

Post-exposure prophylaxis

11

Anna Pierce

Infectious Diseases Unit, The Alfred Hospital, Melbourne, VIC

This chapter covers antiretroviral post-exposure prophylaxis (PEP) in both occupational and non-occupational settings. It provides an understanding of the rationale for PEP, the risks of HIV transmission in both occupational and non-occupational settings as well as recommendations for management including consideration and initiation of PEP. It is not a replacement or substitute for detailed guidelines which should be referred to for more specific advice. Readers are referred to the Australian national guidelines for post-exposure prophylaxis after non-occupational exposure to HIV and the Centers for Disease Control and Prevention (CDC) Guidelines for the Management of Occupational Exposures.^{1,2} A detailed literature review of non-occupational post-exposure prophylaxis (NPEP) was undertaken in 2007.³

11.1 Rationale

HIV PEP is the prescription of one or more antiretroviral drugs to reduce the risk of transmission of HIV following a known or possible exposure to HIV. This exposure may be in an occupational setting percutaneously, via mucous membranes or non-intact skin, or a non-occupational setting where the most common exposures are via sexual contact, injecting drug use (IDU) or accidental needle-stick injury.

While PEP plays a role in the management of exposure to HIV, the most important management strategy remains prevention of exposure. The availability of PEP does not replace the need for universal precautions for the prevention of HIV in the health care setting and adherence to safe sexual and injection practices in the non-occupational setting.

Most of the evidence to support the efficacy of HIV PEP comes from animal studies performed in non-human primates. These studies have shown that PEP is most effective when given early (within 24 hours of exposure) and efficacy is reduced if administration is delayed (especially beyond 72 hours). Efficacy is also reduced with a large viral inoculum, and if the dose of PEP is reduced or the duration of prophylaxis is too short. These results have led to the recommendation that PEP be commenced as soon as possible after the exposure, within 72 hours, and that PEP should not be offered more than 72 hours after the exposure. The standard duration of treatment has been accepted as 28 days.³

Only one randomised, placebo-controlled study in humans has been performed to determine the efficacy of PEP in the health care setting but this study failed to fully recruit and was never completed.⁴ A multicentre, case-control study of 712 health care workers exposed to HIV demonstrated that the use of zidovudine prophylaxis reduced the odds of HIV infection by 81%.⁵ This study led to the implementation of PEP as part of standard

management for occupational exposure to HIV. Although the CDC published guidelines for occupational exposure and PEP in 1998, they declined to make recommendations for NPEP until 2005 due to lack of evidence.^{6,7} Australian national guidelines recommending NPEP were first published in 2001.⁸

There is no direct clinical trial evidence to support the use of PEP in the non-occupational setting. In addition to evidence from animal models, the data from the above case control study as well as results of postnatal, antiretroviral prophylaxis studies have been extrapolated to the non-occupational setting.⁷

11.2 Risk

In order to calculate the risk of HIV transmission, both the risk carried by the specific exposure and the risk of the source being HIV positive need to be known.

Risk of HIV transmission = Risk carried by the exposure X Risk of source being HIV positive.

11.2.1 Occupational exposure

In the occupational setting, the source is usually able to be identified and tested for HIV, and PEP is prescribed only for those who have definitely been exposed to HIV. The risks carried by exposures that occur in the occupational setting are outlined below.

Percutaneous needle-stick injuries

Prospective studies in health care workers have estimated the risk of HIV transmission after percutaneous exposure to HIV-infected blood to be approximately 0.3% (95% confidence interval [CI]; 0.2%-0.5%).⁹ Although the average risk is estimated to be 0.3%, the case-control study in health care workers by Cardo and colleagues identified potential risk factors associated with increased transmission,⁵ including: visible blood on the device; needle used in artery or vein; deep injuries; and large bore hollow needle. These potential risk factors are presumed to be surrogate markers of a greater volume of blood from the source patient. Terminal illness in the source patients was also associated with increased risk of transmission. It is presumed that this is due to higher plasma HIV RNA levels. While there is evidence that risk of HIV transmission is related to plasma HIV RNA levels in cohort studies, there is no evidence from clinical studies to demonstrate that undetectable plasma HIV RNA due to combination antiretroviral therapy (cART) is not associated with HIV transmission.^{10,11} In addition, genotypic and phenotypic features of the virus potentially influencing transmission have not been studied. Thus, every significant exposure where the source is known to have HIV infection should be treated seriously.

