Postexposure prophylaxis for HIV infection following sexual exposure

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Individuals will often present to their GPs with concerns of HIV infection following a perceived risky sexual exposure. In such situations, an awareness of the infection risks, postexposure management and referral pathways is important.

Postexposure prophylaxis (PEP) is a prevention strategy for HIV infection involving the provision of antiretroviral medications to individuals following a recent potential or definitive high-risk exposure to the virus. Following an assessment, two or three antiretroviral drugs can be prescribed to such individuals for a total of 28 days.

PEP for HIV infection is not available through community pharmacies in Australia. It can only be accessed through emergency departments and hospital pharmacies by a prescription from sexual health physicians, infectious disease physicians or immunologists. Outside hospital settings, PEP can only be prescribed by GPs who have completed the HIV Community s100 Prescriber's Course (for details see the Australasian Society for HIV Medicine website: www.ashm.org.au).

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Nonetheless, individuals will often present to their GP with concerns following a perceived risky sexual exposure. In such situations, an awareness of the infection risks, postexposure management and referral pathways is important.

There have been no randomised controlled trials investigating the efficacy of PEP for HIV infection in humans. However, offering PEP to individuals who have had high-risk sexual exposures has been introduced throughout the developed world as a result of indirect evidence from human, animal and *in vitro* studies.[1] These studies have provided persuasive evidence that PEP is likely to be effective in preventing HIV infection and have influenced various aspects of prescribing of antiretroviral medications in these situations.

PEP for HIV infection is cost effective in Australia only if used in high-risk situations.[2] Promotion of PEP availability should therefore be targeted at those who have the highest risk of HIV – for example, homosexual men and couples in HIV serodiscordant relationships. In Australia, PEP is appropriately prescribed more often to homosexual men, as this group bears the greatest burden of HIV nationally.[3,4]

Timing of postexposure prophylaxis

The aim of PEP is to limit the spread of the initial viral inoculum, allowing the body's immune system to clear the infection. As HIV quickly disseminates beyond the initial site of inoculation following sexual exposure, the window of opportunity is narrow. PEP is likely to be effective only if the first dose is taken within 72 hours of exposure, although a shorter time from exposure to dosing is associated with higher PEP success.[1]

Assessing the risk of the exposed person

HIV transmission during sexual contact is relatively inefficient compared with the transmission of many other sexually transmissible infections (STIs).[5] The estimated risk of HIV transmission for various sexual exposures with an HIV-infected source is listed in Table 1. Cofactors related to the exposure that may increase the risk of HIV transmission include:[6]

- a high HIV load in the source individual

Table 1. Estimated risk of HIV transmission for various sexual exposures with an HIV-infected source[6]

Sexual exposure	Estimated risk of HIV transmission per act
Receptive anal intercourse	1/120
Receptive vaginal intercourse	1/1000
Insertive anal or vaginal intercourse	1/1000
Fellatio/cunnilingus	Unmeasurable (very low)

continued

Table 2. HIV seroprevalence in Australian and overseas populations[6]

Community group	HIV prevalence (%)	Risk of source being HIV infected
Homosexual men (in Australia)		
Sydney	14.2	≈1/7
Melbourne	9.1	≈1/11
Brisbane	6.0	≈1/16
Perth	4.9	≈1/20
Injecting drug users (in Australia)		
Homosexual	17.0	≈1/6
All others	1.0	1/100
Heterosexuals (in Australia)		
Blood donors	0.0005	1/2000
STI clinic attendees	<0.2	<1/500
Sex workers		
Australian born	0.1	1/1000
HIV prevalence in selected regions		
Oceania, Western and Central Europe, North Africa, the Middle East, East Asia and New Zealand	<0.5	<1/200
Latin and North America, South and South East Asia, Eastern Europe and Central Asia	0.6–1.0	⩽1/100
The Caribbean	1.6	≈1/60
Sub-Saharan Africa	7.2	≈1/14

Adapted from the *National guidelines for post-exposure prophylaxis after non-occupational exposure to HIV*, with permission of the Australian Government Department of Health and Ageing (reference 6).

- an STI, especially genital ulcer disease or symptomatic gonococcal infection, in either the source or exposed individual
- a breach in genital mucosal integrity (e.g. trauma or genital tract infection)
- a breach in oral mucosal integrity when performing oral sex, particularly for the receptive partner.

