Undetectable HIV Doesn't Preclude Transmission

BY DIANA MAHONEY
New England Bureau

BOSTON — Women on highly active antiretroviral therapy for human immunodeficiency virus whose plasma viral load is below detectable levels may continue to shed the virus intermittently in the genital tract, Dr. Susan Cu-Uvin said at the annual meeting of the Infectious Diseases Society for Obstetrics and Gynecology.

"This finding means we cannot rule out the possibility of continued risk of HIV transmission among women in whom the virus appears to be well controlled," said Dr. Cu-Uvin of Brown University, Providence, R.I.

The advent of highly active antiretroviral therapy (HAART) has resulted in significant decreases in the replication of HIV in the blood of infected patients, and in so doing it has substantially reduced the associated morbidity and mortality of the disease, Dr. Cu-Uvin said.

"However, several studies have shown evidence of discordance between the RNA shedding of HIV in the blood and in the female genital tract, and when it comes to sexual transmission of HIV, the big player is the amount of genital tract viral load, not the plasma viral load," she said. "Unfortunately, because the only commercially available tools for assessing HIV viral load are those that look at RNA shedding in plasma, we use plasma viral load as a surrogate for how infectious a given patient is, yet this may not always reflect what is happening in the genital tract."

Dr. Cu-Uvin and colleagues sought to assess the pattern of HIV genital tract shedding among women already on HAART with sustained below detectable plasma viral loads. Of 55 women with HIV enrolled in an ongoing study of HAART, 49 with below detectable plasma viral load for at least 6 months were included in the analysis. Each of the women underwent serum plasma and genital tract sampling every 4 weeks for 12 weeks. Genital tract secretions were collected from the endocervix, ectocervix, and vagina in 40 of the women, and from the vagina only in 9 women who had previous hysterectomies. The lower limit of viral detection was 80 copies per milliliter for plasma and 3,300 copies per milliliter for the genital tract, Dr. Cu-Uvin noted.

The immune status of all of the patients was "generally good," with a median CD4 count of 412 cells/mm^3, said Dr. Cu-Uvin. In terms of demographics, 45% of the patients were African American, 35% were white, and 15% were Hispanic, and the median patient age was 45 years. An assessment for "classic" STDs showed not much gonorrhea, chlamydia, or syphilis, "which was not surprising, because the population was older," Dr. Cu-Uvin said. All of the patients were positive for herpes simplex virus type 2, she noted.

Patients were grouped based on their genital tract HIV RNA patterns, Dr. Cu-Uvin explained. Nonshedders were those women with no evidence of detectable genital tract HIV during study visits. Indeterminate shedders had at least one episode of genital tract shedding with no available measurement prior to or following the episode. Women who had genital tract shedding between negative visits were described as intermittent shedders, and those who had at least two consecutive episodes of genital tract shedding were persistent shedders.

Of the 49 patients enrolled, 46 maintained below detectable plasma viral loads during the course of the study. "What was astonishing to us is that more than half of those women had some degree of detectable genital tract shedding," Dr. Cu-Uvin said. Specifically, 26% of the women with sustained below detectable plasma viral load were indeterminate shedders, 18% were intermittent shedders, and 8% were persistent shedders, "despite being on HAART and having below detectable levels of virus in their plasma," she said. Among the nine women with total hysterectomy, one demonstrated persistent shedding in the vagina, whereas the others were classified as nonshedders, she said.

Although logistic regression analyses showed the probability of detecting HIV RNA in the genital tract subcompartment was low when plasma viral load was below detectable levels, Dr. Cu-Uvin said, "it worries us that there are some women on antiretroviral therapy who have a very good response in the blood, who, if you look hard enough and at multiple time points, will have evidence of genital tract HIV RNA."