11 Post-exposure prophylaxis

Percutaneous needle-stick injuries occurring in the community most commonly result from needles discarded in public places (in rubbish, parks and on beaches). These injuries frequently result in significant anxiety and media attention; however the actual risk of HIV transmission from such an injury is very low. Laboratory studies have demonstrated viability of virus survival in needle syringes stored at room temperature for up to 30 days, although this depends on a number of factors including: viral titre, volume of blood in syringe, temperature and humidity.^{12,13} However, there have been no published reports of HIV transmission from community needle-stick exposures; NPEP for HIV is generally not indicated for community needle-stick exposures (unless the source is known to be HIV positive). The use of needle and syringe programs in Australia has been successful in keeping the seroprevalence of HIV in the IDU population at around 1%.¹⁴ Therefore, the risk estimate for needle-stick injury from an unknown source is calculated at 1/300 (risk of transmission from known HIV positive source) x 0.01 (1% HIV seroprevalence in IDU population) = 1/30 000. PEP is not recommended. However, in the subgroup of IDUs who identify as men who have sex with men (MSM), the prevalence of HIV is higher and in 2006 was reported as 32.2%.¹⁴

Mucous membrane and non-intact skin exposures

HIV transmission is also known to occur following mucocutaneous exposure, and US National Surveillance data have documented eight cases of HIV seroconversion in health care workers following exposure via this route.¹⁵ However, the actual risk per exposure is less well defined. There has only been one case of documented seroconversion following mucocutaneous exposure in six prospective studies of 1107 health care workers and the risk is estimated at 0.09% (95%

CI; 0.006-0.50).¹⁶ The risk from non-intact skin exposure is thought to be even less, and there have been no documented seroconversions after isolated skin exposure in prospective studies.

11.2.2 Non-occupational exposure

The major difference between occupational and non-occupational exposures is that most people who present for HIV NPEP are not aware of the serostatus of the source involved in the exposure. Table 11.1 provides the current data on HIV seroprevalence within different groups within the Australian community and some overseas countries.¹

HIV transmission is heterogeneous and infection depends not only on the nature of the exposure, but also on other cofactors such as the HIV plasma viral load of the source, the presence of sexually transmissible infections (STIs) (especially genital ulcer disease and symptomatic gonococcal infections) and breaches in genital mucosal integrity.³ Calculating risk estimates for a particular exposure type is also hampered by the lack of prospectively conducted epidemiological studies, with many studies also deriving estimates from mathematical modelling. For a further detailed discussion about transmission risk, refer to the ASHM literature review for NPEP.³

The estimated rates of transmission for a variety of sexual exposures are listed in Table 11.2.¹ In cases where the source or the HIV status of the source is unknown, the risk is estimated by multiplying the risk per single exposure by the risk that the source has HIV infection. For example, in Australia, the seroprevalence of HIV in MSM is estimated to be between 3 and 15%, hence for an episode of unprotected, receptive anal intercourse where the HIV status of the source is unknown,

Table 11.1 HIV seroprevalence in Australian and overseas populations

Community group	HIV seroprevalence % (year)
Homosexual men and MSM in Australia:	
Sydney	14.2 (2005)
Melbourne	9.1 (2005)
Brisbane	6.0 (2005)
Perth	4.9 (2004)
Injecting drug users in Australia:	
Homosexual	17 (2000) ¹
All others	1.0
Heterosexuals in Australia:	
Blood donors	0.0005
STI clinic attendees	<0.2
Australian-born commercial sex workers in Australia	0.1
HIV seroprevalence in selected regions: ²	
Oceania, Western and Central Europe, North Africa and Middle East, East Asia, New Zealand;	≤0.5
Latin America, North America, S and SE Asia, Eastern Europe and Central Asia;	0.6–1.0
Caribbean;	1.6
Sub-Saharan Africa.	7.2

1 The rates of HIV in MSM injecting drug users (IDU) vary considerably between different studies; they are also based on small samples.¹⁴ Prescribers are recommended to seek out local data to assist management.

