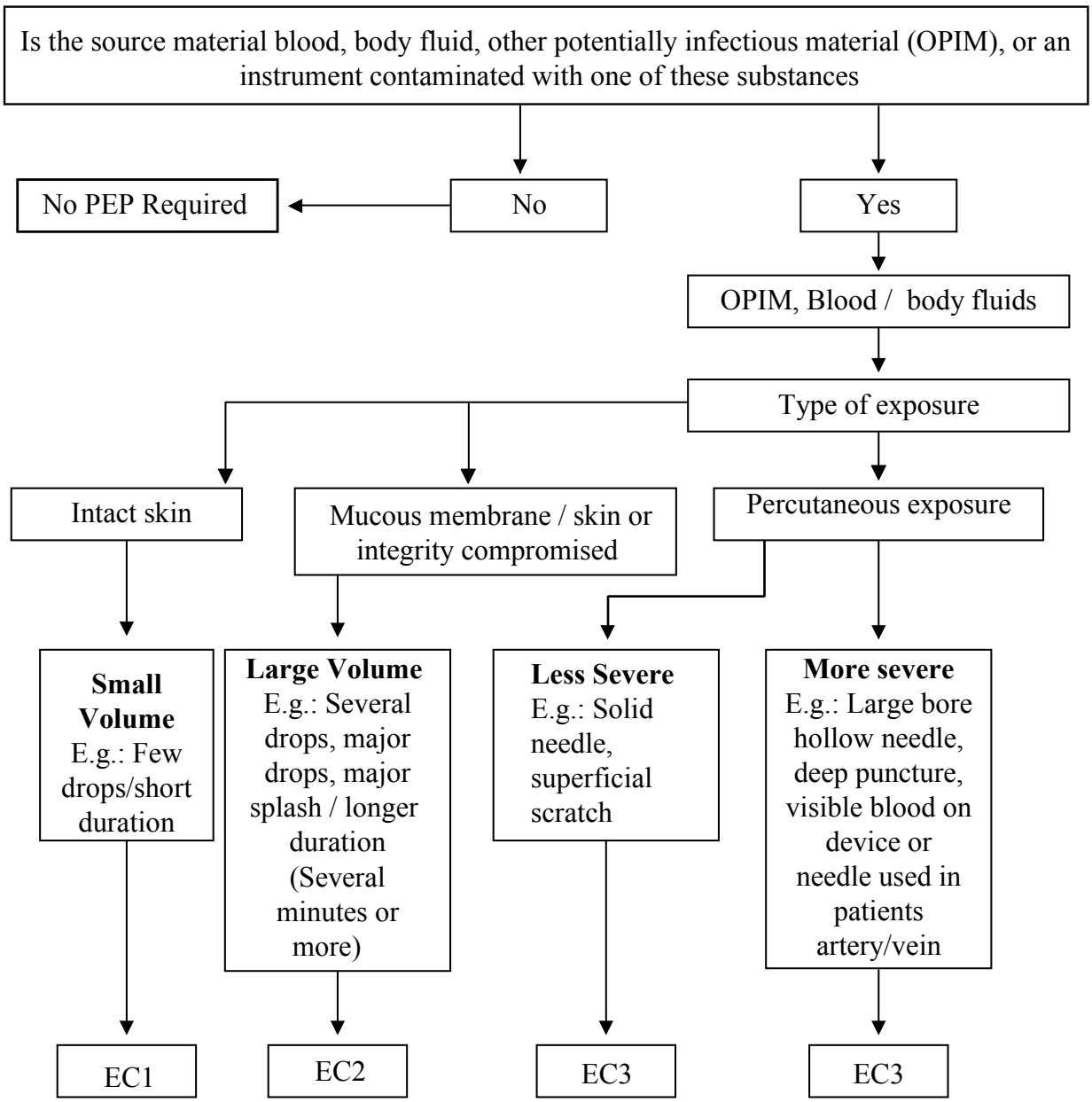
at a societal cost of $2.0 million per case of HIV prevented. The cost per quality-adjusted life year saved was $175,222. A three-drug chemoprophylactic therapy program (postulating 100% effectiveness and 35% source HIV positivity), prevented 66 seroconversions per 100,000 exposures, at a cost of $2.1 million per case of HIV prevented and $190,392 per quality-adjusted life year saved.

