Nonoccupational Postexposure Prophylaxis

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Module 5:	Prevention of HIV
Lesson 4:	Nonoccupational Postexposure Prophylaxis

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Background

In the 1990s, HIV occupational postexposure prophylaxis (PEP) with zidovudine was shown to substantially reduce the risk of HIV acquisition in health care personnel exposed to HIV-contaminated blood or body fluids.[1,2] Soon after these findings were published, the Centers for Disease Control and Prevention (CDC) issued recommendations and guidance for HIV occupational PEP.[3] In 2005, the CDC extended these recommendations to the nonoccupational setting, with the first publication of HIV nonoccupational PEP guidelines, which recommended use of a 3-drug combination antiretroviral regimen for nonoccupational PEP.[4] The initial 2005 HIV nonoccupational PEP guidelines were subsequently updated and revised in 2016 and in 2025.[5,6] The HIV nonoccupational PEP guidelines address exposures to HIV that occur through sexual contact and/or injection drug use, as well as other less common routes.[5] Clinicians evaluating individuals for HIV nonoccupational PEP should provide general HIV prevention counseling, including assessing candidacy for transition to HIV preexposure prophylaxis (PrEP) at the time they complete the 28-day regimen for HIV nonoccupational PEP.[5,7] This lesson will not discuss the use of nonoccupational PEP in children.

Rationale for Providing HIV Nonoccupational PEP

Due to ethical and logistical constraints, it is highly unlikely that a prospective, randomized, placebo-controlled trial to evaluate HIV nonoccupational PEP in humans will ever take place. In addition, HIV nonoccupational PEP studies in humans are challenging because participants may have multiple exposures over the surveillance-testing period, making it difficult to discern the true benefit of HIV nonoccupational PEP for a single exposure event.[8] Thus, the rationale for providing HIV nonoccupational PEP is based on extrapolation from HIV PEP use in other settings, animal studies, retrospective reviews, observational HIV nonoccupational PEP reports, and expert opinion.[5]

Occupational and Perinatal HIV PEP Data

In 1997, investigators reported findings from a case-control study involving health care workers who sustained needlestick injuries from source individuals with HIV; this study demonstrated HIV occupational PEP with oral zidovudine, taken within 4 hours by most of the participants, reduced the risk of HIV seroconversion by 81%.[9] In addition, several important perinatal transmission trials involving mothers with HIV have established a reduction in HIV transmission when using HIV PEP given to the mother during labor and/or to the baby following birth.[10,11,12,13]

Animal PEP Studies

In an early animal HIV PEP study, investigators inoculated macaques intravenously with simian immunodeficiency virus (SIV) and showed that tenofovir PEP reduced the rate of SIV seroconversion, with the greatest reduction in transmission achieved when prophylaxis was initiated as early as possible and continued for 28 days (Figure 1).[14] A later study showed that tenofovir-based HIV PEP is also effective in preventing HIV acquisition after intravaginal inoculation of female macaques with HIV-2: tenofovir prevented seroconversion in all 8 female macaques exposed to HIV-2 when initiated within 12 to 36 hours.[15] A systematic review and meta-analysis of HIV PEP using pooled data from nonhuman primates across 18 studies (mostly involving intravenous inoculation with HIV) further substantiated the efficacy of HIV PEP when initiated as soon as possible after HIV exposure.[16]

Rationale for HIV Nonoccupational PEP in Persons Who Inject Drugs

New HIV infections among persons who inject drugs can result from injection drug use or from sexual activity.[17] Even individuals who typically use safe injection practices may, on occasion, be exposed to HIV. The efficacy of HIV nonoccupational PEP after an at-risk injection drug use exposure may differ from PEP efficacy after a sexual exposure, since the route and HIV inoculum differ in these two situations.[18] It is important that programs that work with people who inject drugs are aware of local resources where their clients can receive HIV nonoccupational PEP if needed. In addition, these programs may consider directly providing services for HIV nonoccupational PEP if they have the capacity and expertise.

HIV Nonoccupational PEP Data in Humans

Although human studies on HIV nonoccupational PEP are observational in nature and limited in sample size, available data involving men who have sex with men (MSM) suggest HIV nonoccupational PEP reduces HIV transmission.[19,20] In addition, a study from San Francisco reported HIV seroconversion among 7 of 702 (1%) persons who received HIV nonoccupational PEP, but only 3 of the seroconversions likely represented true “failure” of HIV nonoccupational PEP.[8] Available data from other reports of HIV transmission in persons who received HIV nonoccupational PEP suggest that most HIV transmissions resulted from poor medication adherence or exposures to HIV that occurred after completing the HIV nonoccupational PEP regimen.[21,22,23,24] In addition, one failure occurred in a 40-year-old woman in France who started HIV nonoccupational PEP more than 72 hours after a sexual exposure.[25] The following summarizes several major studies involving the preferred and alternative regimens recommended for HIV nonoccupational PEP.

- **Bictegravir-tenofovir alafenamide-emtricitabine:** Two studies have been published using bictegravir-tenofovir alafenamide-emtricitabine for HIV nonoccupational PEP.[26,27] In an open-label study, 52 individuals who accessed nonoccupational HIV PEP services at an urban health center were enrolled to receive coformulated bictegravir-tenofovir alafenamide-emtricitabine 1 tablet orally per day for 28 days.[27] This regimen was well tolerated, safe, and there were no HIV seroconversions related to the exposure.[27] In a prospective, open-label study conducted in China, 112 participants received a 28-day course of bictegravir-tenofovir alafenamide-emtricitabine for HIV nonoccupational PEP and no participants acquired HIV (when followed out to 24 weeks).[26]
- **Dolutegravir plus tenofovir DF-emtricitabine**: Three studies have been published that involved dolutegravir plus tenofovir DF-emtricitabine for HIV nonoccupational PEP, including one open-label single-arm trial, one retrospective study, and one cohort study.[28,29,30] In an open-label, single-arm study from Sydney, Australia, 100 men who have sex with men (MSM) received dolutegravir plus tenofovir DF-emtricitabine for 28 days for HIV nonoccupational PEP.[28] The regimen was well tolerated, completion rates were high (90%), and no HIV seroconversions occurred.[28] In a French retrospective analysis involving 19,240 nonoccupational exposures to HIV, including 704 exposures where dolutegravir plus tenofovir DF-emtricitabine was used.[29] Among those taking dolutegravir plus tenofovir DF-emtricitabine, 87.2% completed the course, and there were no new HIV infections.[29] In a cohort study in China, one of the arms included 100 persons who took dolutegravir plus tenofovir DF-emtricitabine, and there were no seroconversions among those who took this regimen.[30]
- **Darunavir (boosted with ritonavir)**: In an observational study, 51 individuals received darunavir boosted with ritonavir plus tenofovir DF-emtricitabine for HIV nonoccupational PEP, and 6 (12%) of the individuals discontinued due to medication side effects.[31] In a 2015 systematic review of 25 HIV nonoccupational PEP studies, the completion rate with darunavir and ritonavir plus tenofovir DF-emtricitabine was 94%, which was significantly higher than the 71% completion rate with lopinavir-ritonavir plus tenofovir DF-emtricitabine.[32] Data on& failure rates with darunavir and ritonavir-based regimens are inadequate.

Evaluation for HIV Nonoccupational PEP

Multiple factors influence the risk of HIV transmission in nonoccupational exposures to HIV. Initial evaluation of a person seeking care after a potential nonoccupational exposure to HIV should rapidly determine whether HIV nonoccupational PEP (nPEP) is indicated.[5] As recommended in the 2025 HIV nPEP Guidelines, this initial evaluation should address the following: (1) details regarding the timing of when the exposure occurred, (2) the type of exposure(s) involved, (3) information, if known, about the HIV status of the person potentially exposed to HIV, (4) information on the source person's HIV status, and (5) any available information on the antiretroviral therapy taken by the source patient, including whether they have sustained suppression of HIV RNA levels.[5] The following summarizes more detailed information about determining whether HIV nonoccupational PEP is indicated.[5]

- **Timing of Exposure:** Determining the timing of the exposure is critical when evaluating a person with a possible HIV nonoccupational PEP. Available data suggest that HIV nonoccupational PEP may not be effective if initiated more than 72 hours after the exposure. It is also important to determine whether multiple exposures have occurred; if multiple exposures have occurred, and, if so, whether any of the exposures have occurred within the previous 72 hours. If the person reports frequent, recurrent HIV exposures, repeated courses of HIV nonoccupational PEP are generally not an optimal long-term HIV prevention strategy; these individuals should ideally receive HIV PrEP.[5]
- **Type of Exposure**: For sexual exposures involving vaginal or anal sex, it is important to determine the type of sex that occurred (anal intercourse, and/or vaginal intercourse, and/or oral genital sex). In addition, it is important to know whether a condom was used, and if so, whether it was used consistently throughout the entire sexual exposure. For exposures involving injection drug use, information should be obtained regarding the sharing of needles (or other drug injection equipment) with other persons.
- **Information on HIV Status of Person Potentially Exposed to HIV**: As part of the initial evaluation, it is important to determine the baseline HIV status of the person seeking medical care for the exposure. In the setting of a nonoccupational exposure to HIV, initiating HIV nonoccupational PEP should not be delayed while determining the HIV status of the exposed person. If HIV nonoccupational PEP is started and the person's baseline test is positive for HIV (indicating they already have HIV), then additional evaluation, including a baseline HIV RNA level and HIV drug resistance testing, should promptly occur. If HIV is diagnosed, the person with HIV should receive long-term continuous antiretroviral therapy, not a 28-day course of HIV nonoccupational PEP.
- **Information Related to Source Person's HIV Status**: During the initial exposure evaluation, it is also important to determine whether the source person is known to have HIV. If the source person's HIV status is unknown, assess their HIV risk factors, if possible. If exposures have occurred with multiple people who may have HIV, every effort should be made to obtain information on the HIV status of all source persons involved. Often, the HIV status of the source person is not known (and not attainable). If this is the case, then initiating HIV nonoccupational PEP should occur on a case-by-case basis, ideally in consultation with an expert.[5] In this situation, if the exposure type warrants HIV nonoccupational PEP and the person has sought care within 72 hours, most experts recommend initiating and completing a 28-day course of HIV nonoccupational PEP.
- **Source Person's Antiretroviral Treatment Information**: If a source person is known to have HIV and takes antiretroviral medications, the clinician should determine what medication the source takes, the most recent HIV RNA levels (ideally a result within the prior 2 months), and if the source person has drug-resistant HIV. The risk of HIV transmission is higher if the source person has elevated HIV RNA levels.[33] In contrast, multiple studies consistently report that persons with HIV who take antiretroviral therapy and maintain plasma HIV RNA levels of less than 200 copies/mL do not transmit HIV sexually to their partners—this concept is referred to as Undetectable = Untransmittable (U=U).[34,35] Similar studies have not been published related to HIV RNA levels and HIV transmission through injection drug use.[35]

Determination of Risk Related to Exposure

The other key element of the initial HIV nonoccupational PEP evaluation is determining the relative risk of HIV transmission based on the exposure.[6,18] Administering HIV nonoccupational PEP should occur only in the setting of substantial risk for HIV transmission, defined as contact involving an area of the body known to be associated with HIV acquisition (vagina, rectum, eye, mouth, or other mucous membranes, non-intact skin, or percutaneous needlestick injuries) with an infectious body fluid (e.g., blood, semen, vaginal secretions, rectal secretions, breast milk, or any other body fluid visibly contaminated with blood). The risk of HIV transmission associated with nonoccupational exposures varies considerably by the type of sexual exposure, with receptive anal intercourse conferring the highest sexual risk.[6,18,36,37,38] The following table summarizes the risk of HIV acquisition by exposure type.[5](Table 1)

Indications for Initiating HIV Nonoccupational PEP

Based on the 2025 HIV nPEP Guidelines, if the following criteria are met, a 28-day course of antiretroviral medications for HIV nonoccupational PEP is recommended:[5]

- A person has had a nonoccupational exposure to blood, genital secretions, or other potentially infectious body fluids from a person known to have HIV (if the HIV status of the source person is unknown, the recommendation is to evaluate on a case-by-case basis, ideally in consultation with an expert), *and*
- The exposure represents a substantial risk for HIV transmission, *and*
- The person seeks care within 72 hours of exposure.

