



Australian Government
Department of Health and Ageing

NATIONAL GUIDELINES FOR POST-EXPOSURE PROPHYLAXIS AFTER NON-OCCUPATIONAL EXPOSURE TO HIV

These guidelines outline the management of individuals who have been exposed (or suspect they have been exposed) to HIV in the non-occupational setting. Since they were originally developed in 2001, there have been advances in knowledge of HIV pathogenesis, treatment and non-occupational post-exposure prophylaxis (NPEP). There are currently no data from randomised controlled trials of the use of NPEP, and still many gaps in the scientific data, with assumptions made accordingly about the direction of management.

THESE NATIONAL NPEP GUIDELINES ARE:

- replacing the guidelines for the management and post-exposure prophylaxis of individuals who sustain non-occupational exposure to HIV, *ANCAHRD Bulletin* No 21 July 2001
- produced by the Australasian Society for HIV Medicine (ASHM)
- located at <http://www.ashm.org.au/guidelines/hiv-guidelines/pep/pep-guidelines/>
- funded by the Australian Government Department of Health and Ageing (DoHA)
- endorsed by the HIV and Sexually Transmissible Infection Subcommittee of the Ministerial Advisory Committee on AIDS, Sexual Health and Hepatitis, the former Intergovernmental Committee on AIDS, Hepatitis C and Related Diseases and ASHM
- to be reviewed on an on-going basis by the Models of Care Panel of ASHM, for advice to DoHA
- supported by a literature review and other documents at:
<http://www.ashm.org.au/guidelines/hiv-guidelines/pep/pep-guidelines/> and <http://www.ashm.org.au/moc/>.

The advice provided is necessarily general.

Specific implementation details in response to regional differences are available through state, territory and local agencies.

Australian Guidelines for Non-Occupational Post Exposure Prophylaxis

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ASSESSMENT OF THE RISK OF HIV TRANSMISSION

The risk of HIV transmission through a single exposure is determined by:

- the method of exposure with its estimated risk/exposure (Table 1)
- the risk that the source is HIV positive, if their status is unknown (Table 2)
- co-factors associated with the source and exposed individuals.

RISK OF HIV TRANSMISSION

= risk/single exposure x risk of source being HIV positive

1. Is the exposure sufficient to recommend NPEP?

Table 1: Exposure and transmission risk/exposure

Type of exposure with known HIV+ source	Estimated risk of HIV transmission/exposure ¹
Receptive anal intercourse (RAI)	1/120
Use of contaminated injecting equipment	1/150
Occupational needlestick injury	1/333
Receptive vaginal intercourse	1/1,000 ²
Insertive anal or vaginal intercourse	1/1,000 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

There is evidence that the following co-factors may increase the risk of HIV transmission. They may be considered in the overall risk assessment:

- high viral plasma load (a low load does not eliminate transmission risk)
- a sexually transmissible infection in either the source or exposed individual, especially genital ulcer disease and symptomatic gonococcal infections
- 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
- penetrating, percutaneous injuries with a hollow bore needle, direct intravenous or intra-arterial injection with a needle or syringe containing HIV-infected blood.

It is important to also consider that:

- the risk of **transmission by a source of unknown HIV status is considerably less** than by a known positive source.

Footnotes

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.

2. What is the HIV status of the source individual?

Provision of NPEP should not be delayed while establishing the source status:

- active attempts should be made to contact the source, by the exposed individual (patient) or, with the patient's consent, treating doctor or contact tracing staff
- if the source discloses they are HIV-positive, consent is gained to seek treatment details from their doctor
- if the source discloses they are not infected with HIV, they are asked to urgently undertake an HIV test (with pre-test discussion provided)
- in cases where the source refuses to disclose their HIV status or have a test for HIV, it should be assumed for the purposes of NPEP prescription that they are HIV-positive
- if the source cannot be contacted, the seroprevalence data in Table 2, below, will assist in determining the need for NPEP.