One course of treatment with the basic regimen costs Rs. 1000 - 1500 as per the cost of drugs in India at the time of writing this. A triple drug prophylaxis will cost around Rs.4000.

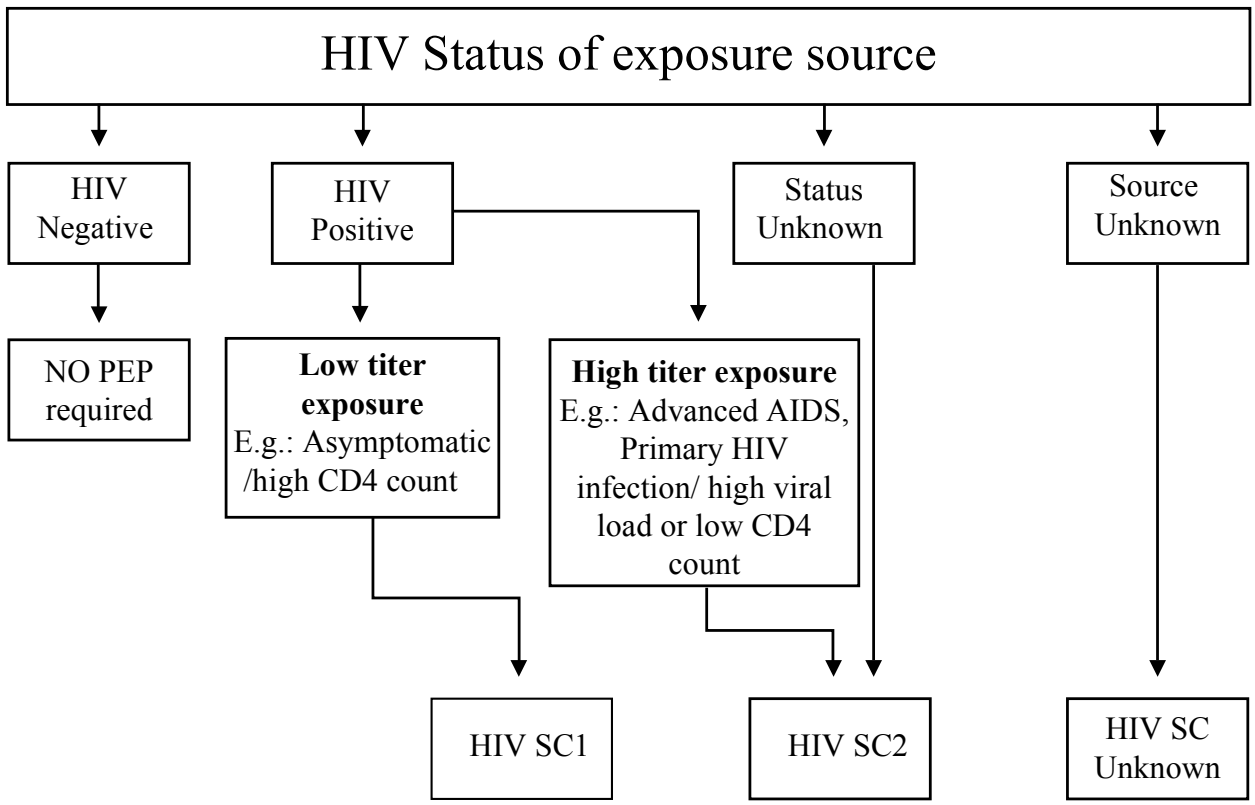
During the last few years it has become more and more likely that an immediate antiretroviral

Flow Chart for Accidental Exposure Inside Hospital

1. Determination of Exposure Code (EC)



2. Determination of HIV Status Code



3. Prophylaxis Recommendations

EC	HIV SC	PEP Recommendation
1	1	PEP may not be warranted
1	2	Consider basic regimen (Negligible risk)
2	1	Recommend Basic Regimen (most exposures are in this category)
2	2	Recommend expanded regimen
3	1 or 2	Recommend expanded regimen
2/3	Unknown	If setting suggests a possible risk (epidemiological risk factors) and EC is 2 or 3, consider basic regimen.

