

HIV PROPHYLAXIS FOLLOWING NON-OCCUPATIONAL EXPOSURE

What's New – July 2013 Update

Significant revisions include the following:

- The Medical Care Criteria Committee now recommends **tenofovir + emtricitabine* plus raltegravir** as the **preferred initial nPEP regimen** because of its excellent tolerability, proven potency in established HIV infection, and ease of administration. **Zidovudine is no longer recommended** in the preferred PEP regimen because it is believed to have no clear advantage in efficacy over tenofovir while having significantly higher rates of treatment-limiting side effects. Appendix D provides payment options for PEP following non-occupational exposures.
- If the source person's HIV screening test result is negative but there has been a risk for HIV exposure in the previous 6 weeks, **plasma HIV RNA testing of the source person** is also recommended. In this situation, nPEP should be initiated and continued until results of the plasma HIV RNA assay are available.
- Table 1 has been updated to more clearly delineate **types of exposures** that should prompt **consideration of nPEP** and those that **do not warrant nPEP**. Appendix B has been added to show both the risk of HIV transmission for various exposures as well as **factors that may increase transmission risk**.
- **Baseline STI testing** is recommended for sexual exposures that *do not* occur as a result of sexual assault. STI management recommendations, including prophylactic treatment, differ for cases of sexual assault. See [HIV Prophylaxis for Victims of Sexual Assault](#).
- Recommendations for follow-up HIV testing of the exposed person have been changed. Regardless of whether the exposed person accepts or declines PEP treatment, **if the post-exposure evaluation determines that nPEP is indicated, repeat HIV testing at 4 weeks and 12 weeks** should be obtained. A negative HIV test result at 12 weeks post-exposure reasonably excludes HIV infection related to the exposure; **routine testing at 6 months post-exposure is no longer recommended**.
- Consideration for **pre-exposure prophylaxis** after completion of the 28-day nPEP regimen is recommended for persons who present with **repeated high-risk behavior or for repeat courses of nPEP**.
- A detailed listing of AIDS Institute-funded HIV prevention programs that provide **risk-reduction counseling** has been added (see Appendix C).

*Lamivudine may be substituted for emtricitabine.

I. INTRODUCTION

The purpose of this chapter is to provide recommendations and guidelines for prescribing PEP following non-occupational exposure to HIV (nPEP). These guidelines will address nPEP for significant risk exposures following sexual and needle-sharing activities, needlesticks outside of occupational settings, and trauma, including human bites. Within the category of sexual exposure, sexual assault merits special focus.

Because of the special considerations regarding evaluation, counseling, and support for sexual assault victims, PEP in the setting of sexual assault is addressed separately (see [HIV Prophylaxis for Victims of Sexual Assault](#)). **PEP regimens for sexual assault are the same as PEP regimens for other types of non-occupational and occupational exposures.**

For guidelines that address HIV PEP following occupational exposure, see [HIV Prophylaxis Following Occupational Exposure](#).

Although the most effective way to prevent HIV transmission is to protect against exposure, nPEP offers the possibility of preventing HIV transmission when potential exposure to HIV has already occurred. Situations that may prompt a request for nPEP include condom slippage, breakage, or lapse in use by serodiscordant partners; unsafe needle-sharing; or other episodic exposure to blood. Treatment of high-risk exposures should be combined with a strong educational component that emphasizes prevention of future exposures.¹

Appendix B shows the risk of HIV transmission for various types of exposure to a known HIV-infected source as well as factors that may increase transmission risk. HIV transmission most frequently occurs during sexual or drug-using exposures; however, there are many factors that can influence transmission risk. Due to the presence of high HIV viral load levels, the probability of transmission when the source person is in the acute and early stage of HIV infection (first 6 months) has been shown to be 8- to almost 12-fold higher than exposures that take place after the viral set point.^{2,3} The presence of sexually transmitted infections (STIs) in either the source or exposed person also increases risk.⁴⁻⁶ Conversely, transmission risk has been shown to be significantly decreased in source persons who are receiving effective antiretroviral therapy (ART).⁷ The Centers for Disease Control and Prevention (CDC) is reviewing the most recent data and constructing mathematical models to update transmission risk.

Evidence Base

Practice guidelines and policy recommendations for nPEP must consider the lack of definitive evidence concerning efficacy to support them. Because randomized, placebo-controlled experimental clinical trials on nPEP have not been conducted and are not feasible to design to generate conclusive data, these guidelines are based on existing published studies and best-practice evidence and constitute the considered opinion of the group of expert clinicians in the field of adult HIV medicine who comprise the [Medical Care Criteria Committee](#).

Although there are no studies that directly demonstrate the efficacy of nPEP, there are data to support its biologic plausibility, including animal studies of prophylaxis following exposure to simian immunodeficiency virus (SIV) and HIV-2,⁸⁻¹⁰ efficacy data from mother-to-child transmission studies,¹¹ and a case-controlled study of occupational exposure.¹² A number of observational studies have been designed to assess the feasibility and potential efficacy of nPEP programs. Initial published reports from San Francisco, Boston, and Brazil have demonstrated the feasibility of such programs in high-risk populations.¹³⁻¹⁵ Cost-effectiveness analyses have suggested that nPEP is cost-effective in high-risk exposures such as receptive anal sex with an HIV-infected partner or a partner of unknown HIV status.^{16,17} However, a 2008 survey of emergency departments in New York State showed that implementation of these guidelines in New York State is not optimal.¹⁸

Developing guidelines for HIV exposures outside of the occupational setting raises a multitude of issues beyond the questions of biologic rationale and transmission risk. Issues include cost of care, payment for medications, feasibility of implementation of guidelines, individual adherence to nPEP, the risks and benefits of prophylactic ART, and the potential public health impact of such guidelines. To develop these guidelines for nPEP, the Medical Care Criteria Committee reviewed the medical literature as well as existing recommendations and guidelines from government and community sources. They also considered specific concerns related to the process of implementing nPEP. Throughout the deliberations of the Committee, a conscious effort was made to weigh both the medical and psychological benefits and risks of medical intervention in the context of a potential HIV exposure.

II. INITIAL ASSESSMENT FOR PEP FOLLOWING NON-OCCUPATIONAL EXPOSURES

RECOMMENDATIONS:

Risk assessment and initiation of nPEP should occur in clinical settings that can provide the following: (AIII)

- **Assessment of HIV risk following exposure**
- **HIV and STI testing and treatment**
- **Prevention and risk-reduction counseling**
- **Clinicians with expertise in the use of ART**
- **Timely access to care and initiation of nPEP**

If all of these services are not available, clinicians should assess the exposure and initiate nPEP when indicated according to the criteria and recommendations in these guidelines. The patient should then be referred for follow-up care to a clinician who has experience in the use of antiretroviral agents and who can provide ongoing prevention counseling.

Treating clinicians who do not have access to experienced HIV clinicians should call the National Clinicians' Consultation Center PEline at 1-888-448-4911 to review the case. When using the PEline, providers from New York State should identify themselves as practicing in the State.

Patients who present for nPEP should be evaluated as soon as possible in order to initiate therapy, if indicated, within recommended timeframes (see Section IV: *Timing of Initiation of PEP for All Non-Occupational Exposures*). **Wound and skin exposure sites should be washed with soap and water. Needlestick injuries should not be squeezed.** (AII)

When an HIV exposure occurs, the events and the subsequent interventions should be clearly documented in order to facilitate determination of the effectiveness of nPEP. (AII)

This section provides guidance for assessing non-occupational exposures that occur from blood and body fluid exposures, including sexual and needle-sharing activities unrelated to sexual assault. (Special considerations for PEP following sexual assault are covered in [HIV Prophylaxis for Victims of Sexual Assault](#).) Situations that may prompt a request for nPEP include condom slippage, breakage, or lapse in use by serodiscordant partners; unsafe needle-sharing; or other exposure to blood or body fluids.

For persons presenting with wounds or needlestick injuries, the site should be washed with soap and water, avoiding irritation of the skin. The wound should not be “milked” or squeezed. Squeezing the wound may promote hyperemia and inflammation at the wound site, potentially increasing systemic exposure to HIV if present in the contaminating fluid.

A. Evaluation of the Exposure: Is nPEP Indicated?

RECOMMENDATIONS:

When deciding whether to recommend the initiation of nPEP, the clinician should assess the patient’s risk of HIV acquisition based on the type of exposure (see Table 1). (AIII)

Non-occupational PEP should not be prescribed when there is negligible or low risk of HIV transmission (see Table 1). (AIII)

Non-occupational PEP should not be routinely dismissed solely on the basis of repeated risk behavior or repeat presentation for nPEP. (AIII) **Persons who present with repeated high-risk behavior or for repeat courses of nPEP should be the focus of intensified education and prevention interventions.**

After completion of the 28-day nPEP regimen, the patient should be evaluated to determine whether initiation of pre-exposure prophylaxis (PrEP) is warranted and feasible. (AII) See the CDC interim guidance documents for use of pre-exposure prophylaxis in [men who have sex with men](#), [heterosexually active adults](#), and [injection drug users](#). See Section III: *Behavioral Intervention and Risk-Reduction Counseling*.

