PRESCRIBE PEP

POST-EXPOSURE PROPHYLAXIS

FAQs

CDC

ACT AGAINST AIDS

FOR THE HEALTH CARE PROFESSIONAL

1. What is PEP?

Post-exposure prophylaxis (PEP) is the use of antiretroviral medication to prevent HIV infection in an HIV-negative person who has had a specific high-risk exposure to HIV. Such an exposure typically occurs through sex or sharing syringes (or other injection equipment) with someone who has or might have HIV. **Nonoccupational post-exposure prophylaxis (nPEP) can be used to clarify exposure type.**

Exposure to HIV is a medical emergency, because HIV establishes infection very quickly, often within 24 to 36 hours after exposure[1,2,3]. Health care providers should evaluate persons rapidly for PEP when care is sought ≤72 hours after a potential exposure. HIV status should be determined in persons being considered for PEP using rapid combined antigen/antibody (Ag/Ab) or antibody blood tests.

If rapid HIV blood test results are unavailable, and PEP is indicated, administration of the first dose of PEP should be started without delay. PEP can be discontinued later if the person is later determined to already have HIV infection, or if the source of the exposure is determined not to have HIV infection.[4]

PEP is not recommended when care is sought >72 hours after exposure.

2. What are the guidelines for prescribing PEP?

National Guidelines from the Centers for Disease Control (CDC) published in 2005 were updated in April of 2016[4]. The update incorporates additional evidence about the use of PEP from animal studies and human observational studies, as well as consideration of new antiretroviral agents introduced after the publications of the last guidelines. One key change from the 2005 recommendations is a new, more effective preferred drug regimen that has fewer side effects.

The new PEP recommendations also include considerations and resources for specific groups, such as pregnant women, victims of sexual assault (including children), and patients without health insurance, as well as a suggested procedure for transitioning patients between PEP and HIV pre-exposure prophylaxis (PrEP) as appropriate.[4]

Find the updated guidelines on www.cdc.gov/hiv/guidelines/index.html

3. Which types of exposure warrant PEP?

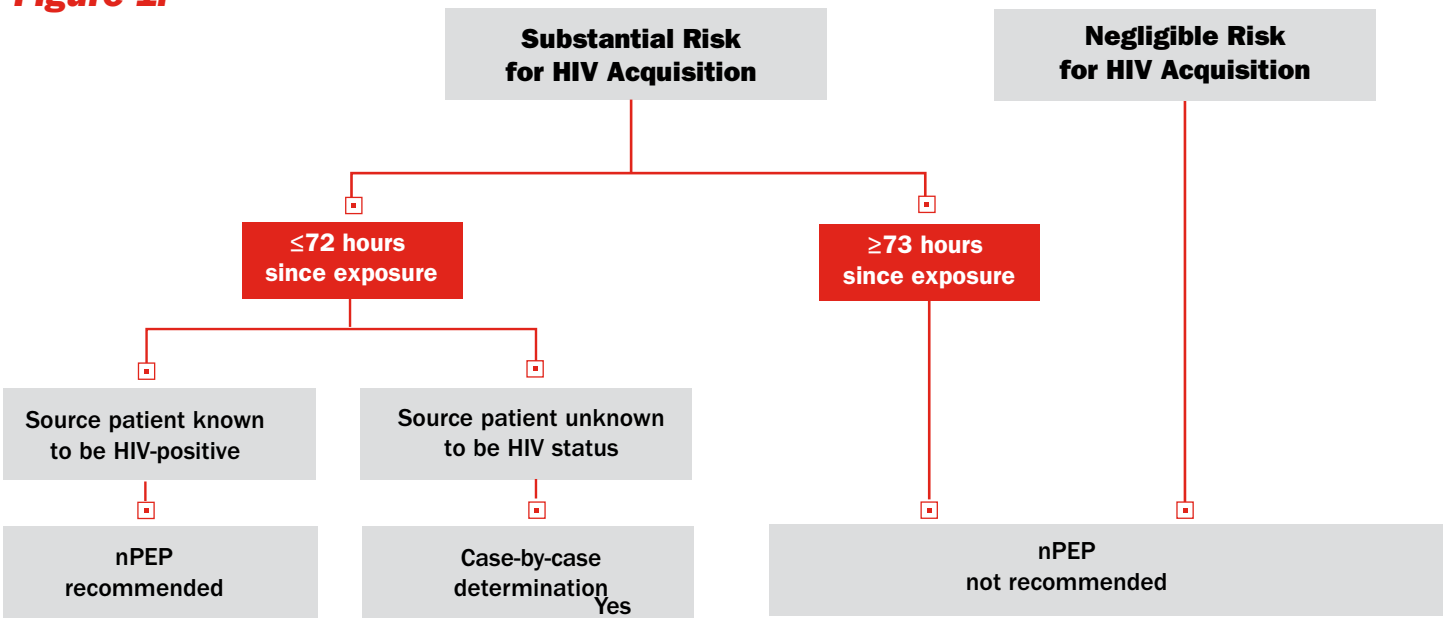
PEP initiation should be considered in people whose vagina, rectum, eye, mouth or other mucuous membrane, non-intact skin, or perforated skin (eg, needle stick) come into contact with potentially contaminated body fluids from an HIV-infected source, as long as exposure has occurred within a 72-hour window. If the source is of unknown HIV status, a case-by-case determination can be made.[4]

