



Cover Sheet

DATE: September 6, 2012

SUBJECT: Antibiotic-resistant Gonorrhea/Revised
Treatment Guidelines

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**DPHHS CDCP
HIV/STD Prevention Section
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Information Sheet

Date: September 6, 2012

Subject: Antibiotic-resistant Gonorrhea/Revised Treatment Guidelines

Information: In response to recent surveillance data suggesting the oral antibiotic cefixime is becoming less effective in treating gonorrhea, CDC has revised its gonorrhea treatment guidelines to preserve the last available effective treatment option for as long as possible. The new guidelines are published in the August 10, 2012 issue of the *Morbidity and Mortality Weekly Report*.

The most significant change in the new guidelines is that CDC no longer recommends cefixime as an effective oral treatment for gonorrhea, leaving only injectable ceftriaxone to be used in combination with one of two oral antibiotics, either azithromycin or doxycycline. Ceftriaxone is more potent against gonorrhea than cefixime, and when paired with the additional oral antibiotic, might slow the emergence of drug resistance by ensuring that Gonococcal infections are quickly cured and not allowed to spread.

RECOMMENDED ACTIONS:

For treatment of uncomplicated urogenital, anorectal, and pharyngeal gonorrhea, CDC recommends combination therapy with a single intramuscular dose of ceftriaxone 250 mg plus either a single dose of azithromycin 1 g orally or doxycycline 100 mg orally twice daily for 7 days.

Clinicians who diagnose gonorrhea in a patient with persistent infection after treatment (treatment failure) with the recommended combination therapy regimen should culture relevant clinical specimens and perform antimicrobial susceptibility testing of *Neisseria gonorrhoeae* isolates. A test-of-cure should be conducted 1 week after re-treatment, and clinicians should ensure that the patient's sex partners from the preceding 60 days are evaluated promptly with culture and treated as indicated.

When ceftriaxone cannot be used for treatment of urogenital or rectal gonorrhea, two alternative options are available: cefixime 400 mg orally plus either azithromycin 1 g orally or doxycycline 100 mg twice daily orally for 7 days if ceftriaxone is not readily available, or azithromycin 2 g orally in a single dose if ceftriaxone cannot be given because of severe allergy. If a patient with gonorrhea is treated with an alternative regimen, the patient should return 1 week after treatment for a test-of-cure at the infected anatomic site.

Report all cases of Gonorrhea immediately to your local health department for assistance with management of sexual contacts.

RESOURCES/REFERENCES:

To obtain further information regarding antibiotic-resistant gonorrhea, please click on the following links:

<http://www.dphhs.mt.gov/publichealth/hivstd/index.shtml>

<http://www.cdc.gov/std/Gonorrhea/arg/default.htm>

<http://www.nejm.org/doi/full/10.1056/NEJMp1112456>

Attached: CDC Fact Sheet: Gonorrhea Treatment Guidelines

Gonorrhea Treatment Guidelines

Revised Guidelines to Preserve Last Effective Treatment Option

In response to recent surveillance data suggesting that the oral antibiotic cefixime is becoming less effective in treating gonorrhea, CDC has revised its gonorrhea treatment guidelines to preserve the last available effective treatment option for as long as possible. The new guidelines are published in the August 10, 2012 issue of the *Morbidity and Mortality Weekly Report*. In addition to revising its treatment guidelines, CDC is also urging researchers in the public and private sectors to step up efforts to develop new treatments for this common but potentially serious sexually transmitted disease (STD).

Gonorrhea Treatment: A Shrinking Arsenal

While antibiotics have long been successfully used to treat gonorrhea, the bacteria has eventually grown resistant to every drug ever used to treat it, including sulfonamides, penicillin, tetracycline, and most recently fluoroquinolones. In 2007, due to widespread drug resistance, CDC revised its gonorrhea treatment guidelines to no longer recommend fluoroquinolones. This left only one class of antibiotics, cephalosporins — which includes the oral antibiotic cefixime and the injectable antibiotic ceftriaxone — to effectively treat the disease.

Now, evidence from CDC's Gonococcal Isolate Surveillance Project (GISP) suggests that cefixime is becoming less effective in treating gonorrhea (see sidebar at right).

To date, no patients have failed treatment with either cefixime or ceftriaxone in the United States. However, a small but growing number of cefixime treatment failures have been observed in other countries. This information, coupled with past experience and the latest U.S. surveillance data, suggest that it is only a matter of time before gonorrhea becomes resistant to the only remaining treatments currently available.

Revised Guidelines

CDC's revised treatment guidelines are designed to ensure that patients receive the most effective treatment for gonorrhea.

