NEW YORK CITY DEPARTMENT OF

HEALTH AND MENTAL HYGIENE

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Commissioner

2016 Health Alert #32: Gonorrhea with Reduced Susceptibility to Azithromycin Increasing in New York City

- **Azithromycin is becoming less effective at killing** *Neisseria gonorrhoeae.*
- **Treat gonorrhea with Ceftriaxone 250mg intramuscularly PLUS azithromycin 1g orally. Do not treat with only one antimicrobial.**
- **For patients with persistent symptoms, perform nucleic acid amplification testing and culture that includes ceftriaxone and azithromycin antibiotic susceptibility testing.**
- **Call 866-692-3641 to notify the Health Department of suspected treatment failures.**

August 9, 2016

Dear Colleagues,

In recent years, *Neisseria gonorrhoeae* (gonorrhea or "GC") has developed decreased susceptibility to cephalosporins; this has been observed both in NYC and nationally. GC isolates are now also exhibiting decreased susceptibility to azithromycin, indicating the decreased effectiveness of that drug. Of note, GC isolates in the U.S. have yet to show reduced susceptibility to combined treatment with ceftriaxone (or cefixime) and azithromycin.

During 2013 - 2015, 33 (2.3%) of 1405 GC isolates from men attending NYC Health Department STD clinics exhibited reduced susceptibility to azithromycin ("AZ-RS", defined as minimum inhibitory concentration [MIC] of azithromycin $\geq$ 2 ug/ml). The majority of AZ-RS isolates (76%; 25/33) were from men who have sex with men (MSM). Both the number of such isolates and the azithromycin MIC values have increased each year during this interval. In the first half of 2016, 13 AZ-RS isolates were detected among STD clinic attendees. Some AZ-RS isolates have had high MICs of greater than 256 μg/ml, and AZ-RS have been found among women as well. There have been at least 3 instances of GC treatment failure in NYC among people treated with azithromycin alone.

To preserve the usefulness of current first-line antibiotics, providers should follow guidelines to detect and manage patients with suspected resistant gonorrhea.(1)

1) Treat gonorrhea with the current CDC recommended first-line regimen

Recommended treatment of uncomplicated genital, rectal or pharyngeal gonorrhea (1)
Ceftriaxone 250mg intramuscularly (IM) once PLUS Azithromycin 1g orally once administered together on the same day, preferably simultaneously and directly observed.

Indications for Alternative Regimens for Uncomplicated GC	
Clinical circumstance	Alternative regimen
Intramuscular injection not possible	Cefixime 400mg orally PLUS Azithromycin 1g orally
Azithromycin allergy	Ceftriaxone 250mg IM PLUS Doxycyline 100mg twice daily for 7 days
Cephalosporin or severe/IgE mediated penicillin allergy	Gentamicin 240mg IM PLUS Azithromycin 2g orally OR Gemifloxacin 320mg orally PLUS Azithromycin 2g orally

2) Counsel patients

After treatment, encourage abstinence from all types of sex until symptoms resolve and for one week after treatment. Offer HIV testing, as the presence of an STD is a risk factor for HIV. Advise notification and presumptive treatment of sex partners exposed during the previous 60 days. Patients wishing to notify partners anonymously may want to use an anonymous partner notification website such as www.inspot.org. Reinforce consistent condom use with vaginal, anal, and oral sex. Discuss HIV pre-exposure prophylaxis (PrEP) in HIV-uninfected patients with gonorrhea, particularly MSM and people who inject drugs.

3) Indications for follow-up GC culture and nucleic acid amplification testing (NAAT)

Indications for culture with antimicrobial susceptibility testing and/or NAAT:

- Persistent symptoms 3-5 days after treatment with low risk of reinfection. Post-treatment NAATs should only be performed if ≥ 7 days after treatment completion.
- Pharyngeal GC treated with an alternative regimen. Perform test-of-cure 14 days after treatment.
- GC (at any anatomical site) being treated with monotherapy (culture before treatment)
- Test-of-cure, 7-14 days after treatment for suspected treatment failure (culture preferred)

Clinicians should pre-arrange access to culture with antibiotic susceptibility testing (AST) that includes azithromycin, ceftriaxone, and cefixime. MIC values should be reported in μg/ml. NAAT is more sensitive than culture but cannot provide information on drug susceptibility.

Indications for re-testing after treatment: Irrespective of site infected or regimen given for treatment, men and women with GC should be retested 3 months after treatment.

Indications for general population screening: All sexually active women <25 years, as well as older women with risk factors for infection (new or multiple sex partners, a sex partner with an STD, a sex partner with concurrent partners, unprotected sex, or drug use) should be screened annually. Men who have sex with men should be screened at sites of exposure (pharynx, urethra, and/or rectum) every 3-6 months if risk factors exist. Several laboratories are approved to perform extra-genital NAAT testing for NYC residents (see Resources).

4) Management of treatment failure

Suspect treatment failure if:

- Symptoms persist 3-5 days after appropriate treatment, with no interval sexual exposure
- Test-of-cure GC-positive culture shows decreased susceptibility to the medications administered

Perform culture before re-treatment and re-treat per the table below. Reinfections are more likely than treatment failures. Assure that sex partners are evaluated promptly and treated as indicated. Rule out other conditions with similar presentations such as chlamydia, herpes, and trichomonas.

Clinical circumstances	Treatment regimens
Possible reinfection	Ceftriaxone 250mg IM PLUS Azithromycin 1g orally
Cefixime and Azithromycin were the initial treatment	Ceftriaxone 250mg IM PLUS Azithromycin 2g orally
Reinfection risk low	Gentamicin 240mg IM PLUS Azithromycin 2g orally OR Gemifloxacin 320mