Development of Guidelines on Nonoccupational HIV Postexposure Prophylaxis for the State of Rhode Island

Roland C. Merchant, MD, MPH[a,b,c]
Kenneth H. Mayer, MD[a,d,e]
Carol A. Browning, MS, RN[f]

SYNOPSIS

The Brown University AIDS Program and the Rhode Island Department of Health joined with health care practitioners, researchers, and representatives of community-based health, social service, and advocacy organizations to create comprehensive guidelines on nonoccupational HIV postexposure prophylaxis for the state of Rhode Island. These guidelines offer health care practitioners detailed advice on the evaluation and management of blood or body fluid exposures outside the health care setting, e.g., through sexual assault, consensual sex, injecting-drug use, or needlestick injuries. In these circumstances, HIV postexposure prophylaxis serves those for whom primary prevention measures have failed or were impractical or impossible.

The guidelines represent the end product of coordination among private and public, academic and nonacademic, clinician and layperson groups committed to decreasing the incidence of HIV infections in the state of Rhode Island. The guidelines serve as both a resource for health care practitioners and a means of educating them on this method of HIV prevention.

[a]Division of Infectious Diseases, Brown Medical School, Providence, RI
[b]Section of Emergency Medicine, Brown Medical School, Providence, RI
[c]Department of Emergency Medicine, Rhode Island Hospital, Providence, RI
[d]Brown University AIDS Program, Providence, RI
[e]Department of Medicine, Miriam Hospital, Providence, RI
[f]Office of HIV and AIDS, Rhode Island Department of Health, Providence, RI
Address correspondence to: Roland C. Merchant, MD, MPH, Dept. of Emergency Medicine, Rhode Island Hospital, 593 Eddy St., Davol 141, Providence, RI 02903; tel. 401-444-5109; fax 401-444-4307; e-mail <rmerchant@lifespan.org>.
©2004 Association of Schools of Public Health

In February 1998, a physician assistant in the emergency department of a hospital in Rhode Island attempted to help an adolescent patient who had been sexually assaulted by two assailants of unknown HIV status. He believed that she might benefit from HIV postexposure prophylaxis (HIV PEP), but did not know how to prescribe it. He consulted an infectious disease physician and an obstetrician/gynecologist. Both told him that since no HIV PEP protocol existed for sexual assault, they could not assist him. Not knowing how to proceed and having exhausted his usual sources of consultation, he discharged the patient with good luck wishes instead of anti-HIV medications and referred her to outpatient follow-up for her sexual assault.

This physician assistant was attempting to reduce the transmission risk for this patient by using antiretroviral medications to prevent a potential HIV infection. It is well known that the vast majority of HIV infections arise from sexual exposures, yet it is not known how many follow sexual assaults. Nor is it known whether vaginal or anal trauma during sexual assault confers added transmission risk. Postexposure prophylaxis is a proposed means of reducing HIV risk through antiretroviral medications taken shortly after a potential HIV exposure. Although there is strong evidence that this approach works after needlestick exposures in the health care setting,[1] its efficacy after sexual exposures is not well established. However, evidence from occupational HIV PEP studies,[1] perinatal HIV prophylaxis trials,[2,3] and animal and immunologic research[4,5] indicates that HIV PEP may be an effective means of preventing HIV infection.

Over a period of several years, staff members of the Brown AIDS Program (BRUNAP) and officials of the Rhode Island Department of Health (RIDOH) received reports of failed (such as the physician assistant's experience described above) or even inappropriate attempts to provide HIV PEP in nonoccupational settings in Rhode Island. Some patients unnecessarily received HIV PEP, some received inadequate regimens, and some did not receive adequate follow-up or counseling. Others at risk of HIV infection through sexual exposures, blood or body fluid exposures, and injecting-drug use did not receive HIV PEP when it was indicated. It was clear from these reports that nonoccupational HIV PEP provision in Rhode Island was not optimal. Representatives from BRUNAP and RIDOH feared that because of missed opportunities to properly administer HIV PEP in nonoccupational settings, some people in Rhode Island may have become HIV-infected as a result.

