For a variety of reasons, people without HIV have unprotected intercourse with a partner they know, or think has HIV, or they may discover after sex that their partner had HIV. If an uninfected person is exposed to HIV, post-exposure prophylaxis (PEP) can be used to try and ensure they do not become infected.

‘Prophylaxis’ refers to medical procedures which are designed to prevent, rather than treat, a disease. Other examples of prophylaxis include drugs taken to prevent malarial infection and statins to prevent cardiovascular disease. ‘Post-exposure’ indicates that PEP is taken after a person has been exposed to body fluids which may contain HIV. PEP is normally taken for one month after a single risk event.

Post-exposure prophylaxis is different from ‘pre-exposure prophylaxis’ (PrEP). As its name indicates, pre-exposure prophylaxis is taken before a person exposes themselves to body fluids which may contain HIV. PrEP is a new intervention whose validity is still being tested in clinical trials.

PEP normally consists of three or four anti-HIV drugs, which need to be taken for 28 days, following possible exposure to HIV. The drugs used in PEP are the same as the drugs used for the treatment of diagnosed HIV. To be effective, it is important to start taking PEP as soon as possible, and no later than three days (72 hours) after the risk event, and to take all the doses, at the right time. Although PEP is not 100% effective, there have been few reports of HIV infection after the use of PEP.

WHAT IS PEP?
When an individual is exposed to HIV, the virus first replicates in cells close to the site of infection, before spreading throughout the body. During this time, there is a short ‘window of opportunity’ to use antiretroviral drugs to block the replication of HIV.

When used, PEP must be initiated promptly. Research on monkeys suggests that it is more likely to be effective if it is begun within the first 24 hours after exposure to HIV.

Guidelines do not support starting PEP more than 72 hours after exposure.

A regime of three or four antiretroviral drugs is recommended. This probably provides more powerful protection than a single drug or two drugs together. The disadvantage of taking several drugs can be an increase in the severity of side-effects, although the drugs currently used have been chosen to minimise side-effects as far as possible.

PEP has been used since the mid-1990s for healthcare workers who have had possible exposure to HIV, for example, after accidentally pricking themselves with needles used on patients. Although it was sometimes used in cases of sexual assault, it was almost a decade later that PEP began to be widely used following sexual exposure.
more likely to work than not, it would be unethical to conduct a randomised controlled trial into PEP. To do so would involve withholding PEP from some people at high risk of infection, in order to compare their infections with those given PEP. Also, given the infrequency with which HIV transmission actually occurs, it would be difficult to recruit enough people into a trial that would have statistical validity.

Important early data suggesting that PEP can prevent HIV infection came from a 1997 case-control study. It examined HIV infection rates in 698 healthcare workers who had had needle stick injuries. Those individuals who acquired HIV were less likely to have taken PEP (AZT monotherapy) than their colleagues who remained uninfected. The researchers estimated that PEP reduced the infection risk by 81% (confidence interval 48-94%).

The best available evidence of PEP’s effectiveness following sexual exposure comes from a cohort study of 200 men who have sex with men, in Brazil. PEP was made available to the men during a two year period. In this study, 68 men chose to take PEP at least once, while 132 chose not to. Because men made the decision themselves, rather than through a randomisation process, the results could be biased. Nonetheless, whereas only 1 in 68 men who took PEP acquired HIV, 10 of the 132 men who did not take PEP were infected. While PEP provided some protection, the overall number of infections in the group of 200 men who had access to PEP was very similar to what would have been expected had PEP not been made available. The men were generally at high-risk of HIV infection, and although a third took PEP, they did not take it often enough to make a difference to HIV incidence in the group as a whole. The men’s own evaluations of which sexual encounters were risky were not always accurate.

It has generally been the experience of countries providing PEP that it is an emergency measure used by a limited number of individuals. Because of this, the use of PEP does not usually make a substantial difference to the number of HIV infections in a population.

A more recent analysis of 710 people given PEP following sexual exposure, over a ten-year period at a Swiss hospital had the following outcomes:

- 60% completed the 28 day course;
- 16% were lost to follow up;
- 15% stopped taking PEP because their sexual partner was found to be HIV negative;
- 5% stopped taking PEP because of side effects;
- 3% stopped for other reasons.

Nobody tested HIV positive following their use of PEP. However, two individuals did seroconvert in the months afterwards, following other risk behaviour.

These are not the only case reports of individuals who took PEP becoming HIV-positive. Most commonly this is due to taking other sexual risks after beginning PEP. When it appears that PEP has failed, this has been linked to using only one drug for PEP, starting PEP late, poor adherence and being infected with drug resistant virus.

The UK guideline says that it is “crucial” to consider PEP “as only one strategy in preventing HIV infection and, as such, it should be considered as a last measure where conventional, and proven, methods of HIV prevention have failed.” Currently there are no national statistics on the prescribing of PEP but the Health Protection Agency is setting up a surveillance programme to monitor how PEP is used after sexual exposure in the UK.