In most circumstances the HIV status of the source is unknown or unable to be obtained in a timely manner. Therefore, assessment of the risk of HIV infection often relies on knowledge of local HIV epidemiology and a 'best guess' as to the likelihood that the source was infected with HIV (Table 2).

The risk of the exposure is estimated by multiplying the risk of the exposure by the risk that the source was HIV infected, taking into account any cofactors that may enhance transmission. Table 3 provides examples of the estimated risk of acquiring HIV infection following various sexual exposures, with inclusion of PEP recommendations for each situation.

Drugs used for postexposure prophylaxis

PEP usually consists of two antiretroviral drugs. These can include two nucleoside reverse transcriptase inhibitors (e.g. coformulation of lamivudine and zidovudine; one tablet taken twice daily) or one nucleoside reverse transcriptase inhibitor and one nucleotide reverse transcriptase inhibitor (e.g. coformulation of emtricitabine and tenofovir; one tablet taken once daily). Coformulated, one tablet daily regimens may improve adherence by reducing pill burden.

A third agent from any antiretroviral drug class can be added to the regimen if required for individuals with higher-risk exposures. However, drugs known to cause severe adverse events such as abacavir and nevirapine are not used for PEP, and teratogens such as efavirenz should be avoided in women who are pregnant.[6] Three antiretroviral drugs are recommended for those with higher-risk exposures because of the theoretical improved efficacy over two-drug regimens (Tables 1 and 3).[6]

PEP is not recommended for individuals with very low-risk exposures (see examples in Table 3).[6] As the risk of acquiring HIV infection from oral sex is very low, PEP is not recommended following any oral sexual exposures, but it may be considered if the source is known to be HIV infected, and receptive oral sex with ejaculation on nonintact oral mucosa occurred.[6]

Side effects of postexposure prophylaxis

Individuals receiving PEP experience more frequent side effects than HIV-infected individuals prescribed the same antiretroviral medications for disease management, possibly as a result of anxiety associated with the exposure.[7] There is concern that poor tolerability

Table 3. Estimates of risk of HIV infection following various sexual exposures and PEP recommendations from Australian National Guidelines*[6]

Exposure risk		Source risk		Risk of HIV transmission	PEP
Example 1. Homosexual man in Sydney, receptive anal intercourse, no condom, source known to be HIV infected					
1/120	x	1 (source HIV+)	=	1/120	Recommend three antiretroviral drugs#
Example 2. Homosexual man in Perth, receptive anal intercourse, no condom, unknown HIV status of source					
1/120	x	1/20	=	1/2400	Recommend two antiretroviral drugs#
Example 3. Homosexual man in Melbourne, insertive anal intercourse, no condom, unknown HIV status of source					
1/1000	x	1/11	=	1/11,000	Consider two antiretroviral drugs#
Example 4. Heterosexual man, insertive vaginal intercourse, no condom, with Australian female sex worker of unknown HIV status					
1/1000	x	1/1000	=	1/1,000,000	Not recommended#
Example 5. Heterosexual female, receptive vaginal intercourse with heterosexual injecting drug user, no condom, unknown HIV status of source					
1/1000	x	1/1000	=	1/1,000,000	Not recommended#
Example 6. Female victim of penile-vaginal sexual assault, no condom, unknown HIV status of source					
1/1000	x	1/500 (STI clinic attendees)	=	1/500,000	Not recommended#
or					
1/1000	x	1/2000 (blood donors)	=	1/2,000,000	Not recommended#

* These risk estimates do not take into account cofactors that may increase the risk of acquiring HIV infection.
# In general: three drugs are recommended if transmission risk is 1/1000 or greater; two drugs are recommended if transmission risk is between 1/1000 and 1/10,000; two drugs are considered if transmission risk is between 1/10,000 and 1/15,000 and PEP is not recommended if transmission risk is less than 1/15,000.
ABBREVIATION: PEP = postexposure prophylaxis.

may lead to nonadherence.[1] Regular follow up may improve compliance with PEP and enable management of side effects should they occur. Most of the evidence-base supporting PEP efficacy in man is based on zidovudine. However, zidovudine-containing PEP regimens are often poorly tolerated and as a result are less frequently used.[8]

Addressing ongoing sexual risk behaviours

Prescribing antiretroviral medications as PEP for HIV infection does not appear to increase subsequent sexual risk behaviours of individuals. However, homosexual men who have ever been prescribed antiretroviral medications for prevention of HIV infection are at high risk of subsequent HIV seroconversion.[9] Irrespective of whether PEP is prescribed or not, risk-reduction counselling is an integral part of management for individuals who have had a recent high-risk sexual exposure. Encouraging condom use and identifying factors contributing to the risky exposure such as alcohol and recreational drug use are important to affect sustained behaviour change. Providing information to patients on documented failures and poor tolerability of PEP may discourage its use as a 'morning-after' pill.