- The most significant change in the new guidelines is that CDC no longer recommends cefixime as an effective oral treatment for gonorrhea, leaving only injectable ceftriaxone to be used in combination with one of two oral antibiotics, either azithromycin or doxycycline. Ceftriaxone is more potent against gonorrhea than cefixime, and when paired with the additional oral antibiotic, might slow the emergence of drug resistance by ensuring that gonococcal infections are quickly cured and not allowed to spread.

Trends in Declining Effectiveness of Cephalosporins

Since 1986, GISP has routinely monitored gonorrhea drug susceptibility — or how *Neisseria gonorrhoeae* responds to antibiotics. The project annually collects approximately 6,000 *N. gonorrhoeae* samples from men with urethral gonorrhea at STD clinics in approximately 30 U.S. cities.

Considering the proportion of samples with elevated "minimum inhibitory concentrations" (MICs) of cefixime and ceftriaxone, recent analyses indicate that higher concentrations of cephalosporins are increasingly needed to stop the bacteria's growth in laboratory tests. An MIC is the lowest concentration of antibiotics needed to stop the bacteria's growth in the laboratory.

From January 2006 through August 2011 the percentage of samples exhibiting elevated MICs increased from:

- 0.1% to 1.5% for cefixime
- 0% to 0.4% for ceftriaxone

These increases were most prominent in samples from the western United States and from gay and bisexual men nationwide — the same geographic and population patterns that preceded the emergence of fluoroquinolone resistance less than a decade ago.



- To further guard against the threat of drug resistance, providers should closely monitor for ceftriaxone treatment failure. According to the new guidelines, patients who have persistent symptoms should be retested with a culture-based gonorrhea test, which can identify antibiotic-resistant infections. The patient should return one week after re-treatment for another culture test — or “test-of-cure” — to ensure the infection is fully cured.
- The new guidelines maintain oral cefixime as an alternative treatment option in some instances. If ceftriaxone is not readily available, providers may prescribe a dual therapy of cefixime plus either azithromycin or doxycycline. Azithromycin may be given alone where there is a severe allergy to cephalosporins. However, if either of these alternative regimens is prescribed, providers should perform a test-of-cure one week after treatment.

While these guidelines are necessary, they may make treatment more challenging for some physicians and patients. Health care facilities that may not have previously stocked injectable medications will need to begin carrying ceftriaxone, and all patients will need to undergo an injection in order to ensure effective treatment for gonorrhea. Efforts to treat the partners of those infected may also be complicated by the change. Every effort should be made to ensure that the sex partners of all patients with gonorrhea from the past 60 days are evaluated and treated for gonorrhea with ceftriaxone and either azithromycin or doxycycline, if possible, or an alternative treatment, if ceftriaxone cannot be prescribed. If a partner cannot be brought in for treatment, physicians may consider expedited partner therapy, or having the patient deliver an oral combination regimen consisting of cefixime with azithromycin to their partner.

