STATE OF NEW YORK
DEPARTMENT OF HEALTH
Corning Tower The Governor Nelson A. Rockefeller Empire State Plaza Albany, New York 12237

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Commissioner

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TO: Hospitals and Local Health Departments

FROM: NYSDOH Bureau of Sexually Transmitted Disease Control

HEALTH ADVISORY: FLUOROQUINOLONES ARE NO LONGER RECOMMENDED FOR THE TREATMENT OF GONORRHEA IN THE UNITED STATES

Please distribute immediately to the Infection Control Department; Emergency Department; Employee Health Service; Departments of Infectious Disease, Internal Medicine, Family Practice, Pediatrics, and Obstetrics and Gynecology; Director of Nursing, Medical Director, Laboratory Service, and all patient care areas.

SUMMARY

- On April 12, 2007, the Centers for Disease Control and Prevention announced that fluoroquinolones are no longer recommended for the treatment of gonorrhea in the United States.

- This recommendation was based on analysis of new data from CDC's Gonococcal Isolate Surveillance Project (GISP), a sentinel surveillance system that monitors trends in antimicrobial susceptibilities of strains of *N. gonorrhoeae* in the U.S., which showed that in the first half of 2006 among heterosexual men, the proportion of gonorrhea cases that were fluoroquinolone-resistant (QRNG) reached 6.7%, an 11-fold increase from 0.6% in 2001.

- Recommended options for treating gonorrhea are now limited to a single class of antibiotics, cephalosporins. Within this class, the NYSDOH and CDC recommend ceftriaxone, available only as an injection, as the preferred treatment for all types of gonorrhea infection (genital, anal and pharyngeal).

- Because of the lack of treatment options, CDC strongly encourages state and local health departments to:

    - Maintain or develop capacity to culture for *N. gonorrhoeae*
    - Maintain capacity or develop partnerships with other experienced laboratories to conduct drug susceptibility tests for any patients who fail gonorrhea treatment

- **NYSDOH BSTDC recommends that all patients treated for gonorrhea infection (including those treated with cephalosporins) must have a follow-up physical examination (anogenital and oral) and a test of cure (TOC) from the infected sites identified at the time of the initial diagnosis.** A TOC is essential in all cases, **even those asymptomatic after treatment**. Isolates from treatment failures should be tested for antibiotic resistance.

    - TOC is recommended at 2 weeks post-treatment if using culture or at 4 weeks post-treatment if using nucleic acid amplification tests (NAAT) regardless of whether symptoms have resolved or not.
    - If the post-treatment NAAT is positive, a culture must be performed to assess for resistance

- Providers should report all cases or suspected cases of resistance to state and local public health authorities so that the NYSDOH and CDC can closely monitor and appropriately respond to any emerging resistance

BACKGROUND

On April 12, 2007, CDC announced that fluoroquinolones are no longer recommended for the treatment of gonorrhea in the United States. This recommendation was based on analysis of new data from CDC's Gonococcal Isolate Surveillance Project (GISP), a sentinel surveillance system that monitors trends in antimicrobial susceptibilities of strains of *N. gonorrhoeae* in the U.S. The data on which the recommendation is based were published in the April 13, 2007 MMWR (http://www.cdc.gov/mmwr/) and show that in the first half of 2006 among heterosexual men, the proportion of gonorrhea cases that were fluoroquinolone-resistant (QRNG) reached 6.7%, an 11-fold increase from 0.6% in 2001.

CDC has recommended oral fluoroquinolones (ciprofloxacin, ofloxacin and levofloxacin) as first-line treatments for gonorrhea since 1993, but over the past several years, as QRNG cases increased steadily, CDC advised that they were not recommended for treating gonorrhea, first in Hawaii (2000), then California (2002), and, most recently, in men who have sex with men nationwide (2004).

TREATMENT RECOMMENDATIONS

Recommended options for treating gonorrhea are now limited to a single class of antibiotics, cephalosporins. Within this class, CDC recommends ceftriaxone, available only as an injection, as the preferred treatment for all types of gonorrhea infection (genital, anal and pharyngeal).