PEP is not recommended for use in people whose exposure occurred 73 hours or more before they sought treatment, or in people who are considered to have a negligible risk for HIV exposure because of exposure to non-blood contaminated secretions such as urine, saliva, sweat, tears, or nasal secretions.[4]

Additionally, people who are already adhering to a daily PrEP regimen under the care of their health care practitioner are not in need of PEP if they experience a potential HIV exposure while they are on PrEP.[4]

Algorithm for evaluation and treatment of possible nonoccupational HIV exposures

Figure 1.



Substantial Risk for HIV Acquisition

Exposure of:
vagina, rectum, eye, mouth or other mucous membrane, nonintact skin, or percutaneous contact

With:
blood, semen, vaginal secretions, rectal secretions, breast milk, or any fluid that is visibly contaminated with blood

When:
the source is known to be HIV-positive

Negligible Risk for HIV Acquisition

Exposure of
vagina, rectum, eye, mouth or other mucous membrane, intact skin or nonintact skin, or percutaneous contact

With:
urine, nasal secretions, saliva,sweat, or tears if not visibly contaminated with blood

Regardless:
of the known or suspected HIV status of the source

4. Who can prescribe PEP?

Any licensed prescriber can prescribe PEP. Emergency medicine physicians are among the most frequent prescribers of PEP, given the need for immediate treatment after exposure. Clinicians working in ambulatory care practices can also ensure that their non-HIV-infected patients who report risk behavior are aware of PEP, and know how to access it after-hours.

When health care providers are inexperienced with prescribing or managing patients on antiretroviral medication, or when information from persons who were the exposure source indicates the possibility of

antiretroviral resistance, consultation with an infectious disease or other HIV-care specialist is warranted before prescribing PEP to determine the correct regimen—***but only if these specialists are immediately available.***

Similarly, consulting with specialists who have experience using antiretroviral drugs is advisable when considering prescribing PEP for certain people, e.g., pregnant women, children, or persons with renal dysfunction. However, ***if such consultation is not available, PEP should be initiated promptly, and if necessary, revised after consultation is obtained.***

If questions arise or if prescribing assistance is needed, expert consultation can be obtained by calling the PEPline at the National Clinicians Consultation at 1-888-448-4911. Additional information is available at http://nccc.ucsf.edu/clinician-consultation/pep-post-exposure-prophylaxis/.

