

Azithromycin Matches Penicillin for Syphilis Tx

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CHICAGO — A single 2-g dose of azithromycin cures early syphilis as effectively as injected penicillin G benzathine, Dr. Edward W. Hook III said at a conference on STD prevention sponsored by the Centers for Disease Control and Prevention.

However, Dr. Hook cautioned that the federally sponsored randomized, controlled trial did not include any HIV-positive patients, so its results can't support the use of azithromycin in this population.

"This is the very group in which macrolide-resistant *Treponema pallidum* mutations have emerged in association with azithromycin treatment," said Dr. Hook of the University of Alabama at Birmingham. "I would certainly not recommend treating these patients with azithromycin for early syphilis."

Neither should the drug be used for syphilis in pregnant women. "In light of the history of macrolide treatment failures among pregnant women, I would caution very, very strongly against treating them with azithromycin for syphilis," Dr. Hook said.

The trial compared the efficacy and safety of 2 g of azithromycin given orally with those of 2.4 million U of penicillin G benzathine in 517 patients with early syphilis. Most of the patients (80%) were in Madagascar; the rest were seen at U.S. clinics.

The patients' mean age was 24 years; 26% had primary syphilis, 46% had secondary syphilis, and 28% had presumed early latent syphilis (a sexual partner in the past 12 months with confirmed syphilis).

Serologic cure rates at 3 months were similar in both groups in the intent-to-treat analysis (74% azithromycin vs. 76% penicillin). At 6 months, the cure rates were still not significantly different (77% azithromycin vs. 78% penicillin). Results at 3 and 6 months in the per-protocol analysis were almost identical, Dr. Hook said. U.S. patients exhibited slightly, but not significantly, higher cure rates than did patients in Madagascar.

Serious adverse events were slightly more common in the penicillin group than they were in the azithromycin group (10 vs. 8, respectively). However, none of these were considered related to the study medication. Nonserious adverse events, especially gastrointestinal distress, were significantly more common among the patients taking azithromycin (61% vs. 46% for penicillin). The most common adverse events were gastrointestinal, with 24% of the azithromycin group experiencing some upset, compared with 7% of the penicillin group. However, only three patients taking azithromycin vomited.

Cutaneous reactions were more common among those taking penicillin (4% vs. 1%), as were administration-related adverse events (10% vs. 5%).

Syphilis Infection Rate Rises Most in Gay Men, Blacks

CHICAGO — The rate of syphilis in the United States has increased for the seventh consecutive year, jumping 12% from 2006 to 2007, according to preliminary evidence released by the Centers for Disease Control and Prevention.

The upsurge was driven largely by a 14% rise in cases of primary and secondary syphilis among men, Dr. Hillard Weinstock said at a conference on STD prevention sponsored by the CDC. "As in recent years, the 2007 data show that men—particularly men who have sex with men—account for the vast majority of syphilis cases and contribute significantly to the overall syphilis increases. Men who have sex with men [accounted for] approximately 64% of reported syphilis cases in 2007," said Dr. Weinstock, chief of surveillance at the CDC's division of STD prevention.

The overall 12% increase reflected about 1,300 additional cases reported to the CDC in 2007—a population rate of 6 per 100,000, Dr. Weinstock said at a press briefing during the conference.

The rate among men was six times greater than that among women.

Blacks experienced a disproportionate increase in the disease, compared with whites, Dr. Weinstock noted; the rate of syphilis among blacks was seven times higher than that among whites. Black men were six times more likely to have the disease than white men were, and black women were 13 times more likely to have it than white women were. From 2006 to 2007, the disease rate rose 25% in black men and 12% in black women.

"While men who have sex with men bear the heaviest burden of syphilis infections, ongoing increases among women and African Americans

are also troubling and threaten to undo recent progress," Dr. Weinstock said.

Following a 1999 federal commitment to end syphilis nationwide, infection rates reached an all-time low in 2000, dipping to just two cases per 100,000. The rate has increased each year since then. The new prevalence numbers represent a 76% increase over the 2000 nadir.