In 2001, BRUNAP formed the Nonoccupational HIV Postexposure Prophylaxis Task Force. This group of clinicians, researchers, staff members of community-based health, social service, and advocacy organizations, and representatives from RIDOH discussed the need for a standardized approach to nonoccupational HIV PEP in Rhode Island. In the absence of national guidelines, the group proposed that the Task Force create such guidelines for clinicians. Several important questions arose: What form should the guidelines take? What should they address? Who should issue them? How should they be disseminated?

BRIEF HISTORY OF NONOCCUPATIONAL HIV PEP GUIDELINES

At the Task Force's disposal were a large body of literature and a few guidelines on nonoccupational HIV PEP. The guidelines chiefly differed in their focus (specific vs. all exposures), extent of advice (detailed vs. generalized), format (iterative vs. summarized), and governmental level (local vs. national). Several countries, including France, Germany, and the United Kingdom, have guidelines or recommendations regarding nonoccupational HIV PEP.[6] At present, there are no national guidelines for the United States. Although the Centers for Disease Control and Prevention (CDC) issued guidelines on HIV PEP for health care workers in 1996, the agency has not released guidelines for nonoccupational HIV PEP.[7] In 1998, the CDC advised clinicians on the accumulated evidence and experience regarding nonoccupational exposures, but did not recommend for or against usage of HIV PEP.[8] Since then, the CDC has convened several external advisory reviews of nonoccupational HIV PEP and has drafted recommendations that may receive Department of Health and Human Services approval and be disseminated in 2003 or 2004. Officials in three states have issued guidelines: In 1998, the Department of Health of the State of New York released guidelines on HIV PEP following sexual assault,[9] as did California in 2001.[10] In 2000, the Massachusetts Department of Public Health released an advisory regarding nonoccupational HIV PEP usage.[11]

THE RHODE ISLAND TASK FORCE

After reviewing the aforementioned guidelines and recommendations and the available literature, the Task Force decided that the Rhode Island guidelines (*1*) should address all possible forms of HIV transmission outside the health care setting; (*2*) should explicitly state the exposures for which HIV PEP may be indicated, what medications should be dispensed, their timing, and the follow-up needed; (*3*) were to be

comprehensive, detailed, and iterative yet reader-friendly; and (*4*) should be a consensus document representing the views of health care providers and community organizations that should be endorsed by RIDOH.

From June through December 2001, the Task Force drafted a set of guidelines. The draft was presented at an open forum of the Clinical AIDS Task Force of BRUNAP, which was attended by local physicians, nurses, administrators, pharmaceutical company representatives, addiction medicine specialists and counselors, students, and community activists. The Task Force collected the comments and suggestions of this group, refined the guidelines, and then distributed them once again for review. Over the succeeding months, the Task Force revised the draft using input from BRUNAP members.

OFFICIAL SUPPORT AND DISSEMINATION

In May 2002, the Task Force presented its work to Patricia A. Nolan, MD, MPH, Director of RIDOH. Dr. Nolan and her staff suggested improvements to the proposed guidelines, which were implemented. On August 1, 2002, the official Rhode Island nonoccupational HIV PEP guidelines were released by RIDOH

Figure 1. *Nonoccupational HIV Postexposure Prophylaxis Guidelines for Rhode Island Healthcare Practitioners*: key points

Context

- *Appropriateness:* The majority of blood or body fluid exposures do *not* require HIV PEP provision (e.g., exposures to urine, feces, sputum, saliva, and other sources that cannot possibly transmit HIV or exposures to sources with low likelihood of HIV infection).
- *Ancillary concerns:* HIV PEP is best provided as part of an HIV risk-reduction program.
- *Efficacy:* Efficacy is presumed from the available literature, but HIV PEP is not a proven means of HIV prevention.
- *Medication choice:* The medications listed in the guidelines are based upon recommendations from others' experiences in multiple settings. Other regimens are possible and may or may not be more effective.