5. What is the recommended PEP regimen?

All persons offered PEP should be prescribed a 28-day course of a 3-drug antiretroviral regimen.* Since adherence is critical for PEP efficacy, it is preferable to select regimens that minimize side effects, number of doses per day and the number of pills per dose.[4]

- ***The preferred PEP regimen for otherwise healthy adults and adolescents is:***

tenofovir disoproxil fumarate (tenofovir DF or TDF)(300 mg) + emtricitabine (FTC)(200 mg) once daily

PLUS

raltegravir (RAL)(400 mg) twice daily or dolutegravir (DTG)(50 mg) once daily

(TDF 300 mg + FTC 200mg is available as a fixed-dose combination called Truvada® from Gilead Sciences.)

- ***An alternative regimen for otherwise healthy adults and adolescents is:***

tenofovir DF (300 mg) + FTC (200 mg) once daily

PLUS

darunavir (DRV) (800 mg) and ritonavir* (RTV) (100 mg) once daily

Alternative regimens may be used in cases of potential HIV resistance, toxicity risks, clinician preference or constraints on the availability of particular agents. In those cases, health care providers are encouraged to seek consultation with other providers knowledgeable in using antiretroviral medications for similar patients (e.g., children, pregnant women, and those with comorbid conditions.)

Providers should be aware that abacavir sulfate (Ziagen, ViiV Healthcare) should not be prescribed in any PEP regimen, as the prompt initiation of PEP does not allow for genetic testing for the HLA-B*5701 allele, which is associated with a hypersensitivity syndrome that can be fatal.[4]

*Ritonavir, which is used with some drug combinations as a pharmacokinetic enhancer to increase the trough concentration and prolong the half-life of darunavir and other protease inhibitors, is not considered to be part of the drug combination.

6. What is the evidence base for PEP?

PEP was first attempted for HIV prevention in the 1980s among health care workers who experienced occupational exposures (now called "oPEP"). At that time, only AZT (zidovudine) was available.

Anecdotal evidence of success began to accumulate, leading to the first formal study of PEP effectiveness, a case-control study of occupational exposures. This study demonstrated an 81% reduction in HIV infection in those who received AZT alone compared with those who did not receive any treatment[5]. PEP was only proposed for non-occupational exposures ("nPEP") more recently.

The additional evidence supporting PEP includes:

- **Its biologic plausibility (based on animal studies)[1, 2];**
- **The efficacy of antiretrovirals post-partum in reduction of mother-to-child transmission[3];**
- **Observational studies (such as data from existing PEP programs)[4, 6].**

In an updated series of studies of PEP initiation in men having sex with men, seroconversion was low, and seemed mostly to be related to continued risky behavior after completing PEP or non-adherence to the regimen.[4] Studies of children and adolescents evaluated after sexual assault reported that among 672 children or adolescents offered PEP, 472 were known to have initiated the regimen, and 126 were reported to have completed a 28-day PEP course. No new HIV infections were documented among these patients who initiated PEP.[4] In 15 studies conducted in mixed populations, 2,209 participants completed 28 days of PEP, of whom about 19 individuals seroconverted. However, only 1 seroconversion was attributed to PEP failure. The other 18 seroconversions were attributed, variously, to continued risky behavior after the end of PEP, non-adherence to PEP, and starting PEP after the 72- hour window.[4]

7. Is PEP safe?

The current preferred regimen is generally safe and well tolerated[7,8]. Patients usually experience only mild side effects on the preferred PEP regimen. Most importantly, PEP is only taken for 28 days. In almost all cases, the benefits of HIV prevention outweigh any other risks posed by the medication. In a meta-analysis of 24 PEP-related studies, including 23 cohort studies and 1 randomized clinical trial, nausea, vomiting, diarrhea and fatigue were the most commonly reported side effects.[9]

