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Nonoccupational Postexposure Prophylaxis

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

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Introduction and Background

In the mid-1990s, postexposure prophylaxis (PEP) was recognized as a safe and effective intervention to prevent the acquisition of HIV for health care workers exposed to HIV-contaminated blood or body fluids. In 2005, the Centers for Disease Control and Prevention (CDC) and the Department of Health and Human Services issued nonoccupational HIV PEP guidelines, and these guidelines were updated in 2016 as the Nonoccupational PEP Guidelines.[1,2] These nonoccupational HIV PEP guidelines address the use of antiretroviral therapy postexposure prophylaxis following exposure to HIV that occurred through sexual contact and/or through injection drug use.[1] Clinicians evaluating individuals for nonoccupational HIV PEP should provide general HIV prevention counseling and recognize these individuals may be excellent candidates to transition to HIV PrEP at the time they complete the 28-day regimen for nonoccupational PEP.[2,3]

Rationale for Providing Nonoccupational HIV PEP

Due to ethical and logistical reasons, it is highly unlikely that a prospective, randomized, placebo-controlled trial to evaluate nonoccupational HIV PEP in humans will ever take place. In addition, nonoccupational HIV 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 nonoccupational HIV PEP for a single exposure event.[4] Thus, the rationale for providing nonoccupational HIV PEP is based on extrapolation from the use of HIV PEP in other settings, animal studies, retrospective reviews, observational nonoccupational PEP reports, and expert opinion.

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 occupational HIV PEP with oral zidovudine, taken within 4 hours by most of the participants, reduced the risk of HIV seroconversion by 81%.[5] 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.[6,7,8,9]

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).[10] 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 of the female macaques exposed to HIV-2 when initiated within 12 to 36 hours.[11] A systematic review and meta-analysis of PEP using pooled data of 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.[12]

Nonoccupational HIV PEP Data in Humans

Although human studies on nonoccupational HIV PEP are observational in nature and limited in sample size, available data involving men who have sex with men (MSM) suggest nonoccupational HIV PEP reduces HIV transmission.[13,14] In addition, a feasibility study in San Francisco demonstrated medical providers could appropriately identify and provide recommended nonoccupational HIV PEP to persons exposed to HIV via sexual contact or through injecting drugs.[15] In a separate San Francisco study, investigators reported HIV seroconversion among 7 of 702 (1%) persons who received nonoccupational HIV PEP, but only 3 of the seroconversions likely represented true “failure” of nonoccupational HIV PEP.[4] Available data from other reports of HIV transmission in persons who received nonoccupational HIV PEP suggest that most HIV transmissions resulted from poor medication adherence or from exposures to HIV that occurred after completing the HIV PEP regimen.[16,17,18,19] In addition, one failure occurred in a 40-year-old woman in France who started nonoccupational HIV PEP more than 72 hours after a sexual exposure.[20] Multiple studies involving sexual assault survivors have demonstrated very low HIV transmission rates, despite relatively low rates of adherence to nonoccupational HIV PEP medications.[21,22,23,24,25]

Rationale for Nonoccupational PEP in Persons Who Inject Drugs

New HIV infection among persons who inject drugs can potentially result from injection drug use or from sexual activity.[26] Certain circumstances could arise whereby a person who injects drugs and normally uses safe injection practices has an HIV risk exposure. The use of nonoccupational HIV PEP after an at-risk injection drug use exposure may have different efficacy compared with use after a sexual exposure, since the route

and HIV inoculum differ in these two situations.[27] It is important that programs, including syringe services programs, that work with people who inject drugs are aware of local resources where their clients can receive nonoccupational HIV PEP if needed. In addition, these programs may consider directly providing services for nonoccupational HIV PEP if they have the capacity and expertise.

Evaluation for Nonoccupational HIV PEP

Multiple factors influence the risk of HIV transmission in nonoccupational exposures to HIV. The initial evaluation of persons seeking care after potential nonoccupational exposures to HIV requires gathering information to determine whether nonoccupational HIV PEP is indicated (Figure 2).[2] The initial evaluation, as recommended in the Nonoccupational PEP Guidelines, should address the following: (1) the baseline HIV status of the person potentially exposed to HIV, (2) information related to the source person's HIV status, (3) details regarding the type of exposure involved, (4) timing and frequency of the exposure(s), and (5) any available information related to antiretroviral therapy taken by the source patient if they are known to have HIV.[2] In addition, the initial history intake should include the following.

- **Information on HIV Status of Person Potentially Exposed to HIV:** The first step in evaluating the exposure is to determine the baseline HIV status of the person seeking medical care. Persons with established HIV should receive long-term continuous antiretroviral therapy, not a 28-day course of nonoccupational HIV PEP. In the setting of a nonoccupational exposure to HIV, the HIV status of the exposed person should be determined as soon as possible, although HIV testing should not necessarily delay nonoccupational HIV PEP initiation.
- **Information Related to Source Person's HIV Status**: As part of the initial exposure evaluation, it is also important to determine whether the source person has HIV (or, if the status of the source is unknown, assess their risk factors for HIV, if possible). Often, the HIV status of the source person is not known (and not attainable). The Nonoccupational PEP Guidelines recommend using nonoccupational HIV PEP when the source person is known to have HIV; if the HIV status of the source person is not known, the recommendation is to evaluate on a case-by-case basis, ideally in consultation with an expert.[2] In this situation, if the exposure type warrants HIV PEP, but the HIV status of the source person is not attainable, most experts would recommend initiating and completing a 28-day course of nonoccupational HIV PEP. When asking about information related to the source, it is important to ask whether other recent exposures occurred with this source person (and/or other individuals), as recent additional HIV-related exposures could potentially confound management decisions. Nevertheless, repeated exposures do not negate the need to assess whether the most recent exposure warrants nonoccupational HIV PEP.
- **Determination of Risk Related to Exposure:** The other key element of the initial nonoccupational HIV PEP evaluation is to determine whether the exposure confers actual risk for HIV transmission.[2,27] Nonoccupational HIV PEP should only be used in the setting of "substantial risk for HIV acquisition," defined as contact involving an area of the body known to be associated with HIV acquisition (vagina, rectum, eye, mouth, or other mucous membranes, nonintact 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 conveying the highest sexual risk.[2,27,28,29,30] The following table summarizes the risk of HIV acquisition based on the type of exposure.[2] Table 1.

Estimated Per-Act Probability of 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

Exposure Type	Rate for HIV Acquisition per 10,000 Exposures
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 diseases, acute and late-stage HIV infection, and high viral load. Factors that may decrease the risk include condom use, male circumcision, antiretroviral treatment, and 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:

- Centers for Disease Control and Prevention: U.S. Department of Health and Human Services. Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, and Other Nonoccupational Exposure to HIV—United States, 2016. [CDC]

- **Risk Estimes Specific to Sexual Exposures**: Mucosal disruption in either the source person or the exposed person (as might occur with traumatic intercourse including sexual assault, or in the presence of ulcerative genital disease) increases the risk of sexual HIV transmission; correct condom use markedly lowers the risk of transmission.[27] the following table summarizes risk of HIV acquisition based on a number of factors related to the sexual exposure[27] Table 2.