2 This varies greatly. A predictor of HIV positivity is being born in a country with a high prevalence (hpc) of HIV (>1%). Other predictive factors include injecting drug use, commercial sex work and MSM. Country-specific information for the general population and sub groups is available at the UNAIDS/WHO online database at www.who.int/globalatlas/.

MSM = men who have sex with men.

Source: Adapted from the National Guidelines for post-exposure prophylaxis after non-occupational exposure to HIV. Available at: http://www.ashm.org.au/default2.asp?active_page_id=251

Table 11.2 Exposure and transmission risk and exposure

Type of exposure with known HIV positive source	Estimated risk of HIV transmission/exposure ¹
Receptive anal intercourse	1/120
Use of contaminated injecting equipment	1/150
Occupational needle-stick injury	1/333
Receptive vaginal intercourse	1/1000 ²
Insertive anal or vaginal intercourse	1/1000 ²
Receptive fellatio with or without ejaculation	Not measurable ³
Insertive fellatio	Not measurable
Cunnilingus	Not measurable
Bites etc	Not measurable
Other trauma	Not measurable
Non-occupational exposure of intact mucous membrane ⁴ and skin	Not measurable
Community needle-stick injury	Not measurable

1 These estimates are based on prospective studies, not cross-sectional data or figures derived from modelling.
2 This estimate has been rounded down from 1/909 to 1/1000.
3 Although there have been case reports of transmission, the risk associated with the exposures below is so low that it is not measurable.
4 Conjunctival, oral or nasal mucosa.

Source: Adapted from the National Guidelines for post-exposure prophylaxis after non-occupational exposure to HIV. Available at: http://www.ashm.org.au/default2.asp?active_page_id=251

the risk is 1/120 (risk of the single exposure) multiplied by 10% (seroprevalence of HIV in Melbourne) or 1/1200. The presence of genital ulceration or other STIs increases transmission risk.

11.3 Considerations for non-occupational post exposure prophylaxis including number and choice of antiretroviral drugs

11.3.1 Two versus three drug regimens and choice of antiretroviral drugs for non-occupational post exposure prophylaxis

There are no published data to show that the prescription of a three-drug regimen following a high-risk exposure is more efficacious than prescribing a one- or two-drug regimen. The recommendation to use three drugs is based on the knowledge that cART provides the best suppression of HIV replication in people with HIV infection and may therefore provide the best protection against HIV transmission.⁷ This assumption should be balanced by observations that both toxicity and discontinuation rates are higher for three-drug versus two-drug PEP regimens.^{17,18} In addition, modelling studies have shown that, under many conditions, the benefits of completing a better-tolerated, two-drug PEP regimen may exceed the benefits of a three-drug regimen.¹⁸

There is little evidence to support the choice of drugs used for PEP. Zidovudine is the only drug which has clinical trial evidence to support its use; however other drugs with equivalent efficacy to treat HIV and with an improved side-effect profile such as tenofovir have animal data to support their use in PEP, and clinical trials to examine efficacy are never likely to take place. Common two-drug PEP regimens include:

- zidovudine / lamivudine (Combivir),

- tenofovir plus lamivudine
- tenofovir / emtricitabine (Truvada)

When a third drug is required, a protease inhibitor such as lopinavir / ritonavir (Kaletra) is usually added.