When the source person's HIV status is unknown, administering HIV nonoccupational PEP can be considered on a case-by-case basis if the exposure presents a substantial risk for HIV transmission, and it occurred within the prior 72 hours. If the HIV status of the source person is unknown, but they are available for HIV testing, the initiation of HIV nonoccupational PEP should not be delayed while determining the HIV status.[5]

HIV Nonoccupational PEP After Sexual Exposure

For a possible sexual exposure to HIV, multiple factors are taken into account when considering HIV nonoccupational PEP: when the exposure(s) occurred, type of sex, condom use during sex, HIV PrEP use by the person under evaluation, HIV status of the source person, and the source person's recent HIV RNA level.[5] If the source person's HIV status is unknown, then HIV nonoccupational PEP should be administered on a case-by-case basis.[5] For sexual exposures, HIV nonoccupational PEP is not recommended if the person exposed to HIV is taking HIV PrEP as recommended.[5] In addition, with potential sexual exposures to HIV, the use of HIV nonoccupational PEP is not routinely recommended if the source person with HIV has documented sustained viral suppression.[5] The algorithm below summarizes guidance for administering HIV nonoccupational PEP following a potential sexual exposure to HIV (Figure 2).[5]

HIV Nonoccupational PEP After Possible Injection Drug Exposure

For possible exposures to HIV in the setting of injection drug use, there are three main factors to consider when considering HIV nonoccupational PEP: the timeframe when the exposure(s) occurred, the source person's HIV status, and, if the source person is known to have HIV, whether they have viral suppression.[5] If the source person's HIV status is unknown, then administering HIV nonoccupational PEP should be decided on a case-by-case basis.[5] Similarly, if there is an HIV exposure associated with injection drug use and if the source person has documented sustained viral suppression the decision to administer nonoccupational PEP should be made on a case-by-case basis.[5] Unlike recommendations for possible sexual exposure to HIV, the recommendations for exposure to HIV in the setting of injection drug use do not take into account whether the person who was exposed to HIV is taking HIV PrEP.[5] The rationale for not factoring in HIV PrEP use in these scenarios is that available data suggest HIV PrEP in persons who inject drugs is only approximately 74% effective.[5,39] The algorithm below summarizes recommendations for giving HIV nonoccupational PEP following a potential exposure to HIV in the setting of injection drug use (Figure 3).[5]

HIV Nonoccupational PEP After Possible Other Exposures

In addition to sexual and injection drug-related potential exposures to HIV, individuals may seek evaluation and consideration of HIV nonoccupational PEP after exposures that pose a much lower risk of HIV transmission.[5] These types of exposures have varying risks and include blood or infective body fluids that splash onto non-intact skin or mucous membranes, injury from a discarded needle in the community, human bites, kissing, mutual masturbation, and exposure to body fluids not associated with HIV transmission (e.g., tears, sweat, urine, nasal secretions, and saliva).[5] The algorithm below summarizes recommendations for considering the administration of HIV nonoccupational PEP after these other types of exposures (Figure 4).[5]

Recommendation if Source Person Has Sustained Viral Suppression

Multiple studies have shown that persons with HIV who consistently maintain undetectable plasma HIV RNA levels do not sexually transmit HIV, even during condomless sex.[40,41,42] Accordingly, HIV nonoccupational PEP is not routinely recommended for sexual exposures involving a source person with sustained suppression of plasma HIV RNA levels.[5] In this context, “sustained viral suppression” is stringently defined as HIV treatment longer than 6 months, a consistently high level of antiretroviral adherence, and HIV RNA less than 200 copies/mL or undetectable in all laboratory assessments in the last year, including an HIV RNA result within the prior 1–2 months.[5] From a practical standpoint, however, this level of detailed information about the source person’s HIV RNA test results is often unavailable, particularly HIV RNA test results in the prior 1–2 months. For exposures to HIV associated with injection drug use, the same recommendation applies: HIV nonoccupational PEP is not routinely recommended if the source person is known to have sustained suppression of HIV RNA levels.[5] This recommendation is based on an extrapolation of data from studies on HIV RNA levels and risk of sexual transmission of HIV. Rigorous studies examining plasma HIV RNA levels and risk of HIV transmission through injection drug use have not been published.

Recommendation if Person Exposed to HIV is Taking HIV PrEP

Individuals taking HIV PrEP as recommended do not need HIV nonoccupational PEP following a possible sexual exposure to HIV.[5] This recommendation is based on extensive data showing very high protection against sexual acquisition of HIV when HIV PrEP is taken with high adherence. The 2025 HIV nPEP Guidelines do not provide an adherence cutoff that defines taking HIV PrEP as recommended.[5] In HIV PrEP studies involving men who have sex with men prescribed daily oral tenofovir-DF, adherence with at least 4 doses per week was estimated to provide a greater than 95% risk reduction for acquiring HIV.[43,44] Laboratory studies examining vaginal tissue levels of the active metabolites of tenofovir and lamivudine suggest that 6–7 doses per week (greater than 85% adherence) with oral HIV PrEP is required to achieve drug levels in lower vaginal tract tissues for significant protection against vaginal acquisition of HIV.[45] In a pooled analysis of 11 HIV PrEP clinical studies that involved women prescribed daily oral tenofovir DF-emtricitabine, participants with consistent high adherence (4–7 doses per week) experienced very low HIV incidence.[46] For persons taking injectable HIV PrEP, adherence effectiveness data are limited, but presumably, persons who do not miss doses of injectable cabotegravir or lenacapavir would be expected to have very high protection against HIV. There are insufficient data on medication adherence and HIV prevention related to exposures from injection drug use. Thus, the use of HIV PrEP is not factored into decision-making after a nonoccupational exposure to HIV associated with injection drug use.[5]

Recommended Regimens for HIV Nonoccupational PEP

[5]The 2025 HIV nPEP Guidelines endorse a 3-drug combination antiretroviral regimen administered for 28 days in all cases where HIV nonoccupational PEP is indicated.[6] The recommended 3-drug regimens for HIV nonoccupational PEP have robust antiviral activity, excellent safety, and are well tolerated.[5] The selection of the specific HIV nonoccupational PEP regimen should be individualized and should take into account potential drug interactions with concurrent medications, pregnancy, renal dysfunction, hepatic impairment, and cost.[5] In nearly all situations, a once-a-day regimen can be used for HIV nonoccupational PEP.

Time to Initiation of HIV Nonoccupational PEP

If indicated, HIV nonoccupational PEP should be initiated as soon as possible, ideally within 24 hours of the exposure; initiation any time within 72 hours after the exposure is considered acceptable.[5] In certain circumstances, such as a very high-risk exposure, some experts would consider offering HIV nonoccupational PEP even if the exposure occurred more than 72 hours prior to the person seeking evaluation.[5]

Duration of Therapy

The 2025 HIV nPEP Guidelines recommend that individuals who initiate antiretroviral therapy for HIV nonoccupational PEP should complete a 28-day course.[5] Studies in macaques have shown that HIV PEP given for 28 days is more effective than 10 days, which is more effective than 3 days.[14] In addition, available data and experience with occupational PEP support the use of a 28-day regimen.[9,47] From a conceptual standpoint, HIV PEP is believed to, in some instances, halt a very early and very limited HIV infection, rather than truly preventing any cell in the body from becoming infected with HIV.

HIV Nonoccupational PEP Regimens for Adults and Adolescents

For persons 12 years of age and older without renal dysfunction or hepatic impairment, the preferred regimens for HIV nonoccupational PEP consist of an integrase strand transfer inhibitor plus two nucleoside reverse transcriptase inhibitors.[5] The alternative regimen is a boosted protease inhibitor plus two nucleoside reverse transcriptase inhibitors (Table 2).[5]

HIV Nonoccupational PEP Regimens in Pregnant Women

Ideally, expert consultation is advised when considering HIV nonoccupational PEP for pregnant or breastfeeding women. The preferred and alternative HIV nonoccupational PEP regimens for pregnant women are the same as those for persons 12 years of age and older who are not pregnant, except that when darunavir is used in pregnant women, it should be used only with ritonavir boosting, and both darunavir and ritonavir should be given twice daily instead of the usual once-daily dosing (Table 3).[5]

HIV Nonoccupational PEP Regimens for Breastfeeding Women

There are limited data on the use of HIV nonoccupational PEP in women who are breastfeeding. If a woman has an HIV exposure and is breastfeeding, HIV nonoccupational PEP should be offered, if indicated, based on the exposure. The HIV nonoccupational PEP regimens should be the same as for persons older than 12 years of age who are not pregnant (e.g., if darunavir is used, it should be dosed once daily with either cobicistat or ritonavir). Ideally, expert consultation is advised when considering HIV nonoccupational PEP for breastfeeding women. If a woman who is breastfeeding is going to start HIV nonoccupational PEP, counseling should include a discussion and shared decision-making regarding whether to interrupt breastfeeding during the 28-day course of HIV nonoccupational PEP.

HIV Nonoccupational PEP Regimens with Renal or Hepatic Impairment

For adults and adolescents with renal or hepatic impairment, some adjustments may be needed in the recommended HIV nonoccupational PEP regimens (Table 4).[5]

- **Patients with Renal Insufficiency**: For persons with moderate renal insufficiency (creatinine clearance [CrCl] 30–49 mL/min), the major adjustment is that tenofovir DF is not part of any preferred regimen. When tenofovir DF is used as part of an alternative regimen, the dose should be reduced to 300 mg every 48 hours.[5] For persons with severe renal insufficiency (CrCl less than 30 mL/min) who are receiving hemodialysis, the same options can be used as with moderate renal insufficiency, but use of tenofovir DF and/or lamivudine requires dose adjustment.[5] The management of persons with severe renal insufficiency who are not on dialysis is highly complicated and generally warrants expert consultation.[5]
- **Patients with Hepatic Insufficiency**: For individuals with hepatic impairment classified as Child-Pugh class A or B, the same preferred and alternative HIV nonoccupational PEP regimens can be used as recommended for those without hepatic impairment.[5] For individuals with severe hepatic impairment (Child-Pugh class C), expert consultation is recommended to select an appropriate HIV nonoccupational PEP regimen.[5]

Expert Consultation for HIV Nonoccupational PEP

Indications for Obtaining Expert Consultation

The 2025 HIV nPEP Guidelines provide recommendations for scenarios that warrant expert consultation for HIV nonoccupational PEP.[5] Expert consultation is recommended in any of the following situations:

- The health care worker has limited experience with prescribing antiretroviral medications, *or*
- The individual exposed to HIV is a woman who is pregnant or breastfeeding, *or*
- The exposure event involves a child or adolescent, *or*
- The individual needing HIV nonoccupational PEP has severe renal dysfunction and is not on hemodialysis, *or*
- The individual needing HIV nonoccupational PEP has severe hepatic impairment (Child-Pugh class C), *or*
- The source person has known or suspected antiretroviral resistance.