The use of nPEP involves both significant costs and potential risk of toxicity from medications. As a result, it should only be used when the potential benefits of taking nPEP outweigh its risks. Non-occupational PEP is not indicated for perceived exposures that are of negligible or low-risk (see Table 1).

Determining the degree of risk of HIV transmission is an important factor in guiding the patient and clinician in making a decision concerning nPEP. Table 1 lists types of exposures that should prompt consideration of nPEP and those that do not warrant nPEP. There may be factors which complicate assessment of the exposure. Clinicians who do not have access to experienced HIV clinicians should call the National Clinicians' Consultation Center PEPLine at 1-888-448-4911. When using the PEPLine, providers from New York State should identify themselves as practicing in the State.

TABLE 1 CONSIDERATION OF NPEP ACCORDING TO THE TYPE OF RISK EXPOSURE^a	
Types of Exposures for Which nPEP Should Be Recommended (higher-risk exposures)	<ul style="list-style-type: none"> • Receptive and insertive vaginal or anal intercourse^b • Needle sharing^b • Injuries with exposure to blood or other potentially infected fluids from a source known to be HIV-infected or HIV status is unknown (including needlesticks with a hollow-bore needle, human bites, accidents)
Lower-Risk Exposures That Require Case-by-Case Evaluation for nPEP (lower-risk exposures: assess for factors that increase risk before recommending initiation of nPEP)	<ul style="list-style-type: none"> • Oral-vaginal contact (receptive and insertive) • Oral-anal contact (receptive and insertive) • Receptive penile-oral contact with or without ejaculation • Insertive penile-oral contact with or without ejaculation <p>Factors that increase risk:</p> <ul style="list-style-type: none"> ➤ Source person is known to be HIV-infected with high viral load ➤ An oral mucosa that is not intact (e.g., oral lesions, gingivitis, wounds) ➤ Blood exposure — it is important to note that blood exposure can be minimal and therefore not recognized by the exposed person. If the exposed person reports frank blood exposure, PEP would be indicated ➤ Presence of genital ulcer disease or other STIs
Types of Exposures That Do Not Warrant nPEP (no risk)	<ul style="list-style-type: none"> • Kissing^c • Oral-to-oral contact without mucosal damage (mouth-to-mouth resuscitation) • Human bites not involving blood • Exposure to solid-bore needles or sharps not in recent contact with blood^d • Mutual masturbation without skin breakdown or blood exposure
<p>^a Appendix B provides risk calculations for specific risk behaviors.</p> <p>^b With a source known to be HIV-infected or HIV status is unknown.</p> <p>^c There is no risk associated with close-mouthed kissing. There is a remote risk associated with open-mouthed kissing if there are sores or bleeding gums and blood is exchanged.¹⁹</p> <p>^d Examples of solid-bore needles include tattoo needles and lancets used by diabetics to measure blood-sugar levels.</p>	

HIV Exposure Through Sexual and Drug-Using Activities

The clinician should have a frank discussion with the patient regarding sexual activities, needle-sharing, and other drug-using activities that have a potential for exposure to blood and body fluids (see Table 1 and Appendix B). The behaviors that confer the highest risk are needle-sharing and receptive anal intercourse with an infected source.²⁰⁻²² For more information, refer to [Prevention with Positives: Integrating HIV Prevention into Primary Care](#) and the [PozKit: A Prevention with Positives ToolKit for Clinicians](#).

Clinicians should also discuss factors that influence HIV transmission risk, including trauma at the site of exposure, the presence of genital ulcer disease and/or other STIs,^{5,23} and high plasma viral load in the HIV-infected source person.^{24,25} Other factors that may enhance transmission include cervical ectopy and lack of male circumcision.²⁵⁻²⁷ Factors that may decrease transmission risk include exposure to a source person who is receiving effective ART⁷ and condom use.²⁸ Correct condom use is highly effective in preventing transmission of HIV; however, during the post-exposure evaluation, it often is not possible to reliably ascertain whether condoms were used correctly or whether breakage, slippage, or spillage occurred.

HIV Exposure Through Needlestick Injuries

Another route of exposure that prompts requests for nPEP is needlestick injuries in the non-healthcare setting. Factors associated with risk from needlestick injuries outside of the healthcare setting include the potential source of the needle, type of needle, presence of blood, and skin penetration.

People who incur needlestick injuries from *discarded* needles are often concerned about potential HIV exposure. Consideration of potential risk from discarded needles should include the prevalence of HIV in the community or facility where the exposure occurred and the surrounding prevalence of injection drug use. However, the risk of HIV transmission through exposure to dried blood found on syringes is extremely low.²⁹ Discarded needles should not be tested for HIV because of low yield and the risk of injury to personnel involved in testing. Vaccination to prevent tetanus and administration of hepatitis B immunoglobulin and vaccine may be indicated for needlestick injuries resulting in puncture wounds.

HIV Exposure Through Bites

RECOMMENDATIONS:

When bite wounds result in blood exposure, nPEP should be considered for the person(s) who was exposed to blood; this could be the person bitten, the biter, or both (AII) (see Table 2). PEP should not be initiated when the integrity of the skin is not disrupted.

Clinicians should wash bite wounds with soap and water and should not squeeze the wound. (AII)

An estimated 250,000 human bites occur annually in the United States in a variety of settings.³⁰ Although possible, HIV transmission following bites is thought to be extremely rare. While there have been many reported instances of bites, there have been few cases of HIV transmission as a result of a human bite exposure. The few documented cases of possible HIV transmission following bites were in adults exposed to blood-tinged saliva.^{31,32}

A bite wound that results in blood exposure should prompt consideration of nPEP. When a human bite occurs, it is possible for both the person bitten and the biter to incur blood exposure (see Table 2). Use of nPEP in this setting potentially would be indicated when there is significant exposure to deep, bloody wounds. A bite is not considered a risk exposure to either party when the integrity of the skin is not disrupted.

TABLE 2 SCENARIOS IN WHICH BITES MAY RESULT IN BLOOD EXPOSURE
<ul style="list-style-type: none"> • Blood exposure to the biter: when the biter inflicts a wound that breaks the skin, and blood from the bitten person enters the biter's mouth • Blood exposure to the bitten person: when the biter has blood in his/her mouth (e.g., from bleeding gums or lesions) and inflicts a wound that breaks the skin of the person bitten • Blood exposure to both parties: when there is a break in the skin of the person who was bitten <i>and</i> the biter had blood in his/her mouth (e.g., from bleeding gums or lesions)

B. HIV Status of the Source Person

In most cases of non-occupational exposures, the source person is not available for testing. The HIV status of the source person should not be the main focus at the initial presentation, but rather determination of whether the exposure warrants nPEP and, when indicated, prompt initiation of nPEP. Following are the possible scenarios regarding availability of the source person and how each may affect decision-making:

Source Person is Unavailable or Unwilling to Undergo HIV Testing

RECOMMENDATION:

When assessment of the exposure determines that nPEP is indicated, but the source is anonymous, unavailable, or unwilling to undergo HIV testing, nPEP should be initiated and the 28-day course should be completed. (AII)

Source Person is Known to Be HIV-Infected

RECOMMENDATION:

If the source of contact is known to be HIV-infected, information about his/her viral load, antiretroviral medication history, and history of antiretroviral drug resistance should be obtained when possible to assist in the selection of an nPEP regimen; however, administration of the first dose of nPEP should not be delayed while awaiting this information. (AII)

Source Person's HIV Status Is Unknown and Source Is Available for Testing

RECOMMENDATIONS:

When the source person is available *and* consents to HIV testing, clinicians should obtain the most expeditious HIV test available (ideally with a turnaround time <1 hour), using either an FDA-approved HIV rapid test *or* a conventional, laboratory-based screening test, such as an enzyme immunoassay (EIA) or chemiluminescent immunoassay (CIA). (AI) If the test results are not immediately available, the initiation of nPEP should not be delayed pending the test result. If the source person's HIV screening test result is negative but there may have been exposure to HIV in the previous 6 weeks, a plasma HIV RNA assay should also be obtained. (BIII) In these situations, nPEP should be continued until results of the plasma HIV RNA assay are available: if the result is positive, the 28-day regimen should be completed; if the result is negative, PEP should be discontinued. (BIII)

The source person should also be evaluated for hepatitis B and hepatitis C. (AI)

When the source person is available and consents to HIV testing, HIV testing using rapid technology is strongly recommended as soon as possible in order to aid in decision-making regarding nPEP. Results from rapid testing are usually available in 30 minutes. Laboratory-based screening tests may be used if results can be available within an hour. If the test results are not immediately available, the initiation of nPEP should not be delayed pending the test result.