Drugs not to use for NPEP:

- Nevirapine, a non-nucleoside reverse transcriptase inhibitor (NNRTI): due to severe adverse events including liver failure requiring a liver transplant in health care workers taking PEP regimens containing nevirapine^{7,8,19}
- Co-administration of stavudine and didanosine is not recommended, and is contraindicated in pregnancy^{20,21}
- Abacavir, a nucleoside reverse transcriptase inhibitor (NRTI), is associated with hypersensitivity reactions which make it unsuitable to use as PEP²²
- Efavirenz, a NNRTI, is contraindicated in pregnancy and neurological side-effects may make it less suitable for PEP.²³

When the source is known to have HIV infection, it is important to try and determine the antiretroviral medication history of the source so an appropriate PEP regimen can be constructed.

Toxicity and adherence

NPEP causes side-effects in 45-75% of patients in Australia, the USA and Europe.²⁴⁻²⁶ In an analysis of 648 patients who received NPEP in Australia between 1998 and 2002, the prescription of two or three antiretroviral drugs was associated with side-effects in 72% of those receiving two drugs compared with 76% receiving three drugs. Fifty-six percent of patients taking a three-drug regimen had full adherence compared to 62% of patients taking a two-drug regimen.²⁴ The US National NPEP Registry reported that 22% of prescribed regimens were modified because of side-effects.²⁷

Because the long-term side-effects of a 28-day course of PEP are unknown, the risks of the exposure need to be significantly high to warrant the prescription of PEP.

11 Post-exposure prophylaxis

Cost

The cost effectiveness of NPEP has been assessed in the USA and Canada. It has been shown to be cost effective when a two-drug regimen was used for unprotected, receptive anal intercourse with a person known to have HIV infection or to be at high risk of having HIV infection.²⁸⁻³¹ A retrospective cost analysis in Australia concluded that NPEP may be cost effective for high-risk exposures such as receptive anal intercourse and injecting drug use with a known HIV positive source; the overall cost per seroconversion avoided was \$1,740,134.³²

11.4 Management algorithm

The initial management is the same regardless of whether the exposure occurs in an occupational setting or in the community:

- Wash wounds and skin sites that have been in contact with blood or body fluids with soap and water
- After oral exposure to blood or body fluids, spit out fluids and rinse with water
- Irrigate mucous membranes and eyes (remove contact lenses) with water or saline

- Vaginal or rectal douching is not recommended following sexual exposure
- Do not inject antiseptics or disinfectants into wounds.

Clinical assessment and follow-up are similar for both occupational and non-occupational exposures (Table 11.3).¹ The main difference lies in the assessment of the exposed person. Additional sexual history including other recent exposures, history of NPEP and evaluation for STIs should be obtained in the setting of non-occupational exposure.

Based on the clinical assessment and an estimate of the risk of HIV transmission, a decision regarding the need for PEP should be made. A three-drug regimen is generally recommended for all significant exposures to a person with HIV infection. The exception to this may be a mucous membrane or non-intact skin exposure, where the estimated risk of transmission is lower, and receptive oral intercourse where PEP is generally not recommended, but may be considered if the oral mucosa is not intact. In cases of non-occupational exposure, the Australian guidelines recommend:¹

- Three drugs if the transmission risk is 1/1000 or greater
- Two drugs if it is between 1/1000 and 1/10 000

Table 11.3 Clinical assessment and follow-up for non-occupational post-exposure prophylaxis

These details should be documented in the patient's history:

1. The time of the assessment and first dose, if prescribed

2. Of the exposure (when, what, where and with whom?)

- a) Time of exposure
- b) Place of exposure
- c) Exact mode and details of exposure (including contributory factors)
- d) Amount of blood or body fluid involved, including trauma
- e) First aid measures applied

3. Of the exposed person

- a) Most recent HIV test and result
- b) Potential exposures within the last three months (and earlier as indicated)
- c) Previous post-exposure prophylaxis and history of this treatment
- d) Evaluation of current sexually transmitted infections (STI), hepatitis B virus (HBV) and hepatitis C virus (HCV) infection
- e) Pregnancy risk, contraception and lactation (consider emergency contraception)
- f) Medical history, including illnesses, medications and drug allergies
- g) Psychiatric history
- h) Drug and alcohol history
- i) Their knowledge of the source (if unavailable for interview)

