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# Management of Possible Sexual, Injecting-Drug–Use, or Other Nonoccupational Exposure to HIV, Including Considerations Related to Antiretroviral Therapy

## Public Health Service Statement

**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES**
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**The following CDC staff members prepared this report:**

Dawn K. Smith, M.D., M.S., M.P.H.
Robert S. Janssen, M.D.
David R. Holtgrave, Ph.D.
Kevin M. De Cock, M.D., D.T.M.&H.
*Division of HIV/AIDS Prevention — Surveillance and Epidemiology*
*National Center for HIV, STD, and TB Prevention*

**in collaboration with**

Eric P. Goosby, M.D.
*US Department of Health and Human Services*

Roberta J. Black, Ph.D.
Henry L. Francis, M. D.
Rodney Hoff, D.Sc., M.P.H.
*National Institutes of Health*

Kimberly A. Struble
R. Douglas Pratt, M.D., M.P.H.
*Food and Drug Administration*

Debra L. Parham, Ph.D.
*Health Resources and Services Administration*

# Management of Possible Sexual, Injecting-Drug–Use, or Other Nonoccupational Exposure to HIV, Including Considerations Related to Antiretroviral Therapy

## Public Health Service Statement

***Summary***

*The most effective methods for preventing human immunodeficiency virus (HIV) infection are those that protect against exposure to HIV. Preventive behaviors include sexual abstinence, sex only with an uninfected partner, consistent and correct condom use, abstinence from injecting-drug use, and consistent use of sterile equipment by those unable to cease injecting-drug use. Some health-care providers have proposed offering antiretroviral drugs to persons with unanticipated sexual or injecting-drug–use HIV exposure to prevent transmission. However, because no data exist regarding the efficacy of this therapy for persons with nonoccupational HIV exposure, it should be considered an unproven clinical intervention. Health-care providers and their patients may opt to consider using antiretroviral drugs after nonoccupational HIV exposures that carry a high risk for infection, but only after careful consideration of the potential risks and benefits and with a full awareness of the gaps in current knowledge.*

*To address concerns related to providing antiretroviral agents to persons after nonoccupational HIV exposure, CDC convened a meeting in July 1997 of scientists, public health experts, clinicians, members of professional associations, representatives from industry, ethicists, and members of affected communities. This report reviews the topics raised at the meeting, provides background information on patient management options, and presents considerations for antiretroviral therapy.*

## INTRODUCTION

The most effective methods for preventing human immunodeficiency virus (HIV) infection remain those that protect against exposure to HIV. Antiretroviral therapy should never replace adopting and maintaining behaviors that guard against HIV exposure (e.g., sexual abstinence, sex only with an uninfected partner, consistent and correct condom use, abstinence from injecting-drug use, and consistent use of sterile equipment by those unable to cease injecting-drug use). Medical treatment after sexual, injecting-drug–use, or other nonoccupational HIV exposure* is likely to be a

*In this report, a sexual exposure that can place a person at risk for HIV infection is defined as a discrete penetrative sex act (e.g., acts involving the insertion of the penis into the vagina, anus, or mouth) involving vaginal, anal, penile, or oral contact with the sex partner's potentially infectious body fluids, including substances that have been implicated in the transmission of HIV infection (i.e., blood, semen, vaginal secretions, or other body fluids when contaminated with visible blood).

A nonsexual, nonoccupational exposure (excluding perinatal exposures) that can place a person at risk for HIV infection is defined as a percutaneous penetration (e.g., a needlestick, injection, piercing, or cut with a sharp object); contact with mucous membranes; or contact with skin (especially when the involved skin is chapped, abraded, or affected by dermatitis; when the contact is prolonged; or when the involved area is extensive) and substances that have been implicated in the transmission of HIV infection (i.e., blood, tissues, or other body fluids when contaminated with visible blood).