Table 2: HIV seroprevalence in Australian and overseas populations

Community group	HIV seroprevalence (%)
Homosexual men (MSM – men who have sex with men) 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) ⁵
all others	1.0
Heterosexuals (in Australia)	
blood donors	0.0005
STI clinic attendees	<0.2
Commercial sex workers (in Australia)	
Australian born	0.1
HIV seroprevalence in selected regions⁶	
- Oceania, Western & Central Europe, North Africa & Middle East, East Asia, New Zealand	≤0.5
- Latin America, North America, S & SE Asia, Eastern Europe & Central Asia	0.6–1.0
- Caribbean	1.6
- Sub-Saharan Africa	7.2

3. What is the HIV status of the exposed individual?

- All candidates for NPEP require baseline HIV antibody testing. Where possible, the results are followed up within 24 hours of the specimen being collected. Urgent testing should be available to individuals who are identified as at high risk for HIV⁷.

Risk calculation

Table 3: Contact with an MSM source

Population group and exposure	KNOWN HIV + source status	UNKNOWN HIV+ status ⁸
Receptive anal intercourse	1/120 X 1 = 1/120 (recommend 3 drugs)	1/120 X <i>local seroprevalence</i> ⁹ (recommend 2 or 3 drugs)
Contaminated injecting equipment	1/150 X 1 = 1/150 (recommend 3 drugs)	1/150 X 17% ~ 1/900 ¹⁰ (recommend 3 drugs at this level – may vary locally)
Insertive anal intercourse	1/1,000 X 1 = 1/1,000 (recommend 3 drugs)	1/1,000 X <i>local seroprevalence</i> (consider or recommend 2 drugs or recommend no NPEP) ¹¹
Receptive oral intercourse with ejaculation	Not measurable (not recommended*)	Not measurable (not recommended)
Insertive oral intercourse	Not measurable (not recommended)	Not measurable (not recommended)

*Consider 2 drugs if the oral mucosa is not intact

Footnotes

⁵ The rates of HIV in homosexual injecting drug users (IDU) vary considerably between different studies; they are also based on small samples. Prescribers are recommended to seek out local data to assist.

⁶ 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 (IDU), commercial sex work and men who have sex with men (MSM). Country-specific information for the general population and sub groups is available through the UNAIDS/WHO online database at www.who.int/globalatlas/.

⁷ It is recognised that not all areas can provide test results within 24 hours.

⁸ Calculations are based on local data. Note transmission risk may change if sex partner also is IDU or from HPC (see footnote 11).

⁹ See Table 2, this will include individuals from HPC.

¹⁰ Local seroprevalence may be at a lower level so that 2 drugs may be recommended or considered or NPEP may be not recommended.

¹¹ See textbox at end of this section.

Table 4: Contact with a heterosexual source

Population group and exposure	KNOWN HIV+ source status	UNKNOWN HIV+ status Sero-prevalence assumed as 0.1% for a heterosexual source, 1% for Injecting Drug Users (IDU) and 10% for heterosexual contact from high prevalence country (HPC)¹²
Receptive anal intercourse	$1/120 \times 1 = 1/120$ (recommend 3 drugs)	$1/120 \times 1/1,000 = 1/120,000$ (not recommended) $1/120 \times 1/100 = 1/12,000$ (with IDU) (consider 2 drugs) $1/120 \times 1/10 = 1/1,200$ (with person from HPC) (recommend 2 drugs)
Contaminated injecting equipment	1/150 (recommend 3 drugs)	(assume IDU) $1/150 \times 1/100 = 1/15,000$ (consider 2 drugs) $1/150 \times 1/10 = 1/1,500$ (with person from HPC) (recommend 2 drugs)
Receptive vaginal, insertive anal or insertive vaginal intercourse	1/1,000 (recommend 3 drugs)	$1/1,000 \times 1/1,000 = 1/1,000,000$ (not recommended) $1/1,000 \times 1/100 = 1/100,000$ (with IDU) (not recommended) $1/1,000 \times 1/10 = 1/10,000$ (with person from HPC) (consider 2 drugs)
Receptive oral intercourse with ejaculation	Not measurable (not recommended*)	Not measurable (not recommended)
Insertive oral intercourse	Not measurable (not recommended)	Not measurable (not recommended)

*Consider 2 drugs if the oral mucosa is not intact.