4. Of the source

- a) HIV status and other relevant demographic features
- b) If HIV positive:
 - (i) plasma viral load and CD4 cell count
 - (ii) antiretroviral treatment history (has resistance been an issue, if so with which drugs?)
 - (iii) recent HIV resistance genotyping
- c) Current or past STI, HBV and HCV status

5. Pre-test and pre-NPEP discussion

An explanation of NPEP and its indications and effectiveness, risks and benefits are provided to all potential candidates. Thorough pre-test discussion for HIV, including risk assessment, is a fundamental part of the clinical assessment. Refer to the National HIV Testing Policy 2006.

6. Follow-up

A person found to be infected with HIV on baseline testing or during follow-up requires information, support, counselling, clinical assessment and referral. NPEP should be ceased in these cases. There is a theoretical risk of resistance to antiretroviral therapy developing if NPEP is continued, potentially limiting therapeutic options. Ongoing management must also be provided for those at risk of other infections or pregnancy resulting from the exposure.

NPEP= non-occupational post-exposure prophylaxis.

1 Australian Government Department of Health and Ageing 2006. National HIV Testing Policy, available at: http://www.health.gov.au/internet/wcms/publishing.nsf/content/health-pubhlth-strateg-hiv_hepc-hiv-index.htm#testing

Source: Adapted from the National Guidelines for post-exposure prophylaxis after non-occupational exposure to HIV. Available at: http://www.ashm.org.au/default2.asp?active_page_id=251

- Considering two drugs if the risk ranges from less than or equal to 1/10 000 and greater than or equal to 1/15 000
- Not using NPEP for lower transmission risks less than 1/15 000.

If these figures are also used for occupational exposures, then three drugs would be recommended for a percutaneous needle-stick injury with an HIV-positive source where the risk is estimated at 1/333 (Table 11.2). The CDC guidelines for

occupational exposure also modify recommendations based upon HIV disease status (e.g. asymptomatic, low viral load vs advanced disease with antiretroviral resistance) and nature of exposure. Percutaneous injuries are divided into less severe and more severe categories, and nonintact skin exposure into small volume and large volume categories (Table 11.4).²

Table 11.4. Transmission risk and recommendations for the use of post-exposure prophylaxis.

Exposure route via which a significant exposure has occurred*	Source with HIV infection		Source HIV status unknown ²	
	Risk per single exposure and recommended management ¹		Risk per single exposure and recommended management ¹	
Receptive anal intercourse	1/120 R3 ³ , C2 ⁴		MSM	Heterosexual
			1/120 x local seroprevalence R2 ⁵ or R3	1/120 000 NR ⁶
Needle-sharing injecting drug use	1/150 R3, C2		MSM IDU	Heterosexual IDU
			1/880 (or could be 1/500 see text) R3	1/15 000 C2
Percutaneous needle-stick injury	1/333 R3, C2		MSM	Heterosexual
			1/333 x local seroprevalence R2	1/330 000 NR
Receptive penile-vaginal intercourse	1/1000 R3, C2		1/1 000 000 NR 1/10 000 if source from high prevalence country C2	
Insertive anal intercourse	1/1000 R3, C2		MSM	Heterosexual
			1/1000 x local seroprevalence R2 or C2 or NR	1/1 000 000 NR
Insertive penile-vaginal intercourse	1/1000 R3, C2			
Receptive oral intercourse with ejaculation ⁷	Not measurable NR C2 if the oral mucosa is not intact		MSM	Heterosexual
			Not measurable NR	Not measurable NR
Insertive oral intercourse ⁷	Not measurable NR		MSM	Heterosexual
			Not measurable NR	Not measurable NR
Mucous membrane and non-intact skin exposure*	Small volume	Large volume	MSM	Heterosexual
	≤1/1111 R2	≤1/1111 R2, C3 ⁸	≤1/1000 x local seroprevalence C2 if large volume exposure	≤1/1 000 000 NR

NOTE: These recommendations are based upon risk estimates and practitioners may choose to adopt or modify the recommendations on a case-by-case basis.
* Significant exposure: Exposure of vagina, rectum, eye, mouth or other mucous membrane, non-intact skin, or percutaneous contact with blood, semen, vaginal secretions, rectal secretions, breast milk, or any body fluid that is visibly contaminated with blood when the source is known to be HIV infected or is at high-risk of being HIV infected.