relatively ineffective method for preventing HIV infection compared with preventing exposure in the first place. The Public Health Service (PHS) has recommended using antiretroviral drugs to reduce the acquisition of HIV infection among persons exposed in the workplace (e.g., accidental needlesticks received by health-care workers) (*1,2*). Although health-care providers and others have proposed offering antiretroviral drugs to persons with unanticipated sexual or injecting-drug–use HIV exposures (*3,4*), no data exist regarding the effectiveness of such therapy for these types of exposures.*

In July 1997, CDC sponsored the External Consultants Meeting on Antiretroviral Therapy for Potential Nonoccupational Exposures to HIV. This meeting brought together scientists, public health experts, clinicians, members of professional associations, representatives from industry, ethicists, and members of affected communities to discuss concerns related to providing antiretroviral agents to persons after nonoccupational HIV exposure. This report reviews the topics raised at the meeting, discusses background information on patient management options, and presents considerations for antiretroviral therapy.

## THERAPY AFTER NONOCCUPATIONAL HIV EXPOSURE

Health-care providers may want to provide their patients with a system for promptly initiating evaluation, counseling, and follow-up services after a reported sexual, injecting-drug–use, or other nonoccupational HIV exposure that might put a patient at high risk for acquiring infection. Sexual exposure also can put a patient at risk for other sexually transmitted diseases (STDs) and pregnancy. Injecting-drug–use exposure through shared injection equipment can put a patient at risk for acquiring other viral infections (e.g., hepatitis B and hepatitis C). All persons evaluated for possible nonoccupational HIV exposure should be counseled to initiate, resume, or improve risk-reduction behaviors to avoid future exposure and to prevent possible secondary transmission until their current HIV infection status is determined.

## CONSIDERATIONS FOR USING ANTIRETROVIRAL AGENTS

Decisions to provide antiretroviral agents to persons after possible nonoccupational HIV exposure to prevent the establishment of HIV infection must balance the potential benefits and risks. Factors influencing the potential efficacy of this intervention include the probability that the source contact is HIV-infected, the likelihood of transmission by the particular exposure, the interval between exposure and initiation of therapy, the efficacy of the drug(s) used to prevent infection, and the patient's adherence to the drug(s) prescribed.

### Possible Benefits

The major potential benefit of antiretroviral postexposure prophylaxis is reducing a person's risk for acquiring HIV infection after exposure. Estimates differ for the trans-

*Information included in these recommendations may not represent Food and Drug Administration approval or approved labeling for the particular products or indications in question. Specifically, the terms "safe" and "effective" may not be synonymous with the FDA-defined legal standards for product approval.

mission risk (if the person is not treated) after specific HIV exposures and the possible effect of early treatment after such exposures.

### *Probability of Transmission From One HIV Exposure*

HIV can be transmitted efficiently through blood transfusions: an estimated 95% of recipients become infected from transfusion of a single unit of infected whole blood. The per-contact probability of transmission from an HIV-infected source is much lower for injecting-drug–use and sexual exposures. The risk for HIV transmission per episode of intravenous needle or syringe exposure is estimated at 0.67% (*5* ). The risk per episode of percutaneous exposure (e.g., a needlestick) to HIV-infected blood is estimated at 0.4% (upper limit of 95% confidence interval [CI] = 0.8%) (*6* ). The risk for HIV transmission per episode of receptive penile-anal sexual exposure is estimated at 0.1%–3%; the risk per episode of receptive vaginal exposure is estimated at 0.1%–0.2% (*7* ). No published estimates of the risk for transmission from receptive oral exposure exist, but instances of transmission have been reported (*8,9* ).