There are a variety of scenarios when NPEP may be indicated. Ultimately, the clinician will be evaluating factors that cannot be addressed in these guidelines and will make a clinical judgement considering all these variables. The guidelines are not, therefore, prescriptive, but put forward cases where NPEP is recommended; where NPEP should be considered (where the risks of treatment may assume a greater weight and the evidence of benefit is less) and cases where NPEP is not recommended (where the treatment risks outweigh the risk of exposure). The assessment of risk exposure is based on the limited prospective data (where available). Adverse effects caused by antiretrovirals, used for both NPEP and treatment of HIV, and their impact on adherence are frequent and well recognised. Anticipated ability to complete the full 28-day course is a very important factor to consider before recommending NPEP.

Generally, these guidelines recommend 3 drugs if the transmission risk is 1/1,000 or greater; 2 drugs if it is between 1/1,000 and 1/10,000 and considers 2 drugs if the risk ranges from less than or equal to 1/10,000 and greater than or equal to 1/15,000. NPEP is not recommended for lower-risk exposures.

Recommend 3 drugs	Transmission risk $\geq 1/1,000$
Recommend 2 drugs	$1/1,000 > \text{transmission risk} > 1/10,000$
Consider 2 drugs	$1/10,000 \geq \text{transmission risk} \geq 1/15,000$
Does not recommend NPEP	Transmission risk $< 1/15,000$

Footnote

¹² Country-specific information for the general population and sub groups is available through the UNAIDS/WHO online database at www.who.int/globalatlas/.

INDICATIONS FOR NPEP

NPEP should be prescribed as soon as possible after the exposure and within 72 hours.

NPEP is **recommended** when:

The source is known to be HIV-positive

3 drugs are prescribed where the exposure is:

- receptive anal intercourse or
- shared injecting equipment (needle and/or syringe)
- receptive vaginal intercourse or
- insertive anal intercourse or
- insertive vaginal intercourse.

The source status is unknown

3 drugs in some areas of high prevalence where the exposure is:

- sharing injecting equipment between MSM (see Table 2)
- receptive anal intercourse between MSM (see Table 2).

2 drugs and the exposure is:

- shared injecting equipment between MSM or a person from a HPC (see Table 2)
- receptive anal intercourse between MSM (see Table 2)
- receptive anal intercourse with a partner (*heterosexual or MSM*) from a HPC.

NPEP (2 drugs) is **considered** when:

The source is known to be HIV+ and

- the exposure is receptive oral intercourse with ejaculation AND the oral mucosa is NOT INTACT.

The source status is unknown and the exposure is:

- insertive anal intercourse between MSM
- receptive anal intercourse and the source is a heterosexual IDU
- sharing injecting equipment between heterosexuals
- receptive vaginal or insertive vaginal or anal intercourse with a partner from a HPC.

NPEP is **not recommended** when:

The source is known to be HIV+ and the exposure is

- receptive oral intercourse with ejaculation WITH INTACT oral mucosa
- non-occupational contamination of INTACT mucosa and skin with body fluids.

The source status is unknown and the exposure is:

- heterosexual anal, vaginal or oral intercourse (NOT from HPC)
- a community acquired needle-stick injury.

IMMEDIATE MANAGEMENT OF AN INDIVIDUAL WITH KNOWN OR SUSPECTED EXPOSURE TO HIV

- do not douche the vagina or rectum after sexual exposure
- after oral exposure, spit out blood/body fluids and rinse with water
- wash wounds and skin sites that have been in contact with blood or body fluids
- irrigate mucous membranes and eyes (remove contact lenses) with water or saline
- do not inject antiseptics or disinfectants into wounds.

CLINICAL ASSESSMENT AND FOLLOW-UP

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 Transmissible 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
 - (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. See National HIV Testing Policy 2006¹³.

6. Follow-up

Individuals found to be HIV+ on baseline testing or during follow-up require 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.

Footnote

¹³ Australian Government Department of Health and Ageing 2006. National HIV Testing Policy, Canberra
http://www.health.gov.au/internet/wcms/publishing.nsf/Content/health-pubhlth-strateg-hiv_hepc-hiv-index.htm#testing

LABORATORY ASSESSMENT AND FOLLOW-UP

All individuals seeking care after potential exposure to HIV should have baseline and follow-up testing for HIV and other infectious conditions (depending on the mode of exposure). Those prescribed NPEP will benefit from baseline haematological and biochemical tests. Regular follow-up (weekly for the first two weeks, then weekly or fortnightly) will provide opportunities to minimise and manage side effects and may improve adherence.

