HIV Post-exposure Prophylaxis

Introduction
See separate article Needlestick Injury for more information.

Post-exposure prophylaxis (PEP) may be offered for:

- Occupational exposure to hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV). The management of this risk should form part of an integrated workplace safety plan. Health workers and members of the practice team should be aware of the risk, how to reduce risk and what to do in the event of a needlestick injury.[1, 2, 3]
- Non-occupational exposure to HBV, HCV and HIV (for example, sexual, paediatric and perinatal).[4, 5, 6, 7]

Rationale for post-exposure prophylaxis
Most of the evidence for efficacy has been gathered from occupational exposure. The evidence base is growing, although further randomised studies are needed. The main areas for consideration are:

- Pathogenesis of HIV infection. This suggests a window of opportunity after infection, to prevent viral replication. A combination of primate and human studies suggests PEP is most likely to be effective when initiated as soon as possible (the gold standard is an hour and certainly within 48-72 hours of infection) and continued for at least 28 days.[1]
- Efficacy of antiretroviral treatment (ART) in primates. Results also suggest that early, adequate doses of ART, given for long enough, are important.[5]
- Evidence of efficacy of ART for non-occupational exposure in humans. Evidence from studies of vertical transmission and use of PEP in men who have sex with men (MSM) is supportive but as yet there are no confirmatory systematic reviews.[8]
- Assessment of risks and benefits of PEP.

When to prescribe post-exposure prophylaxis
PEP is unpleasant to take and the drugs used have side-effects and toxic effects. This needs to be balanced against the risk of transmission of HIV infection, estimated to be:[6]

- 3/1,000 percutaneous exposures.
- <1/1,000 mucocutaneous exposures.

Quick guide to important factors when considering PEP and protocols for PEP[1]
- Preventing avoidable exposure is of prime importance and guidance for this should be scrupulously followed.
- All healthcare workers (and students) should be informed and educated about the risks of occupational exposure and the importance of seeking urgent advice following needlestick injury or other occupational exposure.
- The views of the exposed healthcare worker should be taken into account when considering PEP; this is particularly important if the HIV status of the source patient is unknown or test results are delayed.
- Training should ensure that all know to whom to report.
- Every NHS employer should have a policy on how to manage exposures, which ensures 24-hour cover. Occupational health services and accident and emergency departments should have access to expert on-call advice.
- There should be clear channels to gain expert advice about HIV and PEP drugs.
- PEP is up to 80% effective but requires speed of thought and action. The window of opportunity to prevent systemic viral dissemination is narrow.
- The Department of Health (DH) guidance offers help with, amongst other details:[1]
  - Assessing risk.
  - When to recommend PEP.
  - Ensuring healthcare workers have immediate 24-hour access to advice on PEP.
  - Devising local PEP policies and protocols.
  - PEP in relation to non-occupational exposure.

Risk assessment for occupational exposure[1]
Risk assessment should be carried out as quickly as possible so that if PEP is deemed appropriate, it can be started without delay. In hospital this is usually done by a designated doctor, trained for the purpose.

An exposure is defined as exposure to potentially infected blood, tissue or bodily fluids through:
A percutaneous injury.  
Contact with mucous membranes (including the eye).  
Contact with skin that is abraded, inflamed or otherwise not intact.

The level of risk is assessed according to:

- Type of exposure. Percutaneous > mucous membrane > skin (skin exposure risk is very small and difficult to quantify).
- Body fluid involved - blood carries the highest risk but other body fluids and materials which carry a risk if significant occupational exposure occurs include:
  - Amniotic fluid.
  - Blood.
  - Cerebrospinal fluid.
  - Exudative or other tissue fluid from burns or skin lesions.
  - Human breast milk.
  - Pericardial fluid.
  - Peritoneal fluid.
  - Pleural fluid.
  - Saliva in association with dentistry (likely to be contaminated with blood, even when not obviously so).
  - Semen.
  - Synovial fluid.
  - Unfixed human tissues and organs.
  - Vaginal secretions.
  - Any other body fluid if visibly bloodstained.

- Severity of exposure.
- Disease status of the source patient (there is high risk if disease is at a more advanced stage and if resistant strains of HIV are involved). Most source patients in hospital are HIV-negative and rapid testing of HIV status may avoid unnecessary PEP, making it cost-effective. [5]
- Obtaining consent from the source patient may be an ethical minefield. The clinician involved in this task will need to comply with General Medical Council (GMC) guidance and possible consideration of the Human Tissue Act 2004 and the Mental Capacity Act 2005 (or the equivalent legislation in Scotland). See separate article Needlestick Injury for more details on these issues.

Retrospective studies suggest the greatest risk to be from percutaneous exposure to HIV-infected blood, especially if:

- There was visible contamination of a device with blood.
- Procedure involved placement in a vein or artery.
- Injuries were deep.
- The source patient was suffering from terminal stages of HIV infection.
- Injury was with a hollow-bore needle.

The guidelines concerning the viral load of the source patient have recently changed. If the patient is known to have undetectable HIV viral load (<200 copies HIV RNA/ml), PEP was previously not recommended. However, it is now recommended that PEP should be offered to those who are anxious about the risk. [3]

Risk assessment for non-occupational exposure [5]

This includes sexual exposure and exposure through sharing of drug injecting equipment with an HIV-infected source. Transmission via sexual contact depends on several factors, including the viral load of the infected partner, local prevalence, host factors (eg, menstruation increases risk in vaginal contact) and the type of contact.

Types of contact, in descending order of risk, are as follows:

- Blood transfusion.
- Receptive anal intercourse.
- Receptive vaginal intercourse.
- Insertive vaginal intercourse.
- Insertive anal intercourse.
- Receptive oral sex (fellatio).