Basic regimen:

Option 1. Zidovudine (ZDV)-600 mg in divided doses (300 mg/twice a day or 200 mg/ thrice a day for 4 weeks + Lamivudine (3TC) – 150 mg twice a day for 4 weeks.

Option 2. Zidovudine (as above) Plus Emtricitabine 200 mg capsule once each day.

Option 3. Tenofovir (TDF) 300 mg once daily Plus Lamivudine (3TC) 300 mg once daily or 150 mg twice daily

Expanded Regimen : Basic regimen + indinavir – 800 mg/thrice a day, or any other (4 wks therapy) protease inhibitor. Or a combination of Lopinavir / ritonavir or any similar.

Source : MMWR (CDC) May 15, 1998 / 47(RR-7);1-28 & Sep. 30, 2005/ 54(RR-09) 1-17 Public Health Service Guidelines for the Management of Health-Care Worker Exposures to HIV and Recommendations for Postexposure Prophylaxis

postexposure prophylaxis can prevent at least 90% of possible infections.

Management of Possible Sexual, Injecting-Drug-Use, or Other Nonoccupational Exposure to HIV

The most effective methods for preventing human immunodeficiency virus (HIV) infection are those that protect against exposure to HIV. Preventive behaviors include sexual abstinence, sex only with an uninfected partner, consistent and correct condom use, abstinence from injecting-drug use, and consistent use of sterile equipment by those unable to cease injecting-drug use. Some health-care providers have proposed offering antiretroviral drugs to persons with unanticipated sexual or injecting-drug-use HIV exposure to prevent transmission. However, because no data exist regarding the efficacy of this therapy for persons with nonoccupational HIV exposure, it should be considered an unproven clinical intervention. Health-care providers and their patients may opt to consider using antiretroviral drugs after nonoccupational HIV exposures that carry a high risk for infection, but only after careful consideration of the potential risks and benefits and with a full awareness of the gaps in current knowledge.

Sexual activities associated with a risk for HIV transmission also are associated with risk for unintended pregnancy and STDs (e.g., syphilis, gonorrhea, chlamydia, or hepatitis B virus). Treatment for STDs should follow the Guidelines for Treatment of Sexually Transmitted Diseases, and victims of sexual assault should receive additional evaluation and counseling. Women at risk for unintended pregnancy should be offered emergency contraception. (Persons with possible HIV exposure through percutaneous routes from sharing syringes or needles should be assessed for hepatitis B and hepatitis C virus infections and considered for hepatitis B virus vaccination).

Persons who report possible nonoccupational HIV exposure should be evaluated for sexual and injecting-drug-use behavior that might lead to recurrent exposure. In all situations, health-care providers should offer confidential risk-reduction counseling during initial and follow-up visits. Persons who have been sexually assaulted also can be referred for anonymous or confidential voluntary counseling and testing within 72 hours of exposure to establish their HIV status at the time of the assault.

Persons with nonoccupational HIV exposures should receive medical evaluations, including HIV-antibody tests at baseline and periodically for at least 6 months after exposure (e.g., at 4-6 weeks, 12 weeks, and 6 months). All persons evaluated for possible nonoccupational HIV exposure should be counseled to initiate or resume protective behaviors to prevent additional exposure and to prevent possible secondary transmission, if they become infected while receiving antiretroviral therapy.