Table 5 below sets out the minimum recommended schedule of testing for exposed and source individuals (adapted from 2005 Centers for Disease Control guidelines). The management of an exposed patient who seroconverts is not included. The symptoms of seroconversion should be explained to all patients with advice to present if these, or any other symptoms occur.

Table 5: Laboratory evaluation of individuals who present for NPEP 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	E, S	E ^c	E ^d	E ^d	
FBE, LFT, electrolytes ^e	E,				
Pregnancy test ^{b, d}	E,	E			
HIV viral load ^f	S				
HIV resistance testing ^g	S				

E = exposed individual; S=source individual

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

WHICH REGIMEN?

Patients who are prescribed NPEP are fully informed by their clinician of the uncertain efficacy of this intervention, the importance of adherence and the potential adverse effects associated with a 28-day course of antiretrovirals. Other key information includes preventive measures and description of seroconversion symptoms.

1. Time to initiation

Patients presenting for NPEP should be triaged as a priority. Early initiation of NPEP, as soon as possible after exposure, is strongly urged. NPEP should not be offered more than 72 hours after exposure.

2. Duration of treatment

A 28-day course of NPEP is recommended practice. A proactive approach to managing side effects will assist patients to adhere to treatment.

3. Period and frequency of follow-up

HIV antibody testing is conducted at baseline, at 4 to 6 weeks, and 3 and 6 months after exposure where HIV is the only blood-borne pathogen to be potentially transmitted. If there is a possibility of co-infection, expert advice should be sought. More frequent follow-up while the patient is taking the NPEP course may improve adherence. Patients should be referred to appropriate services for support as required.

4. Two vs three drugs

There is no direct evidence to support the greater or lesser efficacy of three over two drug preventive regimens. The recommendation for the number of antiretroviral drugs is based on the estimated risk of exposure. It is an extrapolation of the benefit conferred by increased numbers/classes of drugs for HIV treatment. In some other infections (e.g. malaria), the drug regimens used for prophylaxis are quite distinct from those used for treatment. Side effects, toxicity, adherence and cost effectiveness are important areas to consider when prescribing. Again, there is no clear evidence that two or three drugs have a superior side-effect profile or adherence or cost effectiveness.

5. Which drugs?

The choice of drugs will depend on the clinical status of the exposed and the source. Apart from zidovudine (AZT), there is no evidence to support the use of one drug or class of drug over another. Other factors to consider include the simplicity of the dosing regimen, and minimisation of side effect and drug interactions. Many prescribers provide NPEP starter packs, to encourage follow-up, support adherence and minimise drug waste if the course is not finished.

POSSIBLE REGIMENS¹⁴

Two-drug regimens:

- 2 nucleoside reverse transcriptase inhibitors (NRTIs) (may include a nucleotide reverse transcriptase inhibitor, tenofovir)

Three-drug regimens:

- 2 NRTIs (may include a nucleotide reverse transcriptase inhibitor)
+ protease inhibitor (PI) or non nucleoside reverse transcriptase inhibitor (NNRTI)
- 2 nucleoside RTIs + a nucleotide RTI.

Drugs NOT to use for NPEP:

- Nevirapine (NNRTI) is contraindicated for NPEP
- Combination d4T and ddI is not recommended, and contraindicated in pregnancy
- Abacavir (NRTI) is associated with hypersensitivity reactions that may make it unsuitable to use as NPEP
- Efavirenz (NNRTI) is contraindicated in pregnancy.

If in any doubt, seek expert advice about suitable treatment regimens.

Footnote

¹⁴ Commonly prescribed NRTIs are AZT and lamivudine (3TC) or 3TC and tenofovir or emtricitabine and tenofovir; lopinavir/ritonavir is an enhanced PI; efavirenz is a NNRTI.

MANAGEMENT OF POSSIBLE EXPOSURE TO OTHER CONDITIONS

1. Hepatitis B

All individuals presenting for NPEP are assessed for the possibility of hepatitis B exposure and are managed according to the guidelines from the Australian Immunisation Handbook <http://www9.health.gov.au/immhandbook/pdf/handbook.pdf>.

2. Sexually transmissible infections

Individuals presenting for NPEP are screened for chlamydia, gonorrhoea and syphilis as indicated by the exposure, local epidemiology and guidelines. If symptoms are present, further appropriate tests and follow-up should be performed.