### *Pathogenesis of Early HIV Infection*

Information about the initial physiologic events after HIV exposure suggests that it can take several days for infection to become established in the lymphoid and other tissues. During this time, interventions to interrupt viral replication could represent an opportunity to prevent an exposure from becoming an established infection (*10,11* )

### *Studies of Antiretroviral Agent Use to Prevent HIV Infection in Animals*

Attempts to protect animals with antiretroviral monotherapy after experimental mucosal and intravenous (IV) exposures have produced various results (*12* ). In studies to assess the efficacy of zidovudine (ZDV) administered after IV exposure to simian immunodeficiency virus (SIV), the suppression or delay of viral replication was common but the prevention of infection was rare (*13,14* ). Treatment initiated within 24 hours of exposure and continued for 28 days appeared to have a greater effect than treatment initiated 72 hours after exposure. However, ZDV might not be the optimal agent to demonstrate proof-of-concept because it has not demonstrated potent inhibitory activity against SIV infection in macaques, even when treatment is initiated before viral exposure (*12,15* ). In another study in which a licensed antiretroviral drug was administered to macaques, initiating stavudine (d4T) treatment at the time of IV exposure to human immunodeficiency virus type 2 (HIV-2) resulted in a delay in the onset of viremia and a reduction in viral load (*16* ). Although protection from infection was not observed, most of the treated animals exhibited sustained control of viral replication and normal CD4+ cell levels for >1 year after receiving 16 weeks of drug treatment. More compelling evidence of the efficacy of antiretroviral drugs for postexposure prophylaxis in animal models has been generated by using unlicensed compounds. SIV infection was prevented in 100% of macaques when treatment in phase I/II clinical trials with (R)-9-(2-phosphonylmethoxypropyl)adenine (PMPA), a nucleotide analogue, was started either 4 or 24 hours after IV inoculation and was continued for 28 days (*17* ). Protection was diminished if treatment was delayed >24 hours or if the treatment duration was reduced (*18* ). In another recent study, mucosal or IV infection of macaques with SIV was blocked when a 3-day treatment with the nucleoside analogue 2′,3′-dideoxy-3′-hydroxymethyl cytidine (BEA-005) was initiated

within 8 hours of viral exposure (*19*). Further corroborating the PMPA results, the BEA-005 study demonstrated that increasing the time between exposure and treatment initiation or decreasing the duration of treatment reduced protection.

The animal-model data demonstrate that antiretroviral agents administered after SIV or HIV-2 exposure can prevent infection. However, extrapolating these results to humans is problematic because of several factors, including differences between a) the laboratory-adapted strains of SIV and HIV used in animal studies and the HIV strains that circulate among persons; b) inoculum size; c) routes of inoculation or exposure; d) time of treatment initiation; e) drug(s) used; f) treatment duration; and g) host metabolism, host immunology, and other biological parameters. Animal studies offer proof-of-concept and demonstrate the challenges to understanding the requirements for effective use of antiretrovirals to prevent HIV transmission in humans.

### *Studies of Antiretroviral Agent Use to Prevent HIV Infection in Humans*

In 1995, investigators used case-control surveillance data from health-care workers in France, Italy, the United Kingdom, and the United States to document that ZDV use was associated with an 81% (95% CI = 48%–94%) decrease in the risk for HIV infection after percutaneous exposure to HIV-infected blood (*1,2,20,21*). This study was a retrospective case-control study, rather than a prospective trial, which is the preferred method of assessing clinical drug efficacy. Additional limitations were that a) the number of case-patients was small, b) the case-patients and controls came from separate populations, c) some case-patients were reported anecdotally before formal surveillance was established, and d) some details of exposures in case-patients were obtained retrospectively, whereas information for controls was collected prospectively. Although the health-care worker study demonstrated antiretroviral effectiveness following percutaneous HIV exposure, some researchers have suggested that the magnitude of the effect might be overestimated because of the methodologic questions raised (*22*). ZDV has failed to prevent HIV infection in health-care workers in 13 reported instances (*23*).

In a prospective, randomized controlled trial of ZDV administered to HIV-infected women during pregnancy and labor and to their infants for 6 weeks postpartum, perinatal transmission was reduced 67% among those randomly assigned to the treatment group compared with those in the control group, who received no antiretroviral therapy. Results of multivariate analyses suggested that a prophylactic effect on the fetus during antenatal, intrapartum, or postpartum exposure (*24*) could account for some reduction in perinatal transmission. In a prospective trial of ZDV in Thailand, perinatal HIV transmission was reduced 51% for women treated from 36 weeks' gestation until delivery (*25*). Perinatal transmission despite use of ZDV prophylaxis in pregnancy also has been reported (*26*).