Immediate (30-60 minutes after administration) and accelerated (1-12 hours after administration) immunoglobin E mediated anaphylactic or urticarial reactions to cephalosporins are rare relative to those associated with penicillin. Cephalosporin reactions occur in approximately 5-10% of persons with a history of penicillin allergy. However, medical history and penicillin skin test

results do not reliably predict the probability of allergic reactions to cephalosporins in those with history of penicillin allergy. Persons who cannot tolerate cephalosporins should be treated with spectinomycin, if available. Because spectinomycin is not adequately effective against pharyngeal infections, patients who have suspected or known pharyngeal infection should have a pharyngeal culture evaluated 3-5 days after treatment to verify eradication of infection.

Since there are limited data regarding alternative regimens for treating gonorrhea among persons who have documented severe cephalosporin allergy, expert infectious diseases consultation is recommended; the best available treatment option is cephalosporin treatment following desensitization. If desensitization is not an option, azithromycin may be considered. Azithromycin 2 grams orally is effective against uncomplicated gonococcal infection, but concerns over emerging antimicrobial resistance to macrolides should restrict its use to limited circumstances.

Prior federal treatment guidelines have advised that patients with uncomplicated gonorrhea who were treated with recommended or alternative regimens did not need a test of cure. In light of increasing concerns regarding resistance, the **NYSDOH BSTDC recommends that all patients treated for gonorrhea infection (including those treated with cephalosporins) must have a follow-up physical examination (anogenital and oral) and a test of cure (TOC) from the infected sites identified at the time of the initial diagnosis.** A TOC is essential in all cases, **even those asymptomatic after treatment**. Isolates from treatment failures should be tested for antibiotic resistance.

- TOC is recommended at 2 weeks post-treatment if using culture or at 4 weeks post-treatment if using nucleic acid amplification tests (NAAT) regardless of whether symptoms have resolved or not.
- If the post-treatment NAAT is positive, a culture must be performed to assess for resistance

As a reminder, **treatment failures may also be epidemiologic**. For example: (1) the patient may be re-infected by a new partner or an untreated old partner; (2) the treatment of the patient and partner may not have overlapped, thereby allowing the infection to pass back and forth between partners; or (3) treatment may fail to eradicate organisms from the rectum or pharynx of the patient or their partner.

Updated treatment recommendations are attached below; more details are available at http://www.cdc.gov/std/treatment/. For additional information see Newman, LM, Moran JS, Workowski KA. "Update on Management of Gonorrhea in Adults," *Clinical Infectious Diseases* 2007; 44: S84-101.

NEED FOR ONGOING MONITORING OF RESISTANCE

Because of the lack of treatment options, it is critical that all providers work closely with the New York State Department of Health and their Local Health Departments to monitor resistance. Specifically, the CDC has strongly encouraged state and local health departments to:

- Maintain or develop capacity to culture for *N. gonorrhoeae*
- Maintain capacity or develop partnerships with other experienced laboratories to conduct drug susceptibility tests for any patients who fail gonorrhea treatment

CDC will closely monitor for cephalosporin resistance in the U.S. through GISP and will work with the World Health Organization to strengthen international monitoring for gonococcal drug resistance. CDC will also work with government and industry partners to identify and evaluate promising alternative drug regimens for treating gonorrhea.

REPORTING

Reporting is crucial in the ability of the NYSDOH and CDC to closely monitor and appropriately respond to any emerging resistance. Providers should promptly report any case, including suspected cases, of resistance to the local health department where the patient resides. If the patient resides outside New York State, please notify the NYSDOH Bureau of Sexually Transmitted Disease Control at (518) 474–3598.

LABORATORY ASSISTANCE

Providers should check with their commercial or hospital laboratories about the availability of selective media for gonorrhea culture if a resistant infection is suspected. The Wadsworth Center Bacteriology Laboratories of the NYSDOH are available to assist in the confirmation of suspected drug resistant strains. In addition, for those cases where patients fail to respond to therapy, they also are available to assist in performing culture and antibiotic susceptibility testing. Please contact Nellie Dumas or Kim Musser in the Bacteriology Laboratory at (518) 474-4177 before submission of specimens or bacterial isolates.