The most sensitive screening tests available should be used to allow for detection of early or acute HIV infection. Source persons who are in the "window period" prior to seroconversion may not be identified. When the source person's rapid test result is negative and the clinician has ascertained that the source person could have been exposed to HIV in the previous 6 weeks, a plasma HIV RNA assay should also be obtained. In these situations, nPEP should be initiated and continued until results of the plasma HIV RNA assay are available.

C. Baseline Testing for Patients Who Present with Risk Exposures

HIV Testing

RECOMMENDATIONS:

Clinicians should perform baseline HIV testing of the exposed person within 3 days of the exposure. (AIII) Testing must be performed in full compliance with [New York State Public Health Law](#). Exposed persons who decline baseline HIV testing should not receive nPEP. (AIII)

nPEP should be started without waiting for the results of the exposed person's baseline HIV test. (AII) If the initial test result is positive, nPEP should be continued until the positive result is repeated with a confirmatory assay. Decisions regarding continuation of ART should be based on current treatment guidelines.

Baseline HIV testing of the exposed person identifies individuals who were already infected with HIV at the time of presentation. This allows decisions to be made regarding the initiation of ART to treat established HIV infection rather than nPEP to prevent it (see [Antiretroviral Therapy](#), Section III: *When to Initiate ART in Patients with Chronic Infection*). However, the nPEP regimen should not be discontinued until the positive result is repeated with a confirmatory assay.

Key Point:

A negative baseline HIV test only demonstrates that the exposed person was not previously infected with HIV before the exposure occurred; the baseline HIV test *cannot* determine whether the exposed person was infected as a result of the exposure for which he/she is presenting.

Sexually Transmitted Infections Other Than HIV**RECOMMENDATIONS:**

For patients who are sexually exposed *in non-assault situations*, clinicians should perform STI testing at baseline and should treat as indicated. Testing should include the following:

- **Nucleic acid amplification testing (NAAT) to screen for gonorrhea and chlamydia, based on site of exposure (AII)**
- **Rapid plasma reagin (RPR) for syphilis (AIII)**

Clinicians should counsel patients about the risk of acquiring other STIs and symptoms that may occur; patients should be instructed to call their healthcare provider if symptoms occur. (AII)

For MSM who present with sexual exposures, clinicians should assess for the need to vaccinate against meningococcal disease according to current [New York State Department of Health recommendations](#). (AII)

Risk behaviors leading to HIV infection also put the patient at risk for other STIs. Patients who present for nPEP should be evaluated for other STIs after a sexual exposure.

Baseline testing for STIs generally cannot detect STIs that were acquired as a result of the exposure, but may detect infections prior to the exposure leading to HIV PEP. Presentation for nPEP provides an opportunity to screen and treat individuals at risk for STIs. High rates of concomitant STIs at the time of presentation for nPEP have been found in men who have sex with men.^{33,34} Routine empiric treatment for STIs is not recommended for sexual exposures that are not related to sexual assault. Patients should be educated about STI symptoms and instructed to call their healthcare provider if symptoms occur. Follow-up STI testing should be considered at 2 weeks post-exposure to definitively exclude STI acquisition from the exposure.

Management of exposure to other STIs differs for cases of sexual assault. See [HIV Prophylaxis for Victims of Sexual Assault](#).

Emergency Contraception**RECOMMENDATION:**

Clinicians should obtain baseline pregnancy testing for exposed women. (AII) Emergency contraception should be discussed and offered to women who have the potential of becoming pregnant as a result of the exposure. (AII)

Emergency contraception for female patients should be initiated within 72 hours of the sexual exposure to be effective; optimally, pregnancy prophylaxis should be initiated within 12 hours of the exposure. The following websites offer more information about the use of emergency contraception:

- [The Emergency Contraception Website](#) (for providers and consumers)
- [Emergency Contraception: What You Need to Know](#) (for consumers)

III. BEHAVIORAL INTERVENTION AND RISK-REDUCTION COUNSELING

RECOMMENDATIONS:

The clinician or a member of the HIV care team should provide risk-reduction counseling and primary prevention counseling whenever someone is assessed for nPEP, regardless of whether PEP is initiated. (AII)

Clinicians should assess for emotional, psychological, and social factors that can contribute to risk behavior, such as depression, history of sexual abuse, and drug and alcohol use. (AII)

Clinicians should refer patients to mental health and/or substance use programs when indicated and should consider the need for intensive risk-reduction counseling services. (AII) See Appendix C for a contact list for AIDS Institute-funded HIV prevention programs that provide risk-reduction counseling.

Persons who present with repeated high-risk behavior or for repeat courses of nPEP should be the focus of intensified education and prevention interventions and, after completion of the 28-day nPEP regimen, initiation of pre-exposure prophylaxis (PrEP) should be considered. (AII) See the CDC interim guidance documents for use of pre-exposure prophylaxis in [men who have sex with men](#), [heterosexually active adults](#), and [injection drug users](#).

Non-occupational PEP should not be routinely dismissed solely on the basis of repeated risk behavior or repeat presentation for nPEP. Rather, presentation of persons with repeated high-risk behavior or for repeat courses of nPEP should be viewed as an opportunity for intensification of education and prevention planning in a high-risk individual. Intent to change behavior should be assessed, and an individualized risk-reduction plan should be developed. After completion of the 28-day nPEP regimen, initiation of pre-exposure prophylaxis (PrEP) should be considered.^{35,36} See the CDC interim guidance documents for use of pre-exposure prophylaxis in [men who have sex with men](#), [heterosexually active adults](#), and [injection drug users](#).

For more information regarding risk-reduction counseling, refer to [Prevention with Positives: Integrating HIV Prevention into Primary Care](#) and the [PozKit: A Prevention with Positives Toolkit for Clinicians](#).

IV. TIMING OF INITIATION OF PEP FOR ALL NON-OCCUPATIONAL EXPOSURES

RECOMMENDATIONS:

When a potential non-occupational exposure to HIV occurs, every effort should be made to initiate PEP as soon as possible, ideally within 2 hours. (AII)

Decisions regarding initiation of nPEP beyond 36 hours post exposure should be made on a case-by-case basis with the realization of diminished efficacy when timing of initiation is prolonged. (AII)

Data from animal models of PEP have shown that effective antiretroviral treatment is most likely to prevent infection when initiated within 24 to 36 hours of exposure.^{8-10,37-39} HIV virions can traverse epithelial barriers in just hours, and many antiretroviral medications require an intracellular activation step that delays the onset of antiviral activity. Therefore, every effort should be made to initiate nPEP as soon as possible following an exposure and ideally within 2 hours. **An absolute elapsed time after which nPEP should not be given cannot be stated with certainty.**

Decisions regarding initiation of nPEP beyond 36 hours post exposure should be made by the clinician in conjunction with the patient with the realization of diminished efficacy when timing of initiation is prolonged. Some individuals who are victims of sexual assault or who have higher-risk exposures, such as unprotected anal receptive intercourse with a known HIV-infected partner, may wish to initiate nPEP, even though they may present for treatment more than 36 hours following the exposure. These decisions need to be individualized based on the type of exposure, the patient's desire to initiate nPEP, and the amount of time that has elapsed.

Once a decision has been made that nPEP is indicated, patients should be encouraged to initiate the regimen immediately. After the first dose is administered, telephone or in-person consultation with an experienced HIV provider is recommended. Expert advice may be obtained from the National Clinicians' Consultation Center PEpline at 1-888-HIV-4911 (1-888-448-4911). When using the PEpline, providers from New York State should identify themselves as practicing in the State.

V. COUNSELING AND EDUCATION BEFORE INITIATING nPEP

RECOMMENDATIONS:

The clinician should discuss the following issues with the patient and should document that they were discussed before initiating a regimen (AIII):

- **Potential benefit, unproven efficacy, and potential toxicity of nPEP**
- **Duration of nPEP regimen**
- **Importance of adherence to the treatment regimen to prevent nPEP failure or the development of drug resistance should infection occur**
- **Need to reduce risk and prevent exposure to others**
- **Clinical and laboratory monitoring and follow-up schedule**
- **Signs and symptoms of acute HIV infection**
- **How a full supply of medication will be obtained**

Antiretroviral medications have the potential to cause significant side effects and toxicity. The patient should be made aware of these possibilities and weigh them against the potential but unproven benefit of nPEP. Non-occupational PEP is presumed to be more effective when patients strictly adhere to the prescribed regimen. Follow-up visits will need to occur on a regular basis to assess for adherence, drug tolerance, and medication toxicity (see Section VII: *Follow-Up and Monitoring Following Non-Occupational Exposure*). Supports to facilitate adherence with the treatment regimen should be evaluated and provided to the extent possible.

