



PRACTICE

10-MINUTE CONSULTATION

HIV post-exposure prophylaxis (PEP)

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What you need to know

- HIV post-exposure prophylaxis (PEP) is a safe and effective treatment strategy aimed at preventing infection in those with a recent HIV exposure
- PEP is typically prescribed as three HIV antiretroviral drugs started within 72 hours after exposure, and continued for 28 days
- PEP is most useful for people with a single exposure or infrequent moderate-to-high risk exposures to HIV. Pre-exposure prophylaxis may be better suited to those with ongoing risk^{16 17}

A 22 year old man presented to the emergency department for HIV post-exposure prophylaxis (PEP). Twenty six hours previously, he had anal receptive intercourse without a condom with a man of unknown HIV serostatus. He had immediate testing for HIV (using a fourth generation antibody/antigen assay as recommended^{1 2}), hepatitis B and C serologies, syphilis serology, and urine nucleic acid amplification tests for gonorrhoea and chlamydia. In the emergency department he received a three day supply of combined emtricitabine/tenofovir disoproxil fumarate (TDF/FTC) (one tablet, daily) plus raltegravir (400 mg twice daily). He was referred to be seen urgently in the next three days in an outpatient clinic for continuing management.

PEP is a safe and effective HIV prevention modality for people with a recent (within 72 hours) exposure to HIV. People with HIV exposure often present to primary care clinics and emergency departments, so it is useful for non-specialists to have confidence in prescribing PEP. Clinicians caring for people presenting with a recent HIV exposure require knowledge of recommended diagnostic testing after sexual exposure and blood borne exposure, PEP regimens, schedule of short and long term follow-up, and the potential for physical and psychological trauma (eg, in the case of sexual assault). This article offers practical advice and resources for clinicians caring for individuals who present for care after an actual or potential exposure to HIV that is non-occupational.

What you should cover

The risk of the exposure

Ask your patient for details of the exposure, including the precise time and the nature of the exposure. Table 1 shows estimates of the risk of HIV by type of exposure. Ask the patient if they are aware of having a history of sexually transmitted infections or viral hepatitis to assess their baseline risk. If the HIV exposure was through sexual activity, ask if the person is aware if this sexual partner (the “source patient”) has any sexually transmitted infections. Take a history of other recent potential exposures and of previous use of PEP.

HIV and other communicable disease risks of the source patient

If the medical history of the source is unknown, ask if there is an opportunity to contact the source for diagnostic testing (eg, for HIV, hepatitis B and C). There are often considerable challenges in confirming the source patient’s HIV serostatus; however, establishing this history can meaningfully facilitate decisions about the need (or not) for PEP.

Sources who are known to be HIV positive but have a recently documented undetectable viral load (<200 copies/mL for more than six months) have a zero to negligible risk for sexual HIV transmission³ and PEP is unlikely to provide benefit. PEP may be considered in these situations if the source has questionable adherence to his or her antiretroviral medications, has a known detectable viral load, or if the timing of the most recent undetectable viral load cannot be established.

Balancing the risks and benefit of PEP

PEP is typically initiated when the exposure risk is moderate to high⁴ (table 1) and when the source has a non-negligible risk of HIV,^{1 2 5 6} such as with condomless anal insertive or receptive intercourse or sharing of drug injecting paraphernalia.^{3 6} When adherence or recent viral load data are unknown, PEP is

frequently offered and subsequently discontinued during follow-up if additional data reveal the source to be non-infectious. Share with the patient the uncertainty around risk of acquisition from both the source and the exposure type. This facilitates a decision that takes into account the patient's preferences and perception of risk.

Psychological, social, and safeguarding concerns

The presentation of a patient for PEP after a confirmed or potential HIV exposure is an important opportunity for health promotion and screening for abuse. Take a careful history to explore the possibility of sexual assault, ongoing risk exposure, and/or misuse of alcohol or drugs. Ensure that the patient has access to primary healthcare services and social services, as necessary

What you should do

Prescribing PEP

PEP regimens typically comprise three antiretroviral drugs that are started within 72 hours after a potential or confirmed HIV exposure and continued for 28 days.¹²⁻¹⁶ Common PEP drug regimens include a combination tablet of tenofovir disoproxil fumarate plus emtricitabine (TDF/FTC 300mg/200mg once daily) and an integrase inhibitor such as raltegravir (400 mg twice daily). Until recently, dolutegravir (50 mg daily) was commonly used as a PEP regimen with TDF/FTC. However, recent data relating its use to neural tube defects⁷ have led the World Health Organization, European Medicines Agency, and the US Food and Drug Administration to recommend against using it in women of child bearing age who are not on effective contraceptive therapy. Consequently, raltegravir should be recommended in most cases of PEP in women. Health centres that see patients presenting for PEP that do not provide primary or chronic HIV care (eg, urgent care, walk-in and emergency health providers) can prepare PEP "starter packs" with a three day supply of preferred PEP drugs, to bridge presenting patients to longer term care providers.

Where integrase inhibitors are not readily available, a boosted protease inhibitor based regimen is recommended in addition to combination TDF/FTC, with careful consideration of potential drug interactions between any active medicines the patient is taking and the boosted protease inhibitor. Finally, a combination of zidovudine and lamivudine is typically recommended in place of TDF/FTC in individuals with substantial renal insufficiency (creatinine clearance <60 mL/minute). Infectious disease consultation is recommended where the source is known to have HIV drug resistance or if the patient is on therapy for concomitant tuberculosis.