IDU = injecting drug user; MSM = men who have sex with men

Footnotes:

1. Adapted from Australian national guidelines¹
2. Seroprevalence assumed as: 0.1% for a heterosexual source; 32% for MSM IDUs (may vary locally); 1% for heterosexual IDUs and 10% for heterosexual contact from high prevalence country (see Table 11.1).
3. R3: Recommend three antiretroviral drugs for 28 days
4. C2: Consider two antiretroviral drugs for 28 days.
5. R2: Recommend 2 antiretroviral drugs for 28 days
6. NR: Antiretroviral therapy is not recommended.
7. Refers to oral intercourse performed upon a man.
8. C3: Consider 3 antiretroviral drugs for 28 days.

Source: Adapted from the National Guidelines for post-exposure prophylaxis after non-occupational exposure to HIV. Available at: http://www.ashm.org.au/default2.asp?active_page_id=251

Table 11.5 Laboratory evaluation of people who present for non-occupational post exposure prophylaxis and their sources

Test	Baseline (Week 0)	Week 2	Weeks 4–6	Month 3	Month 6
HIV antibody	e, s		e	e	e
Hepatitis B serology ^a	e, s				e (post-immunisation)
Hepatitis C serology ^b	e, s			e	e
STI screen ^{b,c}	e, s	e ^d	e ^e	e ^e	
FBE, LFT, electrolytes ^c	e				
Pregnancy test ^b	e	e			
HIV viral load ^f	s				
HIV resistance testing ^g	s				

e = exposed individual; s=source individual.

^aIndividuals screened for hepatitis B will be immune and require no further follow up; or non-immune and require immunisation and follow-up; or carriers who require appropriate management; ^b depending upon mode of exposure; ^c baseline and where clinically indicated; ^d repeat testing for chlamydia and gonorrhoea; ^e repeat syphilis serology if negative at baseline after sexual exposure; ^f where HIV status confirmed; ^g specimen to be stored and tested in the event of NPEP failure.

Source: National Guidelines for post-exposure prophylaxis after non-occupational exposure to HIV. Available at: http://www.ashm.org.au/default2.asp?active_page_id=251

All people who have had a potential exposure to HIV in both occupational and non-occupational exposure settings should have baseline testing. This includes testing for HIV and other infections such as hepatitis B and C, as well as baseline haematological and biochemical tests in those who will be prescribed PEP. Table 11.5 shows the recommended laboratory evaluations for a person who receives NPEP, as well as the source (if able to be identified) and is adapted from the 2005 CDC guidelines.^{2,7} Patients who do not have a high risk of an intercurrent STI at the time of presentation for NPEP should have an STI screen performed at week 1 (or their first follow-up visit) following the exposure. The STI screen for MSM should include syphilis serology, first-pass urine for polymerase chain reaction (PCR) analysis for *Chlamydia trachomatis* plus rectal swab for PCR *Neisseria gonorrhoeae* and *C. trachomatis*. In addition, a throat swab for culture for *N. gonorrhoeae* may be performed if clinically indicated. These same tests should be offered to women where appropriate but all women ideally should have a cervical swab sent for *N. gonorrhoeae* and *C. trachomatis* PCR. Heterosexual men should have first-pass urine sent for *N. gonorrhoeae* and *C. trachomatis* PCR, although gonorrhoea is rare in this patient group. All patients with negative baseline syphilis serology should have repeat syphilis serology performed at week 4 or week 6.