Sexual assault victims can access reimbursement through the [Office of Victim Services](#); however, private insurers may refuse to reimburse for other types of nPEP. Strategies should be actively sought to provide medication for those who cannot obtain it. Once treatment is initiated, the initiating provider should assume responsibility for ensuring that the patient has access to a full supply of medication to complete the 28-day course of nPEP. Appendix D lists payment options that may be available for both sexual assault and non-sexual assault exposures. For more information on accessing reimbursement through the [Office of Victim Services](#), see [HIV Prophylaxis for Victims of Sexual Assault](#).

VI. RECOMMENDED NPEP REGIMENS

RECOMMENDATIONS:

The preferred PEP regimen is tenofovir + emtricitabine* plus raltegravir (see Table 3 for dosing and Appendix A for description of each drug). (AII) **The first dose should be given as soon as possible after exposure, ideally within 2 hours. The recommended duration of PEP is 28 days.** (AII)

*Lamivudine may be substituted for emtricitabine.

Starter packs with a 3- to 5-day supply of medication should be available on-site for rapid initiation of treatment, and arrangements should be made for continuation of treatment. (AIII)

If the source person is known to be HIV-infected and information is immediately available regarding past and present ART experience, current level of viral suppression, or resistance profile, the treating clinician, in consultation with a clinician experienced in managing PEP, should individualize the PEP regimen to maximize potential effectiveness against the exposed HIV strain (AII). Initiation of the first dose and continuation of PEP should never be delayed while awaiting this information (AII). If indicated, the regimen can be changed when more information becomes available.

Tables 4 and 5 list recommended alternative PEP regimens that should be used in the setting of potential HIV resistance, toxicity risks, clinician preference, or constraints on the availability of particular agents (AII).

Clinicians should switch exposed persons to an alternative regimen if the initial or subsequent PEP regimen is not well tolerated (AII) (see Appendix A for potential adverse events).

Treating clinicians should consult with a clinician experienced in managing PEP when alternative agents are prescribed or if there is doubt as to whether PEP should be continued after the first dose. (AII)

The prescribing clinician should ensure that the exposed person has access to the full 28-day recommended course of antiretroviral medications (AIII) and is appropriately monitored for toxicities during the treatment (see Section VII: *Follow-Up and Monitoring Following Non-Occupational Exposure*).

Treating clinicians who do not have access to experienced HIV clinicians should call the National Clinicians' Consultation Center PELine at 1-888-448-4911. When using the PELine, providers from New York State should identify themselves as practicing in the State.

Table 3 RECOMMENDED REGIMEN FOR HIV PEP FOLLOWING NON-OCCUPATIONAL EXPOSURE
<p>Tenofovir 300 mg PO qd + Emtricitabine 200 mg PO qd</p> <p>Plus</p> <p>Raltegravir 400 mg PO bid</p>
<p>Notes:</p> <p>When the source is known to be HIV-infected:</p> <ul style="list-style-type: none"> • Past and current ART experience, viral load data, and genotypic or phenotypic resistance data (if available) may indicate the use of an alternative PEP regimen. See Tables 4 and 5. • Consult with a clinician experienced in managing PEP. <p>Renal insufficiency:</p> <ul style="list-style-type: none"> • The dosing of tenofovir and emtricitabine/lamivudine should be adjusted in patients with baseline creatinine clearance <50 mL/min (see Appendix A for dosing recommendations). • Tenofovir should be used with caution in exposed persons with renal insufficiency or who are taking concomitant nephrotoxic medications. • Fixed-dose combinations should not be used in patients who need dose adjustment due to renal failure. <p>Lamivudine/Emtricitabine:</p> <ul style="list-style-type: none"> • Lamivudine 300 mg PO qd may be substituted for emtricitabine. However, a fixed-dose combination is available when tenofovir is used with emtricitabine (Truvada 1 PO qd). <p>Co-administration of raltegravir and rifampin:</p> <ul style="list-style-type: none"> • The dosing of raltegravir should be adjusted when co-administered with rifampin (see Appendix A for dosing recommendations).

A. Rationale for Recommended PEP Regimen

This Committee now recommends tenofovir + emtricitabine* plus raltegravir as the preferred initial PEP regimen because of its excellent tolerability, proven potency in established HIV infection, and ease of administration.

*Lamivudine may be substituted for emtricitabine.

The recommended regimen has a favorable side effect profile, fewer potential drug-drug interactions, and an expected efficacy similar to PEP regimens containing zidovudine or protease inhibitors. Studies have shown increased rates of adherence and regimen completion when tenofovir + either emtricitabine or lamivudine have been used as components of the PEP regimen.^{40,41} Limited data show similar improved tolerability with tenofovir + emtricitabine plus raltegravir.^{42,43} Additionally, tenofovir + emtricitabine has been highly successful in recent studies of pre-exposure prophylaxis.⁴⁴⁻⁴⁶

This Committee no longer recommends that zidovudine must be included in PEP regimens because it is believed to have no clear advantage in expected efficacy over tenofovir while having significantly higher rates of treatment-limiting side effects. As experience with PEP continues to accumulate, it has become increasingly clear that tolerability is one of the most important factors in selecting a PEP regimen, especially when the source person is not available for testing and the patient will need to complete the full 28-day course.

Unlike protease inhibitors, which block HIV replication in steps after integration with cellular DNA, all three drugs in the recommended regimen (tenofovir, emtricitabine, raltegravir) act before viral integration with cellular DNA, providing a theoretical advantage in preventing establishment of HIV infection.

B. Use of a Three-Drug PEP Regimen

Once a decision has been made that a significant risk exposure has occurred and that PEP is warranted, **this Committee recommends a three-drug regimen as the preferred option.**

C. Duration of PEP Regimen

RECOMMENDATIONS:

The recommended duration of nPEP is 28 days.

If the exposed person's baseline test shows evidence of HIV infection acquired before the exposure and initiation of nPEP, decisions regarding continuation of ART should be based on current treatment guidelines (AI) (see [Antiretroviral Therapy](#)). However, the nPEP regimen should not be discontinued until the positive result is repeated with a confirmatory assay. (AI)

If the exposed person's week 4 post-exposure HIV test results are indeterminate or the exposed person has symptoms suggestive of acute HIV infection, clinicians should continue ART beyond 28 days until a definitive diagnosis is established (AII) (see Section VII. B. *Sequential HIV Testing* for recommendations regarding diagnosis of acute infection).

When the source person is confirmed to be HIV-negative, clinicians should discontinue the nPEP regimen before completion (AI) (see Section II.B: *HIV Status of the Source Person*).

The recommended 28-day treatment duration is based on limited animal data and expert opinion.³⁹ If the source person is confirmed to be HIV-negative, the PEP regimen should be discontinued before completion.

If at any time acute HIV infection is suspected, consultation with a clinician experienced in managing acute HIV infection should occur immediately (also see [Diagnosis and Management of Acute HIV Infection](#)). Clinicians who do not have access to experienced HIV clinicians can call the New York State Clinician Education Initiative's CEI Line at 1-866-637-2342 (24 hours/7 days per week) or the National Clinicians' Consultation Center PEPLine at 1-888-448-4911. When using the PEPLine, providers from New York State should identify themselves as practicing in the State.

D. Preferred Alternative PEP Regimens

RECOMMENDATIONS:

The preferred alternative PEP regimen is tenofovir + emtricitabine* plus ritonavir-boosted darunavir, atazanavir, or fosamprenavir (AII) (see Table 4).

*Lamivudine may be substituted for emtricitabine.

Clinicians should carefully assess for potential drug interactions between these agents and other medications (including prescription medications and over-the-counter drugs, such as proton pump inhibitors and H2-blockers) that the patient may be taking. (AI) See Appendix A for information regarding dosing, adverse effects, and drug interactions.

Clinicians should consult a clinician experienced in managing nPEP when using alternative PEP regimens (AII). If consultation cannot be immediately obtained, the first dose of the regimen should be given rather than delaying initiation, with consultation occurring as soon as possible thereafter (AII). Clinicians who do not have access to experienced HIV clinicians should call the National Clinicians' Consultation Center PEPLine at 1-888-448-4911. When using the PEPLine, providers from New York State should identify themselves as practicing in the State.

The regimens in Table 4 are the preferred alternatives to the recommended regimen in Table 3. These regimens are acceptable options when the preferred regimen is not available. They are expected to be less well tolerated than the preferred regimen of tenofovir + emtricitabine plus raltegravir, but significantly better tolerated than regimens containing zidovudine or lopinavir/ritonavir. Effectiveness of the preferred alternative regimens is expected to be equivalent to other alternative regimens (Section VI. E: *Other Alternative Regimens*); however, effectiveness will differ if the source person's HIV strain is resistant to one or more of the agents.