STI/HIV testing and follow up

A full screen for STIs, including HIV infection, is mandatory at baseline in individuals being prescribed antiretroviral medications as PEP for HIV infection. Some candidates for PEP are found to be HIV infected at baseline and the use of PEP could potentially lead to the development of antiretroviral resistance, limiting future treatment options.[1] Clinical and laboratory follow up for individuals receiving PEP will usually be performed by the

continued

GP checklist for patients presenting with concerns over a recent unprotected sexual encounter

- **Assess exact time of exposure**
  PEP is only indicated within 72 hours of exposure
- **Assess risk of exposure of HIV infection**
  Determined by risk of exposure x risk of source being HIV infected
- **Assess any cofactors that may increase risk**
- **Provide key information to the patient on PEP for HIV infection**
  - not 100% effective: reports of PEP failure
  - possibility of delayed seroconversion: HIV test required at six months postexposure
  - possibility of side effects
  - importance of compliance
- **Assess hepatitis B vaccination status**
  If any doubt, give vaccination dose as hepatitis B PEP
- **Assess pregnancy risk in females**
  Consider emergency contraception
- **Provide brief risk-reduction counselling**
  e.g. condom use, assessment of alcohol/recreational drug use during exposure
- **Advise against douching vagina or rectum following receptive anogenital exposure**
- **Advise against brushing teeth following receptive oral sexual exposure**
- **Consider advice from PEP hotline**
  Phone: 1800 737 669 or 1800-PEP-NOW
- **Refer patient immediately to nearest sexual health clinic or hospital emergency department if PEP for HIV is being considered or if patient requests PEP for a low-risk exposure.**

prescribing doctor. As HIV seroconversion may be delayed by PEP,[1] the standard six-week to three-month postexposure 'window period' no longer applies and an HIV antibody test is required at six months postexposure. During this period, exposed individuals should be advised to avoid potential onward transmission of HIV. This includes adopting 100% condom use with all sexual partners, safe injecting practices if required, no blood or body fluid/tissue donation and avoiding exposure of their blood to others if an accident occurs. In females, pregnancy status is assessed at baseline, and follow-up pregnancy testing at two weeks is required. Patients are advised to return if symptoms of HIV seroconversion occur, which often include severe and prolonged symptoms of a viral-type illness such as fevers, headaches, generalised rash, malaise and lethargy.[10]

If PEP is not prescribed following a risk assessment and discussion with the patient, follow-up testing for HIV infection and other STIs is recommended and can easily be performed in general practice. This may include gonorrhoea and chlamydia testing of exposed sites (genital, anal) and gonorrhoea testing of the pharynx approximately one to two weeks following exposure. HIV, syphilis and hepatitis B serology should be performed at three months postexposure.

If the patient has no history of a complete course of hepatitis B vaccination, a three-dose schedule should be offered at baseline and at one and six months postexposure. A dose of hepatitis B vaccination given up to 14 days following a sexual exposure can be an effective preventative measure against hepatitis B infection.[11] The need for hepatitis A vaccinations should be assessed in all homosexual men and the two-dose schedule can be offered at baseline and six months postexposure.

Postexposure prophylaxis after sexual assault

For victims of sexual assault, acquisition of HIV infection is a common fear.[12] However, the risk of acquiring HIV infection in a female who has experienced a vaginal assault by an unknown Australian assailant is minimal (see example 6; Table 3). There is no evidence that perpetrators of sexual violence have a higher HIV seroprevalence rate than the general population in Australia. Anogenital injury may increase the risk of acquiring HIV infection, but occurs in the minority of sexual assault victims.[13] The psychological trauma of an assault can compound side effects of antiretroviral medications, and PEP completion rates in victims are low.[14] In sexual assault situations, the risk assessment of HIV infection should be no different from that following consensual sexual exposures. It is important not to prescribe PEP for HIV infection based on victims' anxiety over a perceived high-risk assault, when the actual risk of HIV infection is often minimal.