Although these studies suggest that antiretroviral agents are potentially valuable for treating HIV exposures in these settings, the data might not be directly relevant to nonoccupational exposures. Health-care workers often are exposed to HIV in settings where antiretroviral therapy can begin within 1–2 hours of exposure and where the HIV status of the source patient usually can be determined quickly. These circumstances are unlikely for many nonoccupational exposures. The perinatal transmission model also might not be directly relevant to nonoccupational exposures. If most perinatal infections occur at the time of delivery, the observed effectiveness of ZDV

therapy could represent a preexposure not a postexposure effect. Despite the apparent usefulness of antiretroviral agents in perinatal and occupational settings, it is unclear whether these findings can be extrapolated to other settings. Further studies are needed before one can conclude whether using antiretroviral agents to prevent HIV infection after nonoccupational exposures is effective.

## Possible Risks

Potential risks of antiretroviral postexposure prophylaxis include drug toxicity, reduced effectiveness of behavioral HIV-prevention measures, and the acquisition of antiretroviral-resistant HIV strains. Also, the cost of medications could tax already scarce public funds for antiretroviral agents for HIV-infected persons, which offer cost-effectiveness and therapeutic benefit. Many insurers will not cover the cost of this unproven therapy, so any possible benefit will be limited based on the patient's ability to pay.

### *Side Effects and Toxicity of Antiretroviral Agents*

The frequency, severity, duration, and reversibility of side effects must be weighed against the usefulness of antiretroviral agents for any patient. All antiretroviral agents have been associated with side effects. Adverse events have been reported for persons with advanced HIV disease (and longer treatment courses), but persons with less advanced disease or those who are uninfected might have different experiences (*27*). Many side effects can be managed symptomatically, but when the probability of transmission is low, one must weigh this probability against the risk of a severe side effect. Although the most common side effects are mild, studies have demonstrated that 50%–75% of health-care workers receiving ZDV alone for possible HIV exposure reported one or more subjective complaints, and as many as 35% did not complete the full course of therapy because of side effects (*6,28,29*). Preliminary information on health-care workers receiving combination therapy for postexposure prophylaxis demonstrated that 50%–90% reported subjective side effects and 24%–36% reported side effects severe enough to discontinue therapy (*30–33*).

Many antiretroviral agents are associated with gastrointestinal side effects (e.g., nausea, vomiting, and diarrhea). In general, using combinations of agents has not caused more instances of adverse effects, but serious drug interactions have occurred when antiretrovirals were used with certain other medications. Current medications must be evaluated before patients are prescribed any antiretrovirals, and health-care providers must monitor patients closely for toxicities. Protease inhibitors recently have been associated with the occurrence of lipid abnormalities (*34–36*), as well as the development of diabetes mellitus, hyperglycemia, and diabetic ketoacidosis, and they can exacerbate preexisting diabetes mellitus (*27,37*). Some health-care workers using combination drugs for postexposure prophylaxis of occupational HIV exposure have developed serious side effects—including nephrolithiasis, hepatitis, and pancytopenia—sometimes within 3 days of initiating therapy (*31,32,38*).

### *Behavior Changes Potentially Related to Prophylactic Antiretroviral Therapy*

Some persons actively seek and repeatedly participate in high-risk behaviors (e.g., unprotected sex or needle-sharing injecting-drug use). The widespread availability of

antiretroviral agents for treating possible nonoccupational HIV exposure could undermine public health efforts aimed at increasing and maintaining sexual and injecting-drug–use behaviors that prevent HIV exposure. If persons perceive that postexposure antiretroviral prophylaxis prevents HIV infection, they could increase the frequency of risk behaviors or shift from lower-risk to higher-risk activities. If many persons increase higher-risk behaviors, the widespread availability of antiretroviral agents for treating HIV exposure paradoxically could increase the number of new infections because the treatment's effectiveness will be <100%. One study of 54 men who had sex with men (recruited as part of an intervention counseling study) documented that 15% already had taken "a chance of getting infected when having sex" because of the availability of new treatments. It is unclear whether this reported behavior was a response to the existence of antiretroviral postexposure prophylaxis or a decreased fear of HIV disease because of the effectiveness of combination antiretroviral therapy (*39*).