8. Who is not eligible for PEP?

- **PEP is only indicated for potentially exposed people without HIV infection.**
- **PEP is unlikely to be effective in people who have been exposed more than 72 hours before seeking medical assistance.**
- **PEP should be provided only for infrequent exposures. People who engage in behaviors that result in frequent, recurrent exposures to HIV should be considered for intensive sexual or injection risk-reduction interventions and pre-exposure prophylaxis (PrEP) with daily oral doses of combination TDF+FTC (Truvada®). However if the most recent recurring exposure is within the 72-hour window prior to an evaluation, PEP may be indicated with transition of the patient to PrEP after completion of 28 days of PEP medication.[4]**

However, there are few absolute contraindications to the recommended PEP regimen. All medications in this regimen have minimal drug-drug interactions. In almost all cases, the first dose of a PEP regimen should be given and then further consultation obtained.

If questions arise or if prescribing assistance is needed, expert consultation can be obtained by calling the PEPline at the National Clinician Consultation Center at 1-888-448-4911. Additional information is available at http://nccc.ucsf.edu/clinician-consultation/pep-post-exposure-prophylaxis/.

Because pregnancy has been demonstrated to increase susceptibility to sexual HIV acquisition, PEP can be especially important for women who are pregnant. If the person exposed to HIV is pregnant, expert consultation should be sought. In general, however, PEP is indicated at any time during pregnancy when a significant exposure has occurred, despite a possible risk to the woman and the fetus. The recommended PEP regimen remains the same.

In people with compromised renal function (creatinine clearance <50mL/min), the dose of TDF-FTC must be adjusted.

9. What baseline assessment is required for individuals beginning PEP?

Guidelines recommend the following baseline screening before initiating PEP[4]:

- HIV rapid test at baseline
  If baseline rapid test indicates existing HIV infection, PEP should not be started. However, if rapid HIV baseline testing is not available, there should be no delay in starting PEP. Oral HIV tests are not recommended for use among persons being evaluated for PEP.
- Pregnancy test
  If a woman is of reproductive age, not using highly effective contraception, eg IUDs or other long-acting reversible contraceptives (LARCs), oral contraceptives, or properly used condoms, and with vaginal exposure to semen.
- Serum Liver Enzyme Testing
- Blood Urea Nitrogen (BUN)/Creatinine Test
- STI screening
  Persons being evaluated for PEP because of a sexual encounter should have STI-specific nucleic acid amplification testing (NAAT) for chlamydia and gonorrhea at each site of potential exposure, and a blood test for syphilis.
- Hepatitis B (HBV) testing, including hepatitis B surface antigen, surface antibody, and core antibody
- Hepatitis C (HCV) antibody

[Note: The first dose of PEP should always be expedited; testing can wait until after PEP has been initiated.]

10. What additional support is required for patients on PEP?

Providers should maintain contact with their patients on PEP, either by telephone or in a clinic visit for the entire duration of PEP. This is both to support adherence and to facilitate follow-up HIV testing at 30 and 90 days to determine if HIV infection has occurred. Additionally, people whose sexual or injection-related exposures result in concurrent acquisition of HCV and HIV infection might have delayed HIV seroconversion. ***See Table 1*** for the recommended schedule of laboratory evaluations for exposed persons.

Patients should be counseled to take measures that reduce the risk of transmission during the 12-week follow-up period, such as using condoms consistently, avoiding pregnancy/breastfeeding, avoiding needle-sharing and refraining from donating blood, plasma, organs, tissue or sperm.

Recommended schedule of laboratory evaluations of source and exposed persons for providing nPEP with preferred regimens

Table 2.