Relative Risks of Factors that Alter Per-Act HIV Transmission Risk for Sexual Exposures*

Cofactor	Relative Risk
Factors that Increase Transmission Probability	
High plasma HIV RNA level (log_{10} copies/mL)	2.89
Genital ulcer disease	2.65
Acute versus asymptomatic stage of disease	7.25
Late versus asy	5.81

Cofactor	Relative Risk
mptomatic stage of disease	
Factors that Decrease Transmission Probability	
Use of antiretroviral medications by partner with HIV	
Early versus delayed treatment	0.04
Received treatment versus no treatment	0.08
Preexposure Prophylaxis of partner without HIV	
Among heterosexual couples	0.29
Among men who have sex with men	0.56
Among injection drug users	0.52
Condom use	0.20
Male Circumcision (heterosexual partners)	
Partner without HIV is male	0.50
Partner without HIV is female	0.80
Male circumcision (men who have sex with men)	
Insertive	0.27

Cofactor	Relative Risk
partner is partner without HIV	
Receptive partner is partner without HIV	1.20
*For a detailed description of data and factors used to generate estimates, see original table in article referenced below.	

Source:

- Patel P, Borkowf CB, Brooks JT, Lasry A, Lansky A, Mermin J. Estimating per-act HIV transmission risk: a systematic review. AIDS. 2014;28:1509-19. [PubMed Abstract]

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- **Timing of Risk Exposure:** It is important to determine the timing of exposure in persons seeking nonoccupational HIV PEP. Available data suggest that HIV PEP may not be effective if initiated beyond 72 hours after the exposure. Furthermore, HIV PEP is not the optimal HIV prevention strategy for individuals who have frequent, recurrent HIV exposures; these individuals should ideally receive HIV PrEP in conjunction with risk reduction counseling.[2]
- **Source Person Antiretroviral Treatment Information**: If a source person is known to have HIV and takes antiretroviral medications, the medical provider should determine what medication the source takes, the most recent HIV RNA levels, and if the source person has developed resistance to any antiretroviral medications. The risk of HIV transmission is higher if the source person has advanced HIV disease or high HIV RNA levels.[31] After the release of the Nonoccupational PEP Guidelines, multiple studies were subsequently published that consistently showed persons with HIV who take antiretroviral therapy maintain plasma HIV RNA levels less than 200 copies/mL do not transmit HIV sexually to their partners—this concept is referred to as Undetectable = Untransmittable (U=U).[32,33] Similar studies have not been published related to HIV transmission through injection drug use.[33]

Indications for Initiating Nonoccupational HIV PEP

Based on the Nonoccupational PEP Guidelines, if the following criteria are met, a 28-day course of antiretroviral medications for nonoccupational HIV PEP is recommended:[2]

- 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.

Note: Administering nonoccupational PEP with the goal of transitioning to HIV PrEP can be considered beyond the 72-hour window in cases where multiple recent exposures to HIV have occurred more than 72 hours prior, but the most recent exposure occurred within the 72-hour window.

Challenges When Evaluating Whether to Initiate Nonoccupational HIV PEP

A number of challenges may arise during the initial evaluation of persons for nonoccupational HIV PEP.

- With some exposures, the person seeking help may not actually know the HIV status (or any other information) of the source person.
- Individuals often present for care more than 72 hours after the exposure.
- The exposure that brings the person in for medical attention may not consist of an isolated event, but instead may be among multiple recent potential HIV exposure events; if this is the case, it is still necessary to assess the need for nonoccupational HIV PEP for any significant exposures occurring within the last 72 hours.
- Certain sexual exposure events may involve concomitant exposures to other sexually transmitted pathogens or to hepatitis viruses (especially with injection drug use exposures).
- Some nonoccupational HIV PEP cases involve persons recently sexually assaulted, which can involve additional medicolegal concerns and complications.
- Insurance programs may not cover the cost of the 28-day course of nonoccupational HIV PEP, or they may only partially cover the cost. In addition, some facilities or pharmacies may not have recommended HIV PEP medications on hand, and obtaining these medications may take several days.

Recommendation if Source Person Has an Undetectable HIV RNA Level

Multiple studies have shown that persons with HIV who consistently maintain undetectable serum HIV RNA levels do not sexually transmit HIV, even with condomless sex.[34,35,36] These studies led to the concept of undetectable equals untransmittable (U=U).[32] The widespread support of the U=U concept occurred after the publication of the Nonoccupational PEP Guidelines. At the present time, there are no clear recommendations regarding the use of nonoccupational HIV PEP following a sexual exposure with a source person with HIV who has consistently suppressed HIV RNA levels, but most experts would base their recommendation on the reliability of the information and documentation of persistently suppressed HIV RNA levels in the source person with HIV.

Recommendation if Person Exposed to HIV is Taking HIV PrEP

Persons who are taking HIV PrEP (tenofovir DF-emtricitabine, tenofovir alafenamide-emtricitabine, or long-acting injectable cabotegravir) as prescribed do not need nonoccupational HIV PEP following an exposure to HIV.[37] If, however, an individual is receiving HIV PrEP, but is not consistently taking HIV PrEP as prescribed, nonoccupational HIV PEP might be indicated following an HIV exposure.[37] In this situation of sporadic HIV PrEP use, the decision to initiate nonoccupational HIV PEP should be made on a case-by-case basis, and

ideally with the help of expert clinical consultation.

Recommended Therapy for Nonoccupational HIV PEP

Preferred and Alternative Antiretroviral Regimens

The Nonoccupational PEP Guidelines recommend using a three-drug antiretroviral combination regimen given for 28 days in all cases when nonoccupational PEP is indicated.[2]

- **Preferred Nonoccupational HIV PEP Regimen**: The preferred nonoccupational HIV PEP regimen for adults (and adolescents age 13 years and older) who have a baseline creatinine clearance of at least 60 mL/min consists of the fixed-dose combination of tenofovir DF-emtricitabine plus either raltegravir or dolutegravir with the regimen given for 28 days.[2]

Table 3. 2016 CDC and HHS Guidelines for Nonoccupational Exposure to HIV

Preferred and Alternative 28-Day Regimens for Nonoccupational HIV PEP[a,b]

Adults and adolescents aged ≥13 years with normal renal function (creatinine clearance ≥60 mL/min), including pregnant women
Preferred Regimens: • Raltegravir (400 mg twice daily) plus tenofovir DF-emtricitabine (300-200 mg once daily) • Dolutegravir (50 mg once daily) plus tenofovir DF-emtricitabine (300-200 mg once daily) ***Alternative Regimen:*** • Darunavir (800 mg once daily) plus ritonavir (100 mg once daily) plus tenofovir DF-emtricitabine (300-200 mg once daily)
Adults and adolescents aged ≥13 years with renal dysfunction (creatinine clearance ≤59 mL/min)[+]
Preferred Regimens: • Raltegravir (400 mg twice daily) plus zidovudine (dose adjusted) plus lamivudine (dose adjusted) • Dolutegravir (50 mg once daily) plus zidovudine (dose adjusted) plus lamivudine (dose adjusted)

Alternative Regimen: • Darunavir (800 mg once daily) plus ritonavir (100 mg once daily) plus zidovudine (dose adjusted) plus lamivudine (dose adjusted)		
[a]These recommendations do not reflect current Food and Drug Administration-approved labeling for antiretroviral medications listed in this table. [b]Ritonavir is used in clinical practice as a pharmacokinetic enhancer to increase the trough concentration and prolong the half-life of darunavir, lopinavir, and other protease inhibitors. Ritonavir is not counted as a drug directly active against HIV in the above "3-drug" regimens. [+]The dose adjustments for zidovudine and lamivudine are made based on degree of renal function		