TABLE 4
PREFERRED ALTERNATIVE PEP REGIMEN FOLLOWING NON-OCCUPATIONAL EXPOSURE

<p>Tenofovir^a 300 mg PO qd + Emtricitabine^{a,b} 200 mg PO qd</p> <p>Plus</p> <p>Darunavir 800 mg PO qd^c, <i>or</i> Atazanavir 300 mg PO qd^c, <i>or</i> Fosamprenavir 1400 mg PO qd^c</p> <p>and</p> <p>Ritonavir 100 mg PO qd^c</p>
<p>^a The dosing of lamivudine/emtricitabine, and tenofovir should be adjusted in patients with baseline creatinine clearance <50 mL/min (see Appendix A for dosing recommendations). Tenofovir should be used with caution in individuals with renal insufficiency or who are taking nephrotoxic medications. Fixed-dose combinations should not be used in patients who need dose adjustment due to renal failure.</p> <p>^b Lamivudine 300 mg PO qd may be substituted for emtricitabine. A fixed-dose combination is available when tenofovir is used with emtricitabine (Truvada 1 PO qd).</p> <p>^c See Appendix A for dosing recommendations for protease inhibitors in exposed persons with hepatic impairment.</p>

Potential for drug interactions in patients receiving PIs is increased due to the extensive cytochrome P450 interactions. For example, proton pump inhibitors may adversely affect the absorption of atazanavir. Clinicians should assess for potential interactions before prescribing a PEP regimen.

The following online resources provide information on antiretroviral drug interactions:

- *HIV-Drug-Drug Interactions*, available at: www.hivguidelines.org/clinical-guidelines/adults/hiv-drug-drug-interactions
- Department of Health and Human Services *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents*, available at: www.aidsinfo.nih.gov
- Johns Hopkins Poc-IT Center, available at: www.hopkinsguides.com/hopkins/ub
- University of Liverpool drug interactions site, available at: www.hiv-druginteractions.org
- PDR Network, available at: www.pdr.net
- Epocrates medical software, available at: www.epocrates.com

E. Other Alternative PEP Regimens

RECOMMENDATION:

Clinicians who continue to prescribe zidovudine for PEP should recognize and inform patients that the drug has significant side effects and that better-tolerated agents are available (see Appendix A for side effects associated with alternative PEP agents).

Other alternative PEP regimens are listed in Table 5 and may be acceptable in certain situations. For patients who are paying out of pocket, cost is a factor to weigh in selecting a regimen. The Department of Health and Human Services (DHHS) antiretroviral therapy guidelines provide a table of the monthly suggested wholesale price of each antiretroviral drug, available at: <http://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/282/arv-cost-table>

Use of lopinavir/ritonavir has greater potential for drug interactions and side effects than raltegravir or the preferred protease inhibitors (darunavir, atazanavir, or fosamprenavir; each taken with ritonavir 100 mg daily), with little added efficacy benefit expected. Recent studies have demonstrated decreasing protease inhibitor resistance among HIV strains,⁴⁷ suggesting that there may be diminishing benefit to choosing lopinavir/ritonavir for its activity against resistant HIV strains. The other recommended ritonavir-boosted PI regimens listed in Table 4 also have excellent activity against protease inhibitor-resistant strains and are better tolerated than lopinavir/ritonavir.

TABLE 5 ALTERNATIVE PEP REGIMENS FOLLOWING NON-OCCUPATIONAL EXPOSURE^a
<ul style="list-style-type: none"> • Tenofovir + Emtricitabine^b + Zidovudine • Tenofovir + Emtricitabine^b + Lopinavir/ritonavir • Zidovudine + Lamivudine^c + one of the following ritonavir-boosted protease inhibitors: Darunavir, Atazanavir, Fosamprenavir, or Lopinavir
<p>^a See Appendix A for full dosing information for alternative ARV agents that may be used in the PEP regimen. Also see <i>HIV Drug-Drug Interactions</i> for important drug interactions. Dosing interval of zidovudine should be adjusted in patients with baseline creatinine clearance <15 mL/min. The dosing interval of lamivudine, emtricitabine, and tenofovir should be adjusted in patients with baseline creatinine clearance <50 mL/min. (see Appendix A for dosing recommendations in patients with renal impairment). Fixed-dose combinations should not be used in patients who need dose adjustment due to renal failure.</p> <p>^b Lamivudine 300 mg PO qd may be substituted for emtricitabine. However, a fixed-dose combination is available when tenofovir is used with emtricitabine (Truvada 1 PO qd).</p> <p>^c Emtricitabine 200 mg PO qd may be substituted for lamivudine. However, a fixed-dose combination is available when zidovudine is used with lamivudine (Combivir 1 PO qd).</p>

The Committee recommends a three-drug regimen because of the greater likelihood of enhanced effectiveness; however, use of a two-drug regimen would be preferred to discontinuing the regimen completely if tolerability is a concern. An early case control study of occupational exposure demonstrated an 81% reduction in seroconversion with the use of zidovudine monotherapy alone,⁴⁸ suggesting that treatment with any active antiretroviral agent is beneficial in reducing risk.

F. Antiretroviral Drugs to Avoid as PEP Components

Table 6 lists antiretroviral drugs that are generally not recommended as components of PEP. Consultation with a clinician experienced in managing PEP is recommended before using any of the antiretroviral drugs listed in Table 6 (see Section VIII: *Non-Occupational PEP for the Pregnant Patient* for drugs to avoid in exposed persons who are pregnant or breastfeeding). If efavirenz is used in women of childbearing potential, a pregnancy test should be obtained before initiation and the woman should be counseled about the use of effective contraception while taking efavirenz.

TABLE 6
ANTIRETROVIRAL DRUGS TO AVOID AS PEP COMPONENTS

Drug(s) to Avoid	Rationale
Efavirenz	<ul style="list-style-type: none"> • Poor adherence anticipated due to CNS side effects, which are common • CNS side effects may impair work after the initial and subsequent doses • EFV should be avoided in first 6 weeks of pregnancy and in women of childbearing potential who are not using effective contraception • Substantial EFV resistance in community HIV isolates
Nevirapine	Contraindicated for use in PEP due to potential for severe hepatotoxicity ⁴⁹
Abacavir	Potential for hypersensitivity reactions
Stavudine, didanosine	Possibility of toxicities
Nelfinavir, indinavir	Poorly tolerated
CCR5 co-receptor antagonists	Lack of activity against potential CXCR4 tropic virus

Because of limited experience with the use of newer agents as components in a PEP regimen, consultation with a clinician experienced in HIV PEP management is recommended before using [new antiretroviral agents](#), such as rilpivirine and etravirine.

VII. FOLLOW-UP AND MONITORING FOLLOWING NON-OCCUPATIONAL EXPOSURE

RECOMMENDATIONS:

All patients receiving PEP should be re-evaluated within 3 days of the exposure to further clarify the nature of the exposure, review available source person data, evaluate adherence, and monitor toxicities associated with the PEP regimen. (AIII)

The exposed person should be evaluated weekly while receiving PEP to assess treatment adherence, side effects of treatment, interval physical complaints, and emotional status. (AIII) Longitudinal care of the exposed person during PEP treatment and the follow-up period should be provided by or in consultation with a clinician experienced in managing nPEP. Emergency Departments and urgent care centers should establish linkages with local HIV providers to facilitate easy referral of patients for follow-up care. Providers who do not have access to a clinician experienced in PEP should use the National Clinicians' Consultation Center PEpline at 1-888-HIV-4911 (1-888-448-4911) for phone consultation. When using the PEpline, providers from New York State should identify themselves as practicing in the State.

Clinicians should provide risk-reduction counseling to exposed persons to prevent secondary transmission during the 12-week follow-up period. HIV-exposed individuals should be advised to:

- **use condoms to prevent potential sexual transmission (AI)**
- **avoid pregnancy and breastfeeding (AI)**
- **avoid needle-sharing (AI)**
- **refrain from donating blood, plasma, organs, tissue, or semen (AI)**

During the PEP treatment period, other blood tests may be indicated to monitor for side effects of treatment. The timing and specific testing indicated varies based on the PEP regimen used (see Table 7).

Key Point:

Post-exposure care involves simultaneous attention to multiple issues: the emotional state of the exposed person, adherence to the PEP regimen, monitoring for potential adverse effects, and sequential HIV testing to determine infection status.

Clinicians should be aware of the resources within the community that offer medical and supportive counseling/adherence services needed following non-occupational exposure.

TABLE 7 MONITORING RECOMMENDATIONS AFTER INITIATION OF PEP REGIMENS FOLLOWING NON-OCCUPATIONAL EXPOSURES						
	Baseline	Week 1	Week 2	Week 3	Week 4	Week 12
Clinic Visit	√	√ Or by telephone	√ Or by telephone	√ Or by telephone	√	
Pregnancy Test	√					
Serum liver enzymes, BUN, creatinine, CBC^a	√		√		√	
HIV test^b	√				√	√
STI Screening (for exposures unrelated to sexual assault) ^b : <ul style="list-style-type: none"> • GC/CT NAAT (based on site of exposure) • RPR See HIV Prophylaxis for Victims of Sexual Assault for recommendations in cases of sexual assault.	√		√ (consider)			
Hepatitis B and C^b	For post-exposure management for hepatitis B and C, see Section IX: <i>Non-Occupational Exposures to Hepatitis B and C</i>					
^a CBC should be obtained for all exposed persons at baseline. Follow-up CBC is indicated only for those receiving a zidovudine-containing regimen.						
^b Recommended even if PEP is declined.						