Treatment timing

- *Initiation:* Administer the first dose of HIV PEP without delay—preferably within one hour of exposure.
- *Treatment window:* Treat within 72 hours of an exposure. HIV PEP following this period may not be effective, but it may be given in exceptional circumstances.
- *Duration:* Provide 28 days of uninterrupted therapy.
- *Exposure uncertainties:* Provide the highest level of HIV PEP when the available information is unclear. Adjust later as necessary. HIV testing of the source of infection should *not* delay HIV PEP provision.
- *Consultation:* Consultations should be sought as required, but should not delay the first dose of HIV PEP. Medication adjustments, when needed, can be made following consultations.

Patient consent

- *Voluntary:* HIV PEP should only be provided to patients capable of giving consent (or with the consent of a caretaker/parent/guardian) and only to patients who are willing and able to continue treatment for the full period. Some institutions may mandate signed informed consent forms.
- *Disclosure:* Patients must be informed that HIV PEP (*1*) is not a cure for HIV infections; (*2*) is of unknown efficacy; (*3*) cannot be used as prophylaxis prior to risky sexual encounters or injecting drug use; and (*4*) must be taken under the care of a health care provider knowledgeable regarding HIV PEP and (if applicable) in the context of an HIV/STD risk reduction program.
- *Refusal:* Because a patient's recent traumatic experience may adversely affect his or her capacity to accept HIV PEP, patients who decline HIV PEP should be reevaluated within 24 hours and HIV PEP should be offered or recommended when it is indicated.

Testing

- *Baseline testing:* Patients receiving HIV PEP should undergo baseline laboratory testing at the time of receiving their first dose or at least within 72 hours of receiving their first dose. Testing must not delay receipt of HIV PEP. Patients who decline baseline testing should not be refused HIV PEP.
- *HIV source testing:* Testing of the source should occur whenever possible. HIV PEP provision should not be delayed to accommodate source testing.

with the agency's endorsement.[12] The *Nonoccupational HIV Postexposure Prophylaxis Guidelines for Rhode Island Healthcare Practitioners* are available on the Web at www.brown.edu/brunap or http://www.healthri.org. These are the first comprehensive, state-sponsored nonoccupational HIV PEP guidelines in the United States. Figure 1 shows the key points included in the guidelines, and Figure 2 provides a brief overview of the hierarchical scheme used to match exposure risk and medications.

Releasing the guidelines was clearly not enough. The Task Force recognized that the true value of the guidelines was in its educational potential. The important work ahead was in disseminating the guidelines to health care practitioners in the state and informing them on the appropriate usage of nonoccupational HIV PEP. Toward that end, BRUNAP and RIDOH utilized several different approaches to distribute the guidelines. First, copies of the guidelines with a cover letter signed by Dr. Nolan and by Dr. Mayer, Director of BRUNAP, were mailed to Rhode Island emergency departments, sexually transmitted disease clinics, and physicians who were likely to evaluate patients for nonoccupational HIV PEP. Second, both BRUNAP and RIDOH placed the guidelines on their websites, and the largest hospital system in the state provided a link to the guidelines on its intranet. Third, press releases were distributed to media outlets announcing the release of the guidelines, and a news story was featured on radio and television and in various periodicals. Finally, BRUNAP offered an informational meeting for health care practitioners in the state regarding the guidelines, and the guidelines' authors gave presentations to clinicians at several hospitals throughout the state on the use of the guidelines.

NEXT STEPS

Drs. Merchant (principal author of the guidelines) and Mayer are conducting a study of the provision of HIV PEP at Rhode Island's emergency departments as a prelude to a study examining the possible impact of the guidelines on clinician practice. BRUNAP also plans to conduct further didactic programs on nonoccupational HIV PEP. It is hoped that with continued research and provider education, provision of nonoccupational HIV PEP in Rhode Island will be better understood and its usage improved.