Data from clinical trials and rigorous observational studies in humans are lacking. However, decades of observational experience with PEP^{8,9} have shown it to be associated with a substantial reduction in the risk of HIV acquisition after percutaneous needle exposure and condomless sex. Indeed, most PEP "failures" reported in the literature are confounded by ongoing risk or sub-optimal PEP adherence.^{10,11} Animal studies support this protective effect, particularly when PEP is initiated within 72 hours of exposure.^{12,13}

Most patients tolerate PEP without any issues, although nausea, diarrhoea, and headaches may be reported. These frequently resolve within the first 48 hours of initiating PEP. Raltegravir is associated with a small risk¹⁴ of rhabdomyolysis: inform patients about the risk and advise them to let their clinician

know if they experience myalgia and to avoid statins while taking raltegravir. Advise patients to take the medication at roughly the same time of day, and that drug adherence is important to ensure maximum efficacy.

Baseline testing, screening for sexually transmitted infection, and prevention of onward transmission

Major national and international guidelines on HIV prevention differ in recommended investigations and follow-up schedules. In general, initial investigations include a complete blood count, creatinine, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and bilirubin to establish baseline values and also to potentially help choose a PEP regimen as certain components (eg, TDF) are renally metabolised.

Baseline testing for other infectious diseases includes serologic screening for HIV with preference for use of a point of care HIV test, if available. Testing should also be performed for chlamydia, gonorrhoea (urine nucleic acid amplification test; rectal and pharyngeal culture or nucleic acid amplification tests, if indicated by exposure), syphilis serology, hepatitis C serology, immunity to hepatitis A (hepatitis A IgG), immunity or infection with hepatitis B (surface antibody, surface antigen, core-total antibody). Perform a pregnancy screen where appropriate.

Empiric treatment for sexually transmitted infections (STIs) is typically provided to patients who have experienced sexual assault and occasionally to others in whom risk is high.¹²⁻¹⁵ STI treatment should adhere to local guidelines. Advise patients to use barrier protection during sex until at least their four month follow-up HIV screen is confirmed as negative and to avoid sharing drug injecting paraphernalia. Ongoing health promotion strategies in clinic include counselling on safe sex, advice on safer injecting practices, vaccination for hepatitis A and/or hepatitis B viruses if serology results indicate they are appropriate, and referral to appropriate resources for those with a history of abuse, mental health comorbidities, and drug or alcohol misuse.

Follow-up care

After transitioning from a PEP starter pack to the full 28 days of treatment, patients are typically seen again after two weeks in primary care or HIV clinic, where they are evaluated for medication toxicity and adherence. They should be seen again 4-6 weeks after PEP initiation to repeat screening for HIV and STI, and for pregnancy testing if relevant. Attrition rates between the emergency department and clinics are high.¹⁵ We find it useful for patients to identify and designate a friend or relative at the first point of contact to help ensure the patient follows up in clinic and to assist with drug adherence. We also find it helpful to confirm a patient contact information, and we will repeatedly attempt to contact patients should they miss an appointment to facilitate timely follow-up and completion of the recommended course of therapy and follow-up testing schedule.

HIV testing is repeated four months after the inciting exposure to confirm transmission did not occur at the time of exposure. Perform an additional HIV screen at six months if hepatitis C was acquired from the inciting exposure, as acute hepatitis C infection may delay HIV seroconversion.^{12,15}

PEP may be discontinued early if there is evidence of a negative HIV test or confirmation of a recent undetectable HIV-1 RNA viral load in the source patient (and there is no suspicion that the source has acute HIV infection). Patients with ongoing risk factors for HIV acquisition should be considered for HIV

pre-exposure prophylaxis. If seroconversion occurs, refer patients to an HIV treatment provider for immediate initiation of antiretroviral therapy.^{16,17}

Education into practice

- Do you have PEP starter packs at work? If not, what is the local pathway for rapid access to PEP?
- How might you address the high rate of attrition between initiating PEP and attending follow-up appointments?
- Can you identify local data sources of HIV prevalence in your population that might help you assess risk of a source patient?

How this article was created

This article was created by reviewing major national and international HIV prevention guidelines, including those of the UK, USA, Canada, and World Health Organization.^{1,2,4,5} Additionally, other sentinel HIV prevention studies were included that relate to risk of HIV transmission,^{3,4} adherence, and follow-up issues.¹⁵

How patients were involved in the creation of this article

Two patients were consulted and contributed to the creation of this article. Both initiated PEP following a sexual exposure, and one patient ultimately transitioned to pre-exposure prophylaxis care. Both patients had targeted suggestions for abuse screening (eg, drugs, alcohol, sexual) and stressed the importance of connecting patients with appropriate psychosocial support when necessary.

Recommended resources

- Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis¹
- US guidelines for antiretroviral postexposure prophylaxis²
- British HIV Association guidelines for the use of post-exposure prophylaxis after sexual exposure⁵
- WHO guidelines on post-exposure prophylaxis for HIV⁶

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Table

Table 1 | Estimated risk of acquiring HIV from an infected source by type of exposure*

Exposure type	Rate for acquisition of HIV per 10 000 exposures
Needle sharing during injection of drugs	63
Percutaneous (needlestick)	23
Receptive anal intercourse	138
Receptive penile-vaginal intercourse	8
Insertive anal intercourse	11
Insertive penile-vaginal intercourse	4
Receptive oral intercourse	Low
Insertive oral intercourse	Low

* From the US guidelines for antiretroviral post-exposure prophylaxis after sexual and injection drug use exposure to HIV²