References

- 1 Australian Government Department of Health and Ageing. National guidelines for post-exposure prophylaxis after non-occupational exposure to HIV. 2006:1-10. Available at: <http://www.ashm.org.au/guidelines/pep/pep-guidelines>. (cited April 2008)
- 2 Centers for Disease Control and Prevention. Updated U.S. Public Health Service guidelines for the management of occupational exposures to HIV and recommendations for postexposure prophylaxis. MMWR 2005;54(No. RR-9):1-13.
- 3 Australasian Society for HIV Medicine. Literature review for the Australian guidelines for post-exposure prophylaxis after non-occupational exposure to HIV. ASHM Journal Club 2006;15(4):1-32. Available at: <http://www.ashm.org.au/uploads/File/jc-2006-10.pdf> (cited April 2008).
- 4 LaFon SW, Mooney BD, McMullen JP, Pattishall KH, Smiley ML, Roques MO, et al. A double-blind, placebo-controlled study of the safety and efficacy of Retrovir (zidovudine) as a chemoprophylactic agent in healthcare workers exposed to HIV (abstract 489). Program and abstracts of the 30th Interscience Conference on Antimicrobial Agents and Chemotherapy (Atlanta). Washington, DC: American Society for Microbiology, 1990:167.
- 5 Cardo DM, Culver DH, Ciesielski CA, Srivastava PU, Marcus R, Abiteboul D, et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. Centers for Disease Control and Prevention Needlestick Surveillance Group. N Engl J Med 1997;337(21):1485-90.
- 6 Centers for Disease Control and Prevention. Public Health Service guidelines for the management of health-care worker exposures to HIV and recommendations for postexposure prophylaxis. MMWR Recomm Rep 1998;47(RR-7):1-33.
- 7 Centers for Disease Control and Prevention. Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States: recommendations from the U.S. Department of Health and Human Services. MMWR 2005;54 (No. RR-2):1-19.
- 8 Guidelines for the management and post exposure prophylaxis of individuals who sustain nonoccupational exposure to HIV. ANCAHRD Bulletin No. 28 July 2001.
- 9 Bell DM. Occupational risk of human immunodeficiency virus infection in healthcare workers: an overview. Am J Med 1997;102(5B):9-15.
- 10 Gray RH, Wawer MJ, Brookmeyer R, Sewankambo NK, Serwadda D, Wabwire-Mangen F, et al. Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda. Lancet 2001;357(9263):1149-53.
- 11 Wawer MJ, Gray RH, Sewankambo NK, Serwadda D, Li X, Laeyendecker O, et al. Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. J Infect Dis 2005;191(9):1403-9.
- 12 Abdala N, Stephens PC, Griffith BP, Heimer R. Survival of HIV-1 in syringes. J Acquir Immune Defic Syndr Hum Retrovirol 1999;20(1):73-80.
- 13 Thompson SC, Boughton CR, Dore GJ. Blood-borne viruses and their survival in the environment: is public concern about community needlestick exposures justified? Aust N Z J Public Health 2003;27(6):602-7.