A. Adherence to the PEP Regimen

Follow-up care is necessary for patients receiving PEP to monitor for adverse effects of the PEP regimen and to maximize adherence to the prescribed regimen. Adherence to a 28-day PEP regimen has historically been modest (40-60%),⁵⁰⁻⁵² although newer studies using tenofovir + either lamivudine or emtricitabine as components for PEP regimens show increased rates of adherence.^{40,41} Limited data show similar improved tolerability with tenofovir + emtricitabine plus raltegravir.^{42,43}

If the recommended regimen is not well tolerated, an *early* switch to an alternative regimen is encouraged to improve adherence. Again, consultation with a clinician experienced in managing PEP should occur when switching to an alternative regimen due to tolerability or resistance.

B. Sequential HIV Testing

RECOMMENDATIONS:

Sequential confidential HIV testing should be obtained at baseline, week 4, and week 12 post-exposure:

- **HIV testing at 6 months post-exposure is no longer recommended**
- **HIV testing of the exposed person at 4 weeks and 12 weeks should be performed with laboratory-based HIV tests rather than rapid point-of-care HIV tests**
- **If the post-exposure evaluation determined that PEP was indicated, but the exposed person declines PEP, serial testing should still be obtained (see Table 7)**

If at any time the HIV test result is positive, a confirmatory assay must be performed to confirm the diagnosis of HIV infection.

If the exposed person presents with signs or symptoms of acute HIV seroconversion, an HIV serologic screening test should be used in conjunction with a plasma HIV RNA assay to diagnose acute HIV infection. (AII) A fourth-generation HIV antigen/antibody combination test is the preferred serologic screening test if available. Immediate consultation with a clinician experienced in managing ART should be sought for optimal treatment options.

When individuals are potentially exposed to HIV, longitudinal medical follow-up is necessary regardless of whether PEP is initiated or completed, in order to test sequentially for HIV infection.

HIV seroconversion will generally occur within 2 to 4 weeks if HIV infection develops after an exposure. HIV testing at baseline, 4 weeks, and 12 weeks is recommended after significant exposures, regardless of whether the individual accepts or declines PEP treatment. Rapid point-of-care HIV tests are slightly less sensitive than laboratory-based HIV tests; therefore, exposed persons should be tested with laboratory-based HIV tests whenever possible.

HIV testing at 6 months after exposure is no longer recommended. Late seroconversion (i.e., after 3 months) has been rarely reported and has not been described since 1990.^{53,54} It is unclear if these rare events were related to the original or subsequent exposures. The Medical Care Criteria Committee believes that the benefit of routinely testing all exposed persons for HIV at 6 months is outweighed by the negative consequences of routinely extending post-exposure HIV follow-up testing to 6 months because of the infrequency of late seroconversion, the increased sensitivity of standard HIV tests to detect early infection and seroconversion, and the added anxiety and significant consequences of an additional 3 months of precautions and testing for exposed individuals.

Patients acutely infected with HIV will often experience at least some symptoms of the acute retroviral syndrome. Fever and flu- or mono-like symptoms are common in acute HIV infection but are nonspecific. Rash, mucocutaneous ulcers, oropharyngeal candidiasis, and meningismus are more specific. Symptoms may also include fatigue or malaise, joint pain, headache, loss of appetite, night sweats, myalgias, lymphadenopathy, oral and/or genital ulcers, nausea or diarrhea, or pharyngitis. Acute HIV infection is often not recognized in the primary care setting because of the similarity of the symptom complex with that of the flu or other common illnesses. When infection occurs, the ELISA antibody test will generally be positive within 3 weeks of the onset of symptoms and is virtually always positive within 3 months following exposure. A confirmatory Western blot may yield an indeterminate result during the early stages of seroconversion. When acute HIV seroconversion is suspected based on the clinical scenario, an HIV serologic screening test should be used in conjunction with a plasma HIV RNA assay to diagnose acute HIV infection. (AII) A fourth-generation HIV antigen/antibody combination test is the preferred serologic screening test if available.

See the following resources for more information:

- Characteristics of FDA-Approved Rapid HIV Tests for further information on available rapid HIV tests
- [Diagnosis and Management of Acute HIV Infection](#) for further information on management of acute HIV infection
- [AIDS Institute's Voluntary HIV Provider Directory](#) for referral for continued HIV care

VIII. NON-OCCUPATIONAL PEP FOR THE PREGNANT PATIENT

A. HIV-Exposed Women Who Are Pregnant

RECOMMENDATIONS:

Based on increasing clinical experience with ART, nPEP is indicated at any time during pregnancy when a significant exposure has occurred, despite possible risk to the woman and the fetus. (AII) Expert consultation should be sought. When non-occupational exposure to HIV occurs, every effort should be made to initiate PEP as soon as possible, and ideally within 2 hours. The recommended PEP regimen is the same for pregnant women as for non-pregnant adults (AII) (see Section VI: *Recommended nPEP Regimens*).

Before administering nPEP to a pregnant woman, the clinician should discuss the potential benefits and risks to her and to the fetus. (AIII)

Pregnant women presenting for nPEP as a result of risky behavior should be the focus of intensified education and prevention interventions. (AII) After completion of the 28-day nPEP regimen, initiation of pre-exposure prophylaxis (PrEP) should be considered. (AI) See the CDC interim guidance documents for use of pre-exposure prophylaxis in [heterosexually active adults](#).

The agents listed in Table 8 are all not recommended for use in PEP regimens and are not likely to be used; however, clinicians should be aware that these agents should *not* be prescribed in pregnant women. Initiation of PEP at any time during pregnancy requires a careful discussion of the risks and benefits.

TABLE 8 HIV DRUGS TO AVOID DURING PREGNANCY	
Drug(s) to Avoid	Toxicity
Efavirenz	Teratogenicity
Combination of stavudine and didanosine	Mitochondrial toxicity
Nevirapine	Hepatotoxicity
Unboosted IDV in the 2nd or 3rd trimester	Substantially lower antepartum indinavir plasma concentrations; risk for nephrolithiasis

Key Point:

In addition to the risk of seroconversion for the exposed person, the high viral load levels associated with the acute retroviral syndrome markedly increase the risk of transmission to the fetus or breastfeeding infant.

Although birth defects and adverse effects on human fetuses have generally not been associated with the antiretroviral agents that are currently available, exposure of a fetus to antiretroviral agents during pregnancy carries a theoretical risk of embryotoxicity.

B. HIV-Exposed Women Who Are Breastfeeding

RECOMMENDATION:

Clinicians should advise women who may have been exposed to HIV through non-occupational exposure to avoid breastfeeding for 3 months after the exposure. (AII) If HIV infection is definitively excluded in the source person at any time prior to 3 months postexposure, breastfeeding can be resumed. (AI)

Initiation of PEP in exposed women who are breastfeeding requires careful discussion. Both HIV and antiretroviral drugs may be found in breast milk; therefore, breastfeeding should be avoided for 3 months after the exposure to prevent HIV transmission and potential drug toxicities.⁵⁵ Clinicians should discuss the risks and benefits with the woman. The infant’s pediatrician should be informed of any potential exposure to HIV or antiretroviral medications.

IX. NON-OCCUPATIONAL EXPOSURES TO HEPATITIS B AND C

RECOMMENDATION:

When a non-occupational exposure occurs, and the source is available, the source should be evaluated for both hepatitis B and hepatitis C. (AII)

A. Hepatitis B Virus Post-Exposure Management

RECOMMENDATIONS:

The hepatitis B vaccine series should be initiated in *non-HBV-immune* persons who sustain a blood or body fluid exposure. (AI) Decision-making should not be delayed while testing for anti-HBs. If antibody response is unknown, follow recommendations for “antibody response unknown” in Table 9.

Administration of prophylactic hepatitis B immune globulin (HBIG) and the initiation of the hepatitis B vaccine series injected at different sites is recommended when the non-HBV-immune person sustains a blood or body fluid exposure to a source person with known acute or active HBV (see Table 9). (AI) Both HBIG and the first dose of the hepatitis B vaccine series should be ideally administered within 24 hours of exposure (AII); HBIG should not be given later than 14 days post-exposure. The three-dose HBV vaccine series is given at 0, 1 to 2 months, and 6 months. Hepatitis B antibodies should be obtained 1 to 2 months after completion of the third dose of the vaccine.