Test	Source	EXPOSED PERSONS			
	Baseline	Baseline	4–6 weeks after exposure	3 months after exposure	6 months after exposure
	For all persons considered for or prescribed nPEP for **any exposure**				
HIV Ag/Ab testing [a] (or antibody testing if Ag/Ab test unavailable)	✔	✔	✔	✔	✔[b]
Hepatitis B serology, including: hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core antibody	✔	✔	—	—	✔[c]
Hepatitis C antibody test	✔	✔	—	—	✔[d]
	For all persons considered for or prescribed nPEP for **sexual exposure**				
Syphilis serology [e]	✔	✔	✔	—	✔
Gonorrhea [f]	✔	✔	✔[g]	—	—
Chlamydia [f]	✔	✔	✔[g]	—	—
Pregnancy [h]	—	✔	✔	—	—
	For persons prescribed: tenofovir DF + emtricitabine + raltegravir **or** tenofovir DF + emtricitabine + dolutegravir				
Serum creatinine (for calculating estimated creatinine clearance[i])		✔	✔	—	—
Alanine transaminase, aspartate aminotranferase		✔	✔		
	For all persons with HIV infection confirmed at any visit				
HIV viral load	✔	✔[j]			
HIV genotypic resistance	✔	✔[j]			

Abbreviations: **Ag/Ab, antigen/antibody combination test; HIV, human immunodeficiency virus; nPEP, nonoccupational post exposure prophylaxis; tenofovir DF, tenofovir disoproxil fumarate.**

a Any positive or indeterminate HIV antibody test should undergo confirmatory testing of HIV infection status.

b Only if hepatitis C infection was acquired during the original exposure; delayed HIV seroconversion has been seen in persons who simultaneously acquire HIV and hepatitis C infection.

c If exposed person susceptible to hepatitis B at baseline.

d If exposed person susceptible to hepatitis C at baseline.

e If determined to be infected with syphilis and treated, should undergo serologic syphilis testing 6 months after treatment.

f Testing for chlamydia and gonorrhea should be performed using nucleic acid amplification tests. For patients diagnosed with a chlamydia or gonorrhea infection, retesting 3 months after treatment is recommended.
- For men reporting insertive vaginal, anal, or oral sex, a urine specimen should be tested for chlamydia and gonorrhea.
- For women reporting receptive vaginal sex, a vaginal (preferred) or endocervical swab or urine specimen should be tested for chlamydia and gonorrhea.
- For men and women reporting receptive anal sex, a rectal swab specimen should be tested for chlamydia and gonorrhea.
- For men and women reporting receptive oral sex, an oropharyngeal swab should be tested for gonorrhea.

(http://www.cdc.gov/std/tg2015/tg-2015-print.pdf)

g If not provided presumptive treatment at baseline, or if symptomatic at follow-up visit.

h If woman of reproductive age, not using effective contraception, and with vaginal exposure to semen.

i eCrCl = estimated creatinine clearance calculated by the Cockcroft-Gault formula; eCrClCG= [(140 – age) x ideal body weight] ÷ (serum creatinine x 72) (x 0.85 for females).

j At first visit where determined to have HIV infection.

11. Will PEP be covered by my patients' health insurance?

In many states, PEP is covered by insurance, including Medicaid. If the patient is not covered under insurance, there are assistance programs run by various manufacturers.

Gilead, the manufacturer of Truvada®(a fixed dose combination of tenofovir 300 mg + emtricitabine 200 mg) and of Stribild®(a fixed dose combination of tenofovir 300 mg + emtricitabine 200 mg + cobicistat 150 mg + elvitegravir 150 mg), has established several programs to help cover the cost of PEP. Merck, the manufacturer of Isentress®(raltegravir), also has a program.

Providers can assist their patients by:

- Applying for assistance with the medication co-pay if the patient is insured; or
- Applying for complete coverage of the medication if the patient does not have insurance or needs financial assistance. The paperwork must be signed and submitted by a licensed clinical provider.
- Application forms for Gilead's patient assistance programs can be found at **http://www.truvada.com/truvada-patient-assistance**
- Application form for Merck's patient assistance program can be found at **http://www.merckhelps.com**
- In addition, the Partnership for Prescription Assistance can also help qualified patients get the prescriptions they need at a very low cost. For more information visit **https://www.pparx.org**

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For more information go to:
www.cdc.gov/hiv/pdf/programresources/cdc-hiv-nPEP-guidelines.pdf.