**COST-EFFECTIVENESS**

One concern expressed about PEP is cost. However, at around £700 for a month’s combination therapy, the cost for a single individual compares favourably with the lifetime costs of treating the same individual for HIV. High-quality UK studies of cost-effectiveness have not been conducted, but it is thought that PEP may be cost-effective when it is provided to people who were at high risk of being exposed to HIV. Providing it to people at low risk of infection is unlikely to be cost-effective.

**UNDER WHAT CIRCUMSTANCES IS PEP GIVEN?**

Before being prescribed PEP, an individual will be asked detailed questions about the sex they have had in order to establish the likelihood of HIV transmission. PEP will be more readily prescribed following unprotected anal intercourse (especially for the receptive partner) than for other, less risky, sexual practices.

The new UK PEP guideline also asks doctors to take into account other factors which modify the riskiness of a single sexual contact. The most important of these is the viral load of the source partner. A high viral load, due to untreated HIV, especially during the first months of infection, greatly increases the risk of transmission. Similarly, a very low or ‘undetectable’ viral load greatly reduces the risk of transmission.

If either sexual partner has a sexually transmitted infection, this also raises the risk of transmission. A sexually transmitted infection in the HIV-positive partner may raise HIV viral load in genital secretions. An infection in the HIV-negative partner makes him more susceptible, especially if he has genital ulcers. If there is trauma – for example, during sexual assault or fisting – there may be breaks in mucosal surfaces, making transmission more likely.

When someone requests PEP, doctors will assess the likelihood of their sexual partner having HIV. As HIV prevalence is high among gay men, PEP would be more readily prescribed to a man who has had sex with a man than to a
man who has had sex with a woman (especially if she was British-born). But whenever possible, the sexual partner will be asked to come in for HIV testing (if the result is negative, this avoids someone taking PEP unnecessarily).

The table below summarises the 2011 BASHH and BHIVA UK PEP guideline1.

**HOW CAN PEP BE ACCESSED?**

People who think that they may have recently been exposed to HIV should seek medical help as quickly as possible. The sooner PEP is given, the more effective it is. PEP must be started within 72 hours of the risky sexual contact. People should either go to a GUM or sexual health clinic (if it is open), or an Accident & Emergency department. HIV tests need to be done before PEP is begun and again three months after the last dose. To check for side effects and other complications, a series of other tests need to be done before starting PEP and on another occasion while taking it.

Some people have had difficulty getting PEP. When a GUM clinic is open, patients should tell reception they need to be seen immediately as an emergency appointment for PEP. If the GUM clinic is not open, patients should go as soon as possible to the hospital’s A&E department. Since not all clinicians are fully aware of the UK guideline1, when seeking PEP at A&E departments, it can be helpful to have a print-out of the UK guideline or the Chief Medical Officer’s letter. Some NHS settings dispense “starter packs” to ensure PEP is begun within 72 hours. These packs will have 3-5 days supply of the appropriate drugs which can be used prior to completing the HIV and other testing that is recommended prior to full PEP initiation (see Table 6, page 704 of the UK guideline for a list of tests recommended).

A person’s immigration status should not affect access to PEP. It is emergency treatment that should always be provided free of charge.

<table>
<thead>
<tr>
<th>HIV status of the person’s sexual partner (‘the source’)</th>
<th>Known to be HIV positive</th>
<th>HIV positive with undetectable viral load</th>
<th>Gay or bisexual man (or African migrant) of unknown HIV status</th>
<th>Unknown HIV status, NOT from a high prevalence group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receptive anal intercourse</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Insertive anal intercourse</td>
<td>Yes</td>
<td>No</td>
<td>Consider *</td>
<td>No</td>
</tr>
<tr>
<td>Vaginal intercourse (male or female partner)</td>
<td>Yes</td>
<td>No</td>
<td>Consider *</td>
<td>No</td>
</tr>
<tr>
<td>Fellatio (ie. taking a penis in the mouth) with ejaculation</td>
<td>Consider *</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>All other forms of oral sex</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Splash of semen in the eye</td>
<td>Consider *</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

*When the guideline says that PEP should be ‘considered’, it should only be given if there is an additional factor which increases the likelihood of transmission, such as very high local HIV prevalence, a sexually transmitted infection, acute HIV infection in the source partner, trauma or bleeding.

Helpline staff can advise patients who have problems getting PEP while they are still at the A&E department or GUM clinic. Patients can also ask the hospital worker to speak to a helpline adviser if this would help.

- NHS Direct on 0845 4647, open 24 hours a day, 365 days a year.
- THT Direct on 0808 802 1221 (Monday to Friday 10am-10pm, Saturday and Sunday 12 noon to 6pm).

**WHICH DRUGS ARE USED AND WHAT ARE THE SIDE-EFFECTS?**

PEP needs to be taken for 28 days. The most usual combination of drugs given is:

- **Truvada**, a combined pill containing two non-nucleoside inhibitor drugs, tenofovir and FTC (one tablet daily), and
- **Kaletra**, a combined pill containing two protease inhibitor drugs, lopinavir and ritonavir (four tablets daily).

