Management of nonoccupational exposures to HIV and hepatitis B and C in adults

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INTRODUCTION

Patients who are potentially exposed to human immunodeficiency virus (HIV), hepatitis B virus (HBV), or hepatitis C virus (HCV) through a nonoccupational exposure or injury are at risk for acquiring one of these infections. Patients can be exposed through sexual contact or through exposure to infected blood (or blood-contaminated body fluids). Post-exposure prophylaxis (PEP) for HIV and HBV may reduce the risk of transmission if administered soon after the exposure. By contrast, there are no medications or immunizations to reduce the risk of acquiring HCV.

The management of adults with a potential nonoccupational exposure to HIV, HBV, and HCV are reviewed here. Discussions related to the management of occupational exposures and the prevention of mother-to-child transmission of these pathogens are found elsewhere:

- (See "Prevention of hepatitis B virus and hepatitis C virus infection among health care providers".)
- (See "Management of health care personnel exposed to HIV".)

- (See "Antiretroviral selection and management in pregnant individuals with HIV in resource-abundant settings".)
- (See "Prevention of vertical HIV transmission in resource-limited settings".)
- (See "Hepatitis B and pregnancy".)
- (See "Vertical transmission of hepatitis C virus".)

INITIAL MANAGEMENT

Wound care — For patients with a possible exposure to blood or body fluids after a needlestick injury or a skin or mucous membrane exposure, it is important to clean the wound. Discussions of wound management are found elsewhere. (See "Management of health care personnel exposed to HIV", section on 'Initial actions following exposure' and "Prevention of hepatitis B virus and hepatitis C virus infection among health care providers", section on 'Wound care'.)

Assessing the exposure risk — Patients should be evaluated after a possible exposure to HIV, hepatitis B virus (HBV), or hepatitis C virus (HCV) to determine the risk of viral transmission. This will impact the approach to post-exposure prophylaxis (PEP) and monitoring. (See 'HIV post-exposure management' below and 'Hepatitis B post-exposure management' below and 'Hepatitis C post-exposure management' below.)

The risk of transmission after an exposure depends upon both the exposed and the source's status, as well as the specific exposure. As examples:

- **HIV** – HIV infection is acquired through sexual contact, exposure to infected blood (including blood-contaminated body fluids), or perinatal transmission. The distribution of the modes of transmission of HIV infection varies in different countries. In the United States, male-to-male sexual contact and injection drug use account for more than half of cases [1]. In contrast, in certain resource-limited areas (eg, Sub-Saharan Africa), penile-vaginal intercourse is responsible for 70 to 80 percent of HIV infections [2,3].

  The risk of HIV infection varies by the type of sexual or parenteral exposure (table 1). Risk factors for HIV transmission also include the HIV viral load (eg, an HIV RNA ≥1000 copies/mL in the source, with the risk of transmission increasing with increasing viral load) [4], the presence of sexually transmitted infections (STIs), lack of circumcision, and certain host and genetic factors [5-7].

A detailed discussion of HIV transmission is found elsewhere. (See "HIV infection: Risk factors and prevention strategies", section on 'Risk factors for infection'.)

- **HBV** – Most adults who acquire HBV do so through sexual or percutaneous exposures. Transmission between discordant sexual partners ranges from 18 to 44 percent. The risk of acquiring HBV through a percutaneous exposure has been reported to be approximately 30 percent if the source has chronic HBV [8]. Additional discussions of HBV transmission are found elsewhere. (See "Epidemiology, transmission, and prevention of hepatitis B virus infection", section on 'Transmission of HBV' and "Prevention of hepatitis B virus and hepatitis C virus infection among health care providers", section on 'Risk of acquisition following exposure'.)

- **HCV** – Most patients infected with HCV in the United States and Europe acquire the disease through parenteral exposure (eg, injection drug use). Although the risk of sexual transmission appears to be low, among men who have sex with men (MSM) certain sexual practices, such as condomless receptive anal sex with internal ejaculation, carry a higher risk of transmission [9,10]. A 2020 meta-analysis estimated a 3.4 percent global prevalence of HCV among MSM with the greatest burden in Africa and Southeast Asia and an estimated global incidence (per 1000 person-years) of 0.12, 14.80, and 8.46 in HIV-negative MSM not on HIV PrEP, HIV-negative MSM on HIV PrEP, and MSM with HIV, respectively [9]. A more detailed discussion of HCV transmission is presented elsewhere. (See "Epidemiology and transmission of hepatitis C virus infection", section on 'Routes of transmission'.)

For those with a high-risk exposure to HIV or HBV, PEP should be offered to reduce the risk of HIV or HBV transmission. Indications for HIV and HBV PEP based on exposure risk are discussed below. (See 'Indications for HIV post-exposure prophylaxis (PEP)' below and 'Indications for HBV PEP' below.)

There are no medications or immunizations to reduce the risk of acquiring HCV after a possible exposure. However, close monitoring after the exposure allows early diagnosis and treatment. (See 'Hepatitis C post-exposure management' below.)

Laboratory testing — In most situations, the HIV, HBV, and HCV status of the exposed patient and source are not known at the time of presentation. For exposed patients (and sources whenever possible), this information should be obtained at the time of presentation. However, initial treatment decisions should be made based upon the nature of the exposure, even in the absence of immediate test results. (See 'Indications for HIV post-exposure prophylaxis (PEP)' below and 'Indications for HBV PEP' below.)

HIV testing — When HIV testing is performed, a rapid laboratory-based antigen/antibody assay that detects HIV p24 antigen **and** HIV antibodies should be used whenever possible. (See "Screening and diagnostic testing for HIV infection in adults", section on 'Combination HIV antigen and antibody tests'.)

- **Determining the HIV status of the exposed person** – Rapid HIV testing should be performed on all persons seeking evaluation after a potential nonoccupational HIV exposure. The preferred three-drug regimens for nonoccupational post-exposure prophylaxis (nPEP) are adequate for both treatment and prevention of HIV, so early initiation of a three-drug regimen pending laboratory results is appropriate. (See 'Indications for HIV post-exposure prophylaxis (PEP)' below and 'Regimen selection' below.)

- **Determining the HIV status of the source** – If the source is known and is willing, they should be tested for HIV (algorithm 1 and algorithm 2). In most scenarios, a negative rapid HIV test negates the need for continued nPEP. However, if there is concern that the source is acutely infected with HIV, additional RNA testing should be performed since HIV screening tests (eg, antibody/antigen or antibody only) may not detect acute HIV infection. (See "Acute and early HIV infection: Clinical manifestations and diagnosis".)

  If the source is known to have HIV, they should be interviewed, if possible, to determine their HIV treatment history, and the results of their most recent viral load and resistance tests. In addition, we repeat an HIV viral load and genotype at time of exposure whenever possible. This information will provide guidance regarding the need for continued nPEP and/or which regimen should be administered. (See 'Duration of HIV PEP' below and 'Regimen selection' below.)

Testing for hepatitis B and C virus — All patients should be evaluated for HBV and HCV infection after a percutaneous (eg, bite or needlestick) or mucosal exposure to blood or infectious secretions (eg, semen, vaginal secretions, or any body fluids that contain blood). (See 'Hepatitis B post-exposure management' below and 'Hepatitis C post-exposure management' below.)

- **Determining the HBV and HCV status of the exposed patient**

  - **Testing for HBV** – Determining the HBV status of the exposed patient is important for determining the approach to HBV PEP, as discussed below. (See 'Indications for HBV PEP' below.)

If the exposed patient's HBV status is unknown, we test for hepatitis B surface antigen (HBsAg), hepatitis B core antibody (anti-HBc), and hepatitis B surface antibody (anti-HBs). If the exposed patient may require hepatitis B immune globulin (HBIG) for prophylaxis (algorithm 3), this testing should be performed before HBIG is administered. (See 'Approach to HBV prophylaxis' below.)

In addition to determining the need for HBV PEP, the presence of chronic HBV infection (HBsAg-positive), may impact HIV PEP. Tenofovir and emtricitabine are typically included in HIV nPEP regimens, and both are active against HBV as well as HIV. Discontinuing nPEP in patients with chronic HBV, particularly those with cirrhosis, may lead to a flare of their HBV infection. Patients with chronic HBV should be evaluated to see if antiviral therapy for treatment of HBV should be continued after they have completed the 28-day course for nPEP. If treatment is discontinued, such patients should be monitored closely. (See "Hepatitis B virus: Overview of management".)

- **Testing for HCV** – If the exposed patient has no history of HCV infection, we obtain a baseline HCV antibody. We also obtain an HCV viral load if the patient has signs and symptoms of acute HCV infection (eg, elevated aminotransaminase levels) or has a partner who is known to have HCV infection.

  If the exposed patient was treated for HCV in the past, HCV RNA should be obtained rather than an antibody. Such patients are still at risk for reinfection, even if the HCV antibody is positive.

- **Determining the HBV and HCV status of the exposed patient** – If the source's status is unknown, they should also be tested for HBV and HCV, if possible [11] (table 2). For HBV, they should have the same testing as the exposed patient. For HCV, the source should be tested for HCV RNA; if HCV RNA testing not readily available, the source can be tested for HCV antibody and, if positive, have subsequent testing for HCV RNA [12].

Additional considerations after a sexual exposure — After a high-risk sexual exposure, sexual assault survivors should be empirically treated for STIs without testing. (See "Evaluation and management of adult and adolescent sexual assault victims in the emergency department".)

Other patients should be offered testing for STIs, such as gonorrhea, chlamydia, and syphilis. Gonorrhea and chlamydia testing of the oropharynx, genitals, and rectum should be offered. Patients receiving nPEP have been found to be at high risk for STIs [13]. A detailed discussion of screening for STIs (including which sites should be tested) is found elsewhere. (See "Screening for sexually transmitted infections".)

Women with child-bearing potential should have pregnancy testing, and if negative, emergency contraception should be offered. (See "Emergency contraception".)

HIV POST-EXPOSURE MANAGEMENT

Post-exposure prophylaxis (PEP) for HIV involves administering an HIV antiretroviral regimen for a finite period after a known or possible exposure to HIV. Although data are limited, PEP continues to be recommended by most experts after a high-risk exposure given the potential benefits of treatment and the low risk of available therapies [11,14-20].

Indications for HIV post-exposure prophylaxis (PEP) — The indications for HIV PEP depend upon the type of exposure and when the exposure occurred. Additional information on the timing of nonoccupational post-exposure prophylaxis (nPEP) is discussed below. (See 'When to initiate HIV PEP' below.)

Approach for most patients — Nonoccupational post-exposure prophylaxis (nPEP) should be considered for patients who present within 72 hours of having sexual or percutaneous exposure to a source with HIV, or unknown HIV status, if the exposure presents a substantial risk of HIV acquisition (algorithm 1 and algorithm 2 and table 1).

