Neisseria gonorrhoeae Now Sidesteps Fluoroquinolones

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Fluoroquinolones should no longer be used for the treatment of gonorrhea in the United States, the Centers for Disease Control and Prevention has concluded.

The recommendation is based on new evidence suggesting that the prevalence of fluoroquinolone-resistant strains in the United States has now surpassed the prespecified threshold of 5%. Only one antimicrobial class—the cephalosporins—is now still recommended and available for the treatment of gonococcal infections or for other conditions that might be caused by *Neisseria gonorrhoeae*, such as pelvic inflammatory disease, the CDC said (MMWR 2007;56:332-6).

Fluoroquinolones have been used to treat gonorrhea since 1993. Between 1990 and 2001, the CDC's Gonococcal Isolate Surveillance Project (GISP) detected fluoroquinolone-resistant *N. gonorrhoeae* (QRNG) prevalences of less than 1% among urethral gonococcal isolates taken from males attending between 26 and 30 sexually transmitted disease clinics around the country.

But the prevalence rose to 2.2% in 2002, then to 4.1% in 2003, and to 6.8% in 2004. In 2005, 9.4% of 6,199 isolates collected by GISP were resistant to ciprofloxacin, and during January-June of 2006, 13.3% of 3,005 isolates were resistant.

"Gonorrhea has proven to be quite efficient at navigating around the drugs we use to combat it, developing resistance first to penicillin and tetracycline, and most recently to fluoroquinolones," said Dr. John M. Douglas, director of the CDC's division of sexually transmitted diseases prevention, in a telebriefing held in conjunction with the release of the new guidelines.

Recommendations to stop the use of fluoroquinolones to treat gonorrhea had already been issued in 2000 for people who

acquired their infections in Hawaii, and in 2002, the recommendation was extended to California.

In 2004, the CDC advised that fluoroquinolones should no longer be used to treat gonorrhea in men who have sex with men (MSM) throughout the United States. Excluding isolates from Hawaii and California, 6.1% of U.S. isolates in 2005 and 8.6% in 2006 were fluoroquinolone resistant, the CDC reported.

Data from GIST suggest that QRNG has been increasing among both MSM and heterosexual males since 2001. The prevalence among MSM, which was 1.6% in 2001, rose to 7.2% in 2002, 15% in 2003, 24% in 2004, and 29% in 2005. The increase has been slower among heterosexual males, from 0.9% in 2002 to 1.5% in 2003, 2.9% in 2004, and 3.8% in 2005.

Preliminary data from the first half of 2006 indicate that the QRNG prevalence was 38.3% among MSM and 6.7% among heterosexual males, with both numbers surpassing the 5% threshold set by both the CDC and the World Health Organization to ensure that all recommended gonorrhea treatments can be expected to cure 95% or more of infections, the CDC said.

Cephalosporins are now the only agents available in the United States that meet that standard. For the treatment of uncomplicated urogenital and anorectal gonorrhea, the CDC now recommends a single 125-mg intramuscular dose of ceftriaxone. A single oral 400-mg dose of cefixime is also recommended, but cefixime is available only in a suspension in the United States, not as 400-mg tablets.

Single oral doses of 400 mg cefpodoxime or 1 g cefuroxime axetil also are likely to be effective, but the data for those two regimens are more limited than for ceftriaxone, Dr. Douglas said during the briefing.

Alternative parenteral single-dose regimens for urogenital and anorectal gonorrhea include 500 mg ceftizoxime, 2 g cefoxitin with 1 g oral probenecid, or 500 mg cefotaxime.

However, these regimens don't offer any advantages over ceftriaxone, the CDC noted.

A single 125-mg dose of ceftriaxone also is the recommended treatment for uncomplicated gonococcal infections of the pharynx.

Updated regimens for disseminated gonococcal infection, pelvic inflammatory disease, epididymitis, and gonococcal infections in patients with documented severe allergic reactions to penicillins or cephalosporins are available in separate documents at www.cdc.gov/std/treatment.

Unless *Chlamydia trachomatis* has been specifically ruled out, all patients diagnosed with gonococcal disease should also be treated for possible coinfection, with a single dose of 1 g azithromycin by mouth or with 100 mg doxycycline twice a day by mouth for 7 days.

The full gonorrhea treatment guidelines are available at www.cdc.gov/std/gonorrhea/arg.

Test of cure is not routinely recommended, but patients with persistent or recurring symptoms following treatment should be reevaluated by culture for *N. gonorrhoeae,* and any positive isolates should undergo antimicrobial susceptibility testing.

Treatment failures or resistant gonococcal isolates should be reported to the CDC at 404-639-8373 through state and local public health authorities. ■

Specifics of the New Guidelines For Gonorrhea

Because of increased fluoroquinolone resistance of *Neisseria gonorrhoeae* in the United States, the Centers for Disease Control and Prevention no longer recommends the use of that class of antimicrobials for treatment of gonococcal infections in adolescent or adult patients, regardless of travel or sexual behavior.

The CDC's new guidelines include these recommendations:

► **Uncomplicated gonococcal infections of the cervix, urethra, and rectum.** Recommended regimens: Ceftriaxone 125 mg in a single dose IM, or cefixime 400 mg in a single oral dose, *plus* treatment for chlamydia if chlamydial infection is not ruled out. Alternative regimens: Spectinomycin (not available in the United States) 2 g in a single dose IM or cephalosporin single-dose regimens (including ceftizoxime 500 mg IM, or cefoxitin 2 g IM administered with probenecid 1 g orally, or cefotaxime 500 mg IM).

► **Uncomplicated gonococcal infections of the pharynx.** Recommended regimens: Ceftriaxone 125 mg in a single dose IM, *plus* treatment for chlamydia if chlamydial infection is not ruled out.