

Occupational exposure to HIV

A USER'S GUIDE

Updated September 2005



**PREVENTION
AND
TREATMENT**

Cipla



Preamble

Over the years, Cipla has attacked HIV on all fronts - the world's widest range of antiretroviral drugs, user-friendly scientific resources, CME programmes and multilingual patient education tools.

Although preventing exposures to blood and body fluids is the primary means of preventing occupationally acquired HIV infection, appropriate post exposure management is an important element of work place safety.

Cipla has always strived to disseminate information on Post Exposure Prophylaxis (PEP) over the past many years. This booklet is yet another attempt in this direction.

The Centers for Disease Control (CDC) based in Atlanta, USA, has issued updated guidelines (September 2005) for prophylactic treatment for medical personnel who have been exposed to HIV-infected blood and body fluids. These revised guidelines, along with the drugs and dosing regimens, are presented here.

What is 'occupational exposure' to HIV infection?

Medical personnel caring for HIV-infected patients may be at risk for acquiring HIV infection through contact with HIV-infected blood and body fluids. This is referred to as 'occupational exposure' to HIV.

Apart from HIV, other blood-borne pathogens that may be occupationally acquired are the hepatitis B and C viruses.

Who is at risk for 'occupational exposure'?

All healthcare personnel (HCP) who come in contact with blood or bloody fluids of HIV-infected patients in hospitals or laboratories are at risk for occupational exposure to HIV. This includes nurses, laboratory workers, doctors, residents, paramedical staff, emergency doctors, medical students and others.

What is the risk of occupational exposure?

It should be emphasized that HCP are not at an extremely high degree of risk of acquiring HIV from their patients.

An exposure that might place HCP at risk for HIV infection is defined as a percutaneous injury or contact of mucous membrane or nonintact skin with blood, tissue or other body fluids that are potentially infectious. The risk varies depending on the type of exposure.

A percutaneous injury refers to an injury resulting from a needle prick, or a cut with a sharp object. The risk after percutaneous exposure to HIV-infected blood is estimated to

be about 0.3%, i.e. 3 out of a thousand needle pricks may result in HIV infection.

The risk after a mucous membrane exposure is estimated to be lower; about 0.09%. This includes contact with the mucous membranes of the eyes, nose and mouth.

Contact with nonintact skin (e.g. exposed skin that is chapped, abraded or afflicted with dermatitis) may also place the HCP at risk.

Any kind of direct contact (i.e. contact without barrier protection) with concentrated HIV in a laboratory requires clinical evaluation.

Although episodes of HIV transmission after nonintact skin exposure have been documented, the average risk for transmission by this route has not been quantified. It is estimated to be less than the risk for mucous membrane exposures.

The majority of occupational exposures reported have been percutaneous. Most frequent were hollow-bore and solid needlestick injuries; a few involved other sharp objects.

Most reported occupationally acquired infections have occurred in nurses and laboratory workers. Percutaneous and other exposures are also common during surgical procedures. Factors posing a risk to the surgeon are the length of the procedure, the volume of blood loss, and whether the operation involves major vascular or intraabdominal/gynaecologic surgery.

Which factors influence the risk?

Various factors affect the risk for HIV transmission.

With respect to percutaneous injury, exposure to a larger quantity of blood increases the risk. Thus, risk is increased if:

- The device (e.g. needle) was visibly contaminated with blood
- The procedure involved placing a needle directly in an artery or vein
- The injury was deep
- There was exposure to blood from a patient with AIDS
- The needle was a hollow bore needle rather than a solid needle (e.g. suture needle)

Which body fluids transmit HIV?

Blood and visibly bloody fluids are considered infectious. Potentially infectious materials include semen, vaginal secretions, CSF, synovial, pleural, peritoneal, pericardial, amniotic fluids or tissue. Faeces, nasal secretions, saliva, sputum, sweat, tears, urine and vomitus are not considered potentially infectious unless they are visibly bloody. The risk of HIV transmission from these fluids and materials is low.

Which are the most frequent areas of contact for the HCP?

The most frequent areas of contact are the hands. Face contacts are common in orthopaedics and obstetrics. Eye or mucous membrane contacts may occur in cases where there is splattering of blood.

How can risks be reduced?

There are several preventive measures to reduce the risk of HIV transmission. These include:

- The use of universal precautions, which also reduce risk of transmission of other blood-borne pathogens
- The use of two pairs of gloves by surgeons. The obstetrician may use barriers such as face shields, impervious gowns and impervious shoe covers. Goggles can prevent eye contact
- Care should be taken during procedures such as endoscopy, ENT surgery, and other situations where splattering of blood is anticipated
- Avoiding recapping of needles
- The use of impervious needle-disposal containers
- Transport of samples in sealed containers

How is an occupational exposure evaluated?