High-risk exposures include condomless receptive or insertive anal or vaginal intercourse, a percutaneous exposure to blood or body fluids contaminated with blood (this includes use of contaminated syringes), and/or exposure of blood or body fluids contaminated with blood to nonintact skin.

Our approach to initiating HIV nPEP depends in part on the HIV status of the source.

- **Source with HIV** – We suggest initiating nPEP if the source has HIV, regardless of source patient's viral load (algorithm 2). This is particularly important if the source is known to have a viral load >1,000 copies/mL, as viral loads above this threshold are associated with an increased risk of HIV transmission [4]. (See 'Assessing the exposure risk' above.)

  After nPEP has been initiated, if the source is available and willing, an HIV viral load should be collected. In some settings, nPEP can be discontinued, depending upon the results. (See 'Duration of HIV PEP' below.)

- **Source with unknown HIV status** – When the HIV status of the source is unknown, we suggest nPEP in the following settings (algorithm 1):

  - The source is at high risk for having HIV (eg, man who has sex with men [MSM], person who uses injection drugs, someone who engages in sex work, person who lives in a high-prevalence area). (See "HIV infection: Risk factors and prevention strategies".)

    Some patients may desire nPEP if they had an exposure to a source whose HIV risk factors are unknown. To help inform this decision, we discuss the patient's exposure risk, such as the route of exposure (table 1), and other cofactors that heighten risk of transmission (eg, presence of genital ulcer disease).

  - The patient was sexually assaulted. A more detailed discussion of the management of sexual assault victims is found elsewhere. (See "Evaluation and management of adult and adolescent sexual assault victims in the emergency department", section on 'Management'.)

  If the indications for nPEP are unclear, clinicians can call the National Clinician's Post-Exposure Prophylaxis Hotline at 888-448-4911 for expert advice.

Certain patients may repeatedly present with exposures that qualify for nPEP. For such patients, we try to avoid repeated courses of nPEP, and we discuss the possibility of transitioning from a post-exposure regimen to pre-exposure prophylaxis (PrEP) to reduce the risk of subsequent HIV infection [11,21]. (See "HIV pre-exposure prophylaxis", section on 'Determining eligibility for prep' and "HIV pre-exposure prophylaxis", section on 'Persons receiving post-exposure prophylaxis'.)

PEP was first evaluated in pregnant women to decrease the risk of mother-to-child transmission and in health care personnel who had accidental needlestick exposures [22-25]. Among such patients, PEP with zidovudine alone reduced transmission by 70 to 80 percent.

Placebo-controlled clinical trials of PEP for nonoccupational HIV exposures have not been performed [11]. Available data supporting the efficacy of antiretroviral therapy for nPEP are limited to animal studies and observational data [26-33]. Observational studies of patients who were offered nPEP for HIV prevention after sexual exposure suggest there is a benefit [27,32,33]; however, conclusions are limited because of the design of the studies and small sample sizes.

Considerations for persons taking PrEP — Patients who are taking PrEP typically do not require additional PEP for HIV unless they report taking their medication sporadically or, if on oral PrEP, have not taken their PrEP regimen within the week before the exposure [21].

Nonoccupational post-exposure prophylaxis (nPEP) should also be considered in patients taking PrEP if the source is known to have HIV and has confirmed resistance to the nPEP regimens [11,21]. (See 'Preferred regimens' below and 'Special considerations' below.)

When to initiate HIV PEP — Nonoccupational post-exposure prophylaxis (nPEP) should be given within 72 hours of an exposure. Once the need for nPEP has been identified, the patient should receive an immediate dose. The first dose should not be delayed pending HIV testing of either the exposed patient or the source. (See 'Laboratory testing' above.)

Animal data suggest that there is a small window of opportunity to interrupt HIV transmission. A meta-analysis that included data from 25 nonhuman primate studies found a significant association between timing of PEP and reduced seroconversion after exposure to a closely related virus, simian immunodeficiency virus (SIV) [34]. In an early study of 24 macaques who received post-exposure prophylaxis with a tenofovir disoproxil fumarate prodrug (PMPA), there was no evidence of viral replication if treatment was started within 24 hours of exposure; however, the efficacy of PEP decreased when the time between exposure and treatment was extended [35].

Regimen selection — There are limited data on the relative efficacy of nPEP regimens. Regimens are chosen based upon side effect profiles, patient convenience (eg, pill burden and dosing frequencies), drug interactions, penetration into the genital compartment [36-38], and completion rates [39,40].

The approach to regimen selection for nPEP may differ somewhat from the approach used after an occupational exposure, given the potential need for penetration into genital tract. The approach to regimen selection after an occupational exposure is discussed in a separate topic review. (See "Management of health care personnel exposed to HIV", section on 'Regimen selection'.)

Preferred regimens — We suggest a three-drug regimen for nPEP given the efficacy of this combination in patients with HIV, the tolerability of available treatment regimens, extensive experience with these agents, and the demonstrated safety of these agents.

For most patients, we suggest:

- Tenofovir disoproxil fumarate-emtricitabine (TDF-FTC)

plus

- Dolutegravir

Both agents are administered as one pill once daily. Side effects are rare, but may include nausea, headache, and diarrhea. Uncommon adverse reactions include hepatotoxicity (lactic acidosis, hepatomegaly) and nephrotoxicity (acute kidney injury, Fanconi syndrome). (See "Selecting antiretroviral regimens for treatment-naïve persons with HIV-1: General approach".)

We generally prefer TDF-FTC rather than other nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) combinations, since there has been extensive use of this agent as the NRTI combination for nPEP, and there is excellent accumulation of these agents in the genital tract [37]. Although tenofovir alafenamide (TAF) has less bone and renal toxicity compared with TDF, these adverse effects usually occur with long-term administration of TDF, not the short duration used for nPEP.

Dolutegravir is our preferred integrase strand transfer inhibitor because it is administered once daily, can be administered with TDF-FTC, has minimal drug interactions, and is effective if there is concern for transmission of drug-resistant virus.

Regimens that use TDF-FTC plus an integrase strand transfer inhibitor have led to greater rates of nPEP completion compared with older regimens in which the toxicity often resulted in treatment discontinuation [15,29-33]. As an example, in a study of 100 patients using TDF-FTC plus raltegravir for nPEP, 85 percent took all or most of the nPEP regimen [30]. Although side effects included nausea or vomiting (27 percent), diarrhea (21 percent), headache (21 percent), and fatigue (14 percent), they were mild and did not result in drug

discontinuation. Side effects were significantly less common and completion rates were higher than those historically observed on protease inhibitor (PI)-based regimens with zidovudine-lamivudine.

The use of alternative regimens, and the choice of regimen in selected patient groups (eg, persons who are of childbearing potential or are pregnant, persons with reduced kidney function, persons exposed to a source with known HIV) are discussed below. (See 'Alternative regimens' below and 'Special considerations' below.)

Alternative regimens — There are several alternative regimens that can be used for nPEP. We consider these regimens alternatives because there may be less experience compared with the preferred regimen above, they may be associated with an increased risk of side effects, or they may not be suitable for all populations.

- **TAF-FTC instead of TDF-FTC** – For MSM, TAF/FTC can be used as an alternative to TDF/FTC. This combination is particularly suitable for those with reduced kidney function. Although TAF results in lower mucosal tenofovir levels compared with TDF [41,42], a study evaluating TAF for PrEP in MSM and transgender women found tenofovir alafenamide-emtricitabine (TAF-FTC) to be noninferior to TDF-FTC [43].

  However, pending additional data, we generally avoid TAF-FTC in those assigned female at birth who engage in vaginal sex, since it is unclear if TAF achieves protective levels in vaginal fluids.

  If TAF-FTC is used, the coformulated regimen bictegravir-emtricitabine-tenofovir alafenamide (sold as Biktarvy) is a good option since it is administered as a single pill once daily, and available data suggest it is well tolerated [33,44]. Bictegravir-emtricitabine-tenofovir alafenamide is a recommended regimen by some guideline panels [20,45]. Side effects of this regimen are similar to the preferred regimen above.

- **Pharmacologically boosted** darunavir **(a protease inhibitor) instead of an integrase strand transfer inhibitor** – TDF-FTC or TAF-FTC in combination with the pharmacologically boosted darunavir can be used for nPEP and may be particularly suitable if there is concern that the source has drug-resistant virus. (See 'Special considerations' below.)

  However, compared with integrase strand transfer inhibitors, there is an increased risk of adverse reactions and drug interactions with protease inhibitors. Information about specific drug interactions can be found in the drug interaction program within

UpToDate.

- **Other alternatives** – There are several other alternative agents that may be considered on a case-by-case basis. As an example, zidovudine-lamivudine (coformulated as Combivir) may be considered as an alternative to TDF-FTC or TAF-FTC in those who have contraindications to tenofovir. This combination had previously been the mainstay of nPEP but is generally avoided due to twice-daily dosing and adverse reactions, which have been associated with poor nPEP completion rates [29,31,32].

  For integrase strand transfer inhibitors, raltegravir (400 mg twice daily) may be preferred for some individuals to reduce the risk of drug interactions. Although this agent has been used extensively for nPEP, including in persons who are pregnant, it is administered twice daily and may not be effective in those with drug resistance.

Special considerations

Reduced kidney function — The dolutegravir component of the preferred nPEP regimen does not require adjustment for any degree of impaired kidney function or dialysis.

For exposed individuals with reduced kidney function (estimated glomerular filtration rate <60 mL/min/1.73^2 or estimated creatinine clearance [CrCl] <50 mL/min), the standard dose of TDF-FTC should not be used [46]. Our approach to treatment depends upon the degree of kidney dysfunction and the type of exposure:

- For persons with a CrCl ≥30 mL/min or receiving intermittent hemodialysis, dolutegravir in combination with TAF-FTC or bictegravir-tenofovir alafenamide-emtricitabine can be used in individuals whose potential HIV exposure was through anal sex. As discussed above, pending additional data, we generally avoid TAF-FTC in those assigned female at birth who engage in vaginal sex, since it is unclear if TAF achieves protective levels in vaginal fluids. (See 'Alternative regimens' above.)

- For those with severely reduced kidney function (CrCl <30 mL/min but not receiving dialysis) and those whose potential exposure to HIV was through vaginal sex, the approach is less clear. In these settings, one option is to use TDF plus FTC as separate pills at doses of each that are adjusted according to the patient's kidney function. Refer to the tenofovir disoproxil fumarate and emtricitabine separate drug information topics within UpToDate for specific dose adjustments according to the degree of kidney impairment.

The nephrotoxicity associated with TDF typically occurs with long-term administration, and we feel alternative NRTI combinations (eg, zidovudine-lamivudine) are associated with reduced tolerability and even greater toxicity (eg, anemia). However, if the clinician has concern about using a short course of TDF plus FTC for nPEP, consultation with an infectious diseases specialist should be obtained to find an appropriate alternate regimen.

Persons of childbearing potential/persons who are pregnant — Persons who are pregnant or of childbearing potential can use TDF-FTC **plus** either dolutegravir or raltegravir. (See 'Preferred regimens' above and 'Alternative regimens' above.)

Previously, dolutegravir was avoided in persons who were early in their pregnancy or were able to become pregnant but were not using effective birth control [47]. This was based on a preliminary report suggesting an increased rate of neural tube defects in infants born to women in Botswana who were receiving dolutegravir at the time of conception (the risk of a fetus developing a neural tube defect during the first 28 days) [48]. However, after accrual of further data, the risk with dolutegravir exposure was not found to be statistically different compared with exposure to non-dolutegravir-containing antiretroviral therapy around the time of conception [49,50].

TAF-FTC-containing regimens are generally to be avoided in persons assigned female at birth due to reduced drug concentration in vaginal mucosa.

A detailed discussion of the dosing and safety of antiretroviral agents in persons of childbearing potential and during pregnancy is found elsewhere. (See "HIV and women" and "Safety and dosing of antiretroviral medications in pregnancy".)

If the source may have drug-resistant HIV — In most cases, if the source has HIV, the integrase inhibitor-containing regimens described above should provide protection against transmission of HIV. (See 'Preferred regimens' above and 'Alternative regimens' above.)

However, if there is concern that the source may have multidrug-resistant HIV (eg, source is known to take their medication intermittently or has been on multiple regimens), consultation with an infectious diseases specialist should be obtained. In this setting, a pharmacologically boosted PI such as darunavir may be preferred as the third agent instead of dolutegravir or bictegravir. Many patients who have failed multiple regimens will still have virus that is fully sensitive to first-line pharmacologically boosted PIs, since these agents

have a high barrier to resistance. (See "Selecting an antiretroviral regimen for treatment-experienced patients with HIV who are failing therapy", section on 'Patients who have failed multiple regimens in the past'.)

The initial regimen can be modified based upon the results of drug resistance testing, should they become available.

Patient counseling and education — After a potential HIV exposure, all patients should also be counseled about:

- **Acute HIV infection** – Individuals should be educated about the signs and symptoms of acute HIV infection (table 3). Symptomatic patients should undergo immediate HIV testing, which includes both antibody-antigen testing and testing for HIV-1 RNA. The usual time from HIV exposure to the development of symptoms is two to four weeks. More detailed discussions of the clinical manifestations and diagnosis of acute HIV are found elsewhere. (See "Acute and early HIV infection: Clinical manifestations and diagnosis".)

  Patients taking nPEP should be informed that there are instances of nPEP failure [51]. Reasons for failure may include poor adherence to the nPEP regimen, suboptimal treatment regimens, delays in initiation, or ongoing HIV exposures [52]. In situations where nPEP may fail, selection of resistant virus by drug exposure is possible. The management of patients with potential drug-resistant virus is found elsewhere. (See "Evaluation of the treatment-experienced patient failing HIV therapy" and "Selecting an antiretroviral regimen for treatment-experienced patients with HIV who are failing therapy".)

- **Avoiding secondary transmission** – People potentially exposed to HIV should be advised to:

  - Avoid behaviors (eg, unprotected sexual contact or sharing needles) that may expose their partners to potentially infectious fluids (semen, pre-ejaculate, vaginal secretions, or blood) should HIV transmission occur. Persons of childbearing potential should also avoid pregnancy during the follow-up period. This is particularly important during the first 12 weeks after exposure when most persons with HIV are expected to seroconvert.

  - Refrain from donating blood, plasma, organs, tissue, or semen. The usual duration for this precaution is 12 months [53].

  In addition, breastfeeding women in resource-rich settings should discuss the risks and benefits of continuing breastfeeding. (See "Prevention of HIV transmission during breastfeeding in resource-limited settings".)

- **HIV prevention options** – For patients who engage in frequent high-risk behaviors, providers should discuss HIV prevention strategies (eg, condoms, HIV PrEP, substance abuse treatment) [21,54]. These strategies are reviewed elsewhere. (See "HIV infection: Risk factors and prevention strategies", section on 'Clinical approach to HIV prevention' and "HIV pre-exposure prophylaxis".)

Duration of HIV PEP — Guidelines recommend a 28-day course of antiretroviral therapy for persons with a significant HIV exposure, although the optimal duration of nPEP is unknown [11,14,20].

In some settings, nPEP can be discontinued sooner. As examples:

- If the source is available and is willing to be tested, nPEP may be discontinued if an HIV test (preferably a laboratory-based antigen/antibody test) is negative, unless there is concern that the source is acutely infected with HIV (ie, has signs and symptoms of acute HIV (table 3 and algorithm 1)), in which case HIV RNA testing should also be performed. (See 'Testing for hepatitis B and C virus' above and "Acute and early HIV infection: Clinical manifestations and diagnosis".)

- If the source has HIV, it may be reasonable to discontinue nPEP in selected settings. Available data suggest the risk of HIV transmission is unlikely if the exposure was through sexual contact, the source is taking a preferred antiretroviral regimen, and the viral load is <1000 copies/mL (especially when the viral load is <200 copies/mL) [4]. By contrast, treatment is typically continued if the exposure was through nonsexual contact as there are no data evaluating viral load thresholds for HIV transmission when the exposure was through injection drug use.

However, after reviewing the risks and benefits of nPEP, certain patients may prefer to continue the 28-day course, even if transmission is unlikely. (See "HIV infection: Risk factors and prevention strategies", section on 'Treatment as prevention'.)

Patient monitoring on HIV PEP — Patients should be monitored while receiving PEP to ensure adherence to the regimen and evaluate for potential toxicity (table 2).

- **Toxicity** – Patients should follow up with their provider if they develop side effects (eg, rash, nausea, vomiting, diarrhea).

Laboratory monitoring for patients receiving a tenofovir-based nPEP regimen is described in the table (table 2). For persons receiving a regimen that contains zidovudine-lamivudine, additional testing should be performed after two weeks of treatment. This includes a complete blood count with differential, blood urea nitrogen, creatinine, and liver function tests.

On rare occasion, an individual may have difficulty tolerating one of the preferred or alternative regimens described above. In this setting, consultation with an infectious diseases specialist should be obtained to find an appropriate alternative.

- **Adherence** – Regular contact with the patient, either in person or by video visit, telephone, or email, is important to help ensure adherence to prophylaxis [28].

More detailed information on monitoring patients after a sexual assault is presented separately. (See "Evaluation and management of adult and adolescent sexual assault victims in the emergency department", section on 'Follow-up care'.)

After nPEP is discontinued, patients should have repeat HIV testing to assess for seroconversion. (See 'Follow-up HIV testing (regardless of HIV PEP)' below.)

Follow-up HIV testing (regardless of HIV PEP) — Baseline and follow-up testing for HIV should be performed to see if seroconversion occurred (table 2). We prefer HIV testing employing a laboratory-based fourth-generation assay that detects HIV p24 antigen **and** HIV antibodies; this is in agreement with recommendations from the United States Centers for Disease Control and Prevention (CDC) [55-57]. HIV RNA is not routinely used for diagnosis of a new infection, though may be considered in select settings (eg, suspected acute HIV). (See "Screening and diagnostic testing for HIV infection in adults".)

- **Persons who are asymptomatic** – HIV testing should be performed four to six weeks after the exposure and then again three months after the exposure. Testing at three months is particularly important in the setting of nPEP since there may be a delay in forming detectable levels of HIV antibodies [11,58]. In patients who become acutely infected with hepatitis C virus (HCV) after exposure, the CDC recommends that additional HIV testing be performed six months after the exposure since this may also be associated with a delay in HIV seroconversion [11].

  HIV antigen/antibody tests should not be performed before day 28, since tests for HIV have a "window period" during which time HIV cannot be detected [59], and HIV may be suppressed while on PEP. Patients may also erroneously interpret a negative test

performed while receiving nPEP as a reason to discontinue the medications before the full course is completed.

- **Persons with symptoms of acute HIV** – Testing should be performed any time if symptoms suggestive of the acute retroviral syndrome develop. In this setting, testing for HIV RNA should also be performed. (See 'Patient counseling and education' above and "Acute and early HIV infection: Clinical manifestations and diagnosis".)

Barriers to HIV PEP — There are several considerations that may impact access to and uptake of nPEP. It is important that these potential barriers be addressed when developing nPEP programs.

- **Lack of awareness** – While community knowledge of nPEP has increased over the last two decades, communities who have suffered historic health inequities may have lower levels of knowledge. In a survey conducted from 2016 to 2017 in New York City, nPEP awareness was demonstrated in 80, 63, and 34 percent of young minority MSM, transgender women, and minority cisgender women, respectively [60]. Other studies have also demonstrated low nPEP awareness in the United States, ranging from 40 percent of Black transgender women to three percent of incarcerated men [61,62].

- **Limited access** – Access to nPEP is often limited. In a study among minority young MSM and cis- and transgender women at high-risk of HIV infection, 12 percent did not have access to nPEP and only 13 percent had ever used it in the past [63]. The use of nPEP was also found to be low in transgender women at elevated risk of HIV infection in the eastern and southern United States, despite high knowledge and awareness of nPEP [64].

  Although nPEP is felt to be a cost-effective intervention for individuals at high-risk for HIV [29,65], in some settings, lack of access to antiretroviral medications can be a barrier. In the United States, the Affordable Care Act included provisions to include preventive services including nPEP [66]. However, the COVID-19 pandemic disrupted health care systems worldwide, which impacted timely access to nPEP [67]. An international survey of MSM evaluating the impact of COVID-19 on access to nPEP found that only 17 percent reported access to PEP during and after COVID-19 [68].

- **Provider level barriers** – Provider knowledge of and experience with nPEP varies, which may contribute to reduced access to nPEP [69]. In a 2020 study of health care workers who practiced in areas of the United States with a high-prevalence of HIV, 43.5 percent were aware of nPEP but had not prescribed it, and 12.5 percent were unaware of nPEP [70]. In a study of emergency department

clinicians, only 40 percent felt they could select an appropriate drug regimen, despite being willing to prescribe nPEP [71]. Similarly, in a survey of graduate medical trainees in New York City, most were not knowledgeable of current guidelines or comfortable assessing patients for nPEP [72]. In one report, the availability of a written nPEP protocol was associated with nPEP administration [73].

- **Health inequity** – HIV infection rates vary by race in the United States, with Black and Latinx persons experiencing an increased burden of new HIV infections [74]. A study of knowledge of PEP and PrEP among the named sexual contacts of people newly diagnosed with HIV found that Black and Latinx sexual contacts of new HIV infections were significantly less likely to be aware of nPEP and PrEP [75]. A meta-analysis of structural barriers to HIV prevention and care among MSM in the United States, United Kingdom, and Canada found that Black MSM in the United States have significantly elevated rates of structural barriers known to be associated with increased HIV risk and poorer HIV-related outcomes, such as unemployment, lower income, contact with the criminal justice system, and reduced access to higher education [76]. Thus, when developing nPEP programs, it is important to address the structural barriers to care experienced by these populations.

HEPATITIS B POST-EXPOSURE MANAGEMENT

For persons at risk for acquiring HBV, post-exposure prophylaxis (PEP) consists of hepatitis B vaccine and/or hepatitis B immune globulin (HBIG).

Initial evaluation — All patients should be evaluated for HBV PEP after a percutaneous (eg, bite or needlestick) or mucosal exposure to blood or infectious secretions (eg, semen, vaginal secretions, or any body fluids that contain blood).

Baseline testing for HBV should be performed if the exposed patient and/or source's HBV status is unknown, as described above. (See 'Testing for hepatitis B and C virus' above.)

However, the decision to administer PEP should not be delayed, unless the results are immediately available. (See 'Indications for HBV PEP' below.)

Indications for HBV PEP — PEP should be administered to individuals without previously documented immunity to HBV (anti-HBs ≥10 milli-international units/mL) who are exposed to blood or body fluids from a source if:

- The source has chronic or occult HBV (ie, hepatitis B surface antigen [HBsAg]-positive or isolated hepatitis B core antibody [anti-HBc]-positive with a detectable DNA). PEP should be administered even if the source is on treatment.
- The HBV status of the source is unknown.

For exposed patients without prior HBV infection, the approach to prophylaxis depends primarily upon their vaccination history to HBV (algorithm 3). (See 'Approach to HBV prophylaxis' below.)

PEP is **not** needed if the **exposed patient** has known chronic HBV. Special considerations for those with isolated anti-HBc (hepatitis B surface antibody [anti-HBs]- and HBsAg-negative) are discussed below. (See 'If exposed patient or source is isolated anti-HBc-positive' below.)

In addition, PEP is not needed if the source has documentation of a prior anti-HBs level ≥10 milli-international units/mL after vaccination or has resolved HBV infection (anti-HBs and anti-HBc). However, exposed patients who have not completed a hepatitis B vaccine series should still be vaccinated to reduce the risk of future HBV transmission. (See "Hepatitis B virus immunization in adults".)

Timing — When PEP is warranted, it should be administered within 24 hours of an exposure, if possible.

However, if HBIG is indicated, it may be difficult to obtain (algorithm 3). Should this occur, HBIG can be administered within seven days of a percutaneous exposure or 14 days of a sexual exposure. If both hepatitis B vaccine and HBIG are indicated, we give the hepatitis B vaccine as soon as possible and have the patient return for HBIG. Additional information on HBIG is found below. (See 'Administering HBIG' below.)

Approach to HBV prophylaxis — The approach to HBV prophylaxis (hepatitis B vaccination and/or HBIG) depends primarily upon the exposed patient's history of HBV vaccination (algorithm 3).

Patients not fully vaccinated — Patients without a history of HBV who have not received or completed their hepatitis B vaccine series require PEP if they had a potential exposure to a source who is HBsAg-positive or HBV-unknown. Follow-up testing to assess for

transmission is discussed below. (See 'Follow-up testing' below.)

All patients should initiate or complete the hepatitis B vaccine series (even if the source is found to be HBsAg-negative); the dosing schedule depends upon the type of vaccine (table 4). Such patients should be tested for anti-HBs one month after completing the hepatitis B vaccine series. Follow-up testing to assess for HBV transmission is discussed below. (See 'Follow-up testing' below.)

The need for HBIG depends upon the source's HBV status**:**

- **Source is HBsAg-positive** – If the source in HBsAg-positive, we recommend HBIG in addition to the HBV vaccine. The vaccine and HBIG can be given simultaneously but should be administered at different sites. (See 'Administering HBIG' below.)

  The use of PEP with hepatitis B vaccine and HBIG likely reduces HBV transmission by 70 to 90 percent after an exposure to a patient with chronic HBV when administered within 12 to 24 hours of exposure. These findings are based primarily upon studies evaluating the use of PEP to prevent perinatal transmission of HBV to infants from mothers who are HBsAg-positive. Data supporting the use of PEP to prevent mother-to-child transmission are presented elsewhere. (See "Hepatitis B and pregnancy", section on 'Mother-to-child transmission' and "Hepatitis B virus immunization in infants, children, and adolescents".)

- **HBV status of the source is unknown** – If the HBV status of the source is unknown, the role of HBIG is less clear since there are no data to guide treatment decisions and guideline recommendations vary [77-79].

  In this setting, we use a shared decision-making approach with the patient. We weigh the likelihood that the source has chronic HBV based on risk factors (table 5), versus the risk of HBIG (eg, side effects such as allergic reactions, injection site reactions, headaches, and myalgias [80]) and potentially the cost.

- **Source is HBsAg-negative** – In almost all cases, HBIG is **not** needed if the source is HBsAg-negative. The one exception is if the source has isolated anti-HBc and detectable HBV DNA. (See 'If exposed patient or source is isolated anti-HBc-positive' below.)

Patients vaccinated but response unknown — Exposed patients who are uncertain if they completed the hepatitis B vaccine series should be treated as if they are unvaccinated. (See 'Patients not fully vaccinated' above.)

However, many patients know they have completed a hepatitis B vaccine series (table 4), but do not know if they have had an adequate vaccine response (ie, a postvaccination anti-HBs ≥10 milli-international units/mL).

Such patients should receive a booster dose of a hepatitis B vaccine after an exposure if the source is HBsAg-positive or the HBV status is unknown (algorithm 3). Although most patients who complete the HBV vaccine series develop protective immunity or have immune memory, a small proportion of the vaccinated population lose both the protective levels of anti-HBs and an anamnestic response. Thus, repeat vaccination is reasonable given the possible benefit of vaccination and the low risk of adverse reactions to the available hepatitis B vaccines. (See "Hepatitis B virus immunization in adults".)

Further management depends upon the results of baseline serologic testing (see 'Testing for hepatitis B and C virus' above):

- If the exposed patient has an anti-HBs level ≥10 milli-international units/mL, no further intervention is needed.
- If the anti-HBs is <10 milli-international units/mL at the time of exposure, we typically repeat the hepatitis B series. Alternatively, the patient can have the anti-HBs repeated approximately one month after the booster dose and then complete the series if the anti-HBs level returns <10 milli-international units/mL.

  If the source was available for testing at the time of exposure and the HBsAg returns positive, the exposed patient should receive a dose of HBIG within seven days of a percutaneous exposure or 14 days of a sexual exposure. If the source's status remains unknown, we use a shared decision-making approach to see if HBIG should be administered, as discussed above. (See 'Patients not fully vaccinated' above.)

Special considerations if the exposed patient or source have isolated anti-HBc and the approach to follow-up testing to assess for HBV transmission are discussed below. (See 'If exposed patient or source is isolated anti-HBc-positive' below.)

Patients who are vaccine nonresponders — At the time of exposure, some patients know they did not respond to the hepatitis B vaccine series (ie, anti-HBs <10 milli-international units/mL).

- **Role of HBIG** – Exposed patients who are known to be nonresponders to the hepatitis B vaccine series should receive a dose of HBIG at the time of exposure if the source is known to be HBsAg-positive or has occult HBV (algorithm 3). (See 'If exposed

patient or source is isolated anti-HBc-positive' below.)

If the exposed patient was a nonresponder to two hepatitis B vaccine series, a second dose of HBIG should be administered one month later. Additional information regarding HBIG is described below. (See 'Administering HBIG' below.)

If the source's HBV status is unknown, the decision to use HBIG should be made using a shared decision-making approach, as described above. (See 'Patients not fully vaccinated' above.)

- **Role of hepatitis B vaccination** – The need for additional doses of the hepatitis B vaccine depends upon the number of hepatitis B vaccine series the exposed patient received (algorithm 3).
  - **Nonresponders after the initial vaccine series** – Patients who did not respond to the initial hepatitis B vaccine series should initiate a second course of the hepatitis B vaccine series within 24 hours of exposure. Ideally this should be with a high potency vaccine (eg, HepB-CpG, sold as Heplisav). If the second course had already been started, it should be completed as scheduled (table 4). Anti-HBs should be measured approximately six months after HBIG and at least one to two months after last vaccination [81,82].
  - **Nonresponders after two vaccine series** – The role for additional hepatitis B vaccination in patients who are nonresponders after receiving two courses of the hepatitis B vaccine series is unclear. However, it is reasonable to give a third course with a higher potency vaccine (eg, HepB-CpG) if the patient received conventional vaccine during the prior courses. (See 'Follow-up testing' below.)
- **Follow-up testing** – The approach to follow-up testing to assess for transmission is discussed below. (See 'Follow-up testing' below.)

If exposed patient or source is isolated anti-HBc-positive — On rare occasion, testing of the exposed patient or source may reveal that an individual has isolated anti-HBc (HBsAg-negative and anti-HBs-negative, but anti-HBc-positive). Isolated detection of anti-HBc can occur in several settings: during the window period of acute hepatitis B (when the anti-HBc is predominantly IgM class); when anti-HBs has fallen to undetectable levels many years after recovery from acute hepatitis B; or when the HBsAg titer has decreased below the cutoff level for detection in persons who have had chronic HBV for many years. A false-positive anti-HBc can also be seen. The evaluation

of patients with isolated anti-HBc (eg, need for HBV DNA testing) is presented separately. (See "Hepatitis B virus: Screening and diagnosis in adults", section on 'Isolated anti-HBc'.)

- **If the exposed patient is isolated anti-HBc-positive** – Exposed patients with isolated anti-HBc positivity should receive initial HBV prophylaxis like those who do not have evidence of immunity. (See 'Patients not fully vaccinated' above and 'Patients who are vaccine nonresponders' above.)

  However, if HBV DNA is detected on further work up, no additional immunizations are needed.(See "Hepatitis B virus: Screening and diagnosis in adults", section on 'Isolated anti-HBc'.)

- **Source is isolated anti-HBc-positive** – If the source is found to have isolated anti-HBc, additional testing for HBV DNA should be performed to evaluate for occult HBV infection. This testing does not impact the need for hepatitis B immunization in nonimmune patients. However, if HBV DNA is detected (or if HBV DNA cannot be obtained within seven days of a percutaneous exposure or 14 days of a sexual exposure), the exposed patient should be managed the same way as if the source is HBsAg-positive (algorithm 3 and table 2). (See 'Patients vaccinated but response unknown' above and 'Patients who are vaccine nonresponders' above.)

Administering HBIG — The need for HBIG depends upon the HBV status of the exposed patient and the source, as described above (algorithm 3 and table 2). (See 'Approach to HBV prophylaxis' above.)

The standard adult dose is 0.06 mL/kg and should be given intramuscularly. The hepatitis B vaccine and HBIG can be given simultaneously but should be administered at different sites. HBIG should ideally be administered within 24 hours of exposure, but if this is not possible (eg, not immediately available), it should be given within seven days of a percutaneous exposure or 14 days of a sexual exposure. (See 'Timing' above.)

HBIG provides anti-HBs and generally protects against infection with HBV for three to six months. HBIG has been estimated to be 75 percent effective in preventing HBV infection following a percutaneous exposure [77,83]; the efficacy of HBIG in this setting has only been evaluated when given within a week of exposure. The evidence supporting the use of HBIG up to 14 days after a sexual exposure is based on data from an early observational study evaluating the risk of developing symptomatic HBV infection in discordant spouses

after a high-risk exposure [84]. In this report, only 1 of the 25 spouses who received HBIG developed symptomatic HBV versus 9 of the 33 spouses who did not receive HBIG.

Follow-up testing — For patients who receive PEP for HBV, we test for anti-HBc, anti HBs, and HBsAg after six months to assess for evidence of HBV transmission. Testing should be done sooner if the patient develops signs or symptoms of hepatitis. (See "Hepatitis B virus: Clinical manifestations and natural history".)

HEPATITIS C POST-EXPOSURE MANAGEMENT

There are no medications or immunizations to reduce the risk of acquiring hepatitis C virus (HCV) after a possible exposure. Post-exposure management includes close clinical monitoring and follow-up HCV testing, with referral for treatment if infection does occur. The approach to monitoring and testing after an exposure is presented elsewhere. (See "Clinical manifestations, diagnosis, and treatment of acute hepatitis C virus infection in adults", section on 'Patients with discrete HCV exposure' and "Screening and diagnosis of chronic hepatitis C virus infection", section on 'Diagnosis'.)

SOCIETY GUIDELINE LINKS

Links to society- and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: HIV prevention" and "Society guideline links: Diagnosis of hepatitis B" and "Society guideline links: Management of hepatitis B" and "Society guideline links: Prevention of hepatitis B virus infection" and "Society guideline links: Hepatitis C virus infection".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about

a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Preventing HIV after a possible exposure (The Basics)")
- Beyond the Basics topic (see "Patient education: Care after sexual assault (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Initial management after an exposure** – Patients who are potentially exposed to HIV, hepatitis B virus (HBV), or hepatitis C virus (HCV) through a nonoccupational exposure (eg, sexual or percutaneous) are at risk for acquiring one of these infections.

  Initial management includes wound care if appropriate. In addition, exposed patients should be evaluated to determine the need for post-exposure prophylaxis (PEP) or monitoring. This includes assessing the type of exposure, as well as the HIV, HBV, and HCV status of the exposed patient and the source, if possible. (See 'Initial management' above.)

  Patients with a sexual exposure should also be offered and/or treated for other sexually transmitted infections (table 2). (See "Screening for sexually transmitted infections".)

- **HIV post-exposure prophylaxis**

  - **Indications** – Patients who present within 72 hours of a possible substantive exposure to HIV should be evaluated for nonoccupational post-exposure prophylaxis (nPEP) with antiretroviral therapy. These types of exposures include condomless receptive or insertive anal or vaginal intercourse, percutaneous exposure to blood or body fluids contaminated with blood (this

includes use of contaminated syringes), and/or exposure of blood or body fluids contaminated with blood to nonintact skin. (see 'Assessing the exposure risk' above and 'Indications for HIV post-exposure prophylaxis (PEP)' above).

- **If the source has HIV** – If the source has HIV, we suggest nPEP be initiated after a high-risk exposure, regardless of source's viral load (algorithm 2) (**Grade 2C**). This is particularly important if the source is known to have a viral load >1,000 copies/mL, as viral loads above this threshold are associated with an increased risk of HIV transmission. (See 'Assessing the exposure risk' above.)

After nPEP has been initiated, if the source is available and willing, an HIV viral load should be collected. In some settings, nPEP can be discontinued, depending upon the results. (See 'Duration of HIV PEP' above.)

- **If the source's HIV status is unknown** – We also suggest nPEP after a high-risk exposure if the source's HIV status is unknown and the source has risk factors for HIV or the exposed patient has been sexually assaulted (algorithm 1) (**Grade 2C**).

  Some patients may also desire nPEP for HIV if the source's risk factors for HIV are unknown. To help inform this decision, we discuss the route of exposure (table 1), and other cofactors that heighten risk of transmission (eg, presence of genital ulcer disease).

- **When to initiate PEP** – Once the need for HIV PEP has been determined, the patient should be given a dose as soon as possible, and within 72 hours of the exposure. Prophylaxis should **not** be delayed pending HIV testing of the exposed patient or the source; however, in some settings it can be discontinued based on the results. (See 'When to initiate HIV PEP' above and 'Duration of HIV PEP' above.)

- **Regimen selection** – For most patients who initiate nPEP, we suggest a three-drug regimen using tenofovir disoproxil fumarate-emtricitabine (TDF/FTC) **plus** dolutegravir (**Grade 2C**). (See 'Regimen selection' above.)

  There are additional considerations for regimen selection in certain patient groups, such as persons who are of childbearing potential or are pregnant, persons with reduced kidney function, and persons with an exposure to a source with drug-resistant HIV. (See 'Special considerations' above.)

- **Duration and monitoring** – Patients receiving nPEP for HIV should receive a 28-day course of antiretroviral therapy (algorithm 2 and algorithm 1). After nPEP is discontinued, patients should have repeat HIV testing approximately 6 and 12 weeks after the exposure to assess for seroconversion (table 2). (See 'Duration of HIV PEP' above and 'Patient monitoring on HIV PEP' above.)

- **Hepatitis B post-exposure prophylaxis** – Patients with a potential substantive exposure to HIV should also be evaluated for HBV PEP (algorithm 3). (See 'Hepatitis B post-exposure management' above and 'Initial evaluation' above.)

  Post exposure prophylaxis is indicated for persons at risk for HBV transmission (see 'Indications for HBV PEP' above).

  - **Exposed patients who are not fully vaccinated or are vaccine nonresponders** – If the source is known to be HBsAg positive or has occult HBV, we recommend prophylaxis with HBIG and HBV vaccination for most patients (**Grade 1B**). However, if the exposed patient is a nonresponder to two previous vaccine series, the role of repeat hepatitis B vaccination is unclear, and such patients should receive a second dose of HBIG one month later. (See 'Patients not fully vaccinated' above and 'Patients who are vaccine nonresponders' above and 'If exposed patient or source is isolated anti-HBc-positive' above.)

    If the status of the source is unknown, we discuss the use of HBIG using a shared decision-making approach, assessing the likelihood the source has chronic HBV based on risk factors with the risk of complications from HBIG (eg, allergic reactions, injection site reactions, headaches, and myalgias) and potentially cost. (See 'Administering HBIG' above.)

  - **Exposed patients who are fully vaccinated but response is unknown** – For patients who completed their vaccine series but their response is unknown, we suggest hepatitis B vaccine (**Grade 2C**). If baseline serologic testing reveals the exposed patient is immune, no additional intervention is needed regardless of the source's HBV status. By contrast, additional prophylaxis is warranted for those who are not immune (algorithm 3). (See 'Patients vaccinated but response unknown' above.)

- **Hepatitis C post-exposure management** – Patients with a potential substantive exposure to HIV should also be evaluated for exposure to HCV. Although there are no medications or immunizations to reduce the risk of acquiring HCV after a possible exposure, we perform HCV testing unless the source tests negative for HCV RNA. Early diagnosis allows for prompt treatment if infection does occur This is discussed in detail in separate topic reviews. (See "Clinical manifestations, diagnosis, and treatment of

acute hepatitis C virus infection in adults", section on 'Patients with discrete HCV exposure' and "Screening and diagnosis of chronic hepatitis C virus infection", section on 'Diagnosis'.)

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Topic 3768 Version 35.0

GRAPHICS

Estimated per-act risk for acquisition of HIV, by exposure route

Exposure route		Risk per 10,000 exposures to an infected source (risk
Blood-borne exposure	Blood transfusion	9000 (9/10)
	Needle-sharing injection drug use	67 (1/150)
	Percutaneous needle stick	23 (1/435)
	Mucous membrane exposure to blood (eg, splash to eye)	10 (1/1000)
Sexual exposure	Receptive anal intercourse	138 (1/72)
	Insertive anal intercourse	11 (1/900)
	Receptive penile-vaginal intercourse	8 (1/1250)
	Insertive penile-vaginal intercourse	4 (1/2500)
	Receptive or insertive penile-oral intercourse	0-4
Other	Biting, spitting, throwing body fluids (including semen and saliva), sharing sex toys	Negligible

There are scant empiric data on per contact risk of exposure. This table lists the estimated risk by exposure type in the absence of antiretroviral treatment of the HIV-infected source and in the absence of amplifying factors. Most of these estimates are derived through modeling studies of different cohorts. Clinicians need to be aware that estimates of sexual risk are often based on studies of monogamous couples among whom amplifying factors have been treated and repeated exposure may offer as yet unexplained protection from infection. Using a single value for assessing risk of HIV transmission based on route of sexual exposure fails to reflect the variation associated with important cofactors. A variety of amplifying factors and conditions have been identified, and these factors can be expected to increase transmission probability.

Data from:

1. *Donegan E, Stuart M, Niland JC, et al. Infection with human immunodeficiency virus type 1 (HIV-1) among recipients of antibody-positive blood donations. Ann Intern Med 1990; 113:733-9.*
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5. *Cohen MS. Amplified transmission of HIV-1: Missing link in the HIV pandemic. Trans Am Clin Climatol Assoc 2006; 117: 213–225.*
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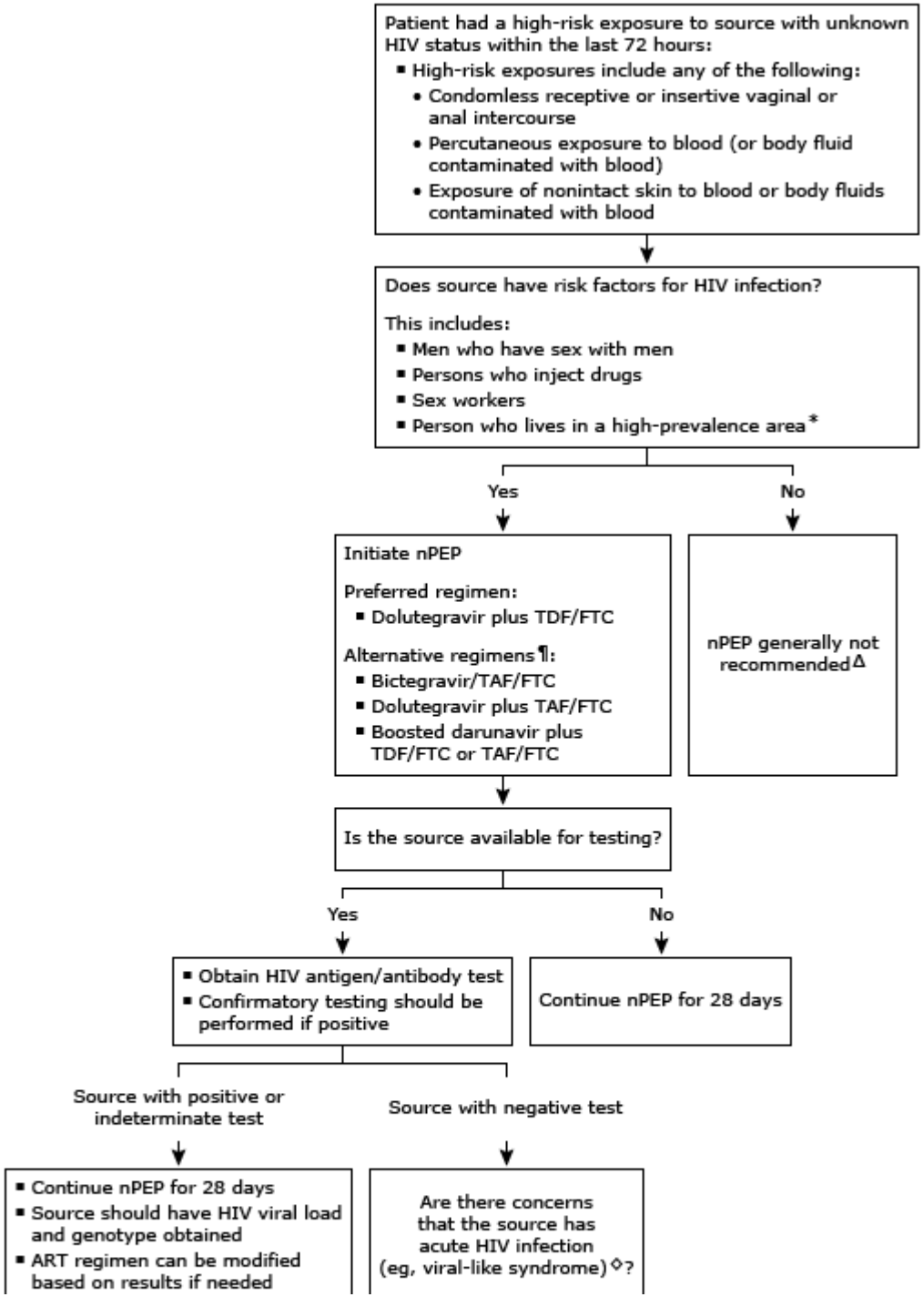
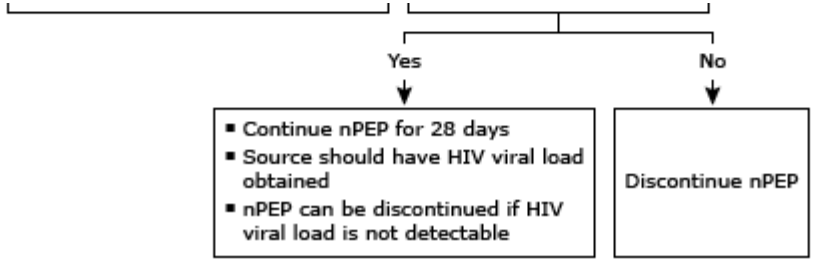
Graphic 60145 Version 6.0

Approach to HIV nPEP: Source with unknown HIV status


Patient had a high-risk exposure to source with unknown HIV status within the last 72 hours:
High-risk exposures include any of the following:
Condomless receptive or insertive vaginal or anal intercourse
Percutaneous exposure to blood (or body fluid contaminated with blood)
Exposure of nonintact skin to blood or body fluids contaminated with blood
Does source have risk factors for HIV infection?
This includes:
Men who have sex with men
Persons who inject drugs
Sex workers
Person who lives in a high-prevalence area*
Yes
No
Initiate nPEP
Preferred regimen:
Dolutegravir plus TDF/FTC
Alternative regimens¶:
Bictegravir/TAF/FTC
Dolutegravir plus TAF/FTC
Boosted darunavir plus TDF/FTC or TAF/FTC
nPEP generally not recommendedΔ
Is the source available for testing?
Yes
No
Obtain HIV antigen/antibody test
Confirmatory testing should be performed if positive
Continue nPEP for 28 days
Source with positive or indeterminate test
Source with negative test
Continue nPEP for 28 days
Source should have HIV viral load and genotype obtained
ART regimen can be modified based on results if needed
Are there concerns that the source has acute HIV infection (eg, viral-like syndrome)◇?



This algorithm describes our suggested approach to nonoccupational post-exposure prophylaxis (nPEP) in persons after a sexual or percutaneous exposure to a person with HIV and should be used in conjunction with UpToDate content on nPEP. A shared decision making approach should be used with all patients since the risks, benefits, costs, and barriers will vary for each individual. Pre-exposure prophylaxis should also be discussed with those who have repeated exposures that put them at risk for acquiring HIV.

ART: antiretroviral therapy; HIV: human immunodeficiency virus; nPEP: nonoccupational post-exposure prophylaxis; TAF/FTC: tenofovir alafenamide-emtricitabine; TDF/FTC: tenofovir disoproxil fumarate-emtricitabine.

* An example of a high-prevalence area is the World Health Organization African Region. Detailed information on the prevalence of HIV in different geographic areas can be found on the WHO website.

¶ Alternative regimens should be considered in certain settings. These include:

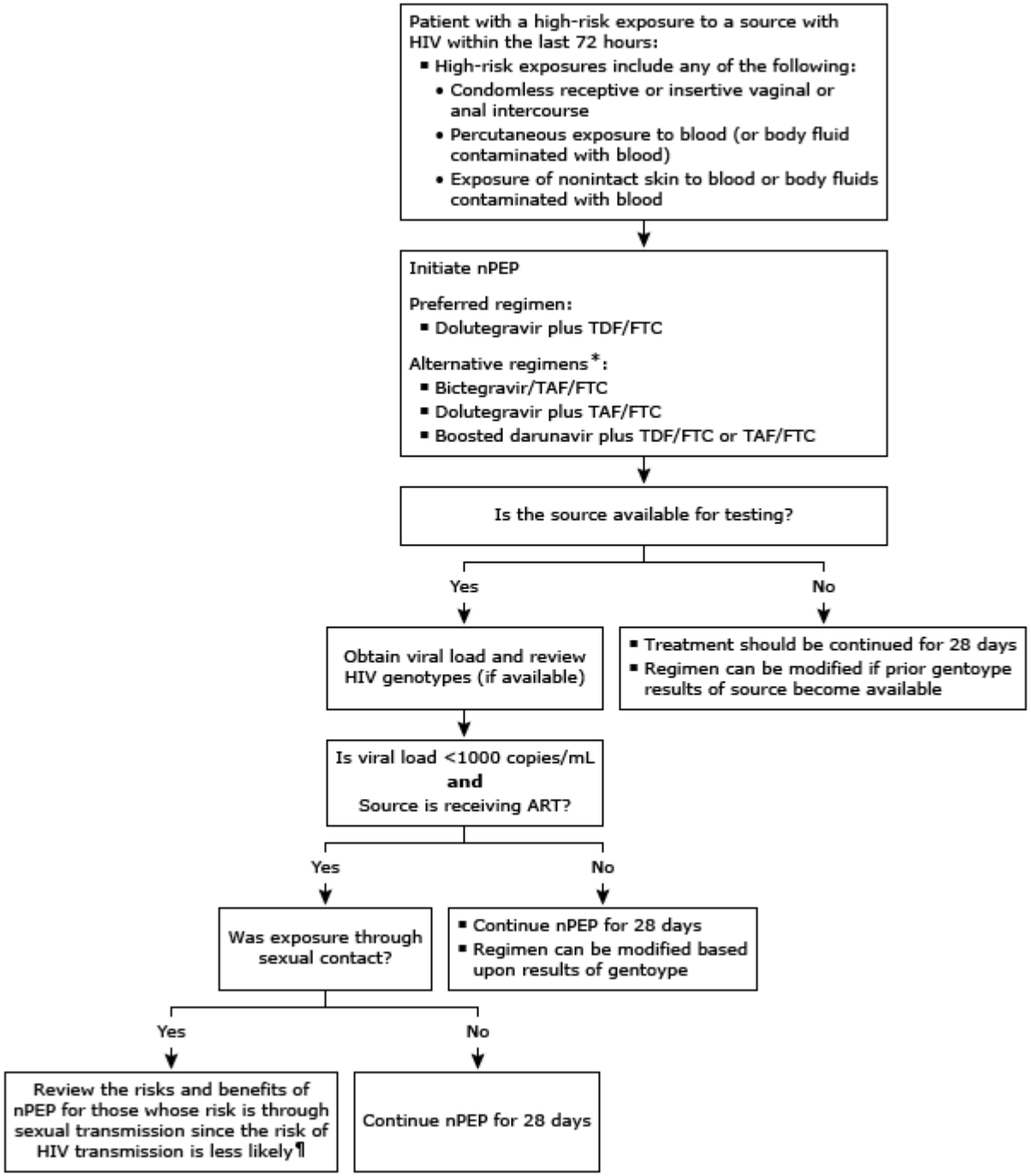
- Reduced kidney function (estimated glomerular filtration rate [GFR] of <60 mL/min/1.73 m^2) or creatinine clearance [CrCl] <50 mL/min) - For nPEP, TDF/FTC should be avoided in persons with reduced kidney function if there are other reasonable alternatives. If the CrCl is between 30 and 50 mL/min and the exposure was through anal sex or injection drug use (IDU), we prefer a TAF/FTC-containing regimen. For those with vaginal exposure or a CrCl <30 mL/min not on dialysis, we typically avoid TAF (uncertain efficacy and potential safety issues, respectively) and instead use dose reduced TDF and FTC in combination with dolutegravir or boosted darunavir. However, the optimal approach is uncertain and infectious diseases consultation may be helpful in these settings. For dose adjustments, refer to the tenofovir disoproxil fumarate and emtricitabine separate drug information topics within UpToDate.
- Exposure to a person with drug-resistant HIV - In this setting boosted darunavir (in combination with TAF/FTC or TDF/FTC) can be considered. This regimen is associated with more side effects than integrase strand transfer inhibitor (INSTI)-containing regimens.
- TAF/FTC-containing regimens are generally avoided in persons assigned female at birth due to reduced drug concentration in vaginal mucosa.

Δ Some patients may choose to initiate nPEP if the source's risk factors are unknown, depending upon the type of exposure.

◇ A variety of symptoms and signs may be seen in association with acute HIV infection. The most common findings are fever, lymphadenopathy, sore throat, rash, myalgia/arthralgia, and headache. Refer to UpToDate topics that discuss clinical manifestations and diagnosis of acute HIV for additional information.

Graphic 144090 Version 1.0

Approach to HIV nPEP: Source with known HIV


Patient with a high-risk exposure to a source with HIV within the last 72 hours:
High-risk exposures include any of the following:
Condomless receptive or insertive vaginal or anal intercourse
Percutaneous exposure to blood (or body fluid contaminated with blood)
Exposure of nonintact skin to blood or body fluids contaminated with blood
Initiate nPEP
Preferred regimen:
Dolutegravir plus TDF/FTC
Alternative regimens*:
Bictegravir/TAF/FTC
Dolutegravir plus TAF/FTC
Boosted darunavir plus TDF/FTC or TAF/FTC
Is the source available for testing?
Yes
No
Obtain viral load and review HIV genotypes (if available)
Treatment should be continued for 28 days
Regimen can be modified if prior gentoype results of source become available
Is viral load <1000 copies/mL
and
Source is receiving ART?
Yes
No
Was exposure through sexual contact?
Continue nPEP for 28 days
Regimen can be modified based upon results of gentoype
Yes
No
Review the risks and benefits of nPEP for those whose risk is through sexual transmission since the risk of HIV transmission is less likely¶
Continue nPEP for 28 days

This algorithm describes our suggested approach to nonoccupational post-exposure prophylaxis (nPEP) in persons after a sexual or percutaneous exposure to a person with HIV and should be used in conjunction with UpToDate content on nPEP. A shared decision making approach should be used with all patients since the risks, benefits, costs, and barriers will vary for each individual. Pre-exposure prophylaxis should also be discussed with those who have repeated exposures that put them at risk for acquiring HIV.

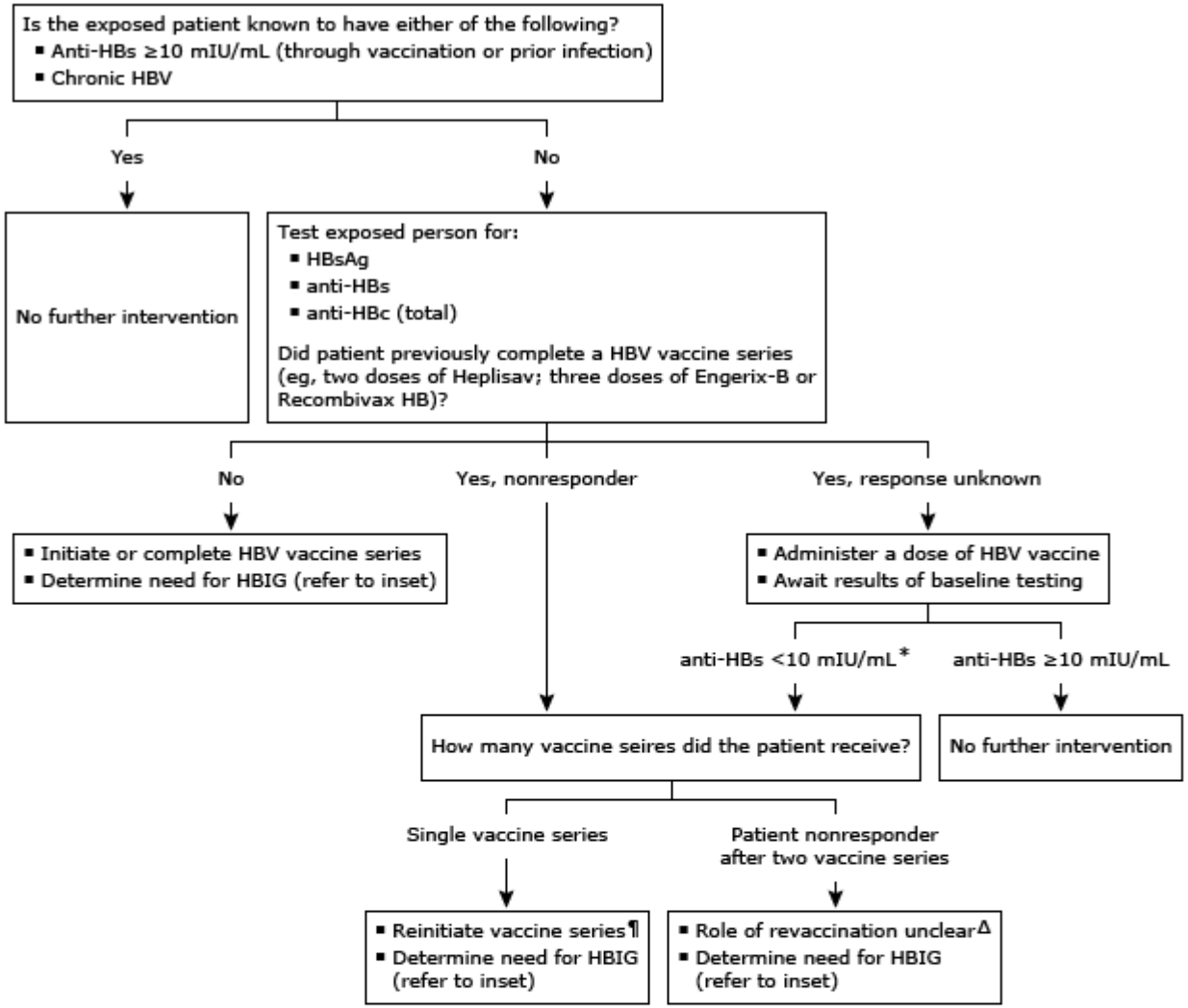
ART: antiretroviral therapy; HIV: human immunodeficiency virus; nPEP: nonoccupational post-exposure prophylaxis; TAF/FTC: tenofovir alafenamide-emtricitabine; TDF/FTC: tenofovir disoproxil fumarate-emtricitabine.

* Alternative regimens should be considered in certain settings. These include:
- Reduced kidney function (estimated glomerular filtration rate [GFR] of <60 mL/min/1.73 m^2 or creatinine clearance [CrCl] <50 mL/min) – For nPEP, TDF/FTC should be avoided in persons with reduced kidney function if there are other reasonable alternatives. If the CrCl is between 30 and 50 mL/min and the exposure was through anal sex or injection drug use (IDU), we prefer a TAF/FTC-containing regimen. For those with vaginal exposure or a CrCl <30 mL/min not on dialysis, we typically avoid TAF (uncertain efficacy and potential safety issues, respectively) and instead use dose-reduced TDF and FTC in combination with dolutegravir or boosted darunavir. However, the optimal approach is uncertain and infectious diseases consultation may be helpful. For dose adjustments refer to the tenofovir disoproxil fumarate and emtricitabine separate drug information topics within UpToDate.
- Exposure to a person with drug resistant HIV – In this setting boosted darunavir (in combination with TAF/FTC or TDF/FTC) can be considered. This regimen is associated with more side effects than integrase strand transfer inhibitors (INSTI)-containing regimens.
- TAF/FTC-containing regimens are generally avoided in persons assigned female at birth due to reduced drug concentration in vaginal mucosa.

¶ Discontinuing nPEP is reasonable in this setting since clinical trials have found that sexual transmission of HIV is unlikley if a persons with HIV is on ART and has a viral load <1000 copies/mL, particularly if the viral load is <200 copies/mL. However, some patients may still choose to continue nPEP after reviewing the risks and benefits. There are no data evaluating viral load thresholds for HIV transmission when the exposure was through IDU.

Graphic 144091 Version 1.0

Overview of HBV prophylaxis after a possible nonoccupational exposure for persons 13 years of age and older



HBV status at time of exposure*	Source HBsAg positive	Source HBsAg negative	Source HBsAg unknown
Exposed person: ▪ Known to be immune to HBV **or** ▪ Has chronic HBV	No HBIG	No HBIG	No HBIG
Exposed person: ▪ Is unvaccinated **or** ▪ Has not completed an HBV vaccine series **or**	HBIG◇	No HBIG	Source is low risk for HBV: No HBIG Source is high risk for HBV: HBIG◇ can be considered§

▪ Has completed an HBV vaccine series but is a nonresponder			

This table provides an overview of post-exposure prophylaxis to prevent HBV after a non-occupational exposure for adults and adolescents over the age of 13. If the source is known and available for testing, they should be tested for HBsAg, anti-HBs, anti-HBc. More detailed information on indications for nPEP and specific dosing recommendations are found in relevant UpToDate content.

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anti-HBc: hepatitis B core antibody; anti-HBs: hepatitis B surface antibody; HBIG: hepatitis B immunoglobulin; HBsAG: hepatitis B surface antigen; HBV: hepatitis B virus; nPEP: nonoccupational post-exposure prophylaxis.

* On rare occasion laboratory testing may reveal the exposed patient or source is isolated anti-HBc positive (HBsAg and anti-HBs negative). Refer to the topic on post-exposure prophylaxis for information on management of this population.

¶ If a patient did not respond to the conventional HBV series (eg, Engerix-B or Recombivax HB), we prefer to administer a higher potency vaccine (eg, Heplisav) if possible.

Δ If the exposed patient received two vaccine series using the conventional HBV vaccine, it is unlikely they will respond to a third series of the conventional vaccine. However, it is reasonable to administer a third series with a higher potency HBV vaccine, although the efficiacy of this approach has not been established.

◇ A second dose of HBIG should be administered one month later if the exposed patient was a nonresponder to two hepatitis B vaccine series.

§ If the source is unknown but felt to be at high risk for HBV (eg, person who uses injection drugs; person who engages in high-risk sexual behaviors), the decision to administer HBIG should be made using a shared decision-making approach with the patient, weighing the risk of acquiring HBV versus risk of HBIG (eg, allergic reaction, injection site reaction, headache, myalgias).

Graphic 143573 Version 1.0

Recommended laboratory evaluation after possible nonoccupational exposure to HIV, HBV, and HCV

Test	Baseline	4 to 6 weeks after exposure	3 months after exposure	6 months after exposure
HIV serologic testing (lab-based fourth-generation HIV antigen-antibody assay preferred test)	E, S (if HIV status unknown)	E	E	E (only if patient became acutely infected with HCV)
Complete blood count with differential*	E			
Serum liver enzymes (ALT, AST)	E	E	E¶	
Blood urea nitrogen/creatinine	E	E		
Sexually transmitted diseases screen if exposure through sexual contact△	E, S◇	E△		E△
Hepatitis B serology (HBsAg, anti-HBs, anti-HBc)	E, S			E§
Hepatitis C testing	E, S¶	E¶	E¶	E¶
Pregnancy test (for women of reproductive age)	E	E (if sexual exposure)		
HIV viral load¥	S (only if HIV-infected or if concern for acute HIV)			
HIV resistance testing¥	S (only if HIV-infected)			

This table provides guidance on monitoring asymptomatic patients receiving HIV nPEP with tenofovir disoproxil fumarate-emtricitabine or tenofovir alafenamide as the nucleoside combination with a third agent (eg, an integrase inhibitor or a boosted protease inhibitor). Additional testing (eg, for pregnancy, sexually transmitted diseases [STIs], hepatitis) should be performed if clinically indicated based on the type of exposure. Refer to

UpToDate content for more detailed information on nPEP regimen selection and HBV postexposure prophylaxis as well as testing for HIV, HCV, and STIs.

ALT: alanine aminotransferase; AST: aspartate aminotransferase; E: exposed patient; HBsAg: hepatitis B surface antigen; HBV: hepatitis B virus; HCV: hepatitis C virus; S: source.

* If zidovudine-lamivudine is used as the nucleoside combination, a complete blood count should be performed while the patient is receiving nonoccupational post-exposure prophylaxis (after approximately two weeks).

¶ The source should be tested for HCV RNA if possible. If the source is HCV-positive or is not available for testing **and** the exposed patient is HCV negative, additional monitoring of the exposed patient should be performed. This includes testing for HCV RNA and serum aminotransferases at four weeks; testing for HCV RNA, anti-HCV antibody, and serum aminotransferases at three to four months; and testing for HCV RNA and anti-HCV antibody at six months.

Δ Routine screening for STIs after a sexual exposure typically includes testing for gonorrhea, chlamydia, and syphilis. Testing should be performed at baseline. Repeat syphilis testing should be performed four to six weeks and six months after a sexual exposure. Chlamydia and gonorrhea testing should be performed four to six weeks after a sexual exposure for those who were not treated empirically at baseline and for those who are symptomatic.

◇ Victims of sexual assault should be empirically treated for STIs (eg, gonorrhea, chlamydia) without need for baseline testing. Refer to UpToDate content on management of sexual assault victims for more detailed information on management.

§ For patients who were not immune at baseline and were exposed to a source who is HBsAg-positive or whose HBsAg status is unknown.

¥ For the exposed patient, testing for HIV RNA should **only** be performed if symptoms of acute HIV infection develop or if the exposed patient is found to have HIV on serologic testing.

Adapted from: Dominguez KL, Smith DK, Thomas V, et al. Updated guidelines for antiretroviral postexposure prophylaxis after sexual, injection drug use, or other nonoccupational exposure to HIV—United States, 2016. United States Centers for Disease Control and Prevention. https://stacks.cdc.gov/view/cdc/38856 (Accessed on April 20, 2016).

Additional information from: Testing and Clinical Management of Health Care Personnel Potentially Exposed to Hepatitis C Virus – CDC Guidance, United States, 2020. MMWR Recommend Rep 2020;69(No. RR-6):1–8.

Graphic 66128 Version 6.0

Clinical manifestations of acute HIV infection

Features (percent)	Overall (n = 378)	Male (n = 355)	Female (n = 23)	Sexual* (n = 324)	IVDU¶ (n = 34)
Fever	75	74	83	77	50
Fatigue	68	67	78	71	50
Myalgia	49	50	26	52	29
Skin rash	48	48	48	51	21
Headache	45	45	44	47	30
Pharyngitis	40	40	48	43	18
Cervical adenopathy	39	39	39	41	27
Arthralgia	30	30	26	28	26
Night sweats	28	28	22	30	27
Diarrhea	27	27	21	28	23

This table lists the most frequent clinical findings reported among patients with acute HIV infection from five prospective cohorts.

* Homosexual or heterosexual route of transmission.

¶ IVDU, intravenous drug use as route of transmission.

Graphic 87682 Version 3.0

Recommended doses of recombinant hepatitis B vaccines licensed in the United States for persons aged 18 years and older

	Age group and associated conditions	Volume (mL)	Dose HBsAg (mcg)	Recommended schedule
Single-antigen vaccines				
Recombivax HB				
Pediatric/adolescent formulation	18 through 19 years	0.5	5	0, 1, and 6 months
Adult formulation	≥20 years	1	10	
Dialysis formulation	Adults on hemodialysis and other immunocompromised adults aged ≥20 years	1	40	0, 1, and 6 months
Engerix-B	18 through 19 years	0.5	10	0, 1, and 6 months
	≥20 years	1	20	
	Adults on hemodialysis and other immunocompromised adults aged ≥20 years	2*	40	0, 1, 2, and 6 months
Heplisav-B¶Δ	≥18 years	0.5	20	0 and 1 months
Combination vaccine				
Twinrix (combined HepB-HepA vaccine)	≥18 years	1	20	Standard: 0, 1, and 6 months Accelerated: 0, 7, and 21 to 30 days, and 12 months

This table should be used in conjunction with UpToDate content on hepatitis B virus immunization in adults. Recommended doses for persons <18 years of age can be found in the UpToDate content on hepatitis B vaccines for children.

HBsAg: hepatitis B surface antigen; HepA: hepatitis A; HepB: hepatitis B.

* This is a double dose of the standard formulation of Engerix-B for patients ≥20 years of age (Engerix-B does not have a separate dialysis formulation).

¶ HepB-CpG (sold as Heplisav-B) is a recombinant yeast-derived vaccine that contains 3000 mcg of immunostimulatory phosphorothioate oligodeoxyribonucleotide as an adjuvant.

Δ Data are not available to assess the effects of Heplisav-B on breastfed infants or on maternal milk production and excretion.

Data from:

1. *Schillie S, Vellozzi C, Reingold A, et al. Prevention of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep 2018; 67:1.*
2. *Schillie S, Harris A, Link-Gelles R, et al. Recommendations of the Advisory Committee on Immunization Practices for use of a hepatitis B vaccine with a novel adjuvant. MMWR Morb Mortal Wkly Rep 2018; 67:455.*
3. *Weng MK, Doshani M, Khan MA, et al. Universal hepatitis B vaccination in adults aged 19–59 years: Updated recommendations of the Advisory Committee on Immunization Practices — United States, 2022. MMWR Morb Mortal Wkly Rep 2022; 71:477.*
4. *Sandul AL, Rapposelli K, Nyendak M, et al. Updated recommendation for universal hepatitis B vaccination in adults aged 19–59 years — United States, 2024. MMWR Morb Mortal Wkly Rep. 2024; 73:1106.*

Graphic 117603 Version 8.0

Groups at increased risk for hepatitis B virus infection

Individuals at risk for HBV due to vertical transmission (ie, mother-to-child transmission)
▪ Individuals born in regions with high (≥8%) or intermediate (≥2%) prevalence rates for HBV, including immigrants and adopted children*
▪ Infants born to pregnant persons who are HBsAg positive¶
▪ US-born persons not vaccinated as infants whose parents were born in regions with high HBV endemicity (≥8%)*
Individuals at risk due to horizontal transmission (ie, percutaneous or mucosal exposure to blood or body fluids contaminated with blood)Δ
▪ Household contacts of HBsAg-positive persons
▪ Needle sharing or sexual contacts of HBsAg-positive persons
▪ Individuals who have ever injected drugs
▪ Individuals with multiple sexual partners and/or history of sexually transmitted infections
▪ Men who have sex with men
▪ Inmates of correctional facilities or other detention settings
▪ Individuals with HIV infection◇
▪ Individuals with current or past HCV infection§
▪ Individuals with end-stage kidney disease on maintenance renal dialysis
Other individuals
▪ Individuals with elevated alanine aminotransferase or aspartate aminotransferase levels of unknown etiology
▪ Individuals who request HBV testing

In the United States, screening for HBV includes[1]:

- **Risk-based screening** – For all individuals (including children and adolescents), screen those who have any of the risk factors listed in the table if they might have been susceptible during the period of increased risk¥. For those with ongoing risk factors (ie, for horizontal transmission) who remain susceptible, continue to test periodically.Δ
- **Universal screening** – For individuals ≥18 years of age, screen at least once in a lifetime. However, for those without risk factors for HBV, screening is generally not needed if there is documentation of completing a hepatitis B vaccine series and evidence of immunity (anti-HBs ≥10

milli-international units/mL) after vaccination.‡

- **Pregnancy screening** – Screen all pregnant people during each pregnancy, regardless of vaccination status of history of prior testing.

Refer to UpToDate content on screening and diagnosis of HBV, HBV immunization, and HBV and pregnancy for more detailed information on screening and vaccination.

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anti-HBc: hepatitis B core antibodies; anti-HBs: hepatitis B surface antibody; HBIG: hepatitis B immune globulin; HBsAg: hepatitis B surface antigen; HBV: hepatitis B virus; HCV: hepatitis C virus; HIV: human immunodeficiency virus; US: United States.

* If HBsAg-positive persons are found in first-generation immigrants of a family, subsequent generations should be tested.

¶ To reduce the risk of perinatal transmission, infants born to HBsAg-positive mothers should receive HBIG and hepatitis B vaccine as soon as possible and within 12 hours of birth and then complete the hepatitis B series. Postvaccination serology should be obtained at 9 to 12 months. Refer to the UpToDate topic that discusses HBV immunization in infants.

Δ In unvaccinated individuals with ongoing HBV risk through percutaneous or mucosal exposure, hepatitis B vaccine should be initiated at the time of screening; the need for subsequent doses will depend upon the results. Postvaccination serology should be performed to ensure immunity. For at-risk persons who do not complete the vaccine series, repeat testing should be performed periodically (eg, every 1 to 2 years).

◇ The presence of HBV coinfection informs the choice of antiretroviral regimen. In addition, patients with HIV who are not immune should be vaccinated regardless of age or risk factors, since HBV infection has an accelerated course in coinfected patients.

§ Patients with chronic HBV are at risk for HBV reactivation with direct-acting antiviral therapy for hepatitis C. Refer to the UpToDate topic that provides an overview of the management of hepatitis C infection.

¥ Susceptible persons include those who have never been infected with HBV (ie, HBsAg-negative, total anti-HBc-negative, and anti-HBs-negative) and either did not complete a hepatitis B vaccine series per the Advisory Committee on Immunization Practices recommendations or who are known to be vaccine nonresponders.

‡ For most patients who remain without risk factors for acquiring HBV, repeat screening is not warranted. However, screening prior to blood, plasma, organ, tissue, or semen donation is routinely performed, regardless of the person's prior history. In addition, screening is warranted prior to initiating immunosuppressive therapy (eg, corticosteroids, biologics, cancer chemotherapy, antirejection therapies) since persons with HBV are at risk for HBV reactivation. Refer to the UpToDate topic on HBV reactivation.

Reference:

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