Although other states may choose to use Rhode Island's guidelines as a basis for developing programs, a national version would be preferable. We are hopeful that the CDC will release guidelines on nonoccupational HIV PEP within the coming year. In the interim, perhaps locally developed guidelines such as those in Rhode Island may expedite the development of a nationally endorsed normative standard for nonoccupational HIV PEP. This standard will serve to educate providers on this important form of secondary

Figure 2. Overview of nonoccupational HIV postexposure prophylaxis hierarchy

Exposure	*Course of action*
Exposure to known HIV-infected source(s).	Recommend HIV PEP: • If source's medication history is unknown or source is known not to be on anti-HIV medications: Recommend zidovudine (AZT/ZDV) or stavudine (d4T) + lamivudine (3TC/Epivir) and nelfinavir (Viracept) or indinavir (Crixivan). • If source's medication history is known: Under advisement of a specialist knowledgeable in HIV PEP and HIV medications, choose a medication regimen that takes into account the source's medication history and drug resistance. If this advice and information is unavailable, a regimen that is different from the medications the source currently uses can be used for the initial dose.
Exposure to unknown HIV status source(s) at high risk of HIV infection.	Offer HIV PEP: zidovudine or stavudine + lamivudine. A protease inhibitor can be added if the source has multiple high-risk factors for HIV infection.
Exposure to unknown HIV status source(s) at low risk of HIV infection.	Consider HIV PEP on a case-by-case basis. Zidovudine or stavudine + lamivudine may be offered when compelling circumstances exist.

HIV prevention and help reduce the incidence of HIV infections in the United States.

The authors gratefully acknowledge the assistance of the members of the Nonoccupational HIV Postexposure Task Force in the creation of the Rhode Island guidelines.

Dr. Merchant is supported by a National Institutes of Health training grant from the National Institute on Drug Abuse (5 T32 DA13911-02) through the Division of Infectious Diseases, Brown Medical School, Miriam Hospital, Providence, RI.

REFERENCES

1. Cardo DM, Culver DH, Ciesielski CA, Srivastava PU, Marcus R, Abiteboul D, et al. Centers for Disease Control and Prevention Needlestick Surveillance Group. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. N Engl J Med 1997;337:1485-90.
2. Connor EM, Sperling RS, Gelber R, Kiselev P, Scott G, O'Sullivan MJ, et al. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. N Engl J Med 1994; 331:1173-80.
3. Shaffer N, Chuachoowong R, Mock PA, Bhadrakom C, Siriwasin W, Young NL, et al. Bangkok Collaborative Perinatal HIV Transmission Study Group. Short-course zidovudine for perinatal HIV-1 transmission in Bangkok, Thailand: a randomised controlled trial. Lancet 1999; 353(9155):773-80.
4. Blauvelt A. The role of skin dendritic cells in the initiation of human immunodeficiency virus infection. Am J Med 1997;102:16-20.
5. Tsai CC, Emau P, Sun JC, Beck TW, Tran CA, Follis KE, et al. Post-exposure chemoprophylaxis (PECP) against SIV infection of macaques as a model for protection from HIV infection. J Med Primatol 2000;29:248-58.
6. Rey D, Bendiane M-K, Moatti JP, Wellings K, Danziger R, MacDowall W. European Study Group on HIV Testing Policies and Practices in Europe. Post-exposure prophylaxis after occupational and non-occupational exposures to HIV: an overview of the policies implemented in 27 European countries. AIDS Care 2000;12:695-701.
7. Update: provisional Public Health Service recommendations for chemoprophylaxis after occupational exposure to HIV. MMWR Morb Mortal Wkly Rep 1996;45:468-80.
8. Management of possible sexual, injecting-drug-use, or other nonoccupational exposure to HIV, including considerations related to antiretroviral therapy: Public Health Service statement. MMWR Recomm Rep 1998; 47(RR-17):1-14.
9. AIDS Institute, New York State Department of Health. HIV prophylaxis following sexual assault: guidelines for adults and adolescents. New York: New York State Department of Health, AIDS Institute; 1998.
10. Myles JE, Bamberger J. Offering HIV prophylaxis following sexual assault: recommendations for the state of California. San Francisco: California HIV Postexposure Prophylaxis after Sexual Assault Task Force; 2001.
11. Commonwealth of Massachusetts, Department of Health. Clinical advisory: HIV prophylaxis for nonoccupational exposures. Boston: Massachusetts Department of Public Health; 2000.
12. Merchant RC, Mayer KH, Browning CA. Nonoccupational HIV Postexposure Prophylaxis Task Force. Nonoccupational human immunodeficiency virus postexposure prophylaxis guidelines for Rhode Island healthcare practitioners. Providence: Brown University AIDS Program and Rhode Island Department of Health; 2002.