Source:

- Centers for Disease Control and Prevention: U.S. Department of Health and Human Services. Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, and Other Nonoccupational Exposure to HIV—United States, 2016. [CDC]

- **Alternative Nonoccupational HIV PEP Regimen**: The recommended alternative regimen is darunavir boosted with ritonavir plus tenofovir DF-emtricitabine, with the regimen given for 28 days.[2] For women of childbearing age, note that darunavir boosted with ritonavir can potentially cause significant drug interactions with oral contraceptives, resulting in reduced levels of ethinyl estradiol and norethindrone.[38]
- **Nonoccupational HIV PEP Regimen for Persons with Renal Insufficiency**: For adults and adolescents who have a baseline creatinine clearance less than 60 mL/min, the preferred and alternative regimens listed above should be modified by replacing tenofovir DF-emtricitabine with zidovudine and lamivudine; in this situation, the fixed-dose combination zidovudine-lamivudine should not be given, so that doses of zidovudine and lamivudine can be adjusted individually based on renal impairment.[39]

Medications with Insufficient Data

There are several antiretroviral medications that are commonly used in the treatment of persons with HIV but have not been adequately studied for use in nonoccupational HIV PEP.

- **Tenofovir alafenamide**: Many commonly used antiretroviral regimens used to treat persons with established HIV have tenofovir alafenamide as a component of the regimen. In addition, tenofovir alafenamide-emtricitabine is also used for HIV PrEP. For nonoccupational HIV PEP, however, the use of any regimen that contains tenofovir alafenamide is not recommended in the Nonoccupational PEP

Guidelines, primarily due to lack of data with the use of tenofovir alafenamide-containing regimens for nonoccupational HIV PEP or occupational HIV PEP. Further, the advantages of using tenofovir alafenamide over tenofovir DF-emtricitabine when used for long-term treatment of persons with HIV (lower rates of nephrotoxicity and osteopenia) are not generally relevant when only prescribing a short 28-day regimen for nonoccupational HIV PEP. The major potential use of tenofovir alafenamide would occur in a person with known renal insufficiency.

- **Bictegravir-tenofovir alafenamide-emtricitabine**: The antiretroviral regimen bictegravir-tenofovir alafenamide-emtricitabine is now widely used to treat adults with HIV. This regimen was not FDA-approved at the time the 2016 Nonoccupational PEP Guidelines were generated; therefore, it is not recommended in the guidelines. At this time, there are limited data on the use of bictegravir-tenofovir alafenamide-emtricitabine for nonoccupational HIV PEP.[40,41]

Medications Not Recommended

There are several antiretroviral medications that are used as a component of treatment regimens for persons with HIV but are not recommended for use in nonoccupational HIV PEP. Special considerations for medications to avoid in pregnancy is discussed below in the section Nonoccupational HIV PEP in Special Populations.

- **Abacavir**: The nucleoside reverse transcriptase inhibitor (NRTI) abacavir, which is commonly used to treat HIV infection, is not recommended for nonoccupational HIV PEP because of the risk of developing a potentially fatal abacavir hypersensitivity reaction. Although HLA-B*5701 testing can be performed and can predict those at risk of developing the hypersensitivity reaction, it may take several days for results to return; thus, abacavir should not be used as part of the initial nonoccupational HIV PEP regimen. It is possible, however, that a switch to abacavir while taking a nonoccupational HIV PEP regimen could be indicated, assuming HLA-B*-5701 testing is negative and there is a strong reason to consider a medication switch, such as renal insufficiency or intolerance to tenofovir DF.
- **Tenofovir alafenamide**: Many of the antiretroviral regimens commonly used to treat persons with established HIV have tenofovir alafenamide as a component of the regimen. In addition, tenofovir alafenamide-emtricitabine is also used for HIV PrEP. For nonoccupational HIV PEP, however, the use of any regimen that contains tenofovir alafenamide is not recommended in the Nonoccupational PEP Guidelines, primarily due to lack of data with the use of tenofovir alafenamide-containing regimens for nonoccupational HIV PEP or occupational HIV PEP. Further, the advantages of using tenofovir alafenamide over tenofovir DF-emtricitabine when used for long-term treatment of persons with HIV (lower rates of nephrotoxicity and osteopenia) are not generally relevant when only prescribing a short 28-day regimen for nonoccupational HIV PEP. The most likely potential use of tenofovir alafenamide would occur in a person with known renal insufficiency.
- **Nevirapine**: The non-nucleoside reverse transcriptase (NNRTI) nevirapine is now rarely used to treat HIV. The use of nevirapine for nonoccupational HIV PEP is strongly contraindicated since the use of nevirapine in occupational HIV PEP has been associated with life-threatening hepatotoxicity.[42]

Nonoccupational HIV PEP Medication Studies with Newer Medications

The following summarizes major studies involving more contemporary three-drug antiretroviral regimens for nonoccupational HIV PEP.

- **Bictegravir-tenofovir alafenamide-emtricitabine:** In this 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.[41] For the participants, this regimen was well tolerated, safe, and highly acceptable; in this study, there were no HIV seroconversions related to the exposure.[41]
- **Dolutegravir plus Tenofovir DF-Emtricitabine (Sydney Study)**: In an open-label, single-arm study, investigators from Sydney, Australia, enrolled 100 men who have sex with men (MSM) to receive dolutegravir plus tenofovir DF-emtricitabine for 28 days for nonoccupational HIV PEP. The regimen was well tolerated, adherence levels were very high (98%), completion rates were high

(90%), and no HIV seroconversions occurred; elevations in alanine aminotransferase occurred in 22% of the participants, but none developed clinical hepatitis.[43]

- **Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine (Fenway Health Study)**: In an open-label, single-arm study, investigators from Fenway Health Clinic in Boston, Massachusetts, enrolled adults (98% men) to receive the fixed-dose single tablet elvitegravir-cobicistat-tenofovir DF-emtricitabine for 28 days for nonoccupational HIV PEP.[44] The regimen was completed as prescribed by 71% of the participants and was moderately well tolerated.[44] At the day 90 follow-up visit, none had HIV seroconversion.[44]
- **Raltegravir plus Tenofovir DF-Emtricitabine (Fenway Health Study)**: The Fenway Health Clinic also reported their experience with a 28-day course of the three-drug regimen raltegravir plus tenofovir DF-emtricitabine as nonoccupational HIV PEP in 100 adult men, most of whom were men who have sex with men (MSM).[45] This regimen was completed as prescribed by 57% of the participants and was relatively well tolerated, with nausea/vomiting (27%) and diarrhea (21%) the most commonly reported side effects.[45] Among the 85 men who were able to undergo evaluation at 3 months, none had acquired HIV.[45]
- **Raltegravir plus Tenofovir DF-Emtricitabine (Sydney Study)**: Investigators from Sydney, Australia performed an open-label, prospective study that enrolled 86 MSM to receive a 28-day course of raltegravir plus tenofovir DF-emtricitabine for nonoccupational HIV PEP.[46] The regimen was well tolerated, adherence levels were high (89%), completion rates were very high (92%), and no HIV seroconversions occurred.[46] In this study, investigators also enrolled 34 men to receive the two-drug regimen tenofovir DF-emtricitabine, and no HIV seroconversions occurred in this group as well.[46]
- **Rilpivirine-Tenofovir DF-Emtricitabine (Sydney Study)**: Investigators from Sydney, Australia, performed an open-label, single-arm, prospective study that enrolled 100 adult MSM to receive a 28-day course of the fixed-dose tablet rilpivirine-tenofovir DF-emtricitabine for nonoccupational HIV PEP.[47] The regimen was well tolerated, adherence rates were very high (98%), completion rates were very high (92%), and no HIV seroconversions had occurred among the 70 men who had completed the 12-week follow-up visit.[47] The most commonly reported adverse effects were fatigue (34%) and nausea (23%).