Assessment of risk is much more difficult. Information about the source is likely to be less readily available (especially in cases of rape).

If assessing risk is difficult then it becomes equally difficult to tailor optimum treatment. [1]

PEP is likely to be effective in cases of non-occupational exposure if:

- The risk of HIV transmission is high.
- The exposure is unlikely to be repeated.
- PEP can be started promptly.
- Good adherence is likely. [1]
The British Association for Sexual Health and HIV recommends that PEP should be given after the following exposure with an infected individual:

- Receptive anal sex.
- Insertive anal sex.
- Receptive vaginal sex.
- Insertive vaginal sex.

PEP should be considered after:

- Fellatio with ejaculation.
- Splash of semen into the eye.

PEP is not recommended after:

- Fellatio without ejaculation.
- Cunnilingus.

What to prescribe

Antiretroviral agents from three different classes of drugs are currently licensed for first-line treatment of HIV infection:

- Nucleoside/nucleotide analogue reverse transcriptase inhibitors (NRTIs).
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs).
- Protease inhibitors (PIs).
- No antiretroviral drug is currently licensed for PEP, so they have to be prescribed on an 'off-label' basis.
- The starting regime currently recommended by the DH for most patients is one Truvada® tablet (245 mg tenofovir and 200 mg emtricitabine - a combination of NRTIs) once a day plus two Kaletra® film-coated tablets (200 mg lopinavir and 50 mg ritonavir - a combination of PIs) twice a day.
- However, the Expert Advisory Group for AIDS has recently stated that the preferred first-line regimen for PEP should be raltegravir/Truvada® for 28 days. One Truvada® tablet (245 mg tenofovir disoproxil (as fumarate) and 200 mg emtricitabine (FTC)) once a day with one raltegravir tablet (400 mg) twice a day. This is because there are no significant safety issues with this combination from extensive testing in HIV-infected patients and raltegravir is better tolerated than Kaletra®, so switching is likely to improve adherence, and hence efficacy, of PEP.
- This regime is suitable for both occupational and non-occupational exposure.
- Completion of four weeks of treatment is the goal, although this may be compromised by side-effects. About 50% have significant adverse effects and 30% stop taking the PEP because of this.
- Resistant strains have been detected only rarely when PEP has failed but the relationship of this to exposure to resistant strains is poorly understood.
- The choice of starting regimen can be reviewed at 72 hours if information on the source of infection is awaited but PEP should not be delayed whilst waiting for this further information.[1]
- In pregnancy the choice of drug will be more limited.

Now that safe and effective agents have been developed, encouraging at-risk individuals to take up the benefits of PEP is considered as important as searching for new drugs. PEP immediately after acute high-risk exposures and for those who engage in recurrent high-risk behaviours are promising bio-behavioural approaches to decreasing HIV transmission.[10] There is growing evidence supporting the benefits of pre-exposure prophylaxis in high-risk individuals.[11]

How to prescribe

- PEP should be initiated according to agreed protocols, usually involving reference to appropriate specialists.
- The protocols and guidelines should define in detail the procedures to be followed, incorporating assessment of risk, assessment of the PEP recipient, assessment of the source patient, etc.[1, 5]
- GPs may be more involved in initiating PEP as part of an agreed protocol when caring, for example, for a dying HIV-infected patient at home. Access to advice, drugs and testing should form part of the protocol covering occupational exposure to HIV infection.

Monitoring and follow-up

- HIV testing (antibody with enzyme immunoassay (EIA) - not direct virus assays, as these give false positives) should be for twelve weeks after the HIV exposure event or, if PEP was taken, for at least twelve weeks after the PEP was stopped.
- The longer period of monitoring previously advised is no longer supported by evidence unless:
  - The individual is immunocompromised.
  - The illness is compatible with an acute retroviral syndrome (regardless of the interval since exposure).
  - The source patient is dually infected. In the case of HIV and HCV co-infection, delayed seroconversion for HIV (documented at seven months post-sexual exposure) has been reported.
- One audit suggested that there was poor attendance at follow-up clinics and the reasons for this needed to be explored.[12] Counselling at the time of prescribing PEP improves compliance to follow-up.[13]
- Safe-sex counselling should be part of the follow-up protocol. One study reported an increase in the sexual risk behaviour of MSM following a course of PEP.[14]
Prompt referral for treatment if patients become HIV-positive.
- Monitoring for toxicity is recommended with baseline FBC, U&Es and LFTs.
- Symptoms such as nausea are very common and should be treated.
- Encouragement to facilitate completion of the course of PEP is important.
- Counselling and education are important:
  - To help with the emotional impact.
  - To educate about breast-feeding, sex, seroconversion, rationale for PEP, etc. [5, 7]

**Failure of post-exposure prophylaxis**

Factors cited are:
- Delay in initiation of PEP.
- Large inoculum.
- Resistant strains of HIV.
- Short duration of PEP.
- Host factors.
- Non-adherence to regime.

**Practice tips**
- Review local policies on needlestick injuries.
- Review practice and local policies on reduction of risk and prevention of needlestick injuries.
- Review local policies on PEP.
- Inform and educate all practice staff about the policies.

**Further reading & references**

2. Updated recommendation for HIV post-exposure prophylaxis (PEP) following occupational exposure to a source with undetectable HIV viral load; Public Health England, 2013
3. Guidelines for the management of HIV infection in pregnant women (2014 interim review); British HIV Association
4. Antiretrovirals for reducing the risk of mother-to-child transmission of HIV; British Association for Sexual Health and HIV (2011)
5. Risk of infection; aidsmap.com, 2015

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