Excerpt from “Non-occupational Post-exposure Prophylaxis (nPEP) and Pre-Exposure Prophylaxis (PrEP) for HIV Prevention in Adolescents and Young Adults” by D. Straub MD, MPH and T. Mullins MD, MS. *Advances in Pediatrics*. In Press.

Non-occupational Post-Exposure Prophylaxis (nPEP)

nPEP is the use of antiretroviral medication after isolated sexual, injection drug use, or other non-occupational HIV exposure in order to prevent HIV infection. The U.S. Centers for Disease Control and Prevention (CDC)/Department of Health and Human Services released its most recent nPEP recommendations in 2016.[1]

A summary of the 2016 U.S. CDC nPEP guidelines[1] is as follows:

- Clinicians should evaluate persons rapidly for nPEP when care is sought ≤72 hours after a potential non-occupational exposure that presents a substantial risk for HIV acquisition (see Figure 1 for algorithm). “Substantial risk” and “negligible risk” as defined by the CDC are shown in Figure 1. If the source of the exposure is known to be HIV-infected, nPEP is recommended. If the HIV status of the source of exposure is unknown, recommendation for nPEP should be determined on a case-by-case basis. nPEP should not be initiated ≥73 hours after exposure or if there is negligible risk for HIV acquisition.
- At the initial evaluation visit, the clinician should determine the HIV status of the potentially exposed person and the exposure source person (if possible), the timing and characteristics of the exposure for which care is being sought, and the frequency of possible HIV exposures, as well as assessment for other needed treatment or prophylaxis (e.g., STIs, pregnancy).
- All persons considered for nPEP should be tested for HIV, preferably using rapid combined antigen/antibody, or antibody blood tests. If rapid tests are unavailable and nPEP is otherwise indicated, it should be started without delay and can be later discontinued if the patient is determined to *already* be infected or the exposure source is determined to *not* be infected.
- All persons offered nPEP should be prescribed a 28-day course of a 3-drug antiretroviral regimen.
    - The preferred regimen for otherwise healthy adults and adolescents is tenofovir disoproxil fumarate (TDF) 300mg with emtricitabine 200mg once daily PLUS raltegravir 400mg twice daily OR dolutegravir 50mg daily*.
    - The alternative regimen for otherwise healthy adults and adolescents is TDF 300mg with emtricitabine 200mg once daily PLUS darunavir 800mg AND ritonavir 100mg once daily.
    - For regimens for children, persons with impaired renal function, and pregnant women, see the nPEP guidelines.[1]
- All persons evaluated for possible nPEP should also be provided any indicated prevention, treatment, or supportive care for other exposure-associated health risks and conditions (e.g., bacterial sexually transmitted infections, traumatic injuries, hepatitis B and C virus infections, or pregnancy).
- All persons who report behaviors or situations that place them at risk for frequently recurring HIV exposures (e.g., injection drug use, sex without condoms) or who report receipt of ≥1 course of nPEP in the past year should be provided risk-reduction counseling and intervention services, including consideration of pre-exposure prophylaxis (PrEP; discussed below).
- nPEP should only be provided for infrequent exposures. Patients who have frequent, recurrent exposures should be provided with intensive risk-reduction interventions and consideration of prescription of PrEP. However, if the most recent exposure was within 72 hours of the evaluation, nPEP may be indicated with subsequent transition to PrEP.
- Laboratory testing and the recommended follow-up schedule include HIV, STI, pregnancy, and kidney and liver function testing (Table 1). Ideally, follow up should occur at 4-6 weeks, 3 months, and 6 months after exposure. Laboratory testing for the exposure source person and for individuals who seroconvert is also outlined.[1]

*Since the publication of the nPEP guidelines, additional data suggest safety concerns associated with use of dolutegravir in women at risk for pregnancy. In an ongoing NIH-funded observational study in

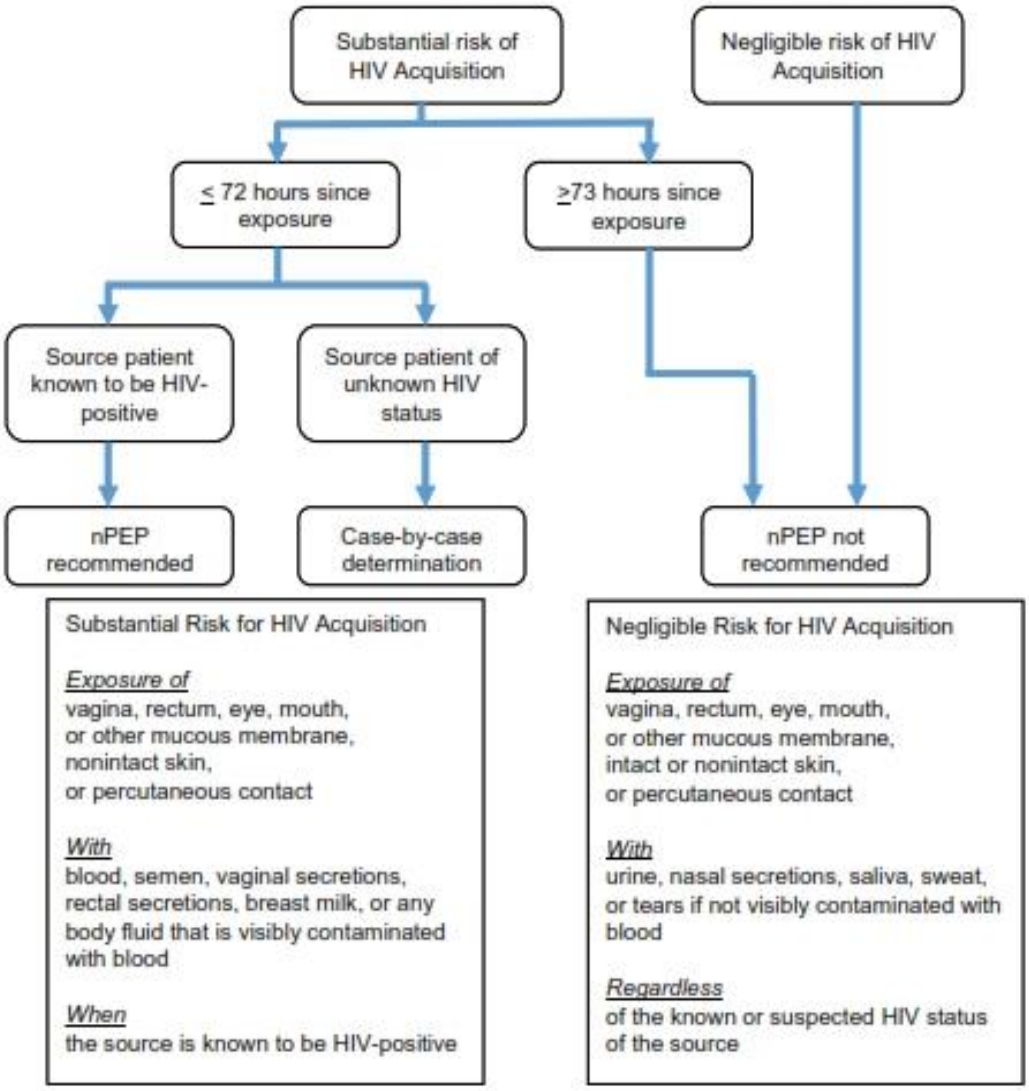
Botswana, a recent preliminary unscheduled data analysis suggested that exposure to dolutegravir-containing regimens at conception may increase the risk of neural tube defects. Four infants with neural tube defects were born to 426 women exposed to dolutegravir at conception, yielding a proportion of 0.9%, as compared to 0.1% in infants of women exposed to other antiretroviral drugs at conception. According to the manufacturer of dolutegravir, a complete package of reproductive toxicology studies showed no evidence of adverse developmental outcomes.[2] While surveillance is ongoing, as a result of this preliminary data, the CDC recommended in May 2018 that clinicians prescribing PEP should avoid the use of dolutegravir for non-pregnant women of childbearing potential who are sexually active or have been sexually assaulted and who are not using an effective birth control method, as well as for women early in pregnancy. The preferred regimen for nPEP for these women includes raltegravir, tenofovir, and emtricitabine (as listed above). Furthermore, all women of childbearing potential starting PEP should have a pregnancy test performed. If the PEP regimen for a non-pregnant woman of child-bearing potential must include dolutegravir (e.g., raltegravir is not available), she should use an effective birth control method until the PEP regimen is completed. Additionally, dietary folic acid 400 mcg is recommended daily.[3]

Pre-exposure Prophylaxis (PrEP)

PrEP is the use of anti-retroviral medications prior to potential exposure in order to prevent HIV infection. The only medication currently approved by the U.S. FDA for PrEP is fixed-dose combination tenofovir disoproxil fumarate 300mg-emtricitabine 200mg (TDF-FTC; Truvada®) administered once daily. The CDC PrEP guidelines were updated in 2017.[4] The CDC also published a clinical provider's supplement that provides resources that can be used to provide PrEP care, including counseling resources for clinicians and educational handouts for patients.[5] These documents have not been updated to reflect the recent FDA approval of PrEP for use in adolescents. Several U.S. organizations, including SAHM,[6] American College of Obstetricians and Gynecologists (ACOG),[7] and the International AIDS Society (IAS)-USA,[8] have released statements supporting the use of PrEP among those at risk of HIV infection.

The CDC PrEP guidelines include suggested indications for PrEP (**Table 2**). Baseline laboratory evaluations should include HIV testing (with an antigen/antibody test [preferred], antibody test, or rapid point-of-care FDA-approved fingerstick blood test), renal function testing (including calculation of estimated creatinine clearance using the Cockcroft-Gault formula), hepatitis B serology, and STI testing. An estimated creatinine clearance <60 ml/min is a contraindication to TDF-FTC PrEP. Evaluating hepatitis B status is important because reactivation of hepatitis B and resultant liver toxicity can occur when PrEP is stopped.[4] Hepatitis C testing is recommended for people who have injected drugs. Patients should be counseled that the time required to achieve protective levels of PrEP ranges from 7 days for the rectal compartment to 20 days for blood and the cervicovaginal compartment.[4] The most common side effects include headache and gastrointestinal distress. The CDC recommends that PrEP be limited to a 3 month supply at a time and that patients be evaluated every 3 months for HIV testing, pregnancy testing, PrEP prescription refills, assessment of side effects and adherence, and STI testing. Creatinine clearance should be monitored every 6 months, and continued need for PrEP should be evaluated every year.[4]

Figure 1: Algorithm for Evaluation and Treatment of Possible Nonoccupational HIV Exposure[2]



Reproduced from the Centers for Disease Control and Prevention. Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV—United States, 2016. 2016; https://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf.

Table 1. Recommended Schedule of Laboratory Evaluations of Source and Exposed Persons for Providing nPEP with Preferred Regimens[1]

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

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

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

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

[c] If exposed person susceptible to hepatitis B at baseline.

[d] If exposed person susceptible to hepatitis C at baseline.

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

[f] Testing for chlamydia and gonorrhea should be performed using nucleic acid amplification tests. For patients diagnosed with a chlamydia or gonorrhea infection, retesting 3 months after treatment is recommended.

- For men reporting insertive vaginal, anal, or oral sex, a urine specimen should be tested for chlamydia and gonorrhea.
- For women reporting receptive vaginal sex, a vaginal (preferred) or endocervical swab or urine specimen should be tested for chlamydia and gonorrhea.
- For men and women reporting receptive anal sex, a rectal swab specimen should be tested for chlamydia and gonorrhea.
- For men and women reporting receptive oral sex, an oropharyngeal swab should be tested for gonorrhea. (http://www.cdc.gov/std/tg2015/tg-2015-print.pdf)

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

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

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

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

Reproduced from the Centers for Disease Control and Prevention. Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV United States, 2016. 2016; https://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf. Accessed 12/2/18.

Table 2: Summary of Current U.S. PrEP Guidance (2017)[4]

	Men Who Have Sex with Men	**Heterosexual Women and Men**	**Injection Drug Users**
Detecting substantial risk of acquiring HIV infection	HIV-positive sexual partner Recent bacterial STI* High number of sex partners History of inconsistent or no condom use Commercial sex work	HIV-positive sexual partner Recent bacterial STI** High number of sex partners History of inconsistent or no condom use Commercial sex work In high-prevalence area or network	HIV-positive injecting partner Sharing injection equipment
Clinically eligible	Documented negative HIV test result before prescribing PrEP No signs/symptoms of acute HIV infection Normal renal function; no contraindicated medications Documented hepatitis B virus infection and vaccination status		
Prescription	Daily, continuing, oral doses of TDF/FTC (Truvada®), $\leq$ 90 day supply		

<table>
<tr><td rowspan="2">Other services</td><td colspan="3">Follow-up visits at least every 3 months to provide the following:
HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment
At 3 months and every 6 months thereafter, assess renal function
Every 6 months, test for bacterial STIs</td></tr>
<tr><td>Do oral/rectal STI testing</td><td>For women, assess pregnancy intent
Pregnancy test every 3 months</td><td>Access to clean needles/syringes and drug treatment services</td></tr>
</table>

* Gonorrhea, chlamydia, syphilis for men who have sex with men including those who inject drugs.
** Gonorrhea, syphilis for heterosexual women and men including those who inject drugs.
STI: sexually transmitted infection
Reproduced from the U.S. Public Health Service, Centers for Disease Control and Prevention. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2017 Update Clinical Practice Guideline.

References:

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