Duration of Therapy

The Nonoccupational PEP Guidelines recommend that individuals who initiate antiretroviral therapy for nonoccupational HIV PEP should complete a 28-day course.[2] Studies involving macaques have shown that HIV PEP given for 28 days is more effective than 10 days, which is more effective than 3 days.[10] In addition, available data and experience with occupational postexposure prophylaxis support the use of a 28-day regimen.[5,48] From a conceptual standpoint, it is believed that HIV PEP, in some instances, halts a very early and limited HIV infection, rather than truly preventing any cell in the body from becoming infected with HIV. Thus, early initiation of nonoccupational HIV PEP, when combined with a 28-day duration of therapy, is believed adequate to minimize tissue involvement and contain any local HIV replication while allowing sufficient time for localized immune responses to clear out the limited HIV infection.

Consideration of HIV Resistance in Source Person

If medical information is available regarding a source person known to have HIV, the choice of a nonoccupational HIV PEP regimen should take into account the source person’s antiretroviral medication history, most recent HIV RNA levels, and prior resistance testing results. In the event the source person has possible or known antiretroviral drug resistance, expert consultation should be obtained to determine the optimal nonoccupational HIV PEP regimen for the exposed individual.

Expert Consultation for Nonoccupational HIV PEP

Indications for Obtaining Expert Consultation

The Nonoccupational PEP Guidelines provide recommendations for scenarios that warrant expert consultation for nonoccupational PEP related to nonoccupational HIV exposure events.[2] 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 nonoccupational PEP has renal dysfunction, *or*
- The source person has known or suspected antiretroviral resistance.

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 888-448-4911; this service is for health care professionals.

Laboratory Testing for Source and Exposed Persons

Initial HIV testing of the individual exposed to HIV should consist of an HIV-1/2 antigen-antibody immunoassay, or HIV antibody testing if HIV antigen-antibody testing is not available.[2] Oral point-of-care HIV tests are not recommended, primarily due to their poor sensitivity in diagnosing acute or very recent HIV infection. Although it is very important to confirm the negative HIV status of the individual presenting for nonoccupational HIV PEP, most experts do not advocate ordering an HIV RNA level (on the exposed person) unless they have signs or symptoms that suggest an acute HIV infection. In addition, persons undergoing evaluation for nonoccupational HIV PEP should be instructed about the signs and symptoms associated with acute HIV and asked to return for evaluation if these occur during or after nonoccupational HIV PEP.[2] The Nonoccupational PEP Guidelines provide recommendations for baseline laboratory studies (for the source and the person exposed to HIV), as well as a schedule of follow-up laboratory tests for monitoring the person exposed to HIV.[2] Table 4.

Nonoccupational HIV PEP: Recommended Laboratory Monitoring of Source and Exposed Persons

Test	Source	Exposed			
	Baseline	Baseline	4-6 Weeks after exposure		3 Months
		For all persons considered for or prescribed			
HIV-1/2 Ag/Ab (or Ab testing if Ag/Ab test unavailable)[a]	√	√	√	√	√[b]
Hepatitis B serology, including: HBsAg anti-HBs anti-HBc	√	√	—	—	√[c]
Hepatitis C antibody test	√	√	—	—	√[d]
		For all persons considered for or prescribed nPEP for sexual expos			
Syphilis serology[e]	√	√			√
Gonorrhea[f]	√	√			√[g]
Chlamydia[f]	√	√			√[g]
Pregnancy[h]	—	√			√
		For persons prescribed: Tenofovir DF-emtricitabine + raltegravir Tenofovir DF-emtricitabine + dolutegravir			
Serum creatinine (for calculating estimated creatinine clearance)[i]		√			√
Alanine aminotransferase, aspartate aminotransferase		√			√
	For all persons with HIV confirmed at any visit				
HIV RNA level	√				√[j]
HIV genotypic drug resistance test	√				√[j]

Abbreviations: Ag/Ab, antigen/antibody combination test; HIV, human immunodeficiency virus; nPEP, nonoccupatior fumarate.
[a] Any positive or indeterminate HIV antibody test should undergo confirmatory testing of HIV status.
[b] Only if hepatitis C infection was acquired during the original exposure; delayed HIV seroconversion has been seen 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 tre
[f] Testing for chlamydia and gonorrhea should be performed using nucleic acid amplification tests. For patients diagr

Test		Source	Exposed		
		Baseline	Baseline	4-6 Weeks after exposure	3 Months
			For all persons considered for or prescribed		

months after treatment is recommended.
- For men reporting insertive vaginal, anal, or oral sex, a urine specimen should be tested for chlamydia and gonorr
- For women reporting receptive vaginal sex, a vaginal (preferred) or endocervical swab or urine specimen should b
- For men and women reporting receptive anal sex, a rectal swab specimen should be tested for chlamydia and gon
- For men and women reporting receptive oral sex, an oropharyngeal swab should be tested for gonorrhea.

[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
[j] At first visit where determined to have HIV infection.

Source:

- Centers for Disease Control and Prevention: U.S. Department of Health and Human Services. Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, and Other Nonoccupational Exposure to HIV—United States, 2016. [CDC]

Baseline Laboratory Evaluation

The baseline laboratory evaluation should include the following tests for the individual exposed to HIV:[2]

- HIV-1/2 antigen-antibody immunoassay (or HIV antibody testing if the HIV-1/2 antigen-antibody immunoassay is not available)
- Serologic testing for hepatitis B virus (HBV) and hepatitis C virus (HCV)
- Testing for sexually transmitted infections, including serologic testing for syphilis and site-specific screening for chlamydia and gonorrhea
- Pregnancy test and emergency contraception, if indicated
- Serum creatinine (for calculating estimated creatinine clearance)
- Hepatic aminotransferase levels

Follow-Up Laboratory Studies

The Nonoccupational PEP Guidelines recommend the following laboratory tests for all persons who seek care for nonoccupational PEP.[2]

- **HIV Testing**: The HIV-1/2 antigen-antibody immunoassay is recommended for follow-up HIV testing, and this should be done at 4 to 6 weeks and 12 weeks after the exposure.[2] If, however, a person is transitioning from nonoccupational HIV PEP to HIV PrEP, then follow-up and testing should occur just before the end of the 28-day course of nonoccupational HIV PEP so that no gap in prevention occurs. In addition, if the exposed person acquires HCV as a result of the original exposure, an additional HIV test should be conducted 6 months after the exposure, since acquisition of HCV can result in delayed HIV seroconversion.[2]
- **HCV Testing**: Follow-up HCV antibody testing for exposed persons who are susceptible to HCV infection is recommended at baseline and at 6 months, but not at 4 to 6 weeks or 3 months.[2]
- **HBV Testing**: For exposed persons not immune to HBV at baseline, providers should ascertain HBV status of the source if possible and administer HBV postexposure prophylaxis as indicated. For exposed persons not immune to HBV at baseline, follow-up testing should be conducted at 6 months and should include hepatitis B surface antigen, hepatitis B surface antibody, and hepatitis B core antibody.[2,49]