### *Acquiring Antiretroviral-Resistant Virus*

The use of antiretroviral agents after possible nonoccupational HIV exposure, particularly if a patient does not adhere to the prescribed drug treatment, poses the theoretical risk that the patient could become infected with an antiretroviral-resistant strain of HIV if postexposure prophylaxis fails to prevent infection. In nonoccupational exposures, information regarding the antiretroviral-susceptibility patterns of the source virus likely will not be known, making it difficult to tailor antiretroviral therapy appropriately.

### *Cost of Antiretroviral Postexposure Prophylaxis*

A 28-day course of antiretroviral agents for a single possible exposure to HIV costs an estimated $800 (range: $600–$1,000), depending on the agents used (*4,40*). This cost generally is more per client than the cost of enrollment in intensive, behavioral, HIV primary prevention programs designed to reduce the likelihood of future exposures (*41*). If postexposure prophylaxis proves effective in reducing HIV transmission after nonoccupational exposure, its cost dictates that use be restricted to high-risk exposures to avoid compromising funds for more cost-effective behavior intervention programs.

Uncertainties about key factors make it difficult to estimate the cost-effectiveness of treating nonoccupational HIV exposure with antiretroviral drugs. However, recent studies have used mathematical modeling to estimate cost-effectiveness ratios for this treatment (*42,43*). These studies demonstrate that antiretroviral drugs could be cost-effective for persons who engage in behaviors with high per-act infectivity (e.g., receptive anal intercourse) with persons known or likely to be HIV-seropositive. However, the drugs might not be cost-effective for treating exposures with low per-act infectivity or involving partners at low risk for HIV infection.

## EVIDENCE OF CURRENT PRACTICE

Some physicians have been asked to provide antiretroviral agents after certain sexual exposures, including rape by an assailant of unknown HIV status and risk history (*44,45*). Other reported exposures that could lead to requests for antiretroviral pro-

phylaxis include injecting-drug–use relapse (*4*); condom breakage during anal sex between HIV-serodiscordant partners (*46*); nonconsensual sex in correctional institutions (*47*); and breast-feeding of newborns by HIV-infected mothers (*48*). Because data have not been collected systematically in the United States, it is not possible to estimate either the frequency of such requests or the actual use of antiretroviral agents in these situations, or the adherence to or effectiveness of the prescribed therapy. No summary information about what specific drug therapies are being prescribed is available, although some physicians have based their practice on published guidelines for treating occupational exposure (*2*).

Outside the United States, some guidelines are in use despite the absence of effectiveness data. In Canada, the British Columbia Centre for Excellence in HIV/AIDS has published *A Guideline for Accidental Exposure to HIV*, which recommends antiretroviral agents for rape victims (in addition to persons with occupational HIV exposure). To allow postexposure antiretroviral therapy to be initiated quickly, the Centre provides a free "starter kit" of 5 days of therapy with ZDV and lamivudine (3TC) to emergency rooms where specialized teams care for the victims of sexual assault or to physicians upon request.

## COMMENTARY

Based on the knowledge of HIV pathogenesis and the possible benefit of antiretroviral agents in preventing transmission (demonstrated in animal and human studies), some physicians believe that antiretroviral agents are indicated for persons with possible sexual, injecting-drug–use, or other nonoccupational HIV exposure (*4*). However, PHS cannot definitively recommend for or against antiretroviral agents in these situations because of the lack of efficacy data on the use of antiretroviral agents in preventing HIV transmission after possible nonoccupational exposure. Efficacy and effectiveness data and additional epidemiologic information are needed, including the number of infections that could be averted by antiretroviral drugs, the number of persons who would need treatment to avert one infection, the effects of antiretroviral drug availability on risk behavior, and physician practices in prescribing antiretroviral drugs.