Contingency plans for dealing with occupational exposures in hospitals should be available. These include:

- Protocols for evaluation, counselling and treatment of occupational exposures
- Access to clinicians during all working hours
- Availability of antiretroviral agents on site or easily
- Availability of trained personnel for postexposure counselling.

An occupational exposure is evaluated based on the following factors:

- What is the source material?
- What is the level of risk for HIV transmission represented by the exposure?
- What is the status of the source person/specimen? (asymptomatic/symptomatic, known low/high viral load, AIDS, primary HIV infection, unknown HIV status)
- Is the HCP pregnant?

What immediate measures should be taken after an occupational exposure?

The immediate measures to be taken after an occupational exposure include:

- Use soap and water to wash any wound or skin site that came into contact with infected blood or fluid
 - Flush exposed mucous membranes with water
 - Irrigate an open wound with sterile saline or disinfectant solution
 - Eyes should be irrigated with clear water, saline or sterile eye irrigants
 - Report to the concerned authority
 - Psychologic counselling should be provided
 - Determine need for antiretroviral therapy
-

What is 'postexposure prophylaxis'?

The term 'postexposure prophylaxis' (PEP) refers to treatment of occupational exposures using antiretroviral therapy. The rationale is that antiretroviral treatment that is started immediately after exposure to HIV may prevent HIV infection.

What are the current guidelines for PEP?

The recommendations provided in these guidelines apply to situations in which HCP have been exposed to a source person who either has or is considered likely to have HIV infection. The guidelines state that:

- Baseline HIV testing should be carried out to rule out any existing HIV infection at the time of exposure.
- HCP with occupational exposure to HIV should receive follow-up counselling, postexposure testing and medical evaluation regardless of whether they receive PEP
- PEP should be initiated as soon as possible, preferably within hours rather than days of exposure, for a period of 4 weeks. HCP should be advised of the importance of completing the prescribed regimen
- 2- and 3-drug PEP regimens that are based on the level of risk for HIV transmission represented by the exposure are recommended
- If a question exists concerning which antiretroviral drugs to use, or whether to use a 2- or 3-drug regimen, the 2-drug regimen should be started immediately rather than delay PEP administration
- Reevaluation of the exposed person should be considered within 72 hours postexposure, especially as additional information about the exposure or source person becomes available
- If the source patient's HIV status is unknown at the time of exposure, decide whether to

give PEP on a case-to-case basis after considering the type of exposure and clinical/epidemiological likelihood of HIV infection in the source

- Potential toxicities of PEP must be considered, keeping in mind that the majority of occupational HIV exposures do not result in transmission of HIV.
- The use of rapid HIV tests for evaluation of source patients has increased. Rapid HIV tests result in decreased use of PEP and spare HCP undue anxiety and adverse effects
- If a source person is determined to be HIV-negative, PEP should be discontinued
- Follow-up counselling and HIV testing by ELISA should be carried out periodically for more than 6 months after occupational exposure (i.e. at baseline, 6 weeks, 12 weeks and 6 months). Extended follow-up (e.g. for 12 months) is recommended for HCP who become infected with hepatitis C Virus (HCV) after exposure to a source coinfecting with HIV and HCV

The development of HIV antibody is considered a reliable indicator of HIV infection, and HIV antibody testing is currently considered the gold standard for following up exposed HCP. The routine use of direct virus assays (e.g. HIV p24 antigen or tests for HIV RNA) to detect infection in exposed HCP is generally not recommended due to the infrequency of seroconversion and expense, as also the relatively high rate of false-positive results of these tests.

What are the recommended regimens for PEP?

The selection of a drug regimen for HIV PEP must balance the risk for infection against the potential toxicities of the agent(s) used. Two types of regimens are recommended for PEP: a “basic” 2-drug regimen that should be appropriate for most HIV exposures and an “expanded” 3-drug regimen that should be used for exposures that pose an increased risk for transmission.

Table 3 (pg. 11) lists the drugs used for the basic and expanded regimens. The duration of therapy for both regimens is 4 weeks.

Offering a 2-drug regimen is a viable option because the benefit of completing a full course of this regimen exceeds the benefit of adding the third drug and risking discontinuation due to side effects. Additionally, the viral load is substantially lower among exposed HCP than among patients with established HIV infection.