Consideration of HIV Drug Resistance in Source Person

If medical information is available regarding a source person with known HIV, the choice of an HIV nonoccupational PEP regimen should consider the source person's antiretroviral medication history, most recent HIV RNA levels, and prior resistance testing results.[5] Drug resistance to the newer generation integrase strand transfer inhibitors (bictegravir and dolutegravir) is uncommon.[5] If the source person has suspected or known antiretroviral drug resistance, expert consultation should be obtained to determine the optimal HIV nonoccupational PEP regimen for the individual exposed to HIV.[5]

PEPline Expert Consultation

Expert consultation for these issues and any other guidance on nonoccupational PEP can be obtained by calling the National Clinician Consultation Center's Post-Exposure Prophylaxis PEPline at 844-275-6222; this service is for health care professionals.

Baseline and Follow-Up Laboratory Testing

Baseline laboratory evaluation and follow-up laboratory studies are key components of nonoccupational HIV PEP evaluation and management, with HIV testing the most essential evaluation component.[5] In addition, the source person should undergo HIV testing, unless the source is unavailable or already known to have HIV.[5] Follow-up laboratory testing for the person exposed to HIV is typically performed 4–6 weeks and 12 weeks after the initial evaluation, with additional testing at 6 months if follow-up for HBV or HCV infection is warranted.[5] The following table and discussion summarize recommendations for baseline laboratory studies (for the source and the person exposed to HIV) and a schedule of follow-up laboratory tests for monitoring the person exposed to HIV.[5] The baseline laboratory evaluation is similar for both, except for three differences: (1) HCV RNA testing is recommended for the source person, whereas HCV antibody with reflex to HCV RNA is recommended for person exposed to HIV; (2) pregnancy testing is considered only for the person exposed to HIV; and (3) baseline serum creatinine and hepatic aminotransferase levels are recommended only for the person exposed to HIV.[5]

Table 5. Laboratory Monitoring with Nonoccupational Exposure to HIV: 2025 CDC Guidelines

Test	Source	Person Exposed to HIV		
	Baseline	Baseline	12 weeks after exposure	6 months after exposure
		All persons evaluated for HIV Nonoccupational PEP		
Rapid (point-of-care) or laboratory-based HIV Ag/Ab test)[†]	√	√	√	—
HIV diagnostic NAT[¶]	√[**]	√[**]	√	—
HBV serology: HBsAg, HBsAb, and HBcAb	√	√[††]	—	If HBV nonimmune at baseline
HCV antibody testing	—	√[§§]	—	If follow-up testing recommended[¶¶]
HCV RNA NAT	√[***]	—	—	—
Syphilis serology[§§§]	√	√	√[§§§]	—
Gonorrhea NAAT[****]	√	√	—	—

Test	Source	Person Exposed to HIV		
	Baseline	Baseline	12 weeks after exposure	6 months after exposure
		All persons evaluated for HIV Nonoccupational PEP		
Chlamydia NAAT****	√	√	—	—
Pregnancy test††††	—	√	—	—
		All persons prescribed HIV Nonoccupational PEP		
Serum creatinine		√	—	—
Alanine aminotransferase and aspartate aminotransferase		√	—	—

Abbreviations: Ag/Ab = antigen/antibody combination test; HBcAb = hepatitis B core antibody; HBsAb = hepatitis B antibody; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCV = hepatitis C virus; NAT = nucleic acid nucleic acid amplification test; PEP = postexposure prophylaxis.

Note: Any person diagnosed with an infection or condition through testing should be informed and treated or referre treatment as needed.

†If a rapid (point-of-care) HIV Ag/Ab test is used, a laboratory-based HIV Ag/Ab test obtained at the same time will in diagnostic sensitivity. PEP should not be delayed awaiting laboratory results. If the preferred HIV diagnostic test is n accessible, the most sensitive available test should be used.

§HIV testing 4–6 weeks post-nonoccupational PEP initiation can be deferred for persons who started nonoccupationa hours of exposure, completed the full PEP course, and are not starting PrEP at this time.

¶NATs that detect HIV RNA include qualitative tests for diagnosis (e.g., HIV-1 RNA assay) and quantitative tests for c monitoring (e.g., viral load). Diagnostic HIV NATs are recommended because they are more likely than viral load tes very low levels of HIV. If the preferred HIV diagnostic test is not accessible, the most sensitive available test should inability to access HIV NAT should not prevent provision of HIV nonoccupational PEP to persons with indications.

**HIV NAT recommended at baseline assessment for persons with injectable ARV exposure during the past 6 month

††HBV PEP recommendations vary by the exposed person's HBV immune status, and by the source's HBV status (wh information available).

§§Reflex to HCV RNA NAT if HCV antibody test is positive. Add HCV RNA NAT to original order if signs and symptoms infection are present (e.g., hepatic enzyme elevation).

¶¶If follow-up testing is recommended based on the source's status (e.g., HCV RNA positive or HCV antibody test is p unavailable HCV RNA, or if the HCV infection status is unknown), and HCV RNA NAT is negative 3–6 weeks postexpo test for HCV antibodies 4–6 months postexposure is recommended

***HCV RNA NAT is preferred for testing of the source, but if not accessible, HCV antibody testing with reflex HCV RI positive is an alternative strategy

†††If follow-up testing is recommended based on the source's status (e.g., HCV RNA positive or positive HCV antibody unavailable HCV RNA, or if the HCV infection status is unknown), HCV RNA NAT is recommended for the exposed pe weeks postexposure.

Test	Source	Person Exposed to HIV		
	Baseline	Baseline	12 weeks after exposure	6 months after exposure
		All persons evaluated for HIV Nonoccupational PEP		

§§§STI testing decisions should be made on an individual basis.
¶¶¶If initial syphilis testing negative and infection in the source cannot be ruled out, follow-up testing may be perforr weeks and 3 months postexposure.
****NAATs are recommended for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* at exposure sites (e.g., pharynx vagina) at initial visit and can be repeated 1–2 weeks postexposure if no presumptive treatment was provided and i results were negative. Repeat testing can also be done if the person reports symptoms concerning for STIs. Certain would also perform a NAAT for *Trichomonas vaginalis* from a urine or vaginal specimen for persons with vaginas.
††††For all women of child-bearing potential who are not known to be pregnant.

Source:

- Tanner MR, O'Shea JG, Byrd KM, et al. Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV - CDC Recommendations, United States, 2025. MMWR Recomm Rep. 2025;74:1-56. [PubMed Abstract]

Baseline Laboratory Studies

The 2025 HIV nPEP Guidelines recommend the following baseline laboratory tests for all persons who undergoing evaluation for HIV nonoccupational PEP.[6]

- **HIV Testing**: Baseline HIV testing for the source person and the individual exposed to HIV should consist of a rapid (point-of-care) test, a laboratory-based HIV antigen-antibody test, or both. If a point-of-care HIV test is used, a laboratory-based HIV antigen-antibody test should also be ordered, primarily because laboratory-based HIV antigen-antibody tests have higher sensitivity. Oral point-of-care HIV tests are not recommended. Obtaining a baseline diagnostic HIV nucleic acid test (NAT) for the source person or the individual under evaluation is recommended if they received an injectable HIV PrEP medication (cabotegravir or lenacapavir) in the prior 6 months.
- **Hepatitis B Virus (HBV)**: The source person and the individual exposed to HIV should undergo an HBV triple screen: hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (HBsAb), and hepatitis B core antibody (HBcAb). Baseline screening is indicated to determine whether nonoccupational PEP against HBV is indicated (the source person has a positive HBsAg test, and the person with the exposure is not immune to HBV). In addition, it is important to determine if the person starting HIV nonoccupational PEP has chronic HBV, since starting one or more medications with activity against hepatitis B (tenofovir DF, tenofovir alafenamide, emtricitabine, or lamivudine) can lead to a hepatic flare after discontinuation. Further, for a person who lacks immunity to HBV and does not have active HBV infection, immunization against HBV is recommended.
- **Hepatitis C Virus (HCV)**: For the source person, HCV RNA NAT testing is recommended. For an individual with a possible exposure to HIV and HCV, the recommended HCV testing consists of HCV antibody with reflex to HCV RNA if the antibody test is reactive. Testing both the source person (if available) and the individual exposed is indicated to determine whether the exposure has the potential for HCV transmission. Although nonoccupational PEP against HCV is not recommended, follow-up for a person exposed to HCV is very important since, in the event they acquire HCV, highly effective and safe treatments for HCV are available.
- **Sexually Transmitted Infection**s: Baseline testing for sexually transmitted infections (syphilis, gonorrhea, and chlamydia) should be individualized based on the exposure and any other indication for screening. Most experts recommend routine testing for syphilis, gonorrhea, and chlamydia in the

setting of a possible sexual exposure to HIV. Ideally, baseline testing for sexually transmitted infection is performed on both the source person and the individual possibly exposed to HIV. In this setting, the evaluation for sexually transmitted infections should include serologic testing for syphilis and nucleic acid amplification tests (NAATs) for chlamydia and gonorrhea (at all exposure sites). If presumptive treatment for these infections is not administered (to the person with the exposure), repeat testing can be ordered approximately 2 weeks later. In addition, for women with a possible sexual exposure to HIV, some experts recommend baseline testing for trichomonas (using a urine or vaginal swab sample).

- **Pregnancy Test:** Although all medications recommended for HIV nonoccupational PEP are considered safe during pregnancy and during breastfeeding, additional counseling may be needed. Therefore, pregnancy testing is recommended for women of childbearing potential undergoing evaluation for HIV nonoccupational PEP.
- **Serum Creatinine**: This test is recommended for persons exposed to HIV who are starting an HIV nonoccupational PEP regimen. The rationale for checking a baseline serum creatinine is twofold: (1) tenofovir DF (and to a lesser extent, tenofovir alafenamide) may cause small, reversible declines in renal function, and (2) for individuals with moderate or severe renal dysfunction, HIV nonoccupational PEP regimens may need modification or dose adjustments.
- **Hepatic Aminotransferase Levels**: Testing for alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels is recommended for persons exposed to HIV who are starting an HIV nonoccupational PEP regimen. Liver injury from nonoccupational PEP medication regimens is extremely rare, but dose adjustments may be needed with severe hepatic impairment (Child-Pugh class C).

