Health Update:

Data Suggest Declining Susceptibility to Cephalosporins Among *Neisseria gonorrhoeae* Isolates

July 12, 2011

This document will be updated as new information becomes available. The current version can always be viewed at http://www.health.mo.gov

The Missouri Department of Health & Senior Services (DHSS) is now using 4 types of documents to provide important information to medical and public health professionals, and to other interested persons:

Health Alerts convey information of the highest level of importance which warrants immediate action or attention from Missouri health providers, emergency responders, public health agencies, and/or the public.

Health Advisories provide important information for a specific incident or situation, including that impacting neighboring states; may not require immediate action.

Health Guidances contain comprehensive information pertaining to a particular disease or condition, and include recommendations, guidelines, etc. endorsed by DHSS.

Health Updates provide new or updated information on an incident or situation; can also provide information to update a previously sent Health Alert, Health Advisory, or Health Guidance; unlikely to require immediate action.

Office of the Director
912 Wildwood
P.O. Box 570
Jefferson City, MO 65102
Telephone: (800) 392-0272
Fax: (573) 751-6041
Web site: http://www.health.mo.gov

Health Update
July 12, 2011

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Data Suggest Declining Susceptibility to Cephalosporins Among *Neisseria gonorrhoeae* Isolates**

On May 10, 2011, the Missouri Department of Health and Senior Services (DHSS) issued a Health Advisory entitled "New Guidelines for the Management of Sexually Transmitted Diseases",[1] which alerted medical providers to new treatment guidelines for sexually transmitted diseases (STDs) from the Centers for Disease Control and Prevention (CDC).[2] Included in these new guidelines, and briefly summarized in the Health Advisory, are revised treatment regimens for gonorrhea.

On July 8, 2011, the *Morbidity and Mortality Weekly Report* (*MMWR*) contained an article entitled "Cephalosporin Susceptibility Among *Neisseria gonorrhoeae* Isolates – United States, 2000-2010."[3] This article presents data which suggest declining susceptibility to cephalosporins – the only remaining class of antibiotics available to treat gonorrhea. This emphasizes the importance of current recommendations that call for dual therapy of gonorrhea with a cephalosporin PLUS either azithromycin or doxycycline. **Based on the findings reported in this *MMWR* article, CDC is now recommending ceftriaxone 250 mg intramuscularly PLUS azithromycin 1 g orally as the most effective treatment for uncomplicated gonorrhea.**

Known or suspected cases of gonorrhea should be reported to the local public health agency (LPHA), or to DHSS at 573/751-6439. In addition, medical providers should be vigilant for treatment failure and report its occurrence to the LPHA, or to DHSS, within 24 hours.

For the *MMWR* article,[3] researchers analyzed 10 years of gonorrhea isolates from male patients in 30 U.S. cities collected through CDC's Gonococcal Isolate Surveillance Project (GISP). The analysis showed an increase in the proportion of isolates with elevated minimum inhibitory concentrations (MICs), the lowest concentration of an antibiotic that inhibits visible growth of the bacteria. Increases in MICs suggest declining antibiotic susceptibility. From 2000-2010, the percentage of isolates exhibiting elevated MICs rose from 0.2% - 1.4% of isolates for cefixime and from 0.1% - 0.3% for ceftriaxone.

The article includes the following comments and recommendations (slightly edited, and including Missouri-specific information):

- The epidemiologic pattern of cephalosporin susceptibility . . . . is similar to that previously observed during the emergence of fluoroquinolone-resistant *N. gonorrhoeae* in the U.S. Although the history of fluoroquinolone-resistant *N. gonorrhoeae* might not predict the patterns of decreasing cephalosporin susceptibility, the observed trends are concerning even though the current prevalence of isolates with elevated MICs remains low overall.

---

1. DHSS *Health Advisory: New Guidelines for the Management of Sexually Transmitted Diseases*, May 10, 2011. http://health.mo.gov/emergencies/ert/alertsadvisories/pdf/had51011.pdf

2. CDC. *2010 STD Treatment Guidelines*. http://www.cdc.gov/std/treatment/2010/default.htm

3. CDC. Cephalosporin Susceptibility Among Neisseria gonorrhoeae Isolates – United States, 2000-2010. *MMWR* 2011;60(26);873-7 http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6026a2.htm?s_cid=mm6026a2_w

- Previously, the emergence and spread of gonococcal antibiotic resistance in the U.S. was addressed by changing the recommended antibiotics for treatment. However, no other well-studied and effective antibiotic treatment options or combinations currently are available other than those now being recommended. The emergence of gonococcal cephalosporin resistance would substantially limit available treatment options.

- In light of the diminished resources available to STD control programs and the past inability to prevent emergence of resistance, the eventual emergence of cephalosporin resistance appears likely. Actions undertaken now could delay the spread of cephalosporin-resistant strains and mitigate the public health consequences. Effective treatment of gonorrhea is essential and now requires two antibiotics.

- The findings in this report suggest that gonococcal resistance to cefixime might emerge in the U.S. before resistance to ceftriaxone. Ceftriaxone is the most effective cephalosporin for treatment of gonorrhea and should be used for treatment of gonorrhea in combination with azithromycin or doxycycline. Azithromycin is preferred over doxycycline for dual therapy with ceftriaxone; of the 2009-2010 isolates with decreased susceptibility to cefixime, none exhibited decreased susceptibility to azithromycin, and all of them exhibited tetracycline resistance.

- **Based on the findings in this report, CDC currently is recommending <u>ceftriaxone</u> 250 mg intramuscularly and <u>azithromycin</u> 1 g orally as the most effective treatment for uncomplicated gonorrhea.**

- In addition to effective treatment, prompt recognition of cephalosporin-resistant gonorrhea is critical. Clinicians should remain vigilant for treatment failures (evidenced by persistent symptoms or a positive follow-up test despite treatment) among patients treated for gonorrhea with CDC-recommended antibiotics and obtain specimens for gonococcal culture from patients with possible treatment failure. Clinicians caring for patients with gonorrhea, particularly men who have sex with men (MSM) in the western U.S., might consider having patients return 1 week after treatment for test-of-cure with culture, preferably, or with nucleic acid amplification tests (NAATs).

- If a patient experiences cefixime treatment failure, clinicians should re-treat the patient with 250 mg ceftriaxone intramuscularly and 2 g azithromycin orally. If a patient experiences a ceftriaxone treatment failure, clinicians should consult with an infectious disease expert and DHSS (573/751-6439) regarding re-treatment. These patients should return for tests-of-cure within 1 week, preferably with culture, or, if culture is not available, with NAAT. If the follow-up NAAT result is positive, a specimen for culture should be obtained. Clinicians also should ensure that the patient's sex partners from the preceding 2 months are tested for gonorrhea (preferably with culture) and empirically treated with ceftriaxone 250 mg intramuscularly and azithromycin 2 g orally. Finally, these treatment failures should be reported to DHSS within 24 hours.

- Laboratorians and clinicians are requested to report gonococcal isolates with decreased cefixime or ceftriaxone susceptibility ($\geq$0.5 μg/mL) to DHSS within 24 hours of identification. Isolates can be submitted to CDC's Neisseria Reference Laboratory for confirmation of susceptibility testing through the Missouri State Public Health Laboratory.

Questions and case reports can be directed to DHSS' Bureau of HIV, STD, and Hepatitis at 573/751-6439, or by faxing to 573/751-6417.