

POSTEXPOSURE PROPHYLAXIS

WHO SHOULD BE TREATED

79. Does the Panel's definition of exposure include high-risk sexual activities, not just occupational exposure? What are the Panel's recommendations for prophylactic anti-retroviral therapy for high-risk sexual exposures?

Dr Fischl: The current postexposure recommendations relate only to occupational exposure. No formal recommendations were made regarding high-risk sexual activities as more definitive data are needed about risks and interventions. However, many members of the Panel regard high-risk sexual exposures as analogous to high-risk occupational exposures and would follow similar guidelines in recommending postexposure prophylaxis.

80. Should therapy be recommended for a patient who may have been exposed to HIV during a surgical procedure in which the surgeon suffered a previous percutaneous exposure (unrecognized or not)? Should testing of the surgeon be mandatory in such a case?

Dr Fischl: Current information would indicate that there is an extremely low risk for patient acquisition of HIV infection from a health care worker and no guidelines for mandatory HIV-testing of health care workers have been made. However, if one surgeon in this case is known to be HIV infected, postexposure prophylaxis would be recommended for the patient.

81. What are the recommendations for prophylaxis for accidental needle injuries in subjects who are not in an identified high-risk setting (eg, a child with an accidental needle puncture)?

Dr Fischl: One would anticipate that the risk for HIV infection would be low in such instances; however, if there is any suspicion that there was a high-risk exposure to HIV-infected blood then the current *Guidelines* should be followed.

82. Should prophylaxis be recommended for

mucosal exposure to HIV? For surface skin exposure?

Dr Fischl: For mucosal membrane exposure, the CDC guidelines suggest offering antiretroviral therapy for exposures to visible blood or other infectious fluids. Skin exposure recommendations have been restricted to increased risk that involves an exposure to a higher titer of HIV, prolonged skin contact, or an extensive area in which the skin integrity is visibly compromised. For increased-risk skin exposure, the CDC guidelines suggest offering antiretroviral therapy for exposures to blood and fluid containing visible blood or other infectious fluids.

83. Is prophylaxis recommended in all accidental injuries (even from healthy sources?)

Dr Fischl: Prophylaxis is recommended for high- and increased-risk exposures from an infected source patient. If the HIV status of the source patient is not known, a decision about prophylaxis should consider the exposure risk and likelihood of HIV infection in the source patient. Once initiated, prophylaxis can always be stopped if subsequent information indicates minimal or no risk of HIV exposure.

THE USE OF LABORATORY MARKERS IN POSTEXPOSURE PROPHYLAXIS

84. Are p24 antigen or PCR tests useful in deciding whether to recommend postexposure prophylaxis? Can plasma HIV RNA testing at 2 to 3 weeks after accidental exposure help to rule out the possibility of infection sufficiently enough to defer the 6 to 12 months antibody testing?

Dr Hirsch: Blood should be drawn acutely (ie, at baseline) and then periodically for at least 6 months postexposure (eg, at 6 weeks, 12 weeks, and 6 months) for conventional anti-HIV testing. The place of plasma HIV RNA or p24 antigen testing for monitoring whether infection has occurred or the need to continue prophylaxis in this setting have not yet been established. At present, it cannot be concluded that an undetectable plasma HIV RNA level or a negative p24 antigen test shortly after exposure rules out the possibility of infection sufficiently enough to defer the 6-month antibody testing.

WHAT REGIMENS SHOULD BE USED FOR POSTEXPOSURE PROPHYLAXIS

85. Postexposure prophylaxis is so rare, and data on zidovudine have not been conclusive. Isn't it too drastic to go for 3 drugs?

Dr Hirsch: The most convincing evidence for zidovudine postexposure prophylaxis is the case-control study published by the CDC in which zidovudine use reduced seroconversion after significant occupational exposure by approximately 80% during the period between 1988 and 1994. Given the greater likelihood of zidovudine resistance currently and the benefits shown for 3-drug combination regimens in other settings of established HIV infection, the recommendations for their use in the most significant exposures are considered appropriate at this time.

Dr Montaner: I would add that postexposure prophylaxis is no longer a rare event. At our institution we have noticed a substantial increase in the demand for intervention after the publication of the CDC study on this issue.

86. What is the role of nevirapine monotherapy for postexposure prophylaxis?

Dr Hirsch: The role of nevirapine monotherapy in postexposure prophylaxis has not been established. However, nevirapine or delavirdine theoretically may be useful drugs for short-term prophylaxis when used in combination with other drugs for high-risk exposures, particularly if the source patient has not received these NNRTIs.