This combination could be modified if the ‘source’ partner was known to be HIV-positive and to have resistance to certain anti-HIV drugs. Another reason to modify the drugs given is if the patient is already taking other medication. Some other drugs, such as statins, may interact with the ARVs.

PEP may cause side-effects, including feeling sick, being sick, diarrhoea, tiredness, and generally feeling unwell. More serious, long-lasting side effects have not been observed in people who have taken PEP. The choice of drugs for PEP is guided, in part, by an attempt to minimise the number of side-effects. The currently recommended regime of Truvada and Kaletra has fewer side effects than other options. A study recently examined side effects in 188 people on this PEP regimen. Just under half the patients had some side effects, with 12% choosing to stop PEP for this reason5.
Problems with side-effects can discourage people from taking the medication. Many UK hospitals report that half (or less) of the people who are given PEP complete the 28 day course of treatment and return for follow-up HIV testing three months after sexual exposure. In some cases, this is because the patient has found out that their sexual partner did not in fact have HIV. Otherwise, these discontinuations will limit the effectiveness of PEP.

People may find it hard to deal with side-effects and adhere to medication when people around them do not know what they are going through. Embarrassment about sexual behaviour and HIV-related stigma means that many people find it difficult to discuss their use of PEP with friends or family.

GAY MEN’S KNOWLEDGE AND USE OF PEP

Men completing the Gay Men’s Sex Survey (GMSS) have been asked a range of PEP questions a number of times. The number having ever heard of PEP has increased from 22.2% in 2003, to 38.5% in 2005, to 56.3% in 2007. Awareness has therefore increased substantially since the first CHAPS campaign on PEP in 2004.

Despite this success, in 2007 just under half of respondents had still not heard of PEP. Moreover significant numbers of men did not know, did not understand or were not sure about the following statements (that is, they were ‘in need’ in some way).

- PEP attempts to stop HIV infection taking place after a person is exposed to the virus (46.2% in need).
- PEP should be started as soon as possible after exposure, preferably within hours (47.9% in need).
- PEP is a one month course of anti-HIV drugs (65.1% in need).
- PEP should be available in most UK hospitals for people exposed to HIV during sex (69.9% in need).
- In practice, PEP may be hard to get hold of (73.4% in need).
- PEP may be particularly hard to get hold of at the weekend (80.4% in need).

Awareness tends to be higher among men who have tested HIV-positive, men in their 30s and 40s, men of ‘white other’ ethnicity and men with more sexual partners.

The 2007 Gay Men’s Sex Survey has also asked about taking PEP. While the numbers have risen since 2003, only a minority of men had ever taken PEP (2.4%) or have tried to get PEP (3.4%). Nonetheless, the vast majority of HIV-negative men would consider using it if they thought they had been exposed to HIV – only 3.8% said they would not consider it.

An Australian study found that the gay men most likely to take PEP were those who have a large number of casual partners (and have unprotected with some of them) and men in a relationship with an HIV-positive man. However PEP was used after only a minority of high-risk events. For example, only 9% of men who had had unprotected sex with an HIV-positive boyfriend in the past six months had taken PEP.

While part of the reason for low uptake is likely to be because obtaining PEP can be time-consuming and difficult, another important factor is that individuals do not always make accurate assessments of the riskiness of their sexual behaviour. Whereas someone may have had unprotected anal intercourse on numerous occasions with a partner of unknown HIV status, they may be motivated to seek PEP when they perceive their sexual behaviour to be out of character, a one-off event, under the influence of drugs or alcohol, with an unusually ‘risky’ sexual partner or linked to a venue such as a sauna or cruising ground.

Most studies show that people take fewer sexual risks after having taken PEP, probably because the experience has made them re-evaluate their behaviour. Moreover, a request for PEP can provide an opportunity for health workers to engage with an individual who has acknowledged that their behaviour is risky. There is evidence that intensive counselling at this stage can have an impact on future behaviour and risk of later HIV infection, especially when the counselling is targeted to those taking the greatest risks.

However, if PEP is delivered as a stand-alone intervention, without enough support, risk behaviour may continue. In Amsterdam, men who have previously taken PEP are more likely to acquire HIV at a later date than other gay men. This reinforces the argument for additional behavioural support for men who access PEP.

While some individuals do request PEP more than once, there is no evidence to suggest that significant numbers of people repeatedly do so.
REFERENCES


FIVE KEY POINTS

- Post-exposure prophylaxis (PEP) consists of anti-HIV drugs taken for one month, in order to reduce the risk of infection after risky behaviour has occurred.
- PEP is more likely to be effective if it is taken within the first 24 hours after possible exposure to HIV.
- The UK PEP guideline recommends giving PEP to gay and bisexual men following unprotected receptive anal intercourse, but PEP is not universally recommended following unprotected insertive anal intercourse.
- While awareness of PEP has risen over the past decade, a substantial minority of gay and bisexual men need to know more about PEP.
- People do not always make accurate assessments of the riskiness of their sexual behaviour – this limits the number of infections which PEP can prevent.

FURTHER READING