- 14 National Centre in HIV Epidemiology and Clinical Research. HIV/AIDS, viral hepatitis and sexually transmissible infections in Australia Annual Surveillance Report 2007. National Centre in HIV Epidemiology and Clinical Research, The University of New South Wales, Sydney; Australian Institute of Health and Welfare, Canberra, 2007.
- 15 Do AN, Ciesielski CA, Metler RP, Hammett TA, Li J, Fleming PL. Occupationally acquired human immunodeficiency virus (HIV) infection: national case surveillance data during 20 years of the HIV epidemic in the United States. *Infect Control Hosp Epidemiol* 2003;24(2):86-96.
- 16 Ippolito G, Puro V, De Carli G. The risk of occupational human immunodeficiency virus infection in health care workers. Italian Multicenter Study. The Italian Study Group on Occupational Risk of HIV infection. *Arch Intern Med* 1993;153(12):1451-8.
- 17 Winston A, McAllister J, Amin J, Cooper DA, Carr A. The use of a triple nucleoside-nucleotide regimen for nonoccupational HIV post-exposure prophylaxis. *HIV Med* 2005;6(3):191-7.
- 18 Bassett IV, Freedberg KA, Walensky RP. Two drugs or three? Balancing efficacy, toxicity, and resistance in postexposure prophylaxis for occupational exposure to HIV. *Clin Infect Dis* 2004;39(3):395-401.
- 19 Centers for Disease Control and Prevention. Serious adverse events attributed to nevirapine regimens for postexposure prophylaxis after HIV exposures worldwide, 1997-2000. *MMWR* 2001;49(51-52):1153-6.
- 20 Mandelbrot L, Kermarrec N, Marcollet A, Lafanechère A, Longuet P, Chosidow D, et al. Case report: nucleoside analogue-induced lactic acidosis in the third trimester of pregnancy. *AIDS* 2003;17(2):272-3.
- 21 Sarner L, Fakoya A. Acute onset lactic acidosis and pancreatitis in the third trimester of pregnancy in HIV-1 positive women taking antiretroviral medication. *Sex Transm Infect* 2002;78(1):58-9.
- 22 Mallal S, Nolan D, Witt C, Masel G, Martin AM, Moore C, et al. Association between presence of HLA-B*5701, HLA-DR7, and HLA-DQ3 and hypersensitivity to HIV-1 reverse-transcriptase inhibitor abacavir. *Lancet* 2002;359(9308):727-32.
- 23 Mofenson LM. Efavirenz reclassified as FDA pregnancy category D. *AIDS Clin Care* 2005;17(2):17.
- 24 Zheng W, Smith D, Kippax S, Grulich A. Epidemiologically targeted non-occupational post exposure prophylaxis (NPEP) in Australia, 1998-2002. Program and abstracts of the 14th Annual Conference of the Australasian Society for HIV Medicine, October 2002, Sydney. Available at: www.ashm.org.au/uploads/148c.ppt (cited June 2008)
- 25 Kahn JO, Martin JN, Roland ME, Bamberger JD, Chesney M, Chambers D, et al. Feasibility of postexposure prophylaxis (PEP) against human immunodeficiency virus infection after sexual or injection drug use exposure: the San Francisco PEP Study. *J Infect Dis* 2001;183(5):707-14.
- 26 Simon BG, Almeda J, Casabona J, et al. Characteristics of demand and prescription of non occupational HIV post exposure prophylaxis (NONOPEP) in Europe. Presented at the XIV International Conference on AIDS, Barcelona, Spain, July 7-12, 2002. (Abstract MoOrD1108)
- 27 Grohskopf LA, Smith DK, Kunches LK, Robert LM, McGowan L, Paxton LA, et al. Surveillance of postexposure prophylaxis for non-occupational HIV exposures through the U.S. national registry. Presented at the XIV International Conference on AIDS, Barcelona, Spain, July 7-12, 2002. (Abstract MoOrD1107).
- 28 Pinkerton SD, Holtgrave DR. Prophylaxis after sexual exposure to HIV. *Ann Intern Med* 1998;129(8):671; author reply 672.
- 29 Pinkerton SD, Holtgrave DR, Bloom FR. Postexposure treatment of HIV. *N Engl J Med* 1997;337(7):500-1.
- 30 Pinkerton SD, Holtgrave DR, Bloom FR. Cost-effectiveness of post-exposure prophylaxis following sexual exposure to HIV. *AIDS* 1998;12(9):1067-78.
- 31 Lurie P, Miller S, Hecht F, Chesney M, Lo B. Postexposure prophylaxis after nonoccupational HIV exposure: clinical, ethical, and policy considerations. *J Am Med Assoc* 1998;280(20):1769-73.
- 32 Guinot D, Ho MT, Poynten IM, McAllister J, Pell C, Grulich AE. Cost-effectiveness of HIV non-occupational post exposure prophylaxis (NPEP) in Australia. Program and abstracts of the 18th Annual Conference of the Australasian Society for HIV Medicine; 2006, October 11-14: Melbourne Australia; p144.