Evaluating level of risk for HIV transmission

The following algorithm is used to evaluate the level of risk for HIV transmission posed by a particular exposure. Accordingly, a basic or expanded regimen may be recommended, as appropriate (Tables 1 and 2).

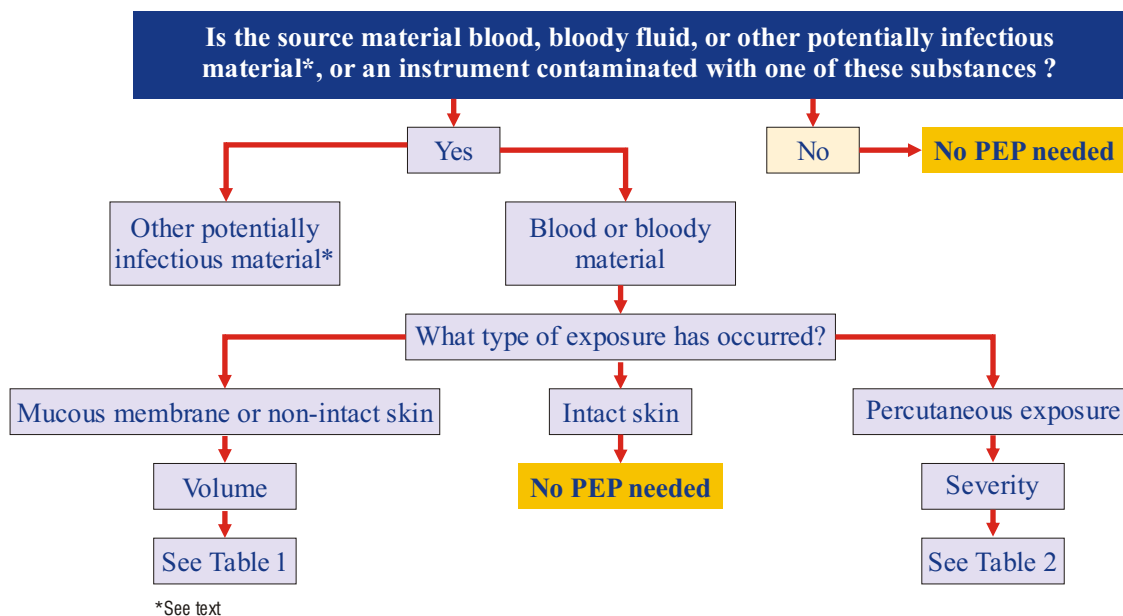


Table 1: Recommended HIV postexposure prophylaxis (PEP) for mucous membrane exposures and nonintact skin* exposures

Exposure type	Infection status of source				
	HIV-positive class 1 [†]	HIV-positive class 2 [†]	Source of unknown HIV status [‡]	Unknown source [§]	HIV-negative
Small volume ^{**}	Consider basic 2-drug PEP ^{††}	Recommend basic 2-drug PEP	Generally, no PEP warranted ^{§§}	Generally, no PEP warranted	No PEP warranted
Large volume ^{**}	Recommend basic 2-drug PEP	Recommend expanded ≥ 3-drug PEP	Generally, no PEP warranted; however, consider basic 2-drug PEP ^{††} for source with HIV risk factors ^{§§}	Generally, no PEP warranted; however, consider basic 2-drug PEP ^{††} in settings in which exposure to HIV-infected persons is likely	No PEP warranted

* 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 HIV RNA 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 counselling, 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

Table 2: Recommended HIV postexposure prophylaxis (PEP) for percutaneous injuries

Exposure type	Infection status of source				
	HIV-positive class 1*	HIV-positive class 2*	Source of unknown HIV status†	Unknown source‡	HIV-negative
Less severe§	Recommend basic 2-drug PEP	Recommend expanded ≥ 3-drug PEP	Generally, no PEP warranted; however, consider basic 2-drug PEP** for source with HIV risk factors††	Generally, no PEP warranted; however, consider basic 2-drug PEP** in settings in which exposure to HIV-infected persons is likely	No PEP warranted
More severe§§	Recommend expanded 3-drug PEP	Recommend expanded ≥ 3-drug PEP	Generally, no PEP warranted; however, consider basic 2-drug PEP** for source with HIV risk factors††	Generally, no PEP warranted; however, consider basic 2-drug PEP** in settings in which exposure to HIV-infected persons is likely	No PEP warranted

* HIV-positive, class 1 --asymptomatic HIV infection or known low viral load (e.g. < 1,500 HIV RNA 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 counselling, 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, a needle from a sharps disposal container