Follow-Up Laboratory Studies

The 2025 HIV nPEP Guidelines recommend the following laboratory tests for all persons who received HIV nonoccupational PEP.[6] In addition, follow-up laboratory studies are recommended for individuals with a significant exposure to HIV who declined HIV nonoccupational PEP.

- **HIV Testing**: Follow-up HIV testing should consist of a laboratory-based HIV antigen-antibody test in combination with an HIV RNA NAT, with testing performed at 4–6 weeks and 12 weeks after the baseline evaluation. If the person started HIV nonoccupational PEP within 24 hours of the exposure and was adherent with the entire 28-day regimen, testing at 4–6 weeks can be omitted. If the person plans to transition from nonoccupational HIV PEP to HIV PrEP, then the first follow-up and testing would ideally occurs at 4 weeks (or a day or two prior to 4 weeks) to coordinate the switch from HIV nonoccupational PEP to HIV PrEP.
- **HBV Testing**: For persons not immune to HBV at baseline, follow-up HBV testing should be conducted at 6 months and should include HBsAg, HBsAb, and HBcAb.
- **HCV Testing**: If the source person has a positive HCV RNA test (or a positive HCV antibody with unknown HCV RNA results), follow-up HCV antibody testing is recommended for the person exposed to HIV and HCV at 6 months.
- **Testing for Sexually Transmitted Infection**s: Routine follow-up testing for syphilis, gonorrhea, and chlamydia is not recommended. If, however, the person is diagnosed with a sexually transmitted infection at baseline, or they are transitioning to HIV PrEP, follow-up testing for sexually transmitted infections should be performed.
- **Pregnancy Testing**: Repeat pregnancy testing should be performed at 4–6 weeks if the woman is of reproductive age and not known to be pregnant.
- **Serum Creatinine**: A serum creatinine should be checked at 4–6 weeks only if the serum creatinine was abnormal at baseline.
- **Hepatic Aminotransferase Levels**: The ALT and AST levels should be checked at 4–6 weeks if the hepatic aminotransferase levels were abnormal at baseline.

HIV Nonoccupational PEP After Sexual Assault

The evaluation and provision of HIV nonoccupational PEP should be part of comprehensive services offered to persons who have experienced sexual assault. Extensive efforts should be made for these services to include a comprehensive evaluation by a sexual assault forensic or nurse examiner, as well as services or referrals for psychological counseling. It is beyond the scope of this lesson to address the extensive issues, including legal issues, that need to be addressed following a sexual assault of an adult, adolescent, or child; these recommendations can be found in published guidelines, including the American College of Obstetricians and Gynecologists (ACOG) Committee Opinion No. 777 (Sexual Assault), the American Academy of Pediatrics, and the CDC Sexually Transmitted Infections Treatment Guidelines section Sexual Assault and Abuse and STIs.[48,49,50] The following will focus on key postexposure medical interventions following a sexual assault.

Emergency Contraception

When a sexual assault victim is a woman, and the assault has the possibility of resulting in pregnancy, emergency contraception should be offered.[5,48]

HIV Nonoccupational PEP

Baseline HIV testing is recommended for all persons who are evaluated after a sexual assault.[5,48] In addition, follow-up HIV testing is recommended at 4–6 weeks and 12 weeks after the sexual assault.[5,48] In most cases of sexual assault, information on the source person's HIV status is unknown, and even when known, detailed knowledge of a recent HIV RNA level is unlikely. Nevertheless, for sexual assault survivors, HIV nonoccupational PEP should be offered if the assault involved contact associated with substantial risk of HIV transmission and the source person is known to have HIV (or the source person's HIV status is unknown).[5] Available data suggest low adherence and low completion rates for HIV nonoccupational PEP among sexual assault survivors.[51,52] Therefore, at the initial visit, it is important to provide counseling and education on the importance of taking the entire 28-day regimen, as well as adherence support. Multiple studies involving sexual assault survivors have demonstrated very low HIV transmission rates, despite relatively low adherence rates with HIV nonoccupational PEP medications.[53,54,55,56,57]

Empiric Treatment for Common Sexually Transmitted Infections

Baseline testing for all persons following sexual assault should include nucleic acid amplification tests (NAATs) for *C. trachomatis* and *N. gonorrhoeae* at all sites of penetration.[48] All sexual assault survivors should have baseline serologic testing for syphilis; if a syphilis diagnosis is not ruled out in the assailant, follow-up syphilis serologic testing should be conducted at 4–6 weeks and 3 months, coinciding with the timing of follow-up HIV testing.[5,48] Women should also have a NAAT for *Trichomonas vaginalis* from a urine or vaginal specimen.[48] Empiric treatment for gonorrhea, chlamydia, and trichomoniasis should be offered to all women following a sexual assault.[48] For pregnant women, azithromycin should be used in place of doxycycline. Men should have empiric treatment for gonorrhea and chlamydia. Empiric initial treatment for STIs should be provided, regardless of whether test results for these pathogens are available. Note that empiric therapy for syphilis is not routinely recommended in sexual assault survivors, but ceftriaxone and doxycycline both have significant activity against *Treponema pallidum* and may provide some protection against incubating syphilis.

2021 STI Treatment Guidelines: Sexual Assault
Table 6. Empiric Antimicrobial Treatment after Sexual Assault

Recommended **Regimen for Adolescent and Adult Female Sexual Assault Survivors**

Ceftriaxone

Ceftriaxone

Tradename:Rocephin

500 mg* IM in single dose

Doxycycline

Doxycycline

Tradename:Doryx, Vibramycin

100 mg orally twice daily for 7 days^+

Metronidazole

Metronidazole

Tradename:Flagyl

500 mg orally twice daily for 7 days+

^For pregnant women, oral azithromycin 1 gram in a single dose is recommended to treat chlamydia in place of doxycycline.

Note: *For persons weighing ≥150 kg, 1 g of ceftriaxone should be administered.

Recommended **Regimen for Adolescent and Adult Male Sexual Assault Survivors**

Ceftriaxone

Ceftriaxone

Tradename:Rocephin

500 mg* IM in single dose

Doxycycline

Doxycycline

Tradename:Doryx, Vibramycin

100 mg orally twice daily for 7 days+

Note: *For persons weighing ≥150 kg, 1 g of ceftriaxone should be administered.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Sexual assault and abuse and STIs. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

Postexposure Prophylaxis for HBV

The indication for HBV postexposure prophylaxis depends on the sexual assault survivor's prior HBV vaccine history and immune status, as well as any available information about the assailant's HBV status. The recommendations for HBV nonoccupational PEP are provided in the section below on *Nonoccupational PEP for Infectious Pathogens Other than HIV*.

Postexposure Prophylaxis for HCV

There are no recommendations to provide HCV postexposure prophylaxis after sexual assault, but recommendations for nonoccupational PEP should be followed with baseline HCV antibody testing, with reflex to HCV RNA if reactive.[5] In addition, if indicated, a follow-up HCV RNA test should be performed at 4–6 weeks after exposure and HCV antibody testing (with reflex to HCV RNA) at 6 months postexposure.[5]

Human Papillomavirus (HPV) Vaccination

For survivors of sexual assault who are 9–26 years of age, the human papillomavirus (HPV) vaccine should be administered if they have not previously received the HPV vaccine series.[48] For healthy persons 9–14 years of age, two doses of the vaccine are recommended. For all others, the vaccine should be administered as a 3-dose series. Individuals who have started the vaccine series but not completed it should complete the vaccine series based on their age when they started the vaccine series.

Herpes Simplex Virus

A sexual assault has the potential to result in transmission of herpes simplex virus (HSV) type 1 and/or type 2 from the assailant to the sexual assault survivor. Although there are no recommendations to perform HSV testing or provide HSV postexposure prophylaxis following sexual assault, clinicians should be aware of this possible complication.

Initial Medication Prescription and Follow-up

Initial Medication Prescription and Timely Follow-Up

The 2025 HIV nPEP Guidelines suggest that health care professionals should consider prescribing HIV nonoccupational PEP antiretroviral medications for 3 to 7 days (i.e., a starter pack) or provide a prescription for the entire 28-day course. Ideally, at the initial visit, the facility would supply a starter pack or a full 28-day supply of medication, both to minimize any delay in receiving the first dose and to address any barriers that could prohibit the patient from filling the prescription at an outside pharmacy. In addition, prior to leaving the facility, the person evaluated for HIV nonoccupational PEP should have an early follow-up visit scheduled or a phone call check-in to assess adherence with HIV nonoccupational PEP, discuss medication-related side effects, and provide additional counseling or education as needed.[5] If the individual receives only a 3- to 7-day supply of antiretroviral medications, coordination for timely follow-up is essential to ensure they do not run out of medication.

Challenges to Follow-Up

One study reported significant patient attrition between the initial emergency department visit for HIV nonoccupational PEP and the first follow-up clinic appointment.[58] Only about half of HIV nonoccupational PEP patients attended their follow-up appointments, and less than a quarter of those who started on nonoccupational HIV PEP completed the full 28-day regimen.[58]

HIV Prevention Counseling

Patients who are evaluated for nonoccupational HIV PEP should receive HIV prevention counseling. This includes counseling on methods to reduce the risk of HIV acquisition (e.g., using barrier methods with sex partners, not sharing equipment used to inject drugs). At follow-up visits, health care professionals should assess for ongoing risk for HIV acquisition, provide additional counseling, and connect patients with services as needed, including assessment for initiation of HIV PrEP.

Transitioning HIV Nonoccupational PEP to HIV PrEP

Individuals who present for HIV nonoccupational PEP following a sexual or injection drug use exposure may be excellent candidates for HIV PrEP, particularly if they report ongoing activities associated with increased risk for HIV acquisition.[7,59] Thus, persons receiving HIV nonoccupational PEP who are interested in HIV PrEP should transition to HIV PrEP without interruption.[5,7] For example, if a person is going to transition from HIV nonoccupational PEP to HIV PrEP, they should take a 28-day course of HIV nonoccupational PEP, and on day 29, transition to taking HIV PrEP.[5,7] The following summarizes several key issues regarding the transition from HIV nonoccupational PEP to HIV PrEP.[7]

- **Timing of Follow-Up**: The recommended first follow-up visit for any individual initiating HIV nonoccupational PEP is 4–6 weeks. Individuals who are a candidate to transition from HIV nonoccupational PEP to HIV PrEP should ideally have their first follow-up visit at 4 weeks (at the completion of the 28-day HIV nonoccupational PEP regimen or ideally several days prior to completing the regimen). At this 4-week follow-up visit, repeat HIV testing should be performed, with a laboratory-based HIV antigen-antibody test and an HIV diagnostic NAT. There is an increased risk of false-negative HIV testing results in persons receiving HIV nonoccupational PEP, since potent antiretroviral therapy may suppress plasma HIV RNA levels and blunt the normal immune reaction to HIV. At this follow-up visit, the individual should have an assessment for any signs or symptoms that would suggest acute HIV.
- **Initiating HIV PrEP**: At the 4-week visit, individuals transitioning to HIV PrEP should receive counseling about HIV PrEP, obtain the HIV PrEP prescription, and understand the need for regular follow-up visits and laboratory testing. They can transition to HIV PrEP at the 28-day visit while HIV results are pending, with the plan to expand to a first-line antiretroviral regimen immediately if the HIV testing reveals HIV infection. If any concern for acute HIV exists, then HIV PrEP should be deferred while evaluation for acute HIV is completed.
- **HIV PrEP Regimen Selection**: The individual taking a 3-drug HIV nonoccupational PEP regimen can transition to any of the HIV PrEP regimens (tenofovir DF-emtricitabine, tenofovir alafenamide-emtricitabine, long-acting injectable cabotegravir, or injectable lenacapavir), as long as the HIV PrEP regimen is indicated for the individual.
- **Additional Prevention Strategies**: For men who have sex with men, doxycycline PEP (Doxy PEP) should be discussed as an option for prevention of bacterial sexually transmitted infection.[60] At this time, Doxy PEP is not recommended for women.[60]

Expert Consultation

Clinicians with questions about transitioning from HIV nonoccupational PEP to HIV PrEP can call the National Clinician Consultation Center's Pre-Exposure Prophylaxis PrEPline at 855-448-7737 for expert consultation.

