

Professionals Briefing

HIV Post-Exposure Prophylaxis following sexual exposure (PEPSE)

This briefing is intended to refresh primary care healthcare practitioners of the essential information needed to manage a patient requesting PEP following sexual exposure (PEPSE). On this matter, the Chief Medical Officers' Expert Advisory Group on AIDS (EAGA) endorses the guidelines published by the British Association for Sexual Health and HIV (BASHH) in February 2006; *UK Guideline for the use of post-exposure prophylaxis for HIV following sexual exposure*¹

What is post-exposure prophylaxis for sexual exposure (PEPSE)?

- PEPSE is an emergency antiretroviral treatment prescribed to individuals who engage in sexual behaviour(s) that places them at risk of HIV infection.
- It consists of a 28-day course of antiretroviral therapy (ART) which must commence within 72 hours of sexual exposure to the virus to ensure the effectiveness of the therapy.
- Individuals on PEPSE may experience unpleasant side-effects.
- Access to PEPSE is based on individual risk assessment.

What is the evidence that PEPSE works?

For ethical and logistical reasons, a randomised, placebo-controlled clinical trial to investigate the effectiveness of PEPSE is unlikely to be performed. Instead evidence of the effectiveness of PEPSE is often taken from data available from animal transmission models, perinatal clinical trials, studies of health care workers receiving prophylaxis after occupational exposures and from observational studies. These data indicate that non-occupational PEP (e.g. PEPSE) might sometimes reduce the risk for HIV infection after non-occupational exposures.²

Animal studies have demonstrated that the effectiveness of PEPSE is very much a function of length of time taken to administer PEPSE to clients following their exposure to the virus and the duration of that therapy; in one study of macaques monkeys intravenously exposed to the simian immunodeficiency virus (SIV) infection, the monkeys who received tenofovir (a single component of the recommended PEPSE regimen) within 24 hours of exposure and continued treatment for 28 days effectively blocked the SIV infection. Conversely in those that therapy was initiated 48 or 72 hours post exposure or who received treatment for only 3 or 10 days, tenofovir was not effective.³

Postnatal Prophylaxis - A review of medical records in New York indicated that zidovudine monotherapy administered to the mother intrapartum (to protect neonates from exposure to maternal HIV) or to the infant within 72 hours of birth decreased perinatal transmission >50% whereas when monotherapy for the infant was started >72 hours after birth, it was less effective⁴. Likewise, an analysis of births in the PACTS study showed that zidovudine administered to infants within 24 hours of birth, when mothers had not been treated either antepartum or intrapartum, compared against no treatment for mothers or infants; lowered perinatal transmission by 48%⁵.

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Observational Studies - A case-control study of needlestick injuries to healthcare workers showed that prompt initiation (i.e. 4 hours after exposure) and continued use (for at least 4 weeks) of zidovudine was linked with an 81% reduction in the risk of acquiring HIV.⁶

In a high-risk HIV cohort of 200 homosexual and bisexual men (in Brazil) administered with 4-day starter packs of zidovudine and lamivudine, it was discovered that seroincidence was 0.7 per 100 person-years (one seroconversion) among men who took non-occupational PEP (nPEP) and 4.1 per 100 person-years among men who did not take nPEP (11 seroconversions)^{7,8}.

To conclude, although data from the studies and case reports do not provide definitive evidence of the efficacy of PEPSE / nPEP after sexual and other non-occupational exposures to HIV, the cumulative data demonstrates that; antiretroviral therapy initiated soon after exposure and continued for 28 days might reduce the risk for acquiring HIV.

Who can prescribe PEPSE?

PEPSE should only be administered under the guidance of a clinician experienced in the management of ART and with expertise in HIV testing and transmission. Patients requesting PEPSE in general practice should be referred immediately to the nearest available specialist HIV treatment centre, usually the Genitourinary Medicine (GUM) or Infectious Diseases (ID) department of the nearest hospital. If the request is made outside of regular clinic hours, responsibility for the provision of PEPSE lies with the Emergency Department (ED). The BASHH guideline recommends that EDs have a policy on PEPSE provision which includes 24-hour access to advice from an experienced GUM, ID or HIV physician.

PEPSE is most effective when taken promptly following exposure. The BASHH guideline recommends that PEPSE be initiated preferably within 24 hours, with a maximum limit of 72 hours, as effectiveness is vastly reduced after this time. **Prompt referral is therefore essential and practices should be aware of the location of their nearest specialist HIV treatment centre.**

Patients can request PEPSE from the settings mentioned without referral from a GP. However, PEPSE will not automatically be prescribed on request. A risk-assessment is first performed to determine the likelihood that the individual has been exposed to HIV, the potential for transmission following any such exposure and the presence of pre-existing undiagnosed (and therefore untreated) HIV infection. PEPSE is then administered following outcome of assessment.

How is the risk of HIV transmission assessed?