- **Pregnancy Testing**: Repeat pregnancy testing should be performed at the follow-up visit (4 to 6 weeks after exposure) if the woman is of reproductive age, is not using effective contraception, and had vaginal exposure to semen.
- **Serum Creatinine**: Repeat serum creatinine should be checked at the 4- to 6-week follow-up visit. Some experts also evaluate the serum creatinine at week 2 of nonoccupational HIV PEP treatment, especially if the person taking nonoccupational HIV PEP has any risk of developing renal complications.
- **Hepatic Aminotransferase Levels**: Repeat hepatic aminotransferase levels should be checked at the 4- to 6-week follow-up visit.
- **Testing for Sexually Transmitted Infection**s: Testing for chlamydia and gonorrhea should be performed at the follow-up visit unless presumptive treatment for these sexually transmitted infections was provided at baseline or if indicated based on active genitourinary symptoms at the follow-up visit.

Nonoccupational HIV PEP in Special Populations and Circumstances

The Nonoccupational PEP Guidelines identify additional considerations for certain special populations as outlined below.[2]

Pregnant Women and Women of Childbearing Potential

Both of the preferred regimens—tenofovir DF-emtricitabine plus raltegravir and tenofovir DF-emtricitabine plus dolutegravir—are considered safe to use during pregnancy and by women of childbearing potential.[50]

Breastfeeding

Specific information is not provided in the Nonoccupational PEP Guidelines regarding the use of antiretroviral regimens for nonoccupational HIV PEP in people who are breastfeeding.[2] Expert consultation should be obtained for these cases.

Children and Adolescents

In many pediatric/adolescent nonoccupational HIV PEP cases, expert consultation will be necessary. In the Nonoccupational PEP Guidelines, the preferred regimen for children aged 4 weeks to less than 2 years of age is zidovudine and lamivudine plus either raltegravir or lopinavir-ritonavir, with all medications given orally and dose-adjusted for age and weight. For children aged 2 to 12 years, the preferred regimen is tenofovir DF plus emtricitabine plus raltegravir (dosed according to age and weight).[2] For children 13 years of age and older with normal renal function, the adult and adolescent preferred and alternative nonoccupational HIV PEP regimens can be used.[2] Following the release of the Nonoccupational PEP Guidelines, dolutegravir, which is a preferred medication for adult nonoccupational HIV PEP, was subsequently approved for use in children; at this time, there are no formal recommendations for the use dolutegravir for nonoccupational HIV PEP in children.

Sexual Assault Survivors

Survivors of sexual assault may be less likely to seek timely care for nonoccupational HIV PEP and may require additional support, clinical follow-up, and adherence counseling. Testing and treatment for other sexually transmitted infections, emergency contraception evaluation, and supportive counseling are also highly recommended in cases of sexual assault.

Individuals in Correctional Settings

The Nonoccupational PEP Guidelines recommend that correctional facilities establish HIV prevention programs. Elements should include confidential and voluntary HIV testing, risk reduction services, and nonoccupational HIV PEP protocols. The Federal Bureau of Prisons published a clinical practice guideline based on the Nonoccupational PEP Guidelines and recommends that each facility develop its own protocol, but the CDC recommends that the most updated guidelines be used whenever possible.[2,51]

HIV Postexposure Prophylaxis in Mass-Casualty Incident

In response to concerns about a potential mass-casualty incidents within the United States, the CDC convened a working group to address management of blood-borne pathogen exposure in persons who are injured in bombings and other mass-casualty incidents, as well as for emergency responders in these catastrophic events. This particular situation does not fall neatly under the guidelines for either occupational or nonoccupational PEP. Accordingly, a separate document was published in 2008, which specifically addresses postexposure prophylaxis for HIV, HBV, HCV, and tetanus in the setting of a mass-casualty

incident.[52] Postexposure prophylaxis for HIV is not routinely indicated for persons exposed to blood or tissue in bombings or mass casualty events. In certain situations, however, nonoccupational HIV PEP might be indicated if the risk for HIV exposure was determined to be high, such as with bombing of a research facility that has blood specimens obtained from persons with HIV, or culture vials growing HIV. If PEP is indicated, the same principles of timing, laboratory testing, and antiretroviral medication selection should apply.

Initial Medication Prescription and Follow-up after Evaluation

Initial Medication Prescription and Timely Follow-Up

The Nonoccupational PEP Guidelines recommend that medical providers should consider giving an initial prescription of antiretroviral medications for 3 to 7 days (i.e., a starter pack) or provide a prescription for an entire 28-day course. Ideally, at the initial visit, the facility would supply the starter pack medication or the 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. In addition, prior to leaving the facility, the person evaluated for nonoccupational HIV PEP should have an early follow-up visit scheduled to assess adherence to nonoccupational HIV PEP, monitor for toxicity, and provide any additional counseling or education that might be needed.[2] If the individual receives only a 3- to 7-day supply of antiretroviral medications, coordination of 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 nonoccupational HIV PEP and the first follow-up clinic appointment.[53] Only about half of nonoccupational HIV PEP patients attended their follow-up appointments, and less than a quarter of those initially started on nonoccupational HIV PEP completed the full 28-day regimen.[53] Older age and self-pay status predicted lower rates of follow-up and poor adherence; women were less likely than men to complete the full course of nonoccupational HIV PEP.

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 a barrier method with sex partners, not sharing equipment used to inject drugs). At follow-up visits, health care providers should assess for ongoing risk activities, provide additional counseling, and connect patients with services as needed, including assessment for initiation of HIV PrEP.

Transitioning from Nonoccupational HIV PEP to HIV PrEP

Individuals who present for nonoccupational HIV 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. The 2021 CDC PrEP Clinical Practice Guideline recommends that persons receiving nonoccupational HIV PEP who are interested in HIV PrEP should have the transition from nonoccupational HIV PEP to HIV PrEP occur without a gap.[3] For example, if a person is going to transition from nonoccupational HIV PEP to HIV PrEP, they should take a 28-day course of nonoccupational HIV PEP, and on day 29, HIV PrEP should be started. The following summarizes several key issues regarding the transition from nonoccupational PEP to PrEP.[3]

- For persons who are candidates for transition from nonoccupational HIV PEP to HIV PrEP, a follow-up visit will be needed at the completion of the 28-day nonoccupational HIV PEP regimen (or several days prior to completing the regimen). To ensure no gap in HIV protection occurs, it is important the visit does not take place on a date after completion of the 28-day course of nonoccupational HIV PEP. At this follow-up visit, the individual should have assessment for any signs or symptoms that would suggest acute HIV. If an individual is presenting with an illness consistent with acute HIV, then HIV PrEP should be deferred while evaluation for acute HIV is undertaken.
- Repeat HIV testing should be performed at this visit, ideally with a laboratory-based HIV-1/2 antigen-antibody immunoassay and an HIV RNA-1 assay. These assays typically require 1 to 3 days before results are available, which practically means they should be ordered several days prior to the end of the 28-day nonoccupational HIV PEP course, or the person can transition to HIV PrEP at the 28-day visit while the results are pending—with the plan to immediately convert the HIV PrEP to HIV treatment if the HIV testing reveals HIV infection.
- At this visit, individuals transitioning to HIV PrEP should receive counseling about HIV PrEP and baseline laboratory studies that are indicated should be obtained. The medication transition can involve a transition from the 3-drug nonoccupational HIV PEP to any of the three HIV PrEP regimens (tenofovir DF-emtricitabine, tenofovir alafenamide-emtricitabine, or long-acting injectable cabotegravir), as long as they are indicated for the individual.
- If HIV testing at any point prior to starting HIV PrEP (or while on HIV PrEP) confirms HIV infection, the individual will need prompt evaluation for the management of newly acquired HIV.