Considerations in Initiating Antiretroviral Therapy

Physicians considering the initiation of antiretroviral therapy in an attempt to reduce the risk for HIV infection in an exposed person should take the following steps in consultation with an expert in the use of antiretroviral agents:

- Evaluate the HIV status and risk-behavior history of the reported source of HIV exposure.
- Provide medical care, supportive counseling, and prevention services to persons who are determined to be HIV-infected when they seek care for a potential HIV exposure.
- Evaluate the risk for HIV transmission (if there is convincing evidence of HIV infection in the reported source). Physicians should determine the specifics of the risk event (e.g., no condom, torn condom, whether receptive or insertive partner, injection before or after others, number of persons sharing injection equipment) and the presence or absence of factors that would modify risk (e.g., vaginal or anal tears or bleeding, visible genital ulcers or other evidence of an

active STD, or bleach treatment of injection equipment).

- Determine the time elapsed between exposure and presentation for medical care. Although animal studies indicate that antiretroviral agents are most effective within 1-2 hours of exposure and probably not effective when started later than 24-36 hours after exposure, the interval during which therapy can be beneficial for humans is unknown.
- Evaluate the frequency of HIV exposure. Uninfected persons who request antiretroviral agents should be evaluated for sexual, injecting-drug-use, and other behaviors that might lead to recurrent HIV exposures. Antiretroviral therapy is not a replacement for adherence to behaviors that reduce the risk of HIV exposure.
- Provide counseling and obtain informed consent. Because postexposure prophylaxis is an experimental therapy of unproven efficacy, informed consent should be obtained and recorded in the medical charts of all persons prescribed antiretroviral agents following nonoccupational exposure. Such consent should document the patient's understanding of
  a. the need to initiate or resume relevant HIV risk-reduction behaviors (e.g., condom use and/or drug treatment);
  b. the limited knowledge about the effectiveness and toxicity of antiretroviral treatment for nonoccupational exposure;
  c. the known side effects of the medications being prescribed;
  d. the name and phone number of a source for follow-up medical care;
  e. the frequency and timing of recommended follow-up HIV testing;
  f. the signs and symptoms associated with acute HIV seroconversion; and
  g. the need for adherence to prescribed medications to maximize efficacy and reduce the risk for infection with a drug-resistant variant. The patient should be told that physicians have diverse opinions about the use of antiretroviral medications to treat possible nonoccupational HIV exposure.
- Persons younger than age 16 years at the time of exposure should be evaluated (before therapy is initiated) by pediatricians, family physicians, or other clinicians with expertise in the specific medical needs, consent issues, and other factors involved in their treatment, including the use of antiretroviral medicines for children and adolescents.
- If antiretroviral therapy is used, drug-toxicity monitoring should include a complete blood count and renal and hepatic chemical function tests when therapy is initiated and again 2 weeks after the patient begins to take the medications. It is possible that antiretroviral therapy during early HIV infection could benefit the patient by reducing the initial level of viral replication (i.e., the set point) and decreasing the extent of lymph node infiltration. Thus, for patients with the highest-risk exposures, health-care providers may consider continuing therapy until HIV test results are received from a specimen drawn after 28 days of treatment. Patients should be monitored for signs and symptoms of acute HIV infection during therapy. If such conditions develop, the patient should be tested for HIV (p24 antigen, HIV viral load assays) during their 4-week course of therapy with confirmation by standard HIV antibody tests. Persons who become infected while taking antiretroviral therapy should be advised to continue taking the medication pending transfer to a health-care provider who specializes in long-term HIV care.
- AIDS service organizations are concerned that the extended provision of PEP therapy in cases of accidental sexual exposure may reduce safer sex practices. Persons may view the PEP therapy as a 'morning after pill' with the ability to halt

the transmission of HIV in all instances.