Table 1: A broad summary of the risk assessment algorithm in the BASHH guidelines.

| | <i>Partner with known HIV-positive status</i> | <i>Partner from high prevalence area/group</i> | <i>Partner meeting neither criterion</i> |
|---|---|--|--|
| <i>Receptive anal sex</i> | Recommended | Recommended | Considered |
| <i>Insertive anal sex</i> | Recommended | Considered | Not recommended |
| <i>Oral sex with ejaculation</i> | Considered | Considered | Not recommended |
| <i>Oral sex with no ejaculation</i> | Not recommended | Not recommended | Not recommended |
| <i>Mucous membrane exposure (e.g. semen in eye)</i> | Considered | not stated | Not recommended |

The BASHH guideline requires an assessment of the risk of HIV transmission to be made using the following formula:
risk of HIV transmission = risk that source is HIV-positive x risk of exposure

See page 4 for references⁶⁻⁸

PEPSE is likely to be recommended under the following conditions: (1) if the source contact is HIV positive and the sexual act engaged in is receptive anal sex; (2) if the source contact is HIV positive and the sexual act engaged in is insertive anal sex or (3) if the source contact is from a high prevalence area/group (eg. IDU's and men who have sex with men (MSM)) and the sexual act engaged in is receptive anal sex. For other conditions under which PEPSE may be considered please see table 1. PEPSE is not recommended / deemed necessary for risk contacts that occurred more than 72 hours prior to clients presenting for PEPSE, and in this case referrals should be made for HIV testing with a clear explanation about the window period. Please see Table 1 for other conditions highlighted by the BASHH guideline under which PEPSE is not recommended.

Other factors determining the prescription of PEPSE

Viral load and STI presence in the source contact may be used as a guide in determining prescription of PEPSE. It is well-known that for individuals who are HIV positive, a high viral load correlates with an increased risk of HIV transmission. Reducing HIV viral load with ART can significantly reduce levels of onward HIV transmission in a population⁹. On this premise and from observations made on sero discordant heterosexual couples, there is the opinion that PEPSE should not be recommended if a source contact, diagnosed as HIV positive and on successful ART has an undetectable viral load and no other sexually transmitted infections. This is because those supporting this view see such individuals as sexually uninfected. However, this position which was officially declared by the SWISS Federal AIDS Commission (January 2008)¹⁰ is controversial for the following reasons: (1) this position can only be generalised to monogamous heterosexual couples as only such couples were observed in the studies that this position is based on (2) this stance carries the unintentional message of promoting reduction of safe sex practices in sero-discordant relationships; (3) STI may be asymptomatic so STI presence is not a good basis for determining PEPSE prescription; (4) there is not enough evidence to support this stance when it comes to the decision to prescribe PEPSE for MSM particularly with regards to probability of HIV transmission through anal sex, in light of trauma to mucous membrane (bleeding) which is not uncommon with MSM; and (5) HIV is sporadically detectable in the semen of men with undetectable viral load¹¹. The threshold level of seminal viral HIV which corresponds to high transmission risk is unknown¹². Consequently in light of such arguments, it will be irresponsible to generalise these markers to all situations when it comes to deciding whether PEPSE is to be prescribed.

Cost effectiveness of PEPSE

There are no guarantees that PEPSE will be prescribed simply because it has been requested. It remains at the discretion of the attending clinician to take account of patients' wishes and balance them against other considerations, including cost-effectiveness. The issue of cost-effectiveness is particularly relevant when the HIV-positive status of the source contact is unknown. Under such circumstances the value of PEPSE as a public health prevention intervention is best tackled at the population level by using techniques like cost-benefit analysis. The outcomes of such analyses have been published: One cost-effectiveness evaluation of non-occupational PEP (nPEP) in different potential exposure scenarios in the United States found it to be cost-effective only in situations in which the source contact was known to be HIV-positive or after unprotected receptive anal intercourse with a homosexual or bisexual man of unknown serostatus^{13,14}. Similarly a recent study from Australia concluded that PEPSE was only cost-effective after receptive unprotected anal intercourse exposure to an HIV-positive source¹⁵.

Recommended drugs for use as PEPSE

The EAGA guidance recommends the use of one Truvada tablet (245mg tenofovir and 200mg emtricitabine (FTC)) once a day plus two Kaletra film-coated tablets (200mg lopinavir and 50mg ritonavir) twice a day as the preferred regimen. At an ED this would be provided in a starter pack of three-to-five days' medication. The regimen can be continued or modified within five days at the follow-up appointment with an HIV clinician. However, the drugs used in any PEP regimen may vary if there is additional information about an HIV-positive source contact's viral load, treatment regimen and resistance profile.

See page 4 for references ⁹⁻¹⁵



Side Effects

There are well known side effects to the drugs when they are used to treat HIV-infected individuals, and these appear to be exacerbated in HIV-negative individuals. The side effects include nausea and vomiting, diarrhoea and body rashes, and have been known to last for more than a week.

PEPSE, HIV testing and confidentiality issues

If an individual is assessed as requiring PEPSE an HIV test will be performed using a rapid testing device. This is to ensure that there is no pre-existing undiagnosed HIV infection which would render PEPSE superfluous and possibly compromise the effectiveness of later ART by creating drug resistance. Where PEPSE is requested in a GUM setting, the normal levels of GUM confidentiality apply. However, concerns have been raised that these protections would not be in force if PEPSE is initiated through an ED. The position of medical records following a request for PEPSE and any subsequent treatment through the ED has been clarified in consultation with one of the major London hospitals which offers PEPSE, that the initial consultation in the ED will be recorded as usual, including any initial investigations and subsequent treatment. Any person seen for PEPSE in the ED will be referred for further assessment and treatment at a specialist HIV centre, so any further records would be treated as at a GUM clinic. It is standard practice for the patient's GP to be informed of any attendance for treatment at an ED, so it is important to emphasise the practice's policy on confidentiality to individuals requesting information on PEPSE in the event of them receiving a positive HIV test result. Patients should also be reassured that a negative HIV test result will not be mentioned in medical reports for applications for life assurance.

Local availability of PEPSE

PEPSE is available at the GUM clinics and EDs of Ealing Hospital, West Middlesex University Hospital and Charing Cross Hospital. It is also available through the Chelsea and Westminster Hospital.

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