Expert Consultation for Transitioning from Nonoccupational HIV PEP to HIV PrEP

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

Concerns with Nonoccupational Postexposure Prophylaxis

Toxicity of Antiretroviral Therapy

Initial concerns about severe side effects and pharmacological toxicities in otherwise healthy persons have been ameliorated by the use of less toxic, well-tolerated antiretroviral agents.[54]

Use of Nonoccupational HIV PEP and HIV Drug Resistance

Selection of drug-resistant HIV can theoretically result from the use of nonoccupational HIV PEP if the exposed person acquires HIV as a result of the exposure. Nevertheless, the development of HIV drug resistance during receipt of nonoccupational HIV PEP appears to occur only rarely. Thus, nonoccupational PEP should not be withheld due to theoretical concerns about the potential selection of drug-resistant HIV.

Use of Nonoccupational PEP and Changes in Sexual Activities

Some clinicians have expressed concern that the availability of nonoccupational HIV PEP could theoretically result in changes in sexual activity that could increase the risk of acquiring HIV.[55] Multiple studies involving MSM have shown that sexual risk activity does not significantly change among individuals who receive nonoccupational HIV PEP.[15,56,57] Of note, no studies have been published that have examined changes in injection drug use practices among people who inject drugs who have received a course of nonoccupational HIV PEP.

Summary Points

- Nonoccupational HIV PEP represents an important tool in the portfolio of strategies to prevent HIV acquisition.
- There are data that support the use of nonoccupational HIV PEP to reduce the risk of HIV acquisition after nonoccupational exposures to HIV.
- The use of antiretroviral medications for nonoccupational HIV PEP is recommended for HIV-seronegative persons following an exposure that has a substantial risk for HIV acquisition, if started within 72 hours of the exposure.
- A 28-day course of three-drug antiretroviral medications is recommended for nonoccupational HIV PEP.
- The preferred nonoccupational HIV PEP regimen for adults and adolescents aged 13 years and older who have a baseline creatinine clearance of at least 60 mL/min consists of the fixed-dose combination of tenofovir DF-emtricitabine plus either raltegravir or dolutegravir.
- The person with a nonoccupational exposure to HIV should have baseline laboratory studies that include HIV testing, screening for sexually transmitted infections, serum creatinine, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels, testing for viral hepatitis, and a pregnancy test (if indicated). Follow-up testing for these laboratory studies should also be performed.
- Expert consultation should be sought for all situations that fall outside the scope of the Nonoccupational PEP Guidelines, including situations when exposure to drug-resistant HIV has occurred. Consultation can be obtained through local expertise (if available) or by calling the National Clinician Consultation Center's Post-Exposure Prophylaxis Hotline (PEPline) at 888-448-4911.
- All persons seeking care for nonoccupational HIV 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 HIV-1/2 antigen-antibody immunoassay is preferred for HIV testing.
- Nonoccupational PEP has not been linked to high rates of adverse side effects, selection of drug-resistant HIV, or increases in activities that are associated with a higher risk of acquiring sexually transmitted infections, including HIV.
- Most individuals who seek nonoccupational HIV PEP should be evaluated as potential candidates to receive HIV PrEP following completion of nonoccupational HIV PEP. The transition from occupational HIV PEP to HIV PrEP, if warranted, should occur without a gap.

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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

Abbreviations: SIV = simian immunodeficiency virus; PEP = postexposure prophylaxis; TFV = tenofovir
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.

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.

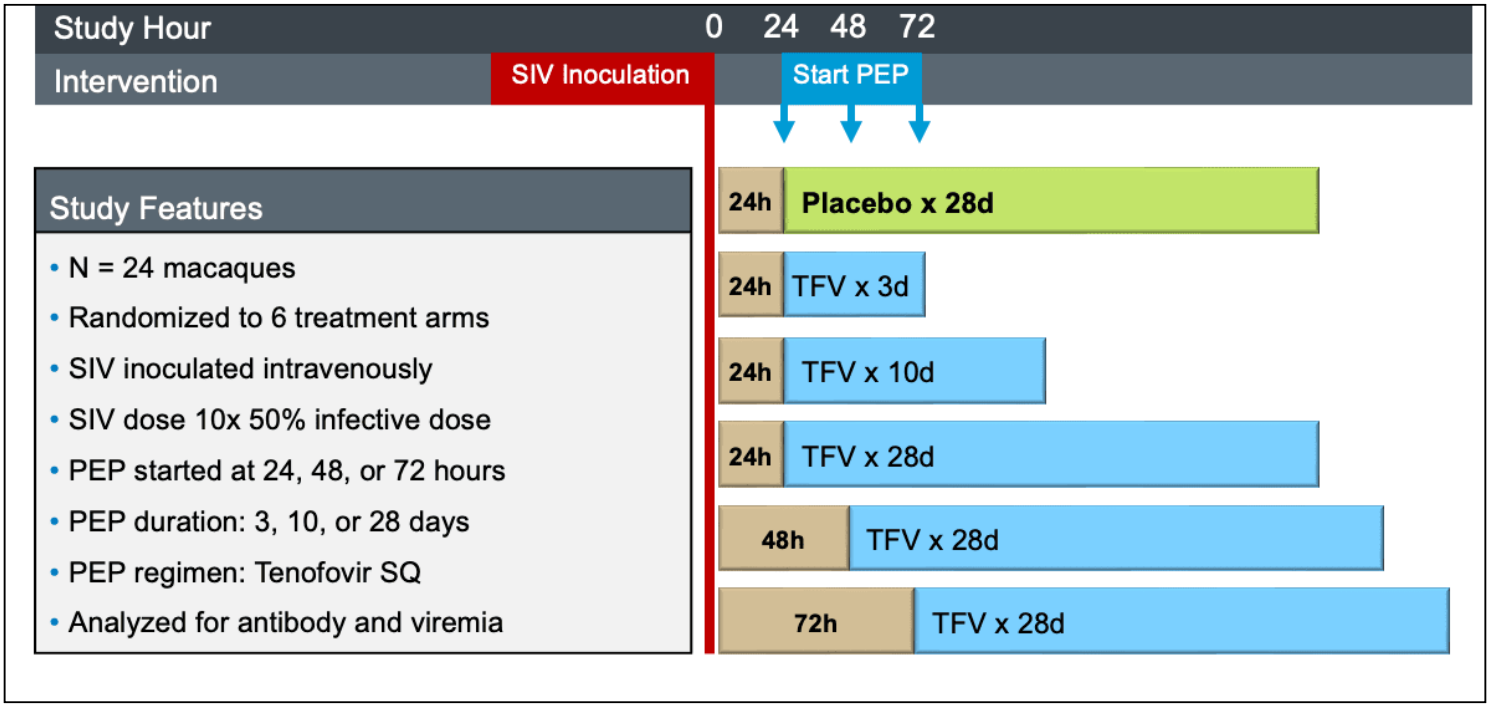

Figure 1 (Image Series) - Tenofovir PEP following SIV-1 Inoculation of Macaques
Image 1B: SIV Transmission Based on Timing of Initiation and Duration of PEP

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.