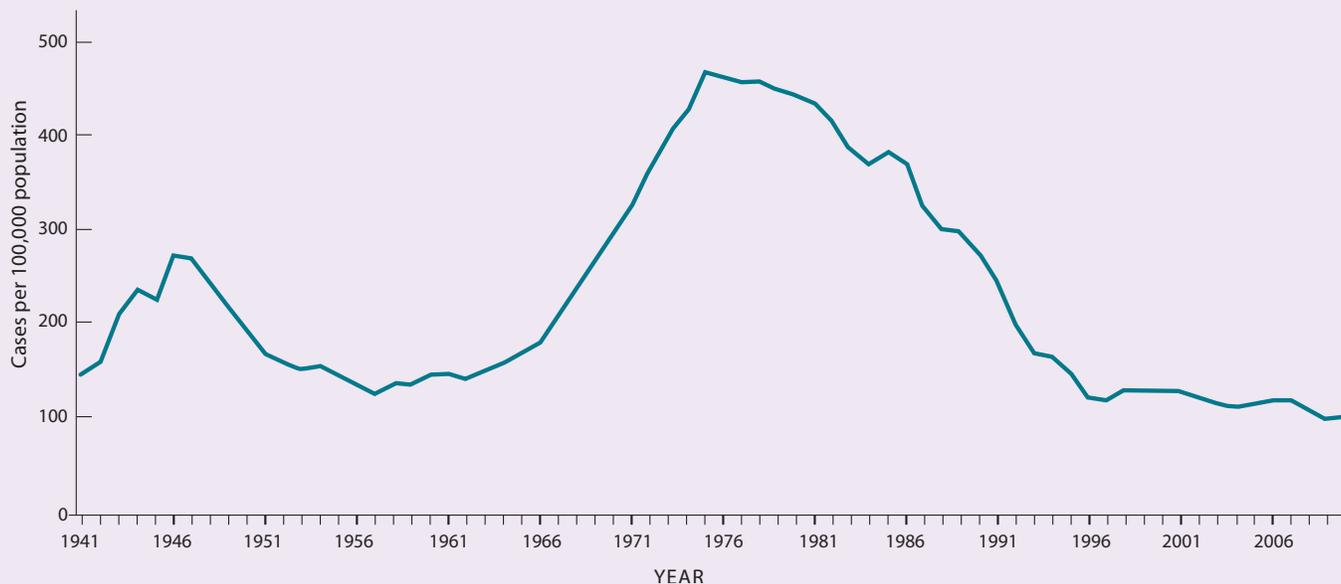
About Gonorrhea

Gonorrhea is the second most commonly reported infectious disease in the United States. Although gonorrhea rates have dropped significantly in recent years, CDC estimates that more than 700,000 Americans still become infected with gonorrhea every year. However, fewer than half of these infections (309,341 in 2010) are diagnosed and reported to CDC.

The disease is caused by *Neisseria gonorrhoeae*, a bacterium that is spread primarily through sexual contact with the penis, vagina, mouth, or anus. Gonorrhea can also be spread from a mother to her baby during delivery.

Untreated gonorrhea can cause serious health consequences, including pelvic inflammatory disease that can lead to infertility and increase the risk of life-threatening ectopic pregnancy in women. In men, gonorrhea can cause epididymitis, a painful condition of the testicles that may lead to infertility if left untreated. Untreated gonorrhea can also increase a person’s risk of acquiring or transmitting HIV.

U.S. Gonorrhea Rates, 1941–2010



Urgent Action Needed

The revised treatment guidelines may help delay the emergence of cephalosporin-resistant gonorrhea, but they do not solve the problem of impending gonorrhea drug resistance. Healthcare providers, state and local health departments, and public and private partners can all take important additional steps to address the potential threat of drug-resistant gonorrhea:

- **Healthcare Providers** — Physicians and other healthcare providers are on the front lines in the fight against gonorrhea and play a critical role in our response. CDC encourages all providers to:
 - Take a sexual history. This will help you know which STDs to test your patient for and at which anatomic sites.
 - Treat all patients diagnosed with gonorrhea promptly according to CDC's updated treatment guidelines, including post-treatment testing to confirm cure when recommended; guidelines available at www.cdc.gov/std/treatment
 - Make every effort to evaluate and treat all patients' sex partners from the previous 60 days
 - Obtain cultures to test for decreased susceptibility from any patients with suspected or documented gonorrhea treatment failures
 - Report any suspected treatment failure to local or state public health officials within 24 hours, helping to ensure that any potential resistance is recognized early
- **Health Departments and Laboratories** — State and local health departments and other laboratories should enhance or rebuild gonorrhea culture capacity so that antibiotic resistance testing can be performed to ensure resistant infections are quickly detected and reported. If antibiotic resistance testing cannot be performed locally, facilities should identify and partner with other labs that can perform such testing. Health departments should develop local response plans and notify CDC of treatment failures immediately. Laboratories should also inform local or state public health officials of any isolates with decreased susceptibility to cephalosporins.
- **Public and Private Partners** — CDC urges scientists and private-sector drug developers to prioritize the identification and study of effective new antibiotic treatments for gonorrhea. Currently, there are few new promising gonorrhea drugs in the pipeline, and only one clinical trial is under way to examine treating gonorrhea using new combinations of existing drugs. While CDC is collaborating with the National Institutes of Health to test new combinations of existing antibiotics for the bacteria, it is likely that many different approaches will need to be tested before suitable treatment options can be found.

Gonorrhea: Protect Yourself

It is critical that individuals protect themselves against infection. Prevention strategies include:

- **Abstinence or mutual monogamy** — The surest way to avoid transmission of gonorrhea is to abstain from sexual intercourse, or to be in a long-term, mutually monogamous relationship with a partner who has been tested and is known to be uninfected.
- **Condoms** — When used consistently and correctly, condoms can reduce the risk of transmission of gonorrhea.
- **Regular screening** — Screening for those at greatest risk is critical. CDC recommends that sexually active gay and bisexual men and high-risk sexually active women be tested for gonorrhea at least once a year.
- **Prompt and effective treatment** — Anyone who becomes infected should get treated with a ceftriaxone injection and either azithromycin or doxycycline right away to cure the infection and prevent transmission to others. Patients receiving a treatment other than dual therapy that includes ceftriaxone should be tested one week after completing treatment to confirm that the infection has been cured.

If you are a member of the news media and need more information, please visit www.cdc.gov/nchstp/Newsroom or contact the News Media Line at CDC's National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention: **404-639-8895** or NCHHSTPMediaTeam@cdc.gov.