Dr Montaner: NNRTIs are attractive drugs for use in postexposure prophylaxis. However, until further data are available they should be regarded as experimental in this setting. Under some specific circumstances I would be prepared to use them as part of a combination therapy scheme.

87. Does it matter what the viral load of the source patient is in deciding future therapy?

Dr Hirsch: The viral load in the source patient is probably very important in determining risk, but this information is rarely available at the time occupational exposures occur. The clinical state of the source patient and his/her treatment history are more frequently known. It is likely that as viral load measurements become more frequent, this information will become very useful in assessing risk.

HOW LONG SHOULD THERAPY CONTINUE AND WHEN SHOULD IT BE STARTED

88. Should the period of the proposed treatment for postexposure prophylaxis be shortened to 2 weeks if the regimen includes a protease inhibitor? Also, why stop at 4 to 6 weeks?

Dr Hirsch: The optimal duration for postexposure prophylaxis is unknown. Based on the biology of the virus, shortened durations of potent 3-drug regimens are reasonable. However, it is unclear whether this should be 2, 3, or 4 weeks, or some other duration. Durations beyond 6 weeks are not recommended because there is no evidence that longer treatment is beneficial, and the toxicity and expense are certainly greater with prolonged therapy.

Dr Fischl: As stated, the optimal duration of prophylaxis is not known. Data from the CDC case-control study suggested that 4 weeks of zidovudine were protective. Therefore, the current recommendations are to treat for 4 to 6 weeks, if tolerated. Whether a more potent regimen can be given for a shorter duration is unknown.

89. What is the maximum time delay that would be acceptable before initiating prophylactic treatment in a high-risk postexposure situation?

Dr Fischl: Ideally, therapy should be started within 1 to 3 hours and certainly within at least 24 to 36 hours. The interval after which prophylaxis is no longer beneficial in humans is unknown. Initiating prophylaxis after a longer period of time, however, should still be considered for a high-risk exposure. Although HIV infection will likely not be prevented, the early treatment of HIV infection may be beneficial, and studies are being conducted to evaluate triple-drug regimens that include protease inhibitors for the treatment of acute seroconversion and early HIV infection.

Dr Hirsch: As noted, we cannot determine today what is the maximum acceptable delay. Data from animal and human studies indicate that the rule to follow should be "the sooner the better," preferably within a few hours.

90. An RN had massive exposure of blood to open blisters on her hands during cardiac arrest of an AIDS patient. She has been on

zidovudine for 3 weeks and then consults you. What do you add now to the regimen?

Dr Hirsch: Given the nature of the exposure and the length of time that has elapsed since the presumed contact, I would not add a second drug to the regimen at this time, unless there is strong evidence that the source patient was likely to have zidovudine-resistant virus.

Dr Fischl: If the exposure was from a patient known to have drug resistance or had been treated with zidovudine for a prolonged period of time, an adjustment in the regimen might be made. Initiating a change in prophylaxis should still be considered because of the high-risk exposure. Although HIV infection may not be prevented, the early treatment of HIV infection may be beneficial, and studies are being conducted to evaluate triple-drug regimens that include protease inhibitors for the treatment of acute seroconversion and early HIV infection. The effectiveness of changing prophylaxis in such a setting, however, is still unknown.

OTHER ISSUES

91. HIV infection acquired through occupational exposure may imply some responsibility on the part of the health care facility—ie, for disability or for other compensation. This implies that periodic HIV testing of health care workers (HCWs) may be necessary to ensure documentation of occupationally acquired infections. What is your position on mandatory testing of HCWs in general?

Dr Fischl: Occupational exposure does not require mandatory HIV testing. HIV testing can be done at the time of the exposure and should be negative if the health care worker was seronegative at the time of the exposure.

A positive HIV antibody test after seroconversion would be expected after 2 to 6 weeks.

Dr Richman: Routine (every 6 to 12 months) blood drawing and serum storage with voluntary testing for HIV should be standard practice in laboratories working with HIV or other biohazardous materials.

92. Please do not forget to emphasize rapid and complete local cleansing of injured/exposed areas.

Dr Fischl: Cleaning of a local injury or exposure with soap and water is always a good hygienic practice and should be done.

93. Would immediate surgical resection of an involved hematoma be recommended in a high-risk needle impaled, for example, in someone's muscle?

Dr Fischl: Virus would likely be rapidly disseminated through the blood stream and resection of the hematoma would not necessarily decrease the risk of seroconversion.

94. Instead of giving a cocktail of drugs, should we reserve one drug for postexposure prophylaxis that will never be given to patients (so there will be no resistance issue)?

Dr Fischl: It would be difficult to withhold therapy from patients in light of the current treatment regimens available. In addition, monotherapy is likely to be less effective and combination therapies are likely to be required.