Public Health – Seattle & King County (PHSKC) Treatment Recommendations for *Neisseria gonorrhoeae* August 2012

New GC treatment guidelines from the CDC

In last week's *Morbidity and Mortality Weekly Report (MMWR)*, CDC released new data demonstrating an increase in the proportion of gonococcal isolates tested through the Gonococcal Isolate Surveillance Project (GISP) with "alert values" to ceftriaxone or cefixime. *Neisseria gonorrhoeae* resistance is evaluated in the laboratory by measuring the minimum inhibitory concentration (MIC) of a drug required to inhibit the growth of a microorganism. For cefixime, *N. gonorrhoeae* isolates with a MIC of ≥0.5 µg/ml are considered resistant, while organisms with an MIC of ≥0.25 µg/ml are defined as having an "alert value." Alert values serve as a warning sign that resistance may be developing. In 2011, the highest proportions of gonococcal isolates with elevated minimum MICs to cefixime were in the West (3.2%) and among men who have sex with men (MSM) (3.8%). It is important to note that the new data are only a warning sign of resistance -- we have not yet seen cases of treatment failure due to cephalosporin resistance in the U.S.

Summary of PHSKC County Recommendations

- Although true cephalosporin resistant gonorrhea has not yet been observed in the U.S., increasing resistance is an important concern, particularly among men who have sex with men (MSM).
- Ceftriaxone 250mg IM po once PLUS Azithromycin 1mg po once is the preferred treatment for gonorrhea.
- Cefixime 400mg po once PLUS Azithromycin 1g po once continues to be an alternative therapy when intramuscular therapy is not an option.
- Medical providers should continue to offer patient delivered partner therapy (PDPT) with cefixime and azithromycin to heterosexual patients with gonorrhea if the provider cannot otherwise assure the partners' treatment. Public Health does not recommend the use of PDPT in MSM.
- Persons with gonorrhea should undergo rescreening 12 weeks after treatment.

The new guidelines place greater emphasis on the primary role of ceftriaxone in the treatment of gonorrhea. However, CDC continues to recommend oral cefixime, in combination with azithromycin or doxycycline, as an alternative treatment. Ceftriaxone is the preferred treatment because it achieves much higher blood levels than cefixime, and the genetic barrier to ceftriaxone resistance is higher than the barrier to cefixime resistance. (Resistance to ceftriaxone requires more genetic changes in *N. gonorrhoeae* than resistance to cefixime.) The use of azithromycin as the second antimicrobial is preferred over doxycycline because of the advantages of single-dose therapy and the higher prevalence of tetracycline resistance. Medical providers should treat gonorrhea patients with allergies to cephalosporins with a single 2g dose of azithromycin.

The CDC also recommends that patients treated with therapies other than ceftriaxone undergo a test of cure (TOC) in 7 days, ideally with culture, though CDC regards nucleic acid amplification tests (NAATs) as acceptable alternatives. If a NAAT TOC is positive, CDC recommends that providers obtain a confirmatory culture. Antimicrobial susceptibility testing is recommended for all positive TOC cultures. CDC's continues to recommend that patients treated for gonorrhea be retested 3 months after treatment.

The full MMWR report is available online: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6131a3.htm?s_cid=mm6131a3_e.

N. gonorrhoeae resistance in King County and PHSKC Recommendations

Washington State monitors *N. gonorrhoeae* resistance through its participation in GISP. Between 2009 and 2011, Washington's GISP evaluated 553 gonorrhea isolates. **No isolates were resistant to cefixime.** However, among MSM, 9 (2.5%) of 362 isolates had alert values for cefixime (MIC=0.25µg/ml). Only 1 of 160 isolates obtained from heterosexuals had an MIC of 0.25µg/ml. Although we have not observed true cephalosporin resistance in Washington State, Public Health remains very concerned about the emergence of resistant *N. gonorrhoeae*. Providers are encouraged to follow the recommendations below:

Treatment Recommendations for uncomplicated gonorrhea of the cervix, urethra or rectum:

RECOMMENDED

- Ceftriaxone 250 mg intramuscularly PLUS Azithromycin 1g orally, both in a single dose;

OR

ALTERNATIVE THERAPY

- Cefixime 400 mg orally in a single dose AND Azithromycin 1g orally in a single dose.

Medical providers should make particular efforts to treat MSM with ceftriaxone and azithromycin. Because gonococcal resistance to doxycycline is much more common than it is to azithromycin, and because doxycycline appears to be less effective than azithromycin for pharyngeal infections, Public Health does not recommend the use of doxycycline as a second agent when treating gonorrhea.

Test-of-cure, Rescreening and Additional Medical Testing

- All persons without a prior HIV diagnosis who are treated for gonorrhea should be tested for HIV infection. MSM should also be tested for syphilis.
- All persons treated for gonorrhea should undergo rescreening for gonorrhea and chlamydial infection 12 weeks following treatment. MSM should also be rescreened for HIV and syphilis.
- The following persons should have a test-of-cure:
    1) Pregnant women
    2) Persons treated for pharyngeal gonorrhea with a regimen that does not include ceftriaxone
- Test of cure should be performed using culture 1-4 weeks following treatment, or using a nucleic acid amplification test 3-4 weeks following therapy.

Because decreased susceptibility *N. gonorrhoeae* remains uncommon, Public Health does not recommend test-of-cure for all patients with gonorrhea treated with cefixime and azithromycin.

Partner Treatment

Sex partner treatment is an integral part of the gonorrhea treatment. Patients' most recent sex partner and all sex partners from the preceding 60 days require treatment. Whenever possible, partners of persons with gonorrhea should undergo a complete medical evaluation. WA State Expedited Partner Therapy Guidelines recommend that medical providers offer patient-delivered partner therapy (PDPT) to all heterosexual patients diagnosed with gonorrhea or chlamydial infection if the treatment of the patients' partners "is not otherwise assured." **Public Health**

continues to recommend the use of expedited partner therapy with cefixime and azithromycin according to current state guidelines. Because few data exist on PDPT in MSM and because MSM with bacterial STI are elevated risk for syphilis, HIV and resistant gonorrhea, Public Health does not recommend the use of PDPT in MSM. Public Health staff currently attempt to contact all MSM with gonorrhea to help ensure their partners treatment.

Suspected Treatment Failure:
Clinicians should obtain specimens for culture from all patients with suspected treatment failure. Clinicians without access to culture should refer patients to the Public Health STD Clinic at Harborview Medical Center. All cases of treatment failure should be reported to Public Health for further investigation (206–744-2275).