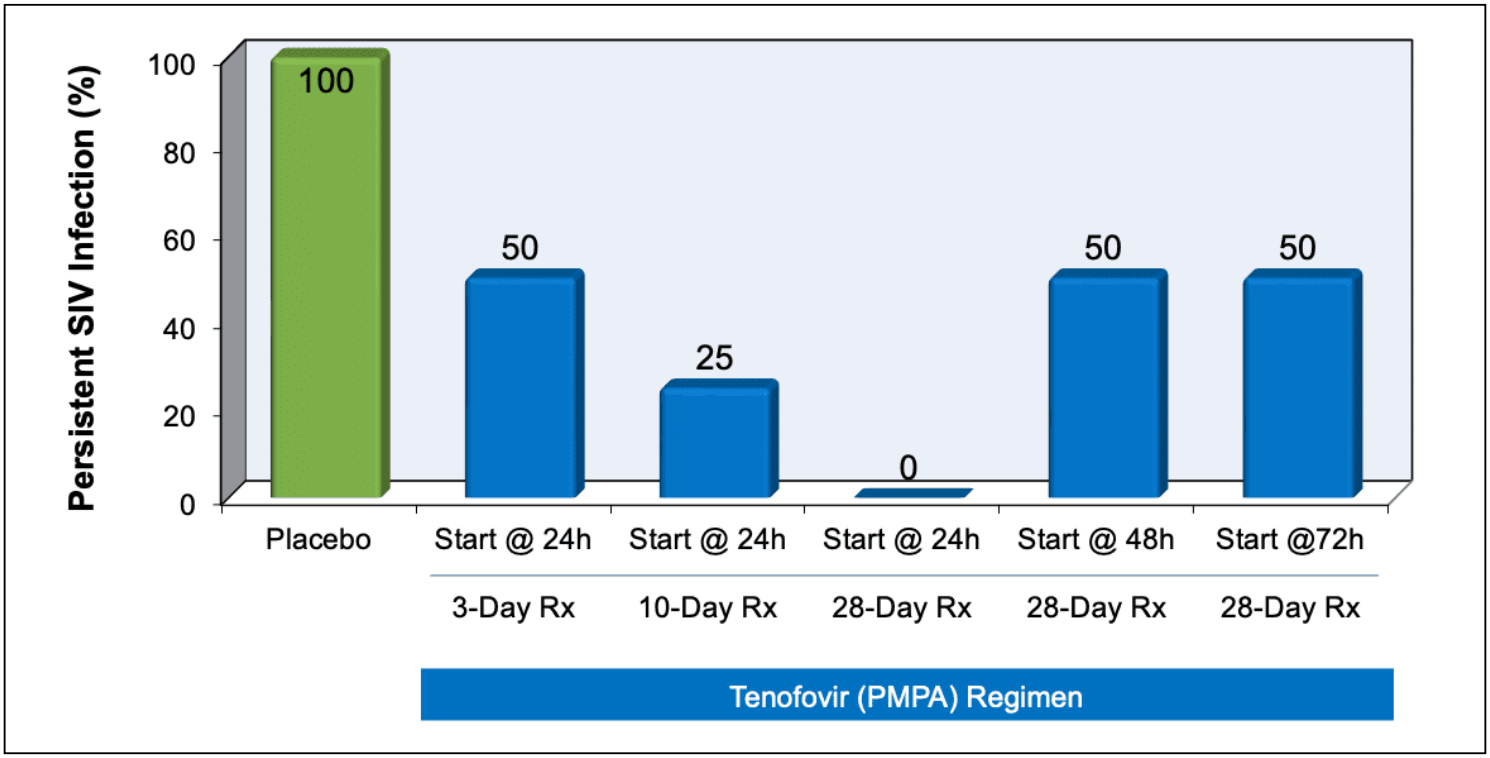

Figure 2 Algorithm for Evaluation and Treatment of possible nonoccupational HIV exposures

Source: Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, and Other Nonoccupational Exposure to HIV – United States, 2016.