Nonoccupational PEP for Pathogens Other Than HIV

In conjunction with HIV nonoccupational PEP, evaluation of other infectious pathogens that can be transmitted as a result of the exposure should occur. The risk for certain pathogens depends on whether the exposure involved sexual contact or injection drug use. For example, the management of potential transmission of *T. pallidum*, *N. gonorrhoeae*, and *C. trachomatis* is more important following nonoccupational sexual exposures than injection drug use-related exposures. In contrast, transmission of HBV or HCV is more likely with injection drug use-related exposures than with sexual exposures. The following outlines key additional considerations for pathogens other than HIV that can be transmitted as a result of a sexual or injection drug use-related exposure. Additional details and recommendations for sexual assault survivors are provided in this lesson in the section on *HIV Nonoccupational PEP after Sexual Assault*.

Hepatitis B Virus

Transmission of hepatitis B virus (HBV) in adults primarily occurs through percutaneous exposure to blood (e.g., by injection drug use) and sexual contact.[61] The risk of HBV transmission from blood contact is substantially higher than from sexual contact. The risk of acquiring HBV with a nonoccupational exposure depends on the type of exposure, the source person's HBsAg status (if known), and the HBV status of the individual with the nonoccupational exposure. The strategy for preventing HBV acquisition for nonoccupational exposure has utilized HBV vaccination and/or hepatitis B immune globulin (HBIG) administration. Although HIV nonoccupational PEP regimens include nucleoside reverse transcriptase inhibitors (tenofovir DF, tenofovir alafenamide, emtricitabine, and/or lamivudine) that have activity against HBV, their impact on preventing HBV acquisition is unknown. Therefore, current HBV nonoccupational PEP recommendations, as outlined in the table below, utilize only the HBV vaccine and/or HBIG (Table 7).[61]

Hepatitis C Virus

Most cases of HCV infection in the United States have resulted from injection drug use.[62] Less often, transmission of HCV can occur through sexual contact, usually with cases involving men who have sex with men (MSM).[62] All persons evaluated for HIV nonoccupational PEP should have baseline HCV antibody testing, with reflex to HCV RNA NAT if positive.[5] They should have follow-up HCV testing if indicated based on the source person's HCV status (e.g., HCV RNA NAT positive, HCV antibody reactive with unavailable HCV RNA NAT, or unknown HCV status).[5] If indicated, follow-up HCV testing should be performed with an HCV RNA NAT at 4–6 weeks postexposure and a final test for HCV antibodies (with reflex to HCV RNA NAT if positive) at 6 months postexposure.[5] There are no recommendations to use HCV direct-acting antiviral (DAA) therapy for nonoccupational PEP, but for persons diagnosed with HCV infection, DAA therapy can provide cure rates of greater than 95%.[5,63] Accordingly, baseline and follow-up HCV testing is an important aspect of the overall nonoccupational PEP evaluation to identify anyone who has HCV infection so they can receive curative antiviral therapy.

Syphilis

For persons under evaluation for HIV nonoccupational PEP, baseline serologic testing for syphilis should be performed on an individual basis.[5] With an HIV nonoccupational sexual exposure, most experts recommend obtaining baseline and follow-up syphilis serologic testing. If the exposure involved sexual assault, baseline syphilis serologic testing should routinely be ordered. There are no recommendations to provide empiric treatment for syphilis, even following sexual assault. For men who have sex with men, doxycycline PEP (a single 200-mg dose taken within 72 hours of the exposure) could be offered and would be expected to provide moderate protection against syphilis.[60] At this time, doxycycline PEP is not recommended for women. Treatment of chlamydia with doxycycline would likely also provide some protection against syphilis.

Gonorrhea

For persons under evaluation for HIV nonoccupational PEP, baseline testing for gonorrhea should be performed on an individual basis.[5] With an HIV nonoccupational sexual exposure, most experts recommend obtaining baseline and follow-up testing for gonorrhea at all exposure sites (e.g., vagina, rectum, pharynx) using NAAT. There are no recommendations to routinely provide empiric treatment for gonorrhea in this setting, but for men who have sex with men, doxycycline PEP (a single 200-mg dose taken within 72 hours of the exposure) could be offered and would be expected to provide moderate protection against gonorrhea.[60] If the exposure involved sexual assault, empiric treatment with a single 500 mg intramuscular dose of ceftriaxone is recommended.[48]

Chlamydia

For persons under evaluation for HIV nonoccupational PEP, baseline testing for chlamydia should be performed on an individual basis.[5] For an HIV nonoccupational sexual exposure, most experts recommend obtaining baseline and follow-up testing for gonorrhea at all exposure sites (e.g., vagina, rectum, pharynx) using NAAT. There are no recommendations to routinely provide empiric treatment for gonorrhea in this setting, but for men who have sex with men, doxycycline PEP (a single 200-mg dose taken within 72 hours of the exposure) could be offered and would be expected to provide moderate protection against chlamydia.[60] If the exposure involved sexual assault, empiric treatment for chlamydia with oral doxycycline (100 mg twice daily for 7 days) is recommended, unless the assault involved a pregnant woman; pregnant women should receive treatment with a single dose of azithromycin 1 gram orally.[48]

Trichomonas

Baseline testing for trichomoniasis is not routinely recommended for persons under evaluation for HIV nonoccupational PEP. Some experts recommend testing women following a sexual exposure with a NAAT for *Trichomonas vaginalis* in a urine or vaginal specimen. There are no recommendations to routinely provide empiric treatment for trichomoniasis for persons evaluated for HIV nonoccupational PEP. If, however, the exposure involved sexual assault, empiric treatment of trichomoniasis for women should be offered with oral metronidazole (500 mg twice a day for 7 days).[48]

Herpes Simplex Virus

There are no recommendations to perform testing or empiric treatment for HSV following a nonoccupational sexual or injection drug use-related exposure. Nevertheless, clinicians should be aware that transmission of HSV-1 and/or HSV-2 could occur with a sexual exposure.

Human Papillomavirus

There are no recommendations to perform human papillomavirus (HPV) testing with HIV nonoccupational PEP evaluations. For persons who have not received HPV immunization, the HPV vaccine series should be offered. For survivors of sexual assault who are 9–26 years of age, the HPV vaccine should be administered to those who have not previously received the HPV vaccine series. It is unknown whether promptly initiating and then completing the HPV vaccine series provides any protection if given after a sexual exposure to HPV.

Summary Points

- Antiretroviral medications for HIV nonoccupational PEP are recommended for HIV-seronegative persons following an exposure that has a significant risk of HIV acquisition, if started within 72 hours of the exposure. The optimal timing for administration of HIV nonoccupational PEP is within 24 hours of the exposure. If the source person's HIV status is unknown, the use of HIV nonoccupational PEP should be evaluated on a case-by-case basis.
- For sexual exposures to HIV involving persons taking HIV PrEP as recommended, HIV nonoccupational PEP is not indicated. In addition, HIV nonoccupational PEP is not routinely recommended when the source person with HIV is known to have sustained suppression of HIV RNA levels.
- The preferred HIV nonoccupational PEP regimens for adults and adolescents aged 12 years and older are fixed-dose combination bictegravir-tenofovir alafenamide-emtricitabine or dolutegravir plus (tenofovir DF or tenofovir alafenamide) plus (emtricitabine or lamivudine). A 28-day course is recommended.
- Regimens for HIV nonoccupational PEP may need to be modified in persons with significant renal dysfunction or severe hepatic impairment.
- Individuals with nonoccupational exposure to HIV should have baseline laboratory studies that include HIV testing (HIV antigen-antibody test), serum creatinine, AST, ALT, HBV, and a pregnancy test (if indicated). If a person has received injectable HIV PrEP in the prior 6 months, then baseline testing should include a diagnostic HIV NAT. Testing for sexually transmitted infections and HCV infection should be guided by the clinical situation.
- Expert consultation should be sought for complex situations and can be obtained through local expertise (if available) or through the National Clinician Consultation Center.
- Individuals receiving HIV nonoccupational PEP should have follow-up HIV testing at 4 to 6 weeks and again at 3 months to determine if HIV infection has occurred. The follow-up HIV testing should consist of the HIV-1/2 antigen-antibody test in tandem with a diagnostic HIV NAT.
- Many individuals who seek HIV nonoccupational PEP services should be evaluated as potential candidates to receive HIV PrEP following completion of HIV nonoccupational PEP. The transition from HIV nonoccupational PEP to HIV PrEP, if warranted, should occur without interruption.

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Figures

Figure 1 (Image Series) - Tenofovir PEP following SIV-1 Inoculation of Macaques (Image Series) -
Figure 1 (Image Series) - Tenofovir PEP following SIV-1 Inoculation of Macaques
Image 1A: Study Protocol

In this study, investigators inoculated 24 macaques with simian immunodeficiency virus (SIV) and then instituted various postexposure prophylaxis regimens with tenofovir (PMPA), which is (R)-9-(2-phosphonylmethoxypropyl) adenine.
Abbreviations: SIV = simian immunodeficiency virus; PEP = postexposure prophylaxis; TFV = tenofovir

Source: Tsai CC, Emau P, Follis KE, et al. Effectiveness of postinoculation (R)-9-(2-phosphonylmethoxypropyl) adenine treatment for prevention of persistent simian immunodeficiency virus SIVmne infection depends critically on timing of initiation and duration of treatment. J Virol. 1998;72:4265-73.