3. Hepatitis C

Individuals who are potentially at risk of hepatitis C infection after exposure require follow-up for this and specialist referral if seroconversion is detected. They should be informed of symptoms of acute hepatitis, with advice to present if these occur.

4. Pregnancy

Pregnancy tests are provided to all sexually active women presenting for NPEP. Emergency contraception is offered to women presenting for NPEP who are at risk of pregnancy. Follow-up pregnancy tests should be offered at two weeks post-exposure where indicated. Specialist advice should be sought urgently for women who require NPEP and are pregnant or breastfeeding.

5. Tetanus

Individuals who sustain wounds or abrasions should have their tetanus status assessed and be offered immunisation as indicated.

ADDITIONAL CLINICAL MANAGEMENT ISSUES

1. Preventive behaviours whilst being managed for HIV exposure

Patients should adopt preventive practices until their seronegative status is confirmed at follow-up. This applies to safe sexual and injecting behaviour as well as preventing others from exposure to their body fluids through means such as accidents or body donation. Women should be counselled about pregnancy, the risk of mother-to-child transmission and contraception.

2. Individuals at risk of HIV transmission who decline NPEP

Education about preventive behaviours and HIV seroconversion is provided to these individuals. It is important that they can maintain a positive relationship with their health service so that they are monitored clinically and tested over the following three months.

3. Individuals at negligible risk of HIV transmission who request NPEP

This response may relate to anxiety and fear about an apparently negligible exposure or undisclosed more serious risks of infection.

It is important that the clinician takes a supportive approach and documents all advice given, including that NPEP was not recommended and if it was prescribed. Early follow-up and a low threshold for psychological and HIV specialist referral is recommended.

4. Individuals who re-present for NPEP

Those who present for repeat NPEP should be supported, with each potential exposure assessed on its merits. Such presentations are an opportunity for ongoing education and counselling and assessment of predisposing medical, psychological and social factors (see 2006 National HIV Testing Policy).

5. Individuals who have been sexually assaulted

Survivors of sexual assault should be assessed for their need for NPEP as early as possible. There are no data on HIV prevalence for convicted sexual assailants in Australia, however studies on HIV point prevalence in Australian jails ranges between 0 and 0.6%, with most jurisdictions reporting below 0.1%. Sexual assaults may involve multiple assailants, unprotected vaginal, anal and oral penetration and result in genital and other physical trauma. While these factors may increase the risk of HIV exposure, it generally remains low.

An individualised assessment of survivors is necessary to address these issues, including informed consent, in a context of psychological stress.

6. Prisoners and detainees

Inmates who are potentially exposed to HIV sexually, through injecting drug use or other means require assessment for NPEP as soon as possible after exposure. HIV point prevalence in Australian jails is estimated as less than 0.1%, although this data is drawn from small and biased samples and should be used carefully. Timely disclosure of exposure is obviously a limiting factor in these circumstances. The provision of assessment and treatment in correctional facilities should be available across all jurisdictions. Responses should be tailored to the circumstances of jurisdictional correctional health services.

7. Risk communication: understanding the risk of exposure

Communicating the risk of an action or consequence can be very difficult. This is compounded by the diversity of interpretations of personal risk.

Table 6: Estimates to quantify risk¹⁵

Risk	Term
1/1 to 1/10	Very High
1/10 to 1/100	High
1/100 to 1/1,000	Moderate
1/1,000 to 1/10,000	Low
1/10,000 to 1/100,000	Very Low
1/100,000 to 1/1,000,000	Minimal
1/1,000,000 to 1 in 1 billion/trillion	Negligible

INFORMATION FOR CLINICIANS

Further information about NPEP and antiretroviral prescribing is available on the ASHM website at:

<http://www.ashm.org.au/guidelines/hiv-guidelines/pep/pep-guidelines/>

<http://www.ashm.org.au/moc/>

http://www.ashm.org.au/aust_guidelines/

Local information may be found on health department websites in each jurisdiction.

INFORMATION FOR PATIENTS

The HIV Patient Fact Sheet was updated by ASHM in 2006 and is available at: www.ashm.org.au/hiv-patient-sheet.

Footnote

¹⁵ Adapted from the draft Victorian NPEP service guidelines, September 2005, citing Paling J. Strategies to help patients understand risks BMJ 2003 327(7417):745-8.