- There are public health departments and AIDS service organizations that believe that in order to combat the possible decrease in safer sex practices, public health campaigns and/or educational materials will have to incorporate information on PEP therapies. Slogans and other educational material will have to be carefully worded so as to relay the correct information and minimize misconceptions. Individual counselling can also assist in relaying correct information.
- It is imperative that the final decision to be tested and/or to take the PEP therapy be made by the client/patient and the right to refuse treatment is respected
- Across studies of HIV-PEP use in non-occupational settings: the indications for HIV-PEP, the time to HIV-PEP initiation, the number and type of drugs used, adherence, side-effects and seroconversion rates are inconsistent. In most cases, however, follow-up has been poor. Risk behavior has not been shown to increase substantially among HIV-PEP users and in communities where HIV-PEP is available. HIV-PEP uptake among sexual assault survivors in most developed countries is low due, in most cases, to low-acceptance rates. Follow-up and completion rates are relatively lower than among men-who-have-sex-with-men (MSM). In other settings such as refugee camps, rape survivors report a great value and motivation regarding PEP.
- It may be noted that very good and large experiences are being reported from the African and Latin American countries on non occupational exposures and prophylaxis.

Summary

Although preventing blood exposures is the primary means of preventing occupationally acquired human immunodeficiency virus (HIV) infection, appropriate postexposure management is an important element of work place safety.

Recommendations for PEP have been modified to include a basic 4-week regimen of two drugs (zidovudine and lamivudine) and many other combinations for most HIV exposures and an expanded regimen that includes the addition of a protease inhibitor (indinavir or nelfinavir) or a boosted PI for HIV exposures that pose an increased risk for transmission or where resistance to one or more of the antiretroviral agents recommended for PEP is known or suspected. An algorithm is provided to guide clinicians and exposed health-care workers in deciding when to consider PEP.

Occupational exposures should be considered urgent medical concerns to ensure timely administration of PEP. Health-care organizations should have protocols that promote prompt reporting and facilitate access to postexposure care.

Many have proposed offering antiretroviral drugs to persons with unanticipated sexual or injecting-drug-use HIV exposures and data do exist regarding the effectiveness of such therapy for these types of exposures. Research is needed to establish if and under what circumstances antiretroviral therapy following non-occupational HIV exposure is effective. Some of the very recent analyses are also presented.

References

1. CDC. Update: Provisional Public Health Service recommendations for chemoprophylaxis after occupational exposure to HIV. *MMWR* 1996;45:468-72.
2. CDC. Public Health Service guidelines for the management of health-care worker exposures to HIV and recommendations for postexposure prophylaxis. *MMWR* 1998;47:1-33.
3. CDC. Public Health Service guidelines for the management of health-care worker exposures to HIV and recommendations for postexposure prophylaxis. *MMWR* 2005;54:1-17.
4. Post-exposure prophylaxis for HIV. *S Afr Med J*. 2000;90:346-51.
5. Chaturvedi S, Gupta P, Rajoura OP, Kumar P, Aggarwal OP. Impact of a multi-method promotional package on awareness and knowledge about STD and AIDS among the trainees of an industrial training institute in a resettlement colony of Delhi, *India*. *J Commun Dis*. 1999;31:209-16.