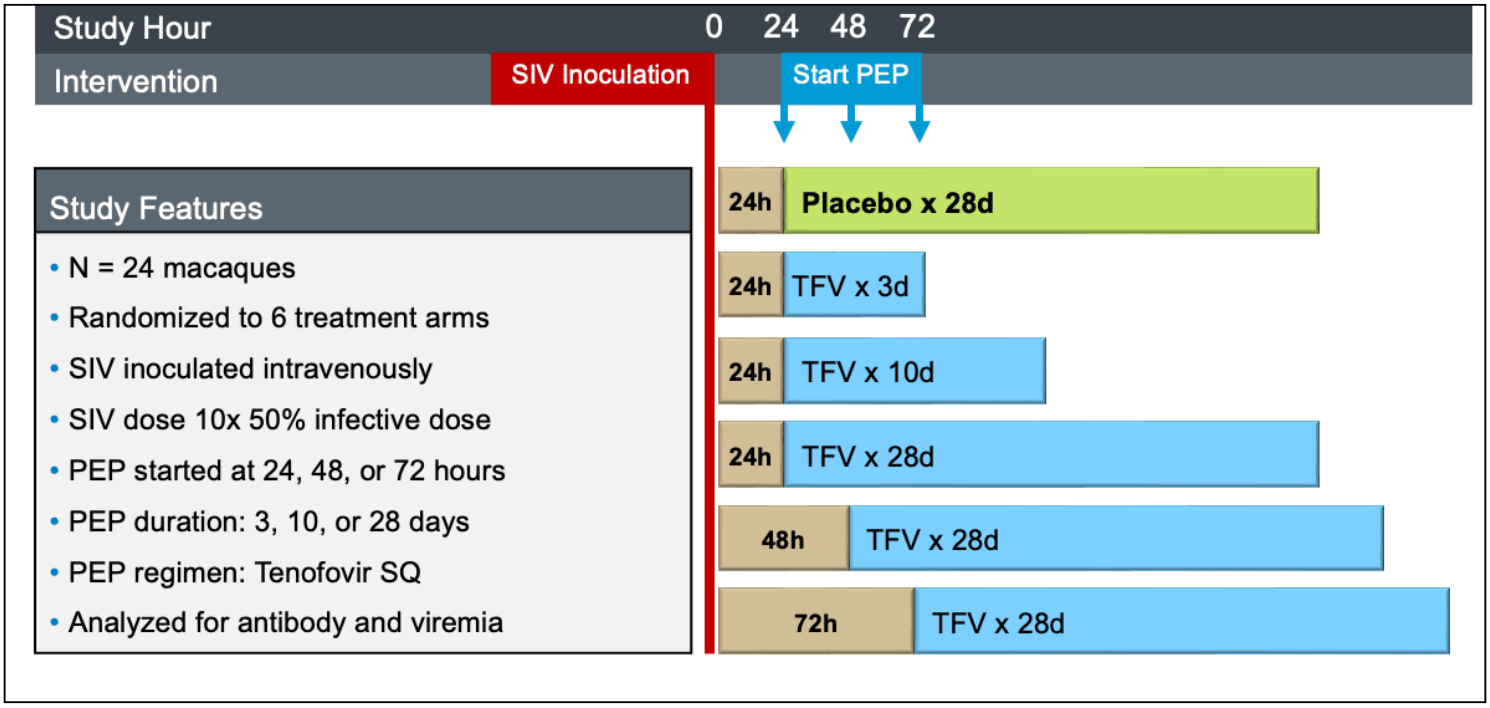

Figure 1 (Image Series) - Tenofovir PEP following SIV-1 Inoculation of Macaques
Image 1B: SIV Transmission Based on Timing of Initiation and Duration of PEP

Source: Tsai CC, Emau P, Follis KE, et al. Effectiveness of postinoculation (R)-9-(2-phosphonylmethoxypropyl) adenine treatment for prevention of persistent simian immunodeficiency virus SIVmne infection depends critically on timing of initiation and duration of treatment. J Virol. 1998;72:4265-73.

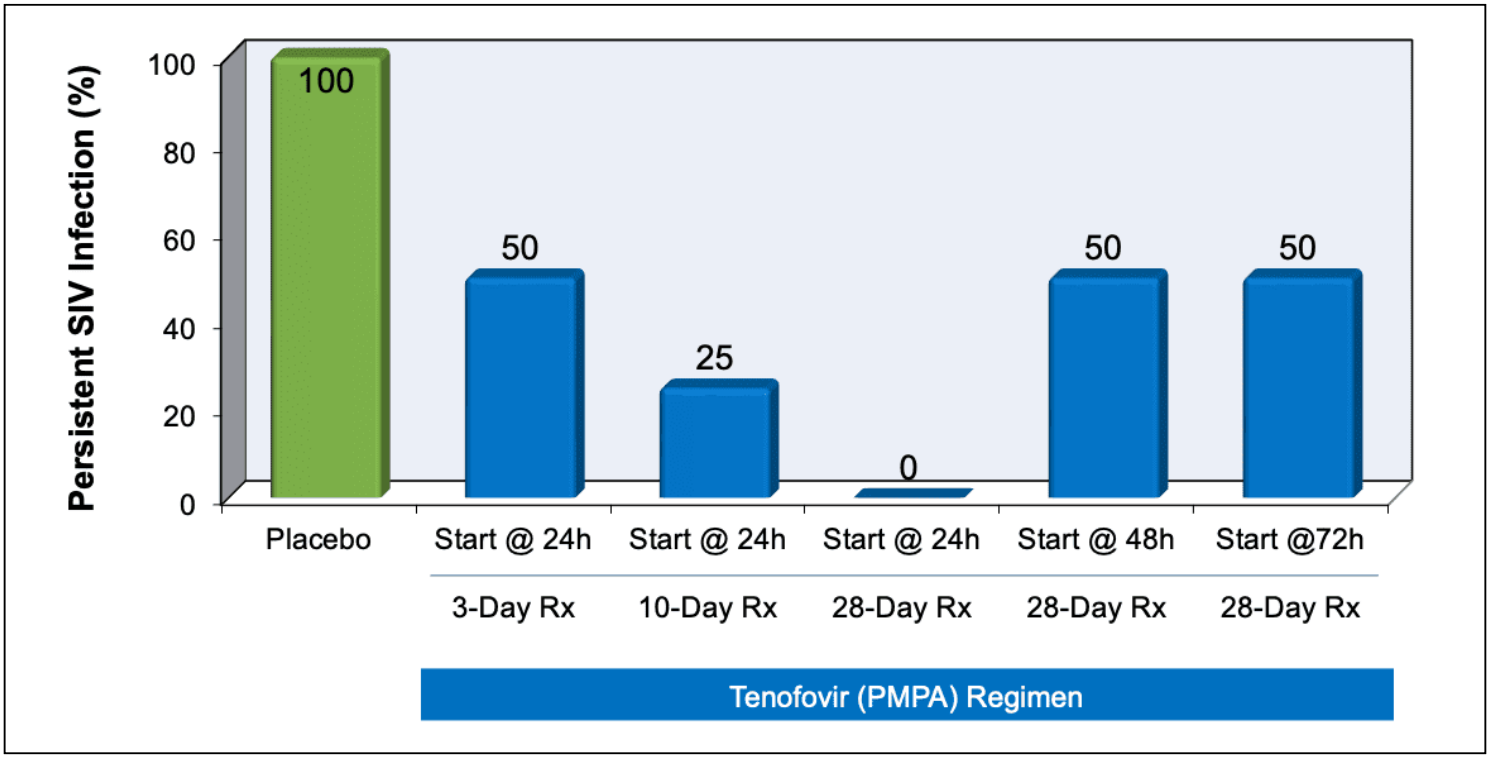

Figure 2 HIV Nonoccupational PEP Use after Possible Sexual Exposure to HIV: 2025 CDC Guidelines

Abbreviations: PrEP = preexposure prophylaxis; nPEP= nonoccupational postexposure prophylaxis

Source: Tanner MR, O'Shea JG, Byrd KM, et al. Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV - CDC Recommendations, United States, 2025. MMWR Recomm Rep. 2025;74:1-56.

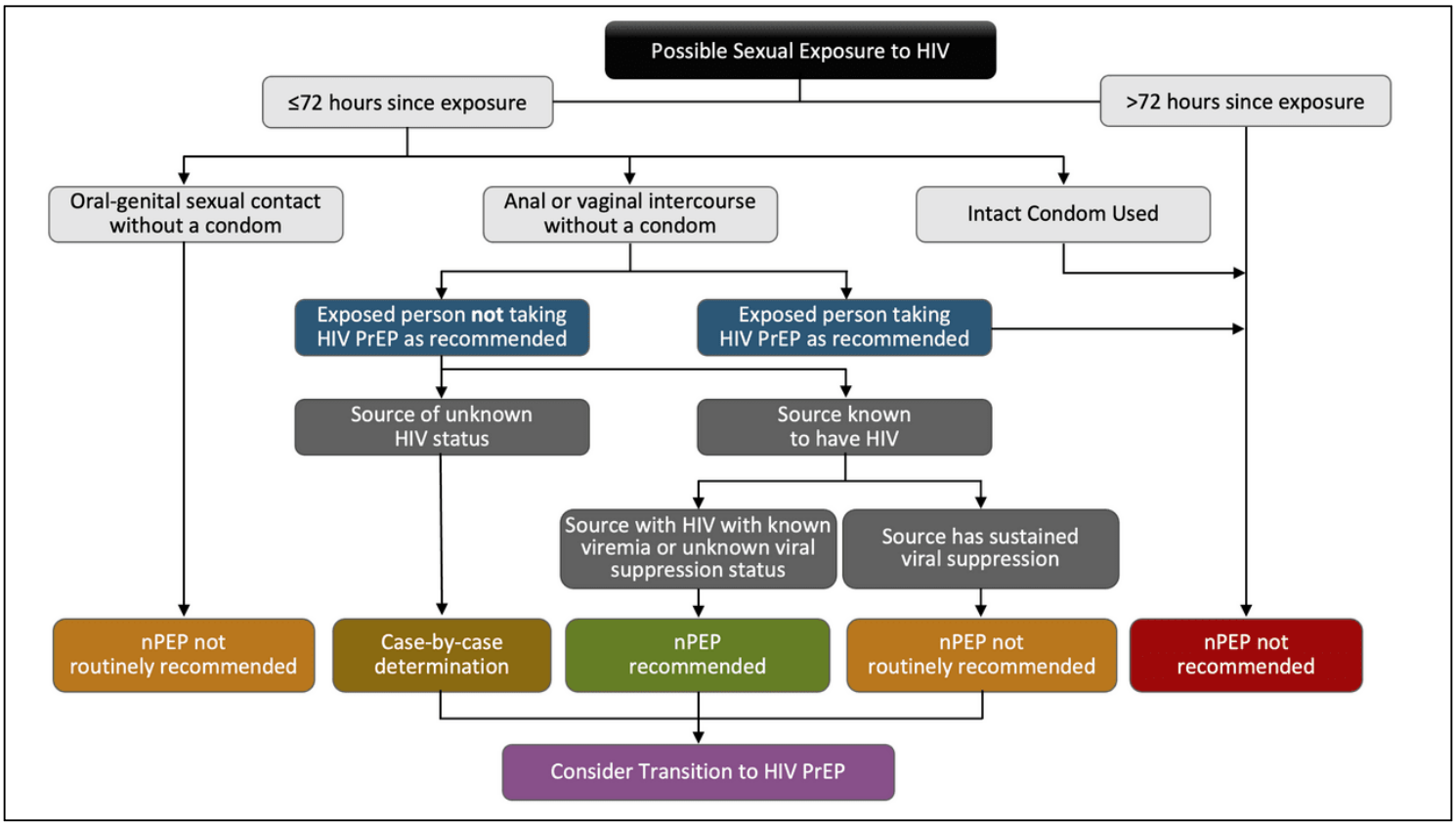

Figure 3 HIV Nonoccupational PEP Use after Possible Injection Drug Use Exposure to HIV: 2025 CDC Guidelines

Abbreviation: nPEP = nonoccupational postexposure prophylaxis

Source: Tanner MR, O'Shea JG, Byrd KM, et al. Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV - CDC Recommendations, United States, 2025. MMWR Recomm Rep. 2025;74:1-56.

