Gonococcal Resistance Continues to Spread

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Contributing Writer

PHILADELPHIA — The rate of fluoroquinolone resistance in *Neisseria gonorrhoeae* doubled from 2.2% in 2002 to greater than 4% in 2003, and resistant isolates are now surfacing at several sites around the country, according to an official with the Centers for Disease Control and Prevention.

In the past, the problem of quinolone-resistant *Neisseria gonorrhoeae* (QRNG) was limited to Hawaii and California, "but we now have big increases in Massachusetts, New Hampshire, New York City, Seattle, and Washington state.

"We also have increased frequency of resistance to a lesser extent in Chicago, Philadelphia, Las Vegas, and many other cities and states," reported Susan Wang, M.D., national coordinator, gonococcal resistance, in the division of STD prevention at the CDC.

According to preliminary estimates of 2003 data, the national rate of QRNG is about 4%, while the rate is about 12% in Hawaii, 19% in California, and 14% in Massachusetts, she said at a conference on STD prevention sponsored by the CDC.

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It's not clear how widespread the problem is, because only a limited number of cities and counties participate in the CDC-sponsored Gonococcal Isolate Surveillance Project (GISP), which monitors the susceptibilities of *N. gonorrhoeae* strains to antimicrobial agents, including ciprofloxacin and cephalosporins.

"In most places, susceptibility testing is not done at the local level. So you and your local health department may not know if gonococcal resistance is a problem for your area, unless you are in a GISP city," Dr. Wang said.

GISP sites include Albuquerque; Atlanta; Baltimore; Birmingham, Ala.; Chicago; Cincinnati; Cleveland; Dallas; Denver; Detroit; Greensboro, N.C.; Honolulu; Los Angeles; Las Vegas; Long Beach County, Calif.; Miami; Minneapolis; New Orleans; Oklahoma City; Orange County, Calif.; Philadelphia; Phoenix, Ariz.; Portland, Ore.; San Diego; San Francisco; Seattle; and St. Louis.

"The prevalence of QRNG in women is increasing but is generally lower than in men who have sex with men [MSM]," Dr. Wang said.

The latter group accounts for a "big portion" of the cases of QRNG. "According to 2002 data, in New York City, Seattle, and Massachusetts, QRNG is especially emerging in MSM," she said.

The lack of data regarding women and QRNG concerns the CDC, Dr. Wang said in an interview.

"Data on women are especially important because the long-term sequelae of the disease have the greatest impact on women in terms of pelvic inflammatory disease, infertility, and chronic pelvic pain," she said.

The lack of QRNG data on women is partly a technical issue, she explained. The national GISP surveillance system uses *N. gonorrhoeae* isolates from the first 25 men with gonorrhea attending sexually transmitted diseases clinics at GISP sites each month; the isolates are then sent for testing at regional labs. "GISP surveillance is limited to male urethral specimens in part because these specimens are less complicated to evaluate than female specimens," she said.

The problem of poor data in women and related treatment problems also is worsened by the increasing inability of community-based physicians and labs to perform culture-based testing, Dr. Wang said.

"To monitor resistance you cannot perform DNA-based testing. You need culture-based testing. Physicians and labs increasingly only perform DNA-based testing."

Physicians who believe that a patient is not responding to treatment with a fluoroquinolone should perform a culture and send the sample to a private lab or local health department for susceptibility testing.

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plicated gonorrhea, the CDC recommends regimens of fluoroquinolones (single-dose, oral therapy with 500 mg ciprofloxacin or 400 mg ofloxacin or 250 mg levofloxacin); or a single oral dose of cefexime 400 mg; or a 125-mg IM injection of ceftriaxone.

The CDC also recommends that clinicians check with their local health departments to learn if treatment recommendations have changed, as is the case in Massachusetts, Washington, and other locales.

Resistance to ciprofloxacin and other fluoroquinolones limits treatment options because of the current absence of cefixime from the market.

"Basically, QRNG threatens the physician's ability to treat with an oral agent. Currently our only other available treatment is a cephalosporin, ceftriaxone, which is an intramuscular injection and doctors may not stock it in private practice," Dr. Wang said.

"Cefixime is also an oral agent and is recommended by the CDC for the treatment of gonorrhea.

But it was taken off the market by Wyeth Laboratories in 2002. However, the Food and Drug Administration recently approved a generic manufacturer of cefixime from India to sell the drug here. Cefixime is also an option for QRNG," she said.

Gonococcal resistance has repeatedly occurred in the United States, noted Dr. Wang.

"Gonococcal resistance has been ongoing since the 1940s, starting with resistance to sulfanilamide. In the 1980s, tetracycline and penicillin were abandoned due to resistance, which led the CDC to recommend treatment with ciprofloxacin or other fluoroquinolones in 1987," Dr. Wang said.

The future of treatment of drug-resistant gonorrhea is cloudy, P. Frederick Sparling, M.D., observed in his plenary lecture at the meeting.

"What drugs will replace ciprofloxacin and cefixime? Pharmaceuticals are abandoning such areas, as they are price-controlled markets, with government as the main buyer. The future of treating gonorrhea is bleak," said Dr. Sparling, J. Herbert Bate Professor of Medicine and Microbiology and Immunology, Emeritus, University of North Carolina at Chapel Hill.

Dr. Sparling added that the implications of emerging vaccines for STDs and attacks from conservative groups on research related to STDs both add to the difficulties in developing new drugs for gonorrhea. ■

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