Prevention of Human Immunodeficiency Virus and AIDS

Postexposure Prophylaxis (Including Health Care Workers)

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KEYWORDS

• HIV • Postexposure prophylaxis • Occupational exposure
• Nonoccupational exposure • HIV PEP

KEY POINTS

- HIV PEP is intended to prevent HIV infection after an exposure.
- HIV PEP is one of several strategies for HIV prevention.
- PEP was first used after occupational HIV exposures.
- A case-control study of HIV seroconversion in health care workers after percutaneous exposure published in 1997 provided the first evidence in humans that PEP with a single antiretroviral agent seemed to be protective against infection.
- Use of PEP has been extended to nonoccupational exposures, including following sexual contact or injection-drug use.

Although human immunodeficiency virus (HIV) incidence in the United States was relatively stable from 2006 to 2009, a total of 48,100 new HIV infections were estimated to have occurred in 2009 in the United States[1] and 2.3 million new cases occurred globally in 2012.[2] Postexposure prophylaxis (PEP), which is designed to prevent HIV infection after an exposure, is one of several strategies for HIV prevention. PEP was first used after occupational HIV exposures in the late 1980s, with the Centers for Disease Control and Prevention (CDC) issuing the first set of guidelines that included considerations regarding the use of antiretroviral agents for PEP after occupational HIV exposures in

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1990.[3] A case-control study of HIV seroconversion in health care workers (HCW) after percutaneous exposure published in 1997 provided the first evidence in humans that PEP with a single antiretroviral agent seemed to be protective against infection.[4] More recently, use of PEP has been extended to nonoccupational exposures, including after sexual contact or injection-drug use.[5] This article provides a brief rationale for PEP, assessment of the need for PEP, and details of its implementation.

RATIONALE FOR POSTEXPOSURE PROPHYLAXIS FOR EXPOSURES TO HUMAN IMMUNODEFICIENCY VIRUS

Biologic Plausibility of Postexposure Prophylaxis

The hypothesis underlying the administration of antiretroviral chemoprophylaxis is that postexposure treatment provided during a "window of opportunity" will attenuate initial HIV replication and prevent systemic HIV infection and allow time for a cellular immune response. Dendritic cells in the mucosa and skin are believed to be the initial target for HIV infection or capture.[6] In a primate model, simian immunodeficiency virus (SIV) remained localized in association with dendritic cells underlying the site of vaginal inoculation for the first 24 hours after exposure to cell-free virus.[7] Within 24 to 48 hours, these cells seemed to migrate to regional lymph nodes and present SIV to T lymphocytes. Cell-free and cell-associated SIV was detected in the peripheral blood within 5 days after inoculation.

Productive HIV infection occurs in a sequence of events involving initial capture and/or infection of dendritic target cells near the exposure site with subsequent transmission of HIV to susceptible T cells in regional lymph nodes. Each step in this sequence is a potential target for intervention. Early antiretroviral treatment plausibly prevents infection by blocking the infection of T cells, presumably in the regional lymph nodes. Interrupting or delaying the productive infection of T cells could also allow time for the development of specific cellular immunity directed against HIV in the exposed individual.

Animal studies provide evidence for an important role for the cellular immune system in HIV PEP. Intact cellular immunity was required for successful PEP in one mouse retroviral model.[8] Putkonen and coworkers[9] demonstrated robust specific cellular responses in macaques in which SIV infection was successfully prevented by PEP. These macaques developed a strong enough immune response that a second challenge with the same viral inoculum resulted in either no or significantly limited infection.

These data suggest that antiretroviral chemoprophylaxis administered soon after an exposure, in concert with cellular immunity, may prevent or inhibit systemic HIV infection. This preventive effect theoretically is caused by limiting proliferation of virus in dendritic cells in skin or in T cells in regional lymph nodes during the time in which the virus remains relatively localized. This effect may be bolstered by a robust cellular immune response.

Animal Models of Postexposure Prophylaxis

In general, PEP is most likely to be effective in animal models where the exposure inoculum is relatively low, when treatment is started soon after exposure (usually within 24 hours), and when treatment is continued for several days to weeks after inoculation.[10,11] In one study of SIV in macaques, all the animals receiving postexposure treatment for 28 days remained uninfected, only half the animals treated for 10 days remained uninfected, and none of the animals that received only 3 days of treatment were protected.[11] Similarly, delay in initiating prophylaxis was detrimental in this model. All of the animals that were treated within 24 hours of intravenous SIV infection remained uninfected, whereas only 50% of the animals that received treatment