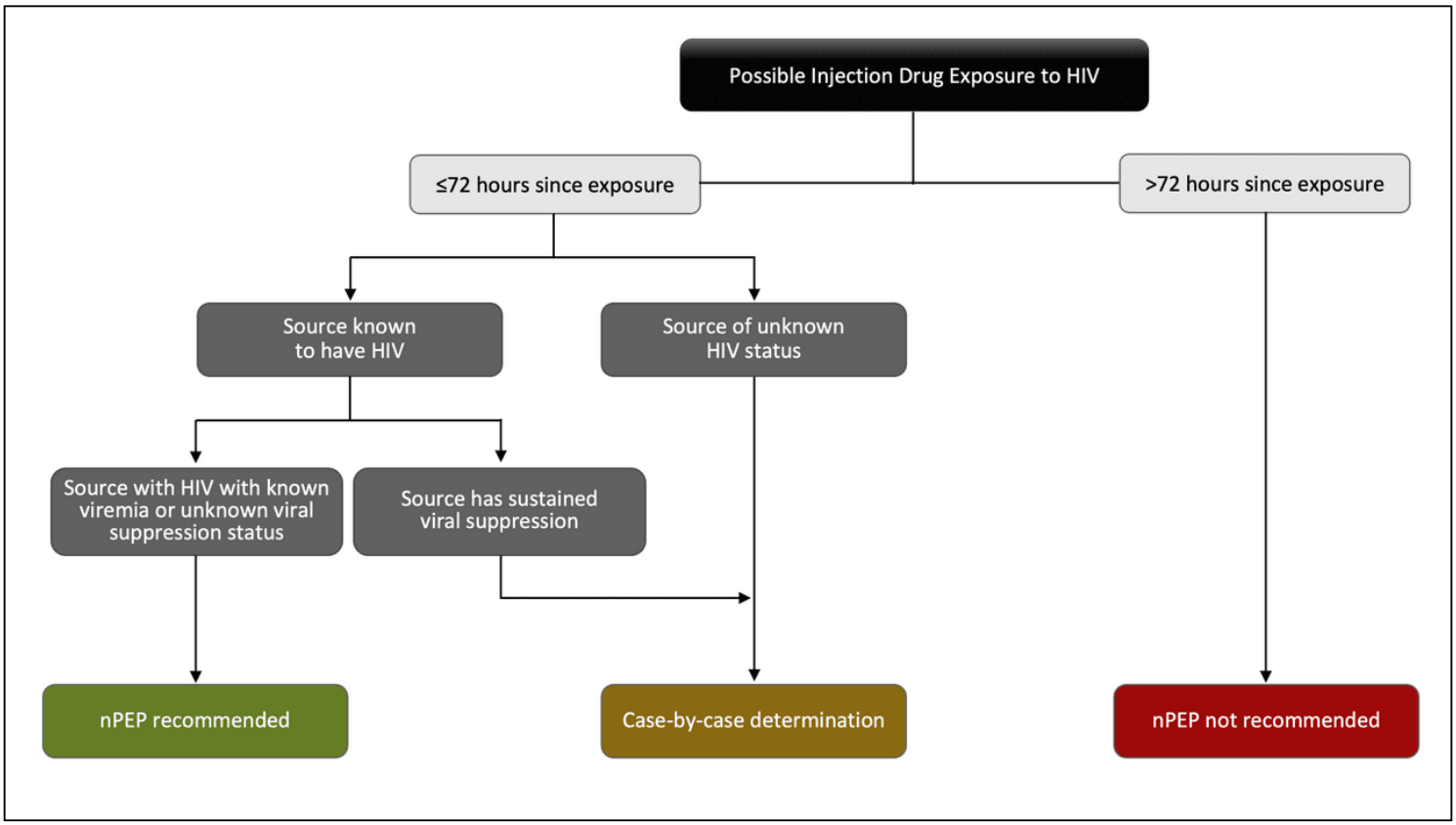

Figure 4 HIV Nonoccupational PEP Use in the Setting of Infective Fluid Splash or Exposure, Needle Injury, or Human Bites: 2025 CDC Guidelines

Abbreviation: nPEP= nonoccupational postexposure prophylaxis

Source: Tanner MR, O'Shea JG, Byrd KM, et al. Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV - CDC Recommendations, United States, 2025. MMWR Recomm Rep. 2025;74:1-56.

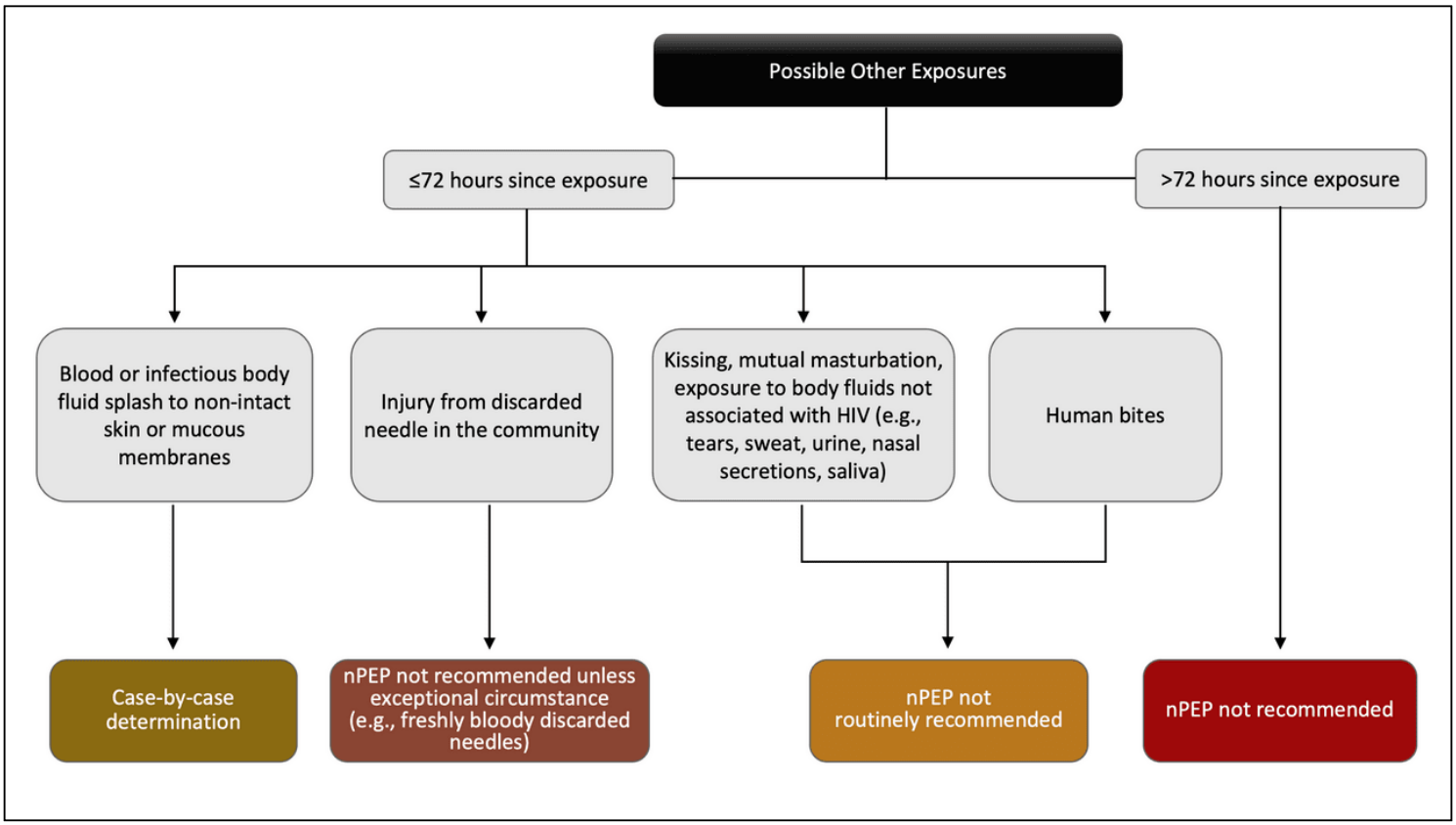

Table 1. Estimated Per-Act Risk for Acquiring HIV from an Infected Source, by Exposure Act*

Exposure Type	Rate for HIV Acquisition per 10,000 Exposures
Parenteral	
Blood transfusion	9,250
Needle sharing during injection drug use	63
Percutaneous (needlestick)	23
Sexual	
Receptive anal intercourse	138
Insertive anal intercourse	11
Receptive penile-vaginal intercourse	8
Insertive penile-vaginal intercourse	4
Receptive oral intercourse	Low
Insertive oral intercourse	Low
Other^	
Biting	Negligible
Spitting	Negligible
Throwing body fluids (including semen or saliva)	Negligible
Sharing sex toys	Negligible

*Factors that may increase the risk of HIV transmission include sexually transmitted infections, acute and late-stage HIV, and high plasma HIV RNA levels. Factors that may decrease the risk include condom use, male circumcision, antiretroviral treatment, and HIV preexposure prophylaxis (PrEP). None of these factors are accounted for in the estimates presented in the table.
^HIV transmission through these exposure routes is technically possible but unlikely and not well documented.

Source:

- Dominguez KL, Smith DK, Thomas V, et al. Updated guidelines for antiretroviral postexposure prophylaxis after sexual, injection drug use, or other nonoccupational exposure to HIV—United States, 2016. Atlanta, GA: US Department of Health and Human Services, CDC; 2016. [CDC]

Table 2. HIV Nonoccupational PEP for Adults and Adolescents Who Are Not Pregnant: 2025 CDC Guidelines*

Adults and Adolescents Aged ≥12 Years (creatinine clearance ≥50 mL/min and not pregnant)	
Preferred	**Integrase Strand Transfer Inhibitor PLUS Two Nucleoside Reverse Transcriptase Inhibitors** • Bictegravir-tenofovir alafenamide-emtricitabine • Dolutegravir PLUS (tenofovir alafenamide OR tenofovir DF) PLUS (emtricitabine OR lamivudine
Alternative	Boosted Protease Inhibitor PLUS Two Nucleoside Reverse Transcriptase Inhibitors • (Darunavir-cobicistat OR Darunavir and ritonavir) PLUS (tenofovir alafenamide OR tenofovir DF PLUS (emtricitabine OR lamivudine)
*The regimens within categories are listed in alphabetical order and not to preference.	

