



HIV MEDICAL ALERT

FOR PRIMARY HEALTH CARE PROVIDERS AND HEALTH PROFESSIONALS

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HIV Medical Alert

provides clinicians with comprehensive and up-to-date information about diagnosis, treatment, and prevention of HIV.

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HIV Medical Alert is also available on-line at www.upstate.edu/cei



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WELCOME to the *HIV Medical Alert* Newsletter Continuing Medical Education (CME) format. This activity has been planned and implemented in accordance with the Essentials and Standards of the Medical Society of the State of New York through the joint sponsorship of Glens Falls Hospital and Upper Hudson Primary Care Consortium. The Glens Falls Hospital is accredited by the Medical Society of the State of New York (MSSNY) to sponsor continuing medical education for physicians. The Glens Falls Hospital designates this continuing medical education activity for a maximum of 1 hour of Category I credit towards the American Medical Association Physician's Recognition Award (AMA-PRA). Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

Non-Occupational HIV Post Exposure Prophylaxis (nPEP): (Finally) Ready for Prime Time

by **Michael Foltzer, MD**

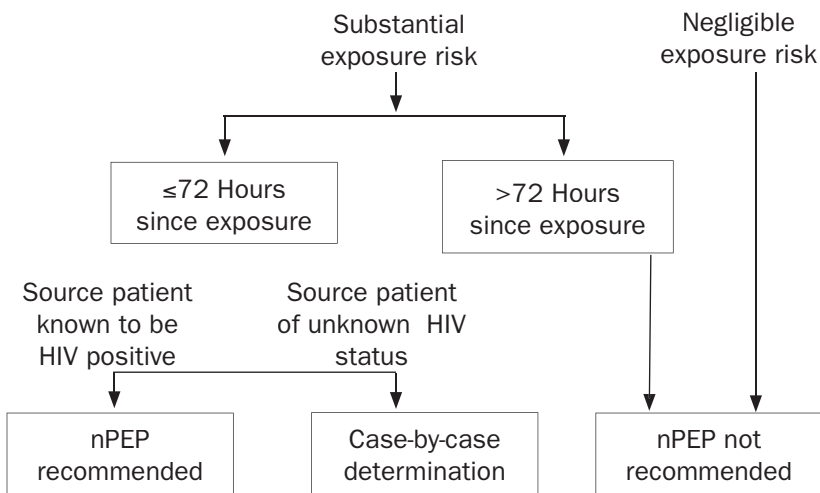
Prophylaxis with antiretrovirals has been recommended following occupational exposure for approximately a decade and more recently for survivors of sexual assault and following occupational exposure in New York State; in January 2005 the CDC issued recommendations for non-occupational exposures including sexual or shared injection needle use. This newsletter reviews the rationale for nPEP, summarizes the recent CDC guidelines and offers practical advice for effective implementation of an nPEP program.

Rationale for nPEP

Zidovudine and other agents such as nevirapine have been shown to be quite effective in reducing rates of vertical transmission from mother to infant. Animal studies have also shown prophylaxis to be effective when administered within 24 hours of mucus membrane inoculation and continued for 28 days. Results of animal studies, a seminal occupational PEP CDC study published in 1997 and the success of perinatal prophylaxis to prevent vertical transmission have collectively driven expanded use of PEP in other scenarios.

nPEP has been effectively implemented in small non-controlled studies reported from Brazil in gay men following a high-risk sexual exposure. For those receiving zidovudine and lamivudine within 96 hours, there was 1 seroconversion compared with 11 seroconversions in the group not re-

Figure 1.
Algorithm for evaluation and treatment of possible nonoccupational HIV exposures



Substantial Risk for HIV Exposure

Exposure of

vagina, rectum, eye, mouth, or other mucous membrane, non-intact skin, or percutaneous contact

With

blood, semen, vaginal secretions, rectal secretions, breast milk, or any body fluid that is visibly contaminated with blood

When

the source is known to be HIV-infected

Negligible Risk for HIV Exposure

Exposure of

vagina, rectum, eye, mouth, or other mucous membrane, intact or non-intact skin, or percutaneous contact

With

urine, nasal secretions, saliva, sweat, or tears, if not visibly contaminated with blood

Regardless

of the known or suspected HIV status of the source

ceiving PEP. Similarly, for Brazilian women presenting within 72 hours of sexual assault, 28 days of zidovudine and lamivudine resulted in 0/180 seroconversions compared with 4/145 seroconversions in the non-treated group.

Arguments against nPEP

Multiple arguments against broad implementation of nPEP have been addressed by small studies. Specifically, the availability of nPEP has not increased high-risk behaviors (not abused as a “morning-after pill”); however several studies report about 15% of nPEP recipients requesting a second nPEP course within a year. Toxicity of nPEP (excluding nevirapine) is generally modest with approximately 22% of recipients in a small nPEP study changing regimen due to toxicity or adverse reaction. However, the cost of nPEP is quite significant; the estimated range is from \$230k to \$530k per HIV infection prevented.

Clinical Considerations

The use of nPEP requires an evaluation of the nature of the

exposure (relative risk), the HIV status of the both the exposed and source and the timing and frequency of the exposure (see Figure 1).

- Baseline HIV testing is recommended for exposed individuals-this should ideally be a rapid test with 1 hour results reporting. If rapid testing is not available, nPEP should not be delayed pending test results.
- Evaluate the source patient-those known to be HIV positive or from high risk groups (gay man, sex worker or IDU) should be factored in the decision to offer nPEP. Of note, the algorithm does not clearly offer nPEP when the source characteristics are unavailable. From a practical perspective, in those situations where the risk characteristics of the source are unknown, the nature of the exposure (risk for transmission) should inform the decision to offer nPEP.
- Is the source patient known to be HIV positive with documented or suspected antiretroviral resistance? Urgent discussion regarding nPEP drug selection with an HIV specialist is recommended in this circumstance.

- Have < 72 hours elapsed since the exposure?
- What is the risk of the exposure? Certain events are associated with magnitudes of higher risk of transmission (see Table 1).
- Is the exposure event one repeated frequently? In this situation a patient could be on nearly continuous PEP, a scenario which should be avoided.

Implementing nPEP

- A 28 day regimen is recommended. This should be initiated as soon as possible with ideally a 3-5 day starter pack of medications physically given to the patient.
- A triple-drug regimen is recommended in all situations. While the CDC recommends either nNRTI or PPI based program, the NYSDOH AIDS Institute Guidelines recommend 2 nucleosides + 1 nucleotide. Preferred regimens are listed in Table 2. Specific recommendations for a particular drug regimen should be based upon drug availability and the choices made by the patient following careful discussion of adverse effect profiles.
- Women of child-bearing potential should not receive efavirenz following vaginal sexual exposure-oral contraceptive efficacy is likely reduced and efavirenz is a known teratogen listed as pregnancy category D by the FDA.
- Patients should be seen within 3-5 days, so that the medical provider may further counsel (including future risk reduction), review baseline HIV results and manage adverse effects. Where available, HIV specialists should manage the patient on antiretrovirals.
- Despite the availability of nPEP, risk reduction counseling must remain the major emphasis of follow-up care.
- Follow-up HIV testing is recommended at 4-6 weeks, 3 months and 6 months post exposure.

The Clinical Education Initiative Line

The New York State AIDS Institute Clinical Education Initiative (CEI) provides a clinical educational line for primary care practitioners that are providing care to people with HIV in New York State.

Table 1
Estimated per-act risk for acquisition of HIV by exposure Route*

Exposure Route	Risk per 10,000 exposures to an infected source
Blood transfusion -----	9,000
Needle-sharing injection-drug use-----	67
Receptive anal intercourse-----	50
Percutaneous needle stick-----	30
Receptive perile-vaginal intercourse-----	10
Insertive anal intercourse -----	6.5
Insertive penile-vaginal intercourse-----	5
Receptive oral intercourse -----	1
Insertive oral intercourse-----	0.5

* Estimates of risk for transmission from sexual exposures assume no condom use.

Table 2. Recommended Regimens for nPEP

CDC Recommendations

- Efavirenz 600 mg once daily + zidovudine/lamivudine (Combivir®) 1 po twice daily **or**
- Efavirenz 600 mg once daily + tenofovir/emtricitabine (Viread®) 1 po daily **or**
- Lopinavir/ritonavir (Kaletra®) 3 po bid + zidovudine/lamivudine (Combivir®) 1 po twice daily

Efavirenz not to be used in women of childbearing potential

NYSDOH Recommendations

- Tenofovir 300 mg daily po + zidovudine/lamivudine (Combivir®) 1 po twice daily **or**
- Tenofovir 300 mg daily po + zidovudine 300 mg po twice daily + lamivudine 150 mg po twice daily
- Other agents can be considered if there is intolerance.

Providers who are working with patients in need of nPEP can access expert clinicians to guide them in tailoring nPEP recommendations to the presenting circumstances. Clinicians can benefit from this one-on-one dialogue with an HIV Specialist who serves their region.

CEI-Lines are located throughout the State. Each regional CEI center has HIV Clinical Specialists that are familiar with the geography and the resources available in their region. HIV Clinical Specialists can direct practitioners to the nearest regional tertiary care center and to providers of advanced HIV care.

To access the CEI-Line in your area, call the CEI site for your region listed at www.hivguidelines.org. CEI-Line services are available 24-hours a day, 7 days a week. HIV Clinical Specialists will return calls within 24 hours from the time of the initial request.

Conclusion

The implementation of PEP has now expanded to all situations in which HIV transmission may occur. Curiously, the CDC recommends a standard 3 drug regimen in nPEP—this is a departure from the current (and dated) recommendations following occupational exposure. The science of PEP continues to evolve as more tolerable, relatively simple drug combinations are employed. New York State providers should be aware of the antiretroviral differences between NYS DOH AIDS Institute and CDC recommended nPEP regimens. Whichever guidelines inform the choices of PEP medications, it is gratifying to know that nPEP has finally arrived.

Sources

http://www.hivguidelines.org/public_html/npep/npep.htm (NYSDOH nPEP Guidelines Dec 2004)

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5402a1.htm> (CDC nPEP Guidelines Jan 2005)

Author

Dr. Foltzer is an HIV Specialist from NYS who is currently serving as Director of the Infectious Diseases Division for Geisinger Health System in Danville, PA. He is a past member and chair of the AIDS Institute Adult Medical Care Criteria Committee.

Continuing Education Test

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To earn credit:

1. Read the CME article.
2. Review the objectives
3. Study and apply the content to the objectives and to your practice.
4. Complete the Post-Test.
5. **Return the answer sheet as directed at the bottom of the evaluation page. (Expires September 2007)**

Objectives: At the conclusion of this activity, the learner will be able to:

1. Describe the fundamentals of implementing post-exposure prophylaxis following a non-occupational exposure to HIV/AIDS.
2. Identify the steps to take in evaluating and treating a patient who requests care following a possible non-occupational HIV exposure.
3. Discuss the clinical considerations of recommending nPEP.

Note: This CME activity and quiz is designated for 1 credit.

Select the best answer for each of the following.

1. **Needle-sharing is at least 10 times more likely to transmit HIV than a needle-stick injury.**
 a. True
 b. False
2. **Which of the following is a risk factor for HIV transmission? (Please check all that apply.)**
 a. Bite
 b. needle stick injury
 c. receptive oral sex
 d. kiss
3. **All of the following antiretrovirals are not teratogenic except:**
 a. lopinavir/ritonavir (kaletra®)
 b. nevirapine
 c. zidovudine
 d. efavirenz
 e. b and d
4. **Randomized controlled trials have been cited to substantiate the use of PEP for survivors of sexual assault.**
 a. True
 b. False
5. **What resource do you most frequently call with questions about nPEP?**