Needlestick injuries and wounds should be washed with soap and water and should not be squeezed. Mucous membranes should be flushed with water. (AIII)

Initiation of the HBV vaccine series within 12 to 24 hours of an exposure has been demonstrated to be 70% to 90% effective in preventing HBV infection. The combination of vaccine and HBIG achieves a similar level of efficacy. Among known non-responders to vaccination, one dose of HBIG is 70% to 90% effective in preventing HBV when administered within 7 days of percutaneous HBV exposure,⁵⁶ and multiple doses have been shown to be 75% to 95% effective.⁵⁷ The maximum effective interval for prophylaxis is likely within 14 days for sexual exposure.⁵⁸⁻⁶² Pregnant women can safely receive both the HBV vaccination and HBIG.

When considering nPEP for HBV exposures, both the source’s HBsAg status and the exposed person’s vaccination status should be considered (see Table 9).

Key Point:

Determination of antibody response of previously vaccinated exposed persons should be based on information available at presentation. It is not recommended that decision-making be delayed while testing for anti-HBs. If antibody response is unknown, follow recommendations for “antibody response unknown” in Table 9.

Both HBIG and the first dose of the hepatitis B vaccine should be ideally administered within 24 hours of exposure; HBIG should not be given later than 14 days post-exposure. The three-dose HBV vaccine series is given at 0, 1 to 2 months, and 6 months. Hepatitis B antibodies should be obtained 1 to 2 months after completion of the third dose of the vaccine.

Even if the risk of exposure to HBV is not deemed significant, HBV vaccination should still be advised for all non-HBV-immune persons (see [Hepatitis B Virus](#) guidelines for more information). Household, sex, and needle-sharing contacts of HBsAg-positive individuals should be identified and vaccinated according to the guidelines for patients exposed to known HBsAg-positive individuals.

TABLE 9
RECOMMENDED POST-EXPOSURE PROPHYLAXIS FOR HEPATITIS B VIRUS

Vaccination and/or antibody response status of exposed patient ^a	Treatment when source patient is:		
	HBsAg positive	HBsAg negative	Source unknown or not available for testing
Unvaccinated/non-immune	HBIG ^b ×1; initiate HB vaccine series	Initiate HB vaccine series	Initiate HB vaccine series
Previously vaccinated, ^c known responder ^d	No treatment	No treatment	No treatment
Previously vaccinated, ^c known non-responder ^d	HBIG ^b ×1 and initiate revaccination ^e or HBIG ^b ×2	No treatment	No treatment unless known high-risk source; if high-risk source, ^f then treat as if source were HBsAg positive
Previously vaccinated, ^c antibody response unknown	Single vaccine booster dose	No treatment	No treatment unless known high-risk source; if high-risk source, ^f then treat as if source were HBsAg positive
If still undergoing vaccination	HBIG ^b ×1; complete series	Complete series	Complete series

HBsAg, hepatitis B surface antigen; HBIG, hepatitis B immune globulin; anti-HBs, antibody to hepatitis B surface antigen.

^a Persons who have previously been infected with HBV are immune to re-infection and do not require PEP.

^b Dose 0.06 mL/kg intramuscularly.

^c Vaccinated with full three-dose series.

^d Based on information available at presentation. Responder is defined as person with previously documented adequate levels of serum antibody to HBsAg (serum anti-HBs >10mIU/mL); non-responder is a person with previously documented inadequate response to vaccination (serum anti-HBs <10mIU/mL). It is not recommended that decision-making be delayed while testing for anti-HBs at presentation.

^e The option of giving one dose of HBIG and re-initiating the vaccine series is preferred for non-responders who have not completed a second three-dose vaccine series. For persons who previously completed a second vaccine series but failed to respond, two doses of HBIG are preferred.

^f High-risk is defined as sources who engage in needle-sharing or high-risk sexual behaviors, and those born in geographic areas with HBsAg prevalence of ≥2%.⁶³

B. Hepatitis C Virus Post-Exposure Management

RECOMMENDATIONS:

Clinicians should consider concurrent exposure to HCV when individuals present with an HIV exposure. (AII)

Neither immunoglobulin nor antiviral agents are recommended for HCV post-exposure prophylaxis. (AII)

When HCV infection is identified, the exposed person should be referred for medical management to a gastroenterologist or other clinician with experience in treating HCV. (AII)

Currently, no effective prophylaxis for HCV has been identified. Immunoglobulin and antiviral agents are not recommended for HCV post-exposure prophylaxis. However, if an individual becomes acutely infected with hepatitis C and is diagnosed at that time, immediate referral to a specialist experienced in the treatment of hepatitis C is strongly recommended. Recent data suggest that early treatment of acute hepatitis C with interferon is highly effective, perhaps as high as 98%.⁶⁴ The best regimen or duration of therapy is unknown. However, observation for a period of 8 to 12 weeks post-infection is reasonable to assess for possible spontaneous resolution of acute hepatitis C.⁶⁵ Whether standard interferon or pegylated-interferon with or without ribavirin is used will depend on the individual scenario, as there have been no randomized, controlled trials to guide this decision.

1. Baseline Management

RECOMMENDATIONS:

Following an exposure to blood or body fluid, the clinician should assess the risk for exposure to HCV. (AII) Wounds should be washed with soap and water, and should not be squeezed. (AII) Mucous membranes should be flushed with water.

Once the clinician has determined that exposure to blood or body fluid has occurred, the following baseline tests should be obtained (AII) (see Table 10 for follow-up according to baseline results):

Exposed Person:

- **HCV antibody, and if positive, HCV RNA test**
- **Liver panel including liver enzymes**

Source Patient:

- **HCV antibody test (e.g., EIA/ELISA), and if positive, HCV RNA test**

If the source patient is tested with an EIA/ELISA and found to be positive, then follow-up testing is necessary to confirm the source person's status. HCV RNA may be used as the confirmatory test. When the source person tests positive with an HCV RNA test, the exposed person should be managed as if the source has chronic HCV.

TABLE 10
HEPATITIS C POST-EXPOSURE MANAGEMENT ACCORDING TO
BASELINE TEST RESULTS

Clinical Scenario	Follow-Up^a
Source is HCV-antibody negative	No further testing or follow-up is necessary for source or the exposed person ^b
Source is unavailable or refuses testing	Exposed person: Follow-up HCV antibody at 3 and 6 months ^b
Source is HCV-antibody positive and HCV RNA negative	Manage the exposed person as if the source has chronic hepatitis C (see Section IX. B. 2: <i>Post-Exposure Follow-Up for HCV</i>) ^c
Source is positive for both HCV antibody and HCV RNA <i>and</i> Exposed person is HCV-antibody negative	Source: Counsel and manage as chronic hepatitis C regardless of status of exposed person Exposed person: Follow up as outlined in Section IX. B. 2: <i>Post-Exposure Follow-Up for HCV</i>
Exposed person tests positive for both HCV antibody and HCV RNA	Counsel and manage as chronic hepatitis C
^a Refer to Appendix E for information about HCV tests and how to interpret results. ^b If at any time the serum ALT level is elevated in the exposed person, the clinician should test for HCV RNA to assess for acute HCV infection. ^c A single negative HCV RNA result does not exclude active infection.	

Clinicians should educate exposed persons about the natural history of HCV infection and should counsel exposed persons about the following:

- **Avoidance of alcohol and, if possible, medications that may be toxic to the liver**
- **Risk of transmission related to:**
 - Blood-to-blood contact, including sharing personal care items that may have come in contact with another person’s blood, such as razors or toothbrushes; occupational needlestick injuries; and sharing needles, syringes, or other equipment to inject drugs
 - Sexual activity
 - Donating blood, plasma, organs, tissue, or semen
 - Perinatal transmission
- **Hepatitis C virus is not spread via food or water and is not transmitted by:**
 - Sharing eating utensils
 - Hugging, kissing, or holding hands
 - Coughing or sneezing
 - Breastfeeding: HCV is not transmitted by breastfeeding; however, clinicians should advise women who may have been exposed to HIV to avoid breastfeeding for 3 months after the exposure⁵⁵

Factors that may increase the risk of sexual transmission include sex with multiple partners, history of STIs, including HIV, or any other practice that might disrupt mucous membranes. The potential need for mental health counseling should be anticipated and offered as needed.