§ For example, solid needle or superficial injury

** 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, large-bore hollow needle, deep puncture, visible blood on device, or needle used in patient's artery or vein

Table 3: Basic and Expanded regimens for PEP

Basic regimen (28 days)	Expanded regimen (28 days)
<p>Duovir* Zidovudine 300 mg + Lamivudine 150 mg 1 tab bid</p> <p>Or</p> <p>Tenofovir 1 tab od + Lamivir 1 tab bid Tenofovir 300 mg + Lamivudine 150 mg</p> <p>Or</p> <p>Lamivir-S 30/40 1 tab bid Stavudine 30/40 mg + Lamivudine 150 mg</p> <p>* Can be used by pregnant HCP</p>	<p>Basic regimen, plus either</p> <p>Lopimune 3 caps bid with food Lopinavir 133.3 mg / Ritonavir 33.3 mg</p> <p>Or</p> <p>Indinavir 2 caps bid + Ritomune 1 cap bid Indinavir 400 mg + Ritonavir 100 mg</p> <p>Or</p> <p>Saquinavir 200 mg, 5 hard gelatin capsules bid + Ritomune 1 cap bid Saquinavir 200 mg, 5 hard gelatin capsules bid + Ritonavir 100 mg</p> <p>Or</p> <p>Efavir-600 1 tab od at bedtime Efavirenz 600 mg</p> <p>Or</p> <p>Nelvir 3 tabs tid Nelfinavir 250 mg</p>

In case the exposed HCP is pregnant, the potential effect of antiretrovirals on the pregnant woman and on her foetus need to be considered.

What is the efficacy of PEP regimens?

Studies conducted in animals and in humans prove the efficacy of PEP regimens. Zidovudine has been the most widely studied agent for prophylaxis. A retrospective study of HCP who used zidovudine as PEP found that the risk of HIV infection was reduced by approximately 81%.

Although the efficacy of combination regimens for PEP is unknown, combination drug regimens are currently recommended for PEP. This is because they are more potent and may be more effective against drug-resistant strains.

What are the possible side effects of PEP?

Data indicate that nearly 50% of HCP experience adverse symptoms while taking PEP and that approximately 24% stop taking PEP because of adverse effects. HCP who are given PEP need to be monitored for drug toxicity at baseline (on starting PEP), and two weeks after therapy begins. Those taking protease inhibitor (PI)-containing regimens have been found to be more likely to discontinue PEP. Minimally, laboratory monitoring for toxicity should include a complete blood count and renal and hepatic function tests. Medical conditions in the exposed person and toxicity of drugs included in the PEP regimen should also be taken into account.

What additional advice should the exposed HCP be given?

Information should be provided to the HCP about potential drug interactions and the drugs that should not be taken with PEP, the side effects of the drugs that have been prescribed, measures to minimize these effects, and the methods of clinical monitoring for toxicity during the follow-up period. HCP should be advised that the evaluation of certain symptoms should not be delayed (e.g. rash, fever, back or abdominal pain, pain on urination or blood in the urine, or symptoms of hyperglycaemia).

Exposed HCP should avoid behaviours that carry a risk of secondary transmission of HIV for the duration of the follow-up period. This is especially true for the first 6 to 12 weeks after exposure, when seroconversion is most likely to occur.

The exposed HCP should be advised on the following:

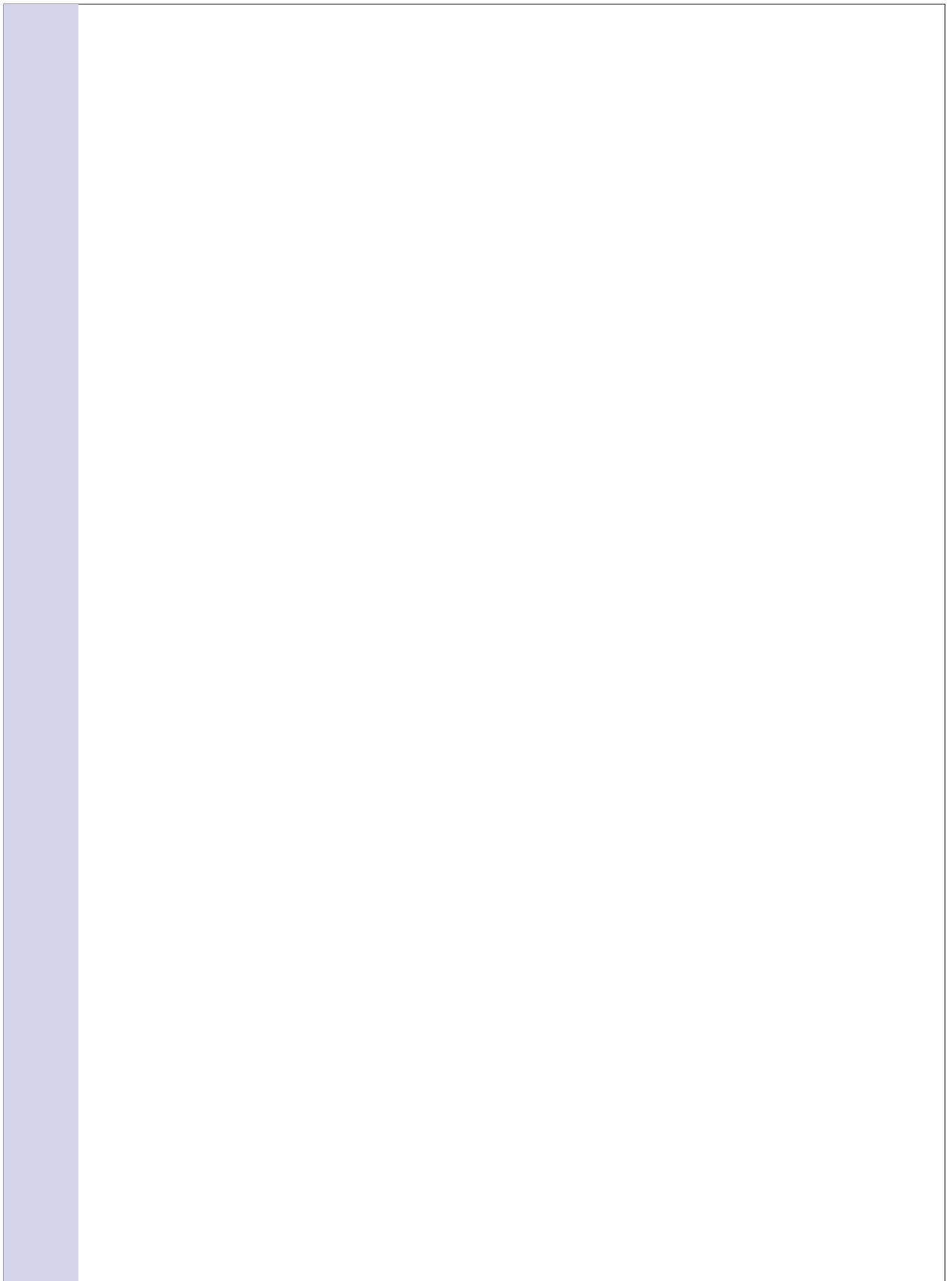
- Use precautions to prevent secondary transmission and pregnancy
- Not to donate blood, plasma, organs, tissue or semen
- HIV and some drugs used in therapy can pass through breast milk. Consider discontinuing breast-feeding, particularly after high-risk exposures.

Conclusion

Occupationally acquired HIV infection represents a health hazard for HCP caring for HIV-positive patients. Although the risk of transmission is low, it is important to institute measures to reduce such risks, as also establish protocols for treating exposed HCP.

Current guidelines recommend commencing prophylactic 2- or 3-drug regimens immediately after an exposure that poses a risk of transmitting HIV infection.

References: 1.MMWR Sept 30, 2005 Vol 54, No RR-9 2.Consultant Jan 1999, p 230-36



Regimens for PEP

Basic regimen (28 days)

Duovir* *1 tab bid*
Zidovudine 300 mg + Lamivudine 150 mg

Or

Tenvir *1 tab od* + **Lamivir** *1 tab bid*
Tenofovir 300 mg + Lamivudine 150 mg

Or

Lamivir-S 30/40 *1 tab bid*
Stavudine 30/40 mg + Lamivudine 150 mg

* Can be used by pregnant HCP

Expanded regimen (28 days)

Basic regimen, plus either

Lopimune *3 caps bid with food*
Lopinavir 133.3 mg / Ritonavir 33.3 mg

Or

Indivan *2 caps bid* + **Ritomune** *1 cap bid*
Indinavir 400 mg + Ritonavir 100 mg

Or

Saquinavir 200 mg, 5 hard gelatin capsules bid + **Ritomune** *1 cap bid*
Ritonavir 100 mg

Or

Efavir-600 *1 tab od at bedtime*
Efavirenz 600 mg

Or

Nelvir *3 tabs tid*
Nelfinavir 250 mg

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