Inadequate routine screening combined with complacency about the disease appear to be influencing the increase, said Dr. John Douglas, the director of CDC's Division of STD Prevention. "When the incidence of a disease decreases so much, we often see an accompanying decrease in recognition of the disease among both providers and the public. And this is especially true among men who are already infected with HIV."

These men might see syphilis and other STDs as a nuisance rather than a serious health threat. But about 2% of syphilis patients suffer permanent neurologic sequelae, including stroke, blindness, and deafness, Dr. Douglas noted.

The CDC recommends that sexually active gay men receive annual testing for both syphilis and HIV, with more frequent testing recommended for men who engage in high-risk same-sex behavior. But the new prevalence numbers, along with other studies, indicate that the rate of screening is too low.

"We really need help from our health care partners," Dr. Douglas said. "A major message is that the word about the need for annual testing is not getting out to providers. We need to work much more closely with these partners both to get the word out and to find resources for testing."



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Azithromycin-Resistant Syphilis Increases in San Francisco

CHICAGO — Azithromycin-resistant strains of *Treponema pallidum* continue to emerge in San Francisco, despite the cessation of the drug's use for syphilis treatment and prophylaxis and for the treatment of nongonococcal urethritis in gay men.

The city's historically low 5% resistance rate jumped dramatically to 40% in 2003, just a year after the San Francisco Department of Public Health began using the drug prophylactically in the sex partners of gay men with symptomatic syphilis, Dr. Kenneth Katz said at a conference on STD prevention sponsored by the Centers for Disease Control and Prevention. During this time, azithromycin also was used to treat both syphilis and nongonococcal urethritis in gay men who were allergic to penicillin. But despite a 2004 decision to stop using the drug for any syphilis treatment, resistance has risen linearly each year, to a high of 77% in 2006, Dr. Katz said at the meeting.

"This finding emphasizes a real need for vigilance in finding treatment failures in patients receiving azithromycin, and a need for surveillance of azithromycin-resistant syphilis in areas where this drug may be used to treat syphilis," he said.

To this end, the CDC recently has launched a nationwide surveillance program to identify azithromycin-resistant *T. pallidum* strains, said Dr. Katz, a public health official with the CDC and the San Francisco Department of Public Health.

In 1998, gay men made up only 20% of the syphilis cas-

es in San Francisco. By early 2002, that proportion had risen to 90%, Dr. Katz said. The dramatic increase spurred the city's health department to launch an aggressive program aimed at decreasing the spread of the disease. "Part of our response was to treat the sex partners of symptomatic patients with a single 1-g dose of azithromycin. Symptomatic patients who were allergic to penicillin were treated with a single 2-g dose."

The protocol began in July 2002. "Shortly thereafter, we began to notice treatment failures in patients with primary or incubating syphilis who had been treated with azithromycin," Dr. Katz said. Azithromycin kills microbes by binding at the ribosome to inhibit protein synthesis. Some strains of *T. pallidum* had developed a mutation that inhibited this ribosomal binding.

In September 2004, the city's health department ceased using azithromycin for any syphilis treatment. But a case-control study showed that the resistant mutation was associated with any azithromycin use within 30 days prior to the syphilis diagnosis. Therefore, Dr. Katz said, the ban on azithromycin was extended; in 2005, the health department discontinued its use in nongonococcal urethritis in gay men.

Despite these precautions, azithromycin resistance has continued to increase in San Francisco, he said. The department conducted a polymerase

chain reaction assay on samples from 39 positive lesions in 2005 and 2006. Almost all of the cases (36) were among gay men. Of the 17 lesions sampled in 2005, 13 (76%) contained the resistant strain. Of the 22 samples examined in 2006, 17 (77%) contained the strain.

Azithromycin-resistant *T. pallidum* also has been found in Seattle and Baltimore, as well as some cities in Canada and Ireland, Dr. Katz noted.