Source:

- Tanner MR, O'Shea JG, Byrd KM, et al. Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV - CDC Recommendations, United States, 2025. MMWR Recomm Rep. 2025;74:1-56. [PubMed Abstract]

Table 3. HIV Nonoccupational PEP in Pregnant Women: 2025 CDC Guidelines*

Pregnant Women (with creatinine clearance ≥50 mL/min)	
Preferred	**Integrase Strand Transfer Inhibitor PLUS Two Nucleoside Reverse Transcriptase Inhibitors** • Bictegravir-tenofovir alafenamide-emtricitabine • Dolutegravir PLUS (tenofovir alafenamide OR tenofovir DF) PLUS (emtricitabine OR lamivudine
Alternative	Boosted Protease Inhibitor PLUS Two Nucleoside Reverse Transcriptase Inhibitors • Darunavir and ritonavir (twice daily) PLUS (tenofovir alafenamide OR tenofovir DF) PLUS (emtricitabine OR lamivudine)
*The regimens within categories are listed in alphabetical order and not to preference.	

Source:

- Tanner MR, O'Shea JG, Byrd KM, et al. Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV - CDC Recommendations, United States, 2025. MMWR Recomm Rep. 2025;74:1-56. [PubMed Abstract]

Table 4. HIV Nonoccupational PEP with Renal Dysfunction or Hepatic Impairment: 2025 CDC Guidelines*

Age ≥12 years with Moderate Renal Dysfunction (CrCl 30-49 mL/min)	
Preferred	**Integrase Strand Transfer Inhibitor PLUS Two Nucleoside Reverse Transcriptase Inhib** • Bictegravir-tenofovir alafenamide-emtricitabine • Dolutegravir PLUS tenofovir alafenamide PLUS (emtricitabine OR lamivudine¶)
Alternative	Integrase Strand Transfer Inhibitor PLUS Two Nucleoside Reverse Transcriptase Inhibitors • Dolutegravir PLUS dose-reduced tenofovir DF**, †† PLUS (emtricitabine OR lamivudine¶) Boosted Protease Inhibitor PLUS Two Nucleoside Reverse Transcriptase Inhibitors • Darunavir-cobicistat-tenofovir alafenamide-emtricitabine • Darunavir and ritonavir) PLUS (tenofovir alafenamide OR dose-reduced tenofovir DF**, ††)
Age ≥12 years with Severe Renal Dysfunction (CrCl <30 mL/min) and on hemodialysis)	
Preferred	**Integrase Strand Transfer Inhibitor PLUS Two Nucleoside Reverse Transcriptase Inhib** • Bictegravir-tenofovir alafenamide-emtricitabine • Dolutegravir PLUS tenofovir alafenamide PLUS (emtricitabine OR dose-reduced lamivudir
Alternative	Integrase Strand Transfer Inhibitor PLUS Two Nucleoside Reverse Transcriptase Inhibitors • Dolutegravir PLUS dose-reduced tenofovir DF** PLUS (emtricitabine OR dose-reduced lam Boosted Protease Inhibitor PLUS Two Nucleoside Reverse Transcriptase Inhibitors • Darunavir-cobicistat-tenofovir alafenamide-emtricitabine • Darunavir and ritonavir PLUS (tenofovir alafenamide OR dose-reduced tenofovir DF**, ††) F
Age ≥12 years with Severe Renal Dysfunction (CrCl <30 mL/min, not on hemodialysis)	
Consult a local HIV specialist or consult the NCCC PEPline at 844-275-6222	
Age ≥12 years with Hepatic Impairment (Child-Pugh class A or B)	
Preferred	**Integrase Strand Transfer Inhibitor PLUS Two Nucleoside Reverse Transcriptase Inhib** • Bictegravir-tenofovir alafenamide-emtricitabine • Dolutegravir PLUS (tenofovir alafenamide OR tenofovir DF) PLUS (emtricitabine OR lamiv
Alternative	Boosted Protease Inhibitor PLUS Two Nucleoside Reverse Transcriptase Inhibitors • (Darunavir and cobicistat OR darunavir and ritonavir) PLUS (tenofovir alafenamide OR te
Aged ≥12 years with Hepatic Impairment (Child-Pugh class C)	
Consult a local HIV specialist or consult the NCCC	

PEPline at 844-275-6222	
Abbreviations: CrCl = creatinine clearance *Regimens within categories are listed in alphabetical order and not to preference. ¶The prescribing information for lamivudine recommends dosage adjustment from 300 mg once daily to 150 mg once daily for patients with CrCl 30–49 mL/min. However, the prescribing information for multiple fixed-dose combination that contain lamivudine recommends no dose adjustment for CrCl 30–49 mL/min. Therefore, no dose adjustment is needed for lamivudine when administered as a standalone tablet or part of a fixed-	

dose combination tablet. **Dose-reduced tenofovir DF = 300 mg every 48 hours ††See manufacturer's package insert for dosing instructions for individual agents or consult the antiretroviral dosing recommendations in adults with renal or hepatic insufficiency	

Source:

- Tanner MR, O'Shea JG, Byrd KM, et al. Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV - CDC Recommendations, United States, 2025. MMWR Recomm Rep. 2025;74:1-56. [PubMed Abstract]

Table 5. Laboratory Monitoring with Nonoccupational Exposure to HIV: 2025 CDC Guidelines

Test	Source	Person Exposed to HIV		
	Baseline	Baseline	12 weeks after exposure	6 months after exposure
		All persons evaluated for HIV Nonoccupational PEP		
Rapid (point-of-care) or laboratory-based HIV Ag/Ab test)[†]	√	√	√	—
HIV diagnostic NAT[¶]	√[**]	√[**]	√	—
HBV serology: HBsAg, HBsAb, and HBcAb	√	√[††]	—	If HBV nonimmune at baseline
HCV antibody testing	—	√[§§]	—	If follow-up testing recommended[¶¶]
HCV RNA NAT	√[***]	—	—	—
Syphilis serology[§§§]	√	√	√[§§§]	—
Gonorrhea NAAT[****]	√	√	—	—
Chlamydia NAAT[****]	√	√	—	—
Pregnancy test[††††]	—	√	—	—
		All persons prescribed HIV Nonoccupational PEP		
Serum creatinine		√	—	—

Test	Source	Person Exposed to HIV		
	Baseline	Baseline	12 weeks after exposure	6 months after exposure
		All persons evaluated for HIV Nonoccupational PEP		
Alanine aminotransferase and aspartate aminotransferase		√	—	—

Abbreviations: Ag/Ab = antigen/antibody combination test; HBcAb = hepatitis B core antibody; HBsAb = hepatitis B antibody; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCV = hepatitis C virus; NAT = nucleic acid nucleic acid amplification test; PEP = postexposure prophylaxis.

Note: Any person diagnosed with an infection or condition through testing should be informed and treated or referre treatment as needed.

[†]If a rapid (point-of-care) HIV Ag/Ab test is used, a laboratory-based HIV Ag/Ab test obtained at the same time will in diagnostic sensitivity. PEP should not be delayed awaiting laboratory results. If the preferred HIV diagnostic test is n accessible, the most sensitive available test should be used.

[§]HIV testing 4–6 weeks post-nonoccupational PEP initiation can be deferred for persons who started nonoccupationa hours of exposure, completed the full PEP course, and are not starting PrEP at this time.

[¶]NATs that detect HIV RNA include qualitative tests for diagnosis (e.g., HIV-1 RNA assay) and quantitative tests for c monitoring (e.g., viral load). Diagnostic HIV NATs are recommended because they are more likely than viral load tes very low levels of HIV. If the preferred HIV diagnostic test is not accessible, the most sensitive available test should inability to access HIV NAT should not prevent provision of HIV nonoccupational PEP to persons with indications.

**HIV NAT recommended at baseline assessment for persons with injectable ARV exposure during the past 6 month

[††]HBV PEP recommendations vary by the exposed person's HBV immune status, and by the source's HBV status (wh information available).

[§§]Reflex to HCV RNA NAT if HCV antibody test is positive. Add HCV RNA NAT to original order if signs and symptoms infection are present (e.g., hepatic enzyme elevation).

[¶¶]If follow-up testing is recommended based on the source's status (e.g., HCV RNA positive or HCV antibody test is p unavailable HCV RNA, or if the HCV infection status is unknown), and HCV RNA NAT is negative 3–6 weeks postexpo test for HCV antibodies 4–6 months postexposure is recommended

***HCV RNA NAT is preferred for testing of the source, but if not accessible, HCV antibody testing with reflex HCV RI positive is an alternative strategy

[†††]If follow-up testing is recommended based on the source's status (e.g., HCV RNA positive or positive HCV antibody unavailable HCV RNA, or if the HCV infection status is unknown), HCV RNA NAT is recommended for the exposed pe weeks postexposure.

[§§§]STI testing decisions should be made on an individual basis.

[¶¶¶]If initial syphilis testing negative and infection in the source cannot be ruled out, follow-up testing may be perforr weeks and 3 months postexposure.

****NAATs are recommended for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* at exposure sites (e.g., pharynx vagina) at initial visit and can be repeated 1–2 weeks postexposure if no presumptive treatment was provided and i results were negative. Repeat testing can also be done if the person reports symptoms concerning for STIs. Certain would also perform a NAAT for *Trichomonas vaginalis* from a urine or vaginal specimen for persons with vaginas.

[††††]For all women of child-bearing potential who are not known to be pregnant.

Source:

- Tanner MR, O'Shea JG, Byrd KM, et al. Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV - CDC Recommendations, United States, 2025. MMWR Recomm Rep. 2025;74:1-56. [PubMed Abstract]

Table 7. HBV Postexposure Prophylaxis Following Nonoccupational Exposure to HBV: CDC Recommendations*

HBV Status of Person Exposed	HBsAg Status of Source		
	HBsAg Positive	HBsAg Status Unknown	HBsAg Negative
Unvaccinated	HBIG x 1, and HBV vaccine series (first dose now)	HBV vaccine series (first dose now)	HBV vaccine series (first dose now)
Partially vaccinated	HBIG x 1, and complete HBV vaccine series	Complete HBV vaccine series (give next dose in series now)	Complete HBV vaccine series (give next dose in series now)
Fully vaccinated but response to vaccine unknown	HBV vaccine booster dose x 1 (give dose now)	HBV vaccine booster dose x 1 (give dose now)	No treatment
Fully vaccinated with documented response to vaccine†	No treatment	No treatment	No treatment
Vaccine nonresponder^	HBIG x 2 (separated by 1 month)	HBIG x 2 (separated by 1 month)	No treatment

Abbreviations: HBV = hepatitis B virus; HBsAg = hepatitis B surface antigen; HBIG = hepatitis B immune globulin
*Exposures include percutaneous (e.g., bite or needlestick) or mucosal exposure to blood or body fluids, sex or needle-sharing contact, or victim of sexual assault/abuse.
†HBV vaccine response is defined as a person with anti-HBs ≥10 mIU/mL after completing a HBV vaccine series.
^HBV vaccine nonresponder is defined as a person with anti-HBs <10 mIU/mL after ≥6 doses of HBV vaccine.

Source:

- Schillie S, Vellozzi C, Reingold A, et al. Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep. 2018;67:1-31. [PubMed Abstract]
- Tanner MR, O'Shea JG, Byrd KM, et al. Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV - CDC Recommendations, United States, 2025. MMWR Recomm Rep. 2025;74:1-56. [PubMed Abstract]