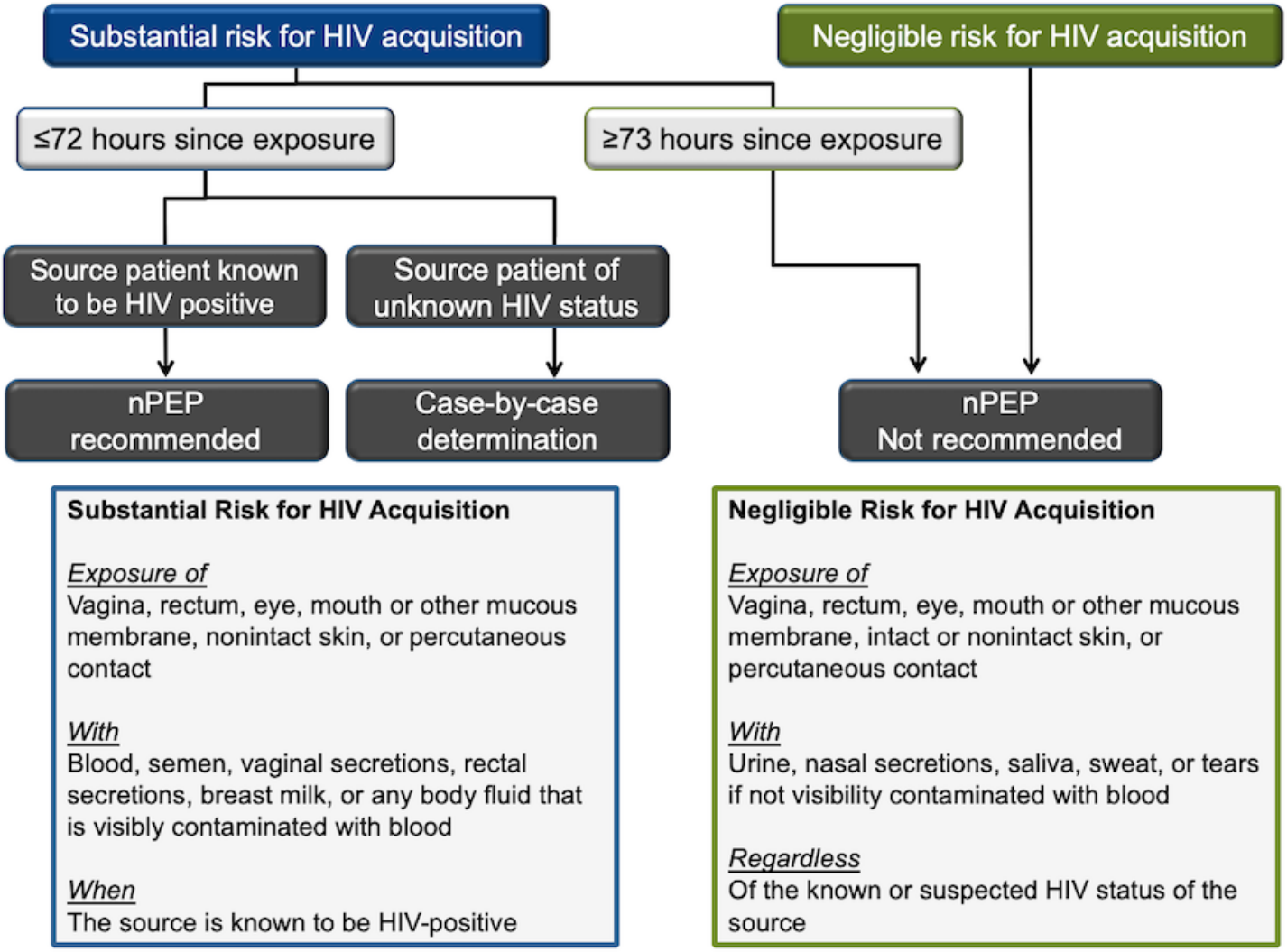

Table 1.

Estimated Per-Act Probability of 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 diseases, acute and late-stage HIV infection, and high viral load. Factors that may decrease the risk include condom use, male circumcision, antiretroviral treatment, and 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:

- Centers for Disease Control and Prevention: U.S. Department of Health and Human Services. Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, and Other Nonoccupational Exposure to HIV—United States, 2016. [CDC]

Table 2.

Relative Risks of Factors that Alter Per-Act HIV Transmission Risk for Sexual Exposures*

Cofactor	Relative Risk
Factors that Increase Transmission Probability	
High plasma HIV RNA level (log_{10} copies/mL)	2.89
Genital ulcer disease	2.65
Acute versus asymptomatic stage of disease	7.25
Late versus asymptomatic stage of disease	5.81
Factors that Decrease Transmission Probability	
Use of antiretroviral medications by partner with HIV	
Early versus delayed treatment	0.04
Received treatment versus no treatment	0.08
Preexposure Prophylaxis of partner without HIV	
Among heterosexual couples	0.29
Among men who have sex with men	0.56
Among injection drug users	0.52
Condom use	0.20
Male Circumcision (heterosexual partners)	
Partner without HIV is male	0.50
Partner without HIV is female	0.80
Male circumcision (men who have sex with men)	
Insertive partner is partner without HIV	0.27
Receptive partner is partner without HIV	1.20

*For a detailed description of data and factors used to generate estimates, see original table in article referenced below.

Source:

- Patel P, Borkowf CB, Brooks JT, Lasry A, Lansky A, Mermin J. Estimating per-act HIV transmission risk: a systematic review. AIDS. 2014;28:1509-19. [PubMed Abstract]

Table 3. **2016 CDC and HHS Guidelines for Nonoccupational Exposure to HIV**

Preferred and Alternative 28-Day Regimens for Nonoccupational HIV PEP[a,b]

Adults and adolescents aged ≥13 years with normal renal function (creatinine clearance ≥60 mL/min), including pregnant women
Preferred Regimens: • Raltegravir (400 mg twice daily) plus tenofovir DF-emtricitabine (300-200 mg once daily) • Dolutegravir (50 mg once daily) plus tenofovir DF-emtricitabine (300-200 mg once daily) ***Alternative Regimen:*** • Darunavir (800 mg once daily) plus ritonavir (100 mg once daily) plus tenofovir DF-emtricitabine (300-200 mg once daily)
Adults and adolescents aged ≥13 years with renal dysfunction (creatinine clearance ≤59 mL/min)[+]
Preferred Regimens: • Raltegravir (400 mg twice daily) plus zidovudine (dose adjusted) plus lamivudine (dose adjusted) • Dolutegravir (50 mg once daily) plus zidovudine (dose adjusted) plus lamivudine (dose adjusted) ***Alternative Regimen:*** • Darunavir (800 mg once daily) plus ritonavir (100 mg once daily) plus zidovudine (dose adjusted) plus lamivudine (dose adjusted)

[a]These recommendations do not reflect current Food and Drug Administration-approved labeling for antiretroviral medications listed in this table.

[b]Ritonavir is used in clinical practice as a pharmacokinetic enhancer to increase the trough concentration and prolong the half-life of darunavir, lopinavir, and other protease inhibitors. Ritonavir is not counted as a drug directly active against HIV in the above “3-drug” regimens.

[+]The dose adjustments for zidovudine and lamivudine are made based on degree of renal function

Source:

- Centers for Disease Control and Prevention: U.S. Department of Health and Human Services. Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, and Other Nonoccupational Exposure to HIV—United States, 2016. [CDC]

Table 4.

Nonoccupational HIV PEP: Recommended Laboratory Monitoring of Source and Exposed Persons

Test	Source	Exposed			
	Baseline	Baseline		4-6 Weeks after exposure	3 Months
		For all persons considered for or prescribed			
HIV-1/2 Ag/Ab (or Ab testing if Ag/Ab test unavailable)[a]	√	√	√	√	√[b]
Hepatitis B serology, including: HBsAg anti-HBs anti-HBc	√	√	—	—	√[c]
Hepatitis C antibody test	√	√	—	—	√[d]
		For all persons considered for or prescribed nPEP for sexual expos			
Syphilis serology[e]	√	√		√	
Gonorrhea[f]	√	√		√[g]	
Chlamydia[f]	√	√		√[g]	
Pregnancy[h]	—	√		√	
		For persons prescribed: Tenofovir DF-emtricitabine + raltegravir Tenofovir DF-emtricitabine + dolutegravir			
Serum creatinine (for calculating estimated creatinine clearance)[i]		√		√	
Alanine aminotransferase, aspartate aminotransferase		√		√	
	For all persons with HIV confirmed at any visit				
HIV RNA level	√			√[j]	
HIV genotypic drug resistance test	√			√[j]	

Abbreviations: Ag/Ab, antigen/antibody combination test; HIV, human immunodeficiency virus; nPEP, nonoccupation
fumarate.
[a] Any positive or indeterminate HIV antibody test should undergo confirmatory testing of HIV status.
[b] Only if hepatitis C infection was acquired during the original exposure; delayed HIV seroconversion has been seen
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 tre
[f] Testing for chlamydia and gonorrhea should be performed using nucleic acid amplification tests. For patients diagr
months after treatment is recommended.
- For men reporting insertive vaginal, anal, or oral sex, a urine specimen should be tested for chlamydia and gonorr
- For women reporting receptive vaginal sex, a vaginal (preferred) or endocervical swab or urine specimen should b
- For men and women reporting receptive anal sex, a rectal swab specimen should be tested for chlamydia and gon
- For men and women reporting receptive oral sex, an oropharyngeal swab should be tested for gonorrhea.
[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
[j] At first visit where determined to have HIV infection.

Source:

- Centers for Disease Control and Prevention: U.S. Department of Health and Human Services. Updated

Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, and Other Nonoccupational Exposure to HIV—United States, 2016. [CDC]