Managing anxious individuals

Anxiety over STIs or HIV infection is also commonly encountered in clinical practice following consensual sexual exposures. A precipitating factor is often not apparent but can frequently be uncovered with sensitive but direct, sexual history questioning. The most common precipitants involve a recent sexual encounter that is out of the ordinary for the patient. They correctly or incorrectly perceive the exposure as high risk, often present with a multitude of nonspecific symptoms in the absence of signs and may be concerned

regarding the risk of HIV transmission to a regular partner. Common scenarios include a married man who has had sexual contact with a sex worker, another man or a casual female partner overseas. Reassurance is often all that is required, although in rare cases referral of the patient to a counsellor or psychiatrist may be indicated. These situations present a challenge for GPs, but it is important that the risk assessment, management and advice provided are not unduly influenced by the patient's angst.

Conclusion

An awareness of HIV and other STI risks following sexual exposures should allow GPs to provide their patients with appropriate information and to refer them for PEP if indicated (see the box on page 70). PEP is an important adjunct to preventing HIV infection in Australia if it is targeted at individuals who have had high-risk sexual exposures. However, the availability of PEP should not undermine primary prevention efforts, which remain the cornerstone of Australia's public health response to HIV. MT

References

1. Australian 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: 1-31. Available online: http://www.ashm.org.au/images/publications/guidelines/jc-2006-10.pdf (accessed September 2009).
2. Guinot D, Ho MT, Poynten IM, et al. Cost-effectiveness of HIV non-occupational post exposure prophylaxis (NPEP) in Australia. HIV Medicine 2009; 10: 199-208.
3. Grulich AE. Epidemiologically targeted post-exposure prophylaxis against HIV: an underutilized prevention technology. HIV Med 2003; 4: 193-194.
4. 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, NSW; Australian Institute of Health and Welfare, Canberra, ACT; 2007. Available online: http://www.nchecr.unsw.edu.au/NCHECRweb.nsf/resources/SurvReports_3/$file/ASR2007 (accessed September 2009).
5. Donovan B, Bradford D, Cameron S, et al. eds. The Australasian Contact Tracing Manual. 3rd ed. Sydney: Australasian Society for HIV Medicine; 2006. Available online: http://www.ashm.org.au/contact-tracing (accessed September 2009).
6. National guidelines for post-exposure prophylaxis after non-occupational exposure to HIV. Canberra: Australian Government Department of Health and Ageing; 2007. Available online: http://www.ashm.org.au/uploads/2007national NPEPguidelines2.pdf (accessed September 2009).
7. Quirino T, Niero F, Ricci E, et al. HAART tolerability: post-exposure prophylaxis in health-care workers versus treatment in HIV-infected people. Antivir Ther 2000; 5: 195-197.
8. Winston A, McAllister J, Amin J, et al. The use of a triple nucleoside-nucleotide regimen for nonoccupational HIV post-exposure prophylaxis. HIV Med 2005; 6: 191-197.
9. Poynten IM, Jin F, Prestage GP, et al. Nonoccupational postexposure prophylaxis, subsequent risk behaviour and HIV incidence in a cohort of Australian homosexual men. AIDS 2009; 23: 1119-1126.
10. Tindall B, Barker S, Donovan B, et al. Characterization of the acute clinical illness associated with human immunodeficiency virus infection. Arch Intern Med 1988; 148: 945-949.
11. The Sexual Health Society of Victoria. National Management Guidelines For Sexually Transmissible Infections. 7th ed. Victoria: The Sexual Health Society of Melbourne; 2008. Available online: http://www.mshc.org.au/Portals/6/NMGFSTI.pdf (accessed September 2009).
12. Templeton DJ, Davies SC, Garvin AL, Garsia RJ. The uptake of HIV post-exposure prophylaxis within a sexual assault setting in Sydney, Australia. Int J STD AIDS 2005; 16: 108-111.
13. Mein JK, Palmer CM, Shand MC, et al. The management of acute adult sexual assault. Med J Aust 2003; 178: 226-230.
14. Wiebe ER, Comay SE, McGregor M, Ducceschi S. Offering HIV prophylaxis to people who have been sexually assaulted: 16 months' experience in a sexual assault service. CMAJ 2000; 21: 780-785.

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