6. Mackie NE, Coker RJ.Post-exposure prophylaxis following non-occupational exposure to HIV: risks, uncertainties, and ethics. *Int J STD AIDS*. 2000 Jul;11:424-7.
7. Grime PR, Risi LJ, Carruthers JR. A survey of the use of post-exposure prophylaxis for occupational exposure to human immunodeficiency virus. *Occup Med* (Lond). 2000;50:164-6.
8. Diprose P, Deakin CD, Smedley J. Ignorance of post-exposure prophylaxis guidelines following HIV needlestick injury may increase the risk of seroconversion. *Br J Anaesth*. 2000;84:767-70.
9. Gisondi MA. Post-exposure prophylaxis for HIV following possible sexual transmission: an ethical evaluation. *Camb Q Healthc Ethics*. 2000 Summer;9:411-7.
10. Donovan B. The repertoire of human efforts to avoid sexually transmissible diseases: past and present. Part 2: Strategies used during or after sex. *Sex Transm Infect*. 2000;76:88-93.
11. Gounden YP, Moodley J. Exposure to human immunodeficiency virus among healthcare workers in south africa. *Int J Gynaecol Obstet*. 2000;69:265-70.
12. Dabis F, Leroy V, Castetbon K, Spira R, Newell ML, Salamon R. Preventing mother-to-child transmission of HIV-1 in Africa in the year 2000. *AIDS*. 2000 26;14:1017-26.
13. Richard VS, Kenneth J, Cherian T, Chandy GM. Preventing transmission of blood-borne pathogens to health care workers. *Natl Med J India*. 2000;13:82-5.
14. Puro V. Post-exposure prophylaxis for HIV infection. Italian Registry of Post-Exposure Prophylaxis. *Lancet*. 2000 29;355:1556-7.
15. Parschalk B, Pernerstorfer-Schon H. Human immunodeficiency virus: post-exposure prophylaxis. *Curr Opin Urol*. 1999;9:51-5.
16. Pinkerton SD, Holtgrave DR, Kahn JG. Is post-exposure prophylaxis affordable? *AIDS*. 2000 18;14:325.
17. Parkin JM, Murphy M, Anderson J, El-Gadi S, Forster G, Pinching AJ. Tolerability and side-effects of post-exposure prophylaxis for HIV infection. *Lancet*. 2000 26;355:722-3.
18. Goldberg D, Johnston J, Cameron S, Fletcher C, Stewart M, et.al. Risk of HIV transmission from patients to surgeons in the era of post-exposure prophylaxis. *J Hosp Infect*. 2000;44:99-105.
19. Henderson DK. Weighing the consequence of doing nothing versus those of doing something: post-exposure chemoprophylaxis for occupational exposures to HIV. *J Hosp Infect*. 1999;43 Suppl:S225-33.
20. Sidwell RU, Green JS, Novelli V.Management of occupational exposure to HIV--what actually happens. Commun Dis Public *Health*. 1999;2:287-90.
21. Papacchini M, Delle Piane R, Palmi S, Tomao P. Prevention, safety and prophylactic measures in occupational HIV infection in Italy, European Union and the USA. *Med Lav*.1999;90:681-92.
22. Gerberding JL, Katz MH. Post-exposure prophylaxis for HIV. *Adv Exp Med Biol*. 1999;458:213-22.
23. Marin MG, Van Lieu J, Yee A, Bonner E, Glied S.Cost-effectiveness of a post-exposure HIV chemoprophylaxis program for blood exposures in health care workers. *J Occup Environ Med*. 1999;41:754-60.
24. Sahlu T, Kassa E, et al. Sexual behaviours, perception of risk of HIV infection, and factors associated with attending HIV post-test counselling in Ethiopia. *AIDS*. 1999 9;13:1263-72.
25. Duff SE, Wong CK, May RE.Surgeons' and occupational health departments' awareness of guidelines on post-exposure prophylaxis for staff exposed to HIV: telephone survey. *BMJ*. 1999 17;319:162-3.
26. Petty TL.When the unthinkable happens: post-exposure prophylaxis of HIV-contaminated percutaneous injuries. *J Can Dent Assoc*. 1999;65:293-4.
27. Laurence J. Post-exposure prophylaxis: a new form of prevention? *AIDS Patient Care STDS*. 1999;13:261-3.
28. Seuffer RH. German-Austrian recommendations for post-exposure prophylaxis after HIV infection. *Dtsch Med Wochenschr*. 1999 26;124:373.
29. Torbati SS, Guss DA. Emergency department management of occupational exposures to HIV-infected fluids.*J Emerg Med*. 1999;17:261-4.
30. Sudre P, San Millan Ruiz D, etal.Post-exposure HIV prevention: eligibility of patients recently infected by sexual exposure. Schweiz *Med Wochenschr*. 1999 27;129:314-8.
31. Battegay M, Zimmerli W. HIV post-exposure prophylaxis after sexual risk contact. *Schweiz Med Wochenschr*. 1999 27;129:311-3.
32. Gamester CF, Tilzey AJ, Banatvala JE. Medical students' risk of infection with bloodborne viruses at home and abroad: questionnaire survey. *BMJ*. 1999 16;318:158-60.
33. Katz MH, Gerberding JL. Postexposure treatment of people exposed to the human immunodeficiency virus through sexual contact or injection-drug use. *N Engl J Med* 1997;336:1097-9.
34. Kaplan EH, Heimer R. A model-based estimate of HIV infectivity via needle sharing. *J Acquir Immune Defic Syndr* 1992;5:1116-8.
35. Schacker T, Collier AC, Hughes J, Shea T, Corey L. Clinical and epidemiologic features of primary HIV infection. *Ann Intern Med* 1996;125:257-64.
36. Pinto LA, Landay AL, Berzofsky JA, Kessler HA, Shearer GM. Immune response to human immunodeficiency virus (HIV) in healthcare workers occupationally exposed to HIV-contaminated blood. *Am J Med* 1997;102:21-4.
37. Saag MS. Candidate antiretroviral agents for use in postexposure prophylaxis. AmJMed 1997;102:25-31.
38. Martin LN, Murphey-Corb M, Soike KF, Davison-Fairburn B, Baskin GB. Effects of initiation of 3'-azido,3'-deoxythmidine (zidovudine) treatment at different times after infection of rhesus monkeys with simian immunodeficiency virus. *J Infect Dis* 1993;168:825-35.
39. Tsai C-C, Folis KE, Sabo A, et al. Prevention of SIV infection in macaques by (R)-9-(2-phosphonylmethoxypropyl)adenine.