Antiretroviral agents should not be used for persons with HIV exposures that have a low risk of transmission (e.g., potentially infected body fluid on intact skin) or for persons who seek care too late for the anticipated interruption of transmission (>72 hours after reported exposure). Physicians considering the use of antiretroviral agents after a nonoccupational HIV exposure should recognize that benefits likely will be restricted to situations in which the risk for infection is high, the intervention can be initiated promptly, and adherence to the regimen is likely. In these instances, the physician and the patient should weigh the low per-act probability of HIV transmission associated with the reported exposure against the uncertain effectiveness, potential toxicities, and cost of antiretroviral drugs, as well as the patient's anticipated adherence to the therapy. If physicians decide to use antiretroviral agents, they should consult with an HIV-care provider experienced with their use.

Postexposure antiretroviral therapy should never be administered routinely or solely at the request of a patient. It is a complicated medical therapy, not a form of primary HIV prevention. It is not a "morning-after pill," but, if proven effective, can

constitute a last effort to prevent HIV infection in patients for whom primary prevention has failed to protect them from possible exposure.

# CONSIDERATIONS IN CARING FOR PERSONS AFTER POTENTIAL NONOCCUPATIONAL EXPOSURE TO HIV WHEN DATA ARE INADEQUATE

## Evaluation for STDs and Substance Abuse

Sexual activities associated with a risk for HIV transmission also are associated with risk for unintended pregnancy and STDs (e.g., syphilis, gonorrhea, chlamydia, or hepatitis B virus). Treatment for STDs should follow the CDC's *1998 Guidelines for Treatment of Sexually Transmitted Diseases* (*49* ), and victims of sexual assault should receive additional evaluation and counseling (*50* ). Women at risk for unintended pregnancy should be offered emergency contraception (*51* ). Persons with possible HIV exposure through percutaneous routes from sharing syringes or needles should be assessed for hepatitis B and hepatitis C virus infections and considered for hepatitis B virus vaccination. They also should be assessed and referred for appropriate substance abuse treatment.

## HIV Evaluation and Management

Persons who report possible nonoccupational HIV exposure should be evaluated for sexual and injecting-drug–use behavior that might lead to recurrent exposure. In all situations, health-care providers should offer confidential risk-reduction counseling (*52* ) during initial and follow-up visits. Persons who have been sexually assaulted also can be referred for anonymous or confidential voluntary counseling and testing within 72 hours of exposure to establish their HIV status at the time of the assault. Some patients (e.g., those who have inconsistently or incorrectly used condoms or relapsed into injecting-drug use) will need to be referred for intensive risk-reduction interventions. Health-care providers evaluating persons for nonoccupational HIV exposure should know where such services are available and help patients obtain them promptly.

Persons with nonoccupational HIV exposures should receive medical evaluations, including HIV-antibody tests at baseline and periodically for at least 6 months after exposure (e.g., at 4–6 weeks, 12 weeks, and 6 months). All persons evaluated for possible nonoccupational HIV exposure should be counseled to initiate or resume protective behaviors to prevent additional exposure and to prevent possible secondary transmission if they become infected while receiving antiretroviral therapy.