2. Post-Exposure Follow-Up for HCV

RECOMMENDATIONS:

If the source is known to be positive for HCV antibody and/or HCV RNA, the follow-up schedule for the exposed person should be as follows (AII):

Week 4:	HCV RNA and liver panel
Week 12:	HCV RNA and liver panel
Week 24:	Liver panel and HCV antibody

If at any time the serum ALT level is elevated, the clinician should repeat HCV RNA testing to confirm acute HCV infection. (AIII)

At any time that exposed persons test positive for HCV RNA, the clinician should refer for medical management and possible treatment by a clinician with experience in treating HCV. (AIII)

For persons exposed to a hepatitis C-infected source, regular follow-up with HCV RNA testing is recommended in addition to HCV antibody testing, because HCV RNA testing can identify acute infection within 2 weeks of exposure, whereas accuracy of the antibody test can be delayed up to several months after acute infection (i.e., “window period”). Seroconversion with the ELISA antibody test occurs in 50% of patients who are infected within 9 weeks of exposure, in 80% of patients within 15 weeks of exposure, and in at least 97% of patients within 6 months of exposure.⁶⁶ The ELISA test is highly sensitive but relatively nonspecific, resulting in a low positive predictive value in low-prevalence populations. Positive HCV ELISA antibody test results require confirmation by a quantitative viral load assay, such as HCV PCR.

X. RESOURCES FOR CONSULTATION

Persons who have responsibility for providing nPEP may need expert advice and consultation, as well as assistance in helping their clients obtain medication.

The following resources are the preferred initial contacts for expert consultation:

- The National Clinicians' Consultation Center PEpline at 1-888-HIV-4911 (1-888-448-4911). When using the PEpline, providers from New York State should identify themselves as practicing in the State.

For providers in New York State:

- For further education of health providers or for consultation regarding setting up PEP services, contact: [CEI PEP, Testing and Diagnosis Center](#)
- To obtain the NYSDOH protocol for sexual assault victims, call the NYSDOH Rape Crisis Program at 518-474-3664.

For information about rape crisis services, see [HIV Prophylaxis for Victims of Sexual Assault](#).

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APPENDIX A. ANTIRETROVIRAL DRUGS

The medications listed below include antiretroviral agents recommended for PEP (tenofovir, emtricitabine, raltegravir) as well as alternative antiretroviral drugs that may be used in the setting of potential HIV resistance, toxicity risks, or constraints on the availability of particular agents. For information on all antiretroviral medications, see [Antiretroviral Therapy](#).

More information about these antiretroviral agents, including dosage and dose adjustment, potential adverse events and drug interactions, and FDA pregnancy categories, can be found in [Antiretroviral Therapy](#), Appendix A: Characteristics of Antiretroviral Drugs. Before using these drugs, package inserts should also be consulted.

Recommended PEP Medications:

[Tenofovir \(TDF\)](#)

[Emtricitabine \(FTC\)](#)

[Raltegravir \(RAL\)](#)

[Lamivudine \(3TC\)](#) – *equivalent substitute for emtricitabine*

Alternative PEP Medications:

[Atazanavir \(ATV\)](#)

[Lopinavir/ritonavir \(LPV/r\)](#)

[Darunavir \(DRV\)](#)

[Fosamprenavir \(FPV\)](#)

[Zidovudine \(ZDV\)](#)

APPENDIX B. PROBABILITY OF ACQUIRING HIV FROM A KNOWN HIV-INFECTED SOURCE

Estimated Per-Act Probability of Acquiring HIV from a Known HIV-Infected Source by Exposure Act and Factors that May Increase Risk		
Type of Exposure	Risk per 10,000 Exposures	Reference
<u>Parenteral</u>		
Blood Transfusion	9,000	Refs 1-3
Needle-sharing during injection drug use	67	
Percutaneous (needlestick)	30	
<i><u>Factors Associated with Increased Risk of HIV Transmission from Needlesharing/Needlestick Injuries</u></i>		
<ul style="list-style-type: none"> • Source person is known to be HIV-infected and is not receiving ART or has incomplete viral suppression; the risk of transmission increases with higher HIV viral load levels in the source person^{4,5} • Hollow-bore needle • Deep skin penetration • Presence of blood on needle; however, risk through exposure to dried blood on discarded needles is extremely low⁶ 		
<u>Sexual</u>		
Type of Exposure	Risk per 10,000 Exposures	Reference
Receptive anal intercourse	50	Refs 7, 8
Receptive penile-vaginal intercourse	10	Refs 7-9
Insertive anal intercourse	6.5	Refs 7, 8
Insertive penile-vaginal intercourse	5	Refs 7, 8
Receptive oral intercourse	Low ^a	Refs 7, 10
Insertive oral intercourse	Low ^a	Ref 7
<i><u>Factors Associated with Increased Risk of Transmission from Sexual Exposure</u></i>		
<ul style="list-style-type: none"> • Source person is known to be HIV-infected and is not receiving ART or has incomplete viral suppression; the risk of transmission increases with higher HIV viral load levels in the source person^{4,5}, most notably during acute HIV infection when the probability of transmission has been shown to be 8- to almost 12-fold higher than exposures that take place after the viral set point^{11,12} • Lack of use of barrier protection, such as male or female condoms • Presence of genital ulcer disease or other STIs^{13,14} • Trauma at the site of exposure • Blood exposure — it is important to note that blood exposure can be minimal and therefore not recognized by the exposed person. If the exposed person reports frank blood exposure, PEP would be indicated • Lack of male circumcision^{15,16} • Cervical ectopy¹⁷ • Oral mucosa is not intact (e.g., oral lesions, gingivitis, wounds) – <i>for oral sex exposure</i> 		

Table continues...

<u>Other^b</u>		
Type of Exposure	Risk per 10,000 Exposures	Reference
Biting	Negligible	Ref 18
Spitting	Negligible	
Throwing body fluids (including semen or saliva)	Negligible	
Sharing sex toys	Negligible	
<i>Factors Associated with Increased Risk of Transmission from Otherwise Negligible-Risk Exposures</i>		
<ul style="list-style-type: none"> • Source person is known to be HIV-infected with high HIV viral load^{4,5} • Activity involved exposure to blood 		
<p>Modified from the Centers for Disease Control and Prevention. HIV Transmission Risk, fact sheet; July 2012. Available at http://www.cdc.gov/hiv/law/transmission.htm</p> <p>^a HIV transmission through oral sex has been documented, but rare. Accurate estimates of risk are not available. It is prudent to recommend nPEP for receptive oral sex with ejaculation, although discussion about the low risk should occur.</p> <p>^b HIV transmission through these exposure routes is technically possible but extremely unlikely and cases are not well documented.</p>		

APPENDIX B REFERENCES

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APPENDIX C. AIDS INSTITUTE-FUNDED HIV PREVENTION COUNSELING PROGRAMS

AIDS INSTITUTE-FUNDED NEW YORK STATE HIV PREVENTION COUNSELING PROGRAMS

The following link contains information about how to contact an AIDS Institute-funded HIV prevention program that provides risk-reduction counseling:

<http://www.hivguidelines.org/wp-content/uploads/2013/04/ai-funded-nys-hiv-prevention-counseling-programs-04-15-2013.pdf>

APPENDIX D. NPEP PAYMENT OPTIONS

PAYMENT OPTIONS FOR POST-EXPOSURE PROPHYLAXIS FOLLOWING NON-OCCUPATIONAL EXPOSURES INCLUDING SEXUAL ASSAULT

The following link lists payment options that may be available for both sexual assault and non-sexual assault exposures.

<http://www.hivguidelines.org/wp-content/uploads/2013/06/npep-payment-options-05-22-2013.pdf>

APPENDIX E. RECOMMENDATIONS FOR INTERPRETING RESULTS OF TESTING FOR ANTIBODY TO HEPATITIS C VIRUS (ANTI-HCV)

RECOMMENDATIONS FOR INTERPRETING RESULTS OF TESTING FOR ANTIBODY TO HEPATITIS C VIRUS (ANTI-HCV) BY TYPE OF REFLEX SUPPLEMENTAL TESTING PERFORMED			
Anti-HCV screening test results	Supplemental test results	Interpretation	Comments
Screening-test-negative*	Not applicable	Anti-HCV-negative	Not infected with HCV, unless recent infection is suspected or other evidence exists to indicate HCV infection
Screening-test-positive* with high signal-to-cut-off (s/co) ratio	Not done	Anti-HCV-positive	Probably indicates past or present HCV infection; supplemental serologic testing not performed. Samples with high s/co ratios usually ($\geq 95\%$) confirm positive, but < 5 of every 100 might represent false-positives; more specific testing can be requested, if indicated
Screening-test-positive	Nucleic acid test (NAT)-positive	Anti-HCV-positive, HCV RNA-positive	Indicates active HCV infection
Screening-test-positive	NAT-negative	Anti-HCV-positive, HCV RNA-negative	The presence of anti-HCV indicates past or present HCV infection; a single negative HCV RNA result does not rule out active infection; repeat HCV RNA testing should be performed after 3 to 6 months to confirm initial negative RNA test

From Centers for Disease Control and Prevention. Guidelines for Laboratory Testing and Result Reporting of Antibody to Hepatitis C Virus. *MMWR Recomm Rep* 2003;52(RR03):1-16. Available at: www.cdc.gov/mmwr/preview/mmwrhtml/rr5203a1.htm

*Screening immunoassay test results interpreted as negative or positive on the basis of criteria provided by the manufacturer.