Science 1995;270:1197-9.

40. CDC. Case-control study of HIV seroconversion in health-care workers after percutaneous exposure to HIV-infected blood -- France, United Kingdom, and United States, January 1988-August 1994. *MMWR* 1995;44:929-33.
41. Jochimsen EM. Failures of zidovudine postexposure prophylaxis. *Am J Med* 1997;102:52-5.
42. Ippolito G, Puro V, and the Italian Registry of Antiretroviral Prophylaxis. Zidovudine toxicity in uninfected healthcare workers. *Am J Med* 1997;102:58-62.
43. Forseter G, Joline C, Wormser GP. Tolerability, safety, and acceptability of zidovudine prophylaxis in health care workers. *Arch Intern Med* 1994;154:2745-9.
44. Bell DM, Gerberding JL, eds. Human immunodeficiency virus (HIV) postexposure management of healthcare workers. *Am J Med* 1997;102(suppl 5B).
45. CDC. Recommendations for prevention of HIV transmission in health-care settings. *MMWR* 1987;36(suppl no. 2S).
46. CDC. Update: universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus, and other bloodborne pathogens in health-care settings. MMWR1988;37:377-82,387-8.
47. Occupational Safety and Health Administration, Department of Labor. 29 CFR Part 1910.1030, occupational exposure to bloodborne pathogens; final rule. Federal Register 1991;56:64004-182.
48. Bell DM. Occupational risk of human immunodeficiency virus infection in healthcare workers: an overview. *Am J Med* 1997;102(suppl 5B):9-15.
49. Cardo DM, Bell DM. Postexposure management. In: DeVita VT Jr, Hellman S, Rosenberg SA, eds. AIDS: biology, diagnosis, treatment and prevention. 4th ed. Philadelphia, PA: Lippincott-Raven Publishers, 1997:701-8.
50. CDC. HIV/AIDS surveillance report 1997;9:15.
51. Ridzon R, Gallagher K, Ciesielski C, et al. Simultaneous transmission of human immunodeficiency virus and hepatitis C virus from a needle-stick injury. *N Engl J Med* 1997;336:919-22.
52. CDC. Immunization of health-care workers -- recommendations of the Advisory Committee on Immunization Practices (ACIP) and the Hospital Infection Control Practices Advisory Committee (HICPAC). *MMWR* 1997;46(no. RR-18):21-2.
53. CDC. Recommendations for follow-up of health-care workers after occupational exposure to hepatitis C virus. *MMWR* 1997;46:603-6.
54. Useful websites: http://www.cdc.gov/ncidod/dhqp/bp_hiv.html, http://www.cdc.gov/niosh, www.unaids.org,