## Considerations in Initiating Antiretroviral Therapy

Physicians considering the initiation of antiretroviral therapy in an attempt to reduce the risk for HIV infection in an exposed person should take the following steps in consultation with an expert in the use of antiretroviral agents:

- Evaluate the HIV status and risk-behavior history of the reported source of HIV exposure.
- Provide medical care, supportive counseling, and prevention services to persons who are determined to be HIV-infected when they seek care for a potential HIV exposure.
- Evaluate the risk for HIV transmission (if there is convincing evidence of HIV infection in the reported source patient). Physicians should determine the specifics of the risk event (e.g., no condom, torn condom, whether receptive or insertive partner, injection before or after others, number of persons sharing injection equipment) and the presence or absence of factors that would modify risk (e.g., vaginal or anal tears or bleeding, visible genital ulcers or other evidence of an active STD, or bleach treatment of injection equipment).
- Determine the time elapsed between exposure and presentation for medical care. Although animal studies indicate that antiretroviral agents are most effective within 1–2 hours of exposure and probably not effective when started later than 24–36 hours after exposure, the interval during which therapy can be beneficial for humans is unknown.
- Evaluate the frequency of HIV exposure. Uninfected persons who request antiretroviral agents should be evaluated for sexual, injecting-drug–use, and other behaviors that might lead to recurrent HIV exposures. Antiretroviral therapy is not a replacement for adherence to behaviors that reduce the risk of HIV exposure.
- Provide counseling and obtain informed consent. Because postexposure prophylaxis is an experimental therapy of unproven efficacy, informed consent should be obtained and recorded in the medical charts of all persons prescribed antiretroviral agents following nonoccupational exposure. Such consent should document the patient's understanding of a) the need to initiate or resume relevant HIV risk-reduction behaviors (e.g., condom use and/or drug treatment); b) the limited knowledge about the effectiveness and toxicity of antiretroviral treatment for nonoccupational exposure; c) the known side effects of the medications being prescribed; d) the name and phone number of a source for follow-up medical care; e) the frequency and timing of recommended follow-up HIV testing (*1,2,52*); f) the signs and symptoms associated with acute HIV seroconversion; and g) the need for adherence to prescribed medications to maximize efficacy and reduce the risk for infection with a drug-resistant variant. The patient should be told that physicians have diverse opinions about the use of antiretroviral medications to treat possible nonoccupational HIV exposure and that PHS cannot make definitive recommendations because of limited knowledge.
- Persons younger than age 16 years at the time of exposure should be evaluated (before therapy is initiated) by pediatricians, family physicians, or other clinicians expert in the specific medical needs, consent issues, and other factors involved in their treatment, including the use of antiretroviral medicines for children and adolescents. These factors can include the investigation of possible child sexual

abuse, state-specific legal reporting requirements for situations that endanger the welfare of minors, and local definitions of emancipation or other consent requirements that define the circumstances under which children and adolescents can give legal consent for their own medical care.

- HIV-exposed women who are pregnant (or could become so as a consequence of the exposure event) should be evaluated before antiretroviral therapy is initiated in consultation with obstetricians or other physicians expert in the care of HIV infection during pregnancy to define which antiretroviral agent(s) would be appropriate to the health of the woman and the fetus. Women should be counseled on a) the limited data available about the short-term safety for the fetus and the long-term safety of in utero antiretroviral exposure for the infant; b) the theoretical risks of suggested antiretroviral agents to the fetus during specific gestational periods; and c) CDC's recommendations regarding antiretroviral therapy for HIV-infected pregnant women (*53,54* ). No studies have been conducted on the safety and effectiveness of antiretroviral agents in preventing HIV infection in uninfected women during attempts to conceive with HIV-infected partners, and this therapy is not recommended for such use.
- If antiretroviral therapy is used, drug-toxicity monitoring should include a complete blood count and renal and hepatic chemical function tests when therapy is initiated and again 2 weeks after the patient begins to take the medications. If subjective or objective toxicity is noted, physicians should consult with their experts on the need for further diagnostic studies and dose reduction or drug substitution. It is possible that antiretroviral therapy during early HIV infection could benefit the patient by reducing the initial level of viral replication (i.e., the set point) and decreasing the extent of lymph node infiltration. Thus, for patients with the highest-risk exposures, health-care providers may consider continuing therapy until HIV test results are received from a specimen drawn after 28 days of treatment. Patients should be monitored for signs and symptoms of acute HIV infection during therapy. If such conditions develop, the patient should be tested for HIV (p24 antigen, HIV viral load assays) during their 4-week course of therapy with confirmation by standard HIV antibody tests. Persons who become infected while taking antiretroviral therapy should be advised to continue taking the medication pending transfer to a health-care provider who specializes in long-term HIV care (*55,56* ).