What this means clinically, she said, is that the potential for sexual transmission of HIV exists even among women whose virus appears to be well controlled. "So, for example, when a woman on HAART comes to me and says she wants to have a baby, there is no way to assure her, even if she has a below detectable plasma viral load, that it's safe to have unprotected sex." ■

MRSA Showing No Mercy in Skin Infections

BY ERIK GOLDMAN
Contributing Writer

NEW YORK — Methicillin-resistant *Staphylococcus aureus* is now the most common cause of serious skin and soft-tissue infections in many communities throughout the United States, Dr. Mark Lebwohl said at the American Academy of Dermatology's annual Academy 2007 meeting.

"If you're getting cultures, you're seeing this, because it is definitely there," said Dr. Lebwohl of the department of dermatology at Mount Sinai Medical Center, New York. "Where's it coming from? Everywhere!"

In one study he cited, methicillin-resistant *Staphylococcus aureus* (MRSA) accounted for 72% of all skin and soft-tissue infections seen at a major medical center and affiliated outpatient clinics in Atlanta (Ann. Intern. Med. 2006;144:309-17). MRSA is particularly common among athletes, military personnel, homeless people, and intravenous drug users, but in reality, everyone is at risk, he stressed.

The bad news is that MRSA isn't just resistant to methicillin. It seems to be increasingly resistant to most antibiotics these days. "Unfortunately, vancomycin resistance is emerging in MRSA organisms. Erythromycin borders on worthless, as almost all MRSA strains are erythromycin-resistant," he said.

Clindamycin is still effective in most communities around the country, but resistance to this drug also is starting to show up. Between 10% and 15% of all MRSA strains identified in the cities of Atlanta and Baltimore and the state of Minnesota are resistant to clindamycin. In Chicago, the number is over 50% for infected adults, Dr. Lebwohl noted.

Fortunately, trimethoprim-sulfamethoxazole (Bactrim) still works almost everywhere. In Baltimore, though, 17% of MRSA strains have been found to be resistant to this drug as well.

All of this bad news might lead one to conclude that antibiotic therapy for MRSA is ultimately futile. A study published several years ago suggested that, when treating MRSA-infected skin and soft-tissue abscesses, there were no significant differences between allegedly effective and ineffective antibiotics, and that the key to treatment was incision and drainage (Pediatr. Infect. Dis. J. 2004;23:123-7).

Dr. Lebwohl cautioned against such antibiotic nihilism. "If there's no difference between the antibiotics, it's reasonable to ask: Why treat? But the point is, it is not the patient you are seeing that you worry about. It is the person you are not seeing: the patient's family members, neighbors, colleagues. MRSA can cause sepsis, coagulopathy, osteomyelitis. It can kill people. It is very serious. You need to use the right antibiotics, because in treating your patient properly you are also treating the whole community."

Clindamycin and Bactrim are still good options, as are doxycycline and minocycline, although they are not recommended for children. For adults, doxycycline and minocycline are the top choices, he said. Daptomycin (Cubicin) is also a good choice for deep-tissue infections, especially in the bones and joints (Curr. Med. Res. Opin. 2005;21:1923-6).

Dr. Lebwohl also had high praise for linezolid (Zyvox), a newcomer to the antibiotic front lines. MRSA seems to be very sensitive to this drug: A recent in vitro study of almost 3,400 MRSA isolates showed that all were sensitive to linezolid (Antimicrob. Agents Chemother. 2005;49:5024-32). Unfortunately, it is very expensive.

Generally, one should stay clear of quinolones and macrolides, as they are ineffective against MRSA at this point. Rifampin may seem to work at first, but resistance develops very quickly.

Dr. Lebwohl strongly advised colleagues to read and practice according to the Infectious Diseases Society of America's 2005 guidelines for the management of skin and soft-tissue infections (Clin. Infect. Dis. 2005;41:1373-406). He also advocated routine culture and sensitivity testing. The more information physicians can gather about the infections they are confronting, the more intelligently they can choose the antibiotic therapy.

Over the past year, Dr. Lebwohl has been a consultant for a number of drug companies, including Galderma (clindamycin) and Pfizer (doxycycline). ■