Postexposure prophylaxis (PEP) has been shown to reduce the risk of HIV transmission by 81% in health care workers, but no information is available about the efficacy of prophylaxis after nonoccupational HIV exposure.

A placebo-controlled study would be difficult to conduct because of ethical considerations, said Dr. Rowland of UCSF.

At press time, the Centers for Disease Control and Prevention was preparing to issue national guidelines on the use of PEP to reduce the risk of HIV infection.

Of the 891 people in the study, all of whom were given PEP within 72 hours after exposure, 700 could be evaluated 12 weeks after PEP was initiated, and 7 (1%) seroconverted. All seven reported having unprotected receptive or insertive anal or vaginal intercourse, receptive oral sex with ejaculation, or shared injection drug equipment. The potential sources of infection had to be known HIV-infected persons, men who have sex with men of unknown HIV status, a past or present injection drug user, a commercial sex worker, or an anonymous contact.

Adherence was fairly good. During week 1, 84% of patients reported no missed doses during the prior 4 days; that figure was 78% during both week 2 and week 4.

Previous studies have yielded estimates that the risk of infection from a single encounter is 0.8% to 5.0% for receptive anal intercourse and substantially lower for other types of exposure. The investigators therefore queried seroconverters about additional risk behavior. Six of the seven reported other high-risk encounters in the 6 months before PEP, and three of the seven reported ongoing high-risk behavior even after starting PEP suggesting that the failure of PEP in these patients may not have been entirely due to medication failure.

"PEP is not just medication. It's also adherence counseling, risk-reduction counseling, and referral, because the whole point of this is to help people stay HIV negative."

There's a tendency to want to divide people presenting for PEP into three groups: those who should be advised to use PEP, those who should be offered PEP, and those who should not be offered PEP. In practice, said, "It's hard for me to recommend PEP to anybody, and it's easy for me to agree to refer it to a fair number of people. The bottom line for me is that it's my job to help that individual person make an individual risk-benefit assessment.

Animal studies and experience with health care workers suggest it's important to begin antiretroviral therapy at most 72 hours after exposure. But many people who are exposed misinterpret that as meaning that they can wait 72 hours before deciding on PEP. "The message we're trying to get across is, 'You want to start this as soon as possible, and we're not going to initiate it after 72 hours,'" she said.

Investigators generally agree that the antiretroviral component of PEP should be continued for 28 days, but there's a great deal of controversy about what antiretrovirals to use and whether two nucleosides are enough or whether a three-drug regimen is better. The practice at UCSF is to use two drugs, but Dr. Rowland would consider using three in certain circumstances. For example, a three-drug regimen might be indicated if a patient reports multiple exposures over 5 days, including several within the required 72-hour period.

She recommended that clinicians be aggressive in getting information about the source of the exposure, to determine whether that person is truly HIV-positive, and to conduct viral resistance testing. This is critical in choosing which antiretrovirals to use.

These results showed that maintaining a normal hemoglobin level in HIV-infected patients may translate into improvements in functional capacity.