## RESEARCH NEEDS

Rigorously designed and executed studies are needed to evaluate the efficacy of antiretroviral agents in preventing HIV infection after nonoccupational exposures. Studies should include assessment of the rates of demand for antiretroviral therapy; the proportion of requests that stem from high-risk exposures; the rates of acceptance of therapy when offered; the patterns of drug prescriptions; the agents, doses, and duration of therapy associated with efficacy; the levels of patient adherence when therapy is prescribed; the rates of toxicity to drugs prescribed; and the costs of therapy. In addition, HIV isolated from patients infected despite therapy should be monitored to document the rates of acquisition of strains with genotypic or pheno-

typic antiretroviral resistance to medications taken. When possible, patient strains should be compared with HIV isolated from the reported source patients.

Studies also are needed to determine a) the distribution of knowledge about antiretroviral postexposure prophylaxis among those with nonoccupational HIV exposure, b) the effect of the availability of antiretroviral prophylaxis on HIV risk behaviors at the individual or community level, and c) the frequency of exposures for which therapy might be recommended.

Animal studies designed to mimic nonoccupational exposure to HIV, the timing of therapy initiation, and the antiretroviral drugs used for humans could provide additional information about the usefulness of drugs prescribed at specific intervals after exposure and for defined durations. Drugs or drug combinations that demonstrate promise for reducing retroviral transmission might be more easily documented in animal models.

## SURVEILLANCE OF DOCUMENTED EXPOSURES

CDC is initiating a surveillance system to collect information about persons who seek medical care after possible sexual, injecting-drug–use, or other nonoccupational HIV exposures. No names or other personal identifiers of patients will be collected. Health-care providers in the United States soon will be encouraged to report all persons who receive or who are considered for antiretroviral agents for nonoccupational HIV exposure to an anonymous registry that CDC is developing. The system will assess utilization, effectiveness, and medication toxicity for those who receive treatment through collection of the following information:

- characteristics of the reported exposure;
- use of antiretroviral medications, including dosage and duration;
- toxicity of and adherence to therapy;
- HIV seroconversion in patients who do and do not receive antiretroviral therapy after exposure to a known HIV-infected source.

CDC will request follow-up information on patients whose nonoccupational HIV exposure is documented and who gave consent to their physician for data reporting. CDC also will assist with HIV testing when asked.

Unusual or severe toxicity from antiretroviral drugs should be reported to the manufacturer or the Food and Drug Administration ([800]-332-1088). The use of antiretroviral drugs for pregnant women should be reported (without patient identifiers) to the Antiretroviral Pregnancy Registry ([800]-258-4263).

For further information about the CDC-sponsored External Consultants Meeting on Antiretroviral Therapy for Potential Nonoccupational Exposures to HIV, which took place in July 1997, contact the National AIDS Clearinghouse ([800]-458-5231 or the Internet website at <http://www.cdc.gov/nchstp/hiv_aids/media.htm>).

## CONCLUSION

Because of the lack of efficacy data for the use of antiretroviral agents to reduce HIV transmission after a possible nonoccupational exposure, PHS is unable to recommend for or against this therapeutic approach. If such therapy is attempted, health-care providers must a) inform patients of the lack of data; b) select antiretroviral agents carefully and monitor their side effects and toxicities closely; c) address their patients' underlying risk-reduction needs (when applicable); and d) restrict the use of this therapy to high-risk exposures (e.g., unprotected receptive anal or vaginal intercourse with a known HIV-positive person). Research is needed to establish if and under what circumstances antiretroviral therapy following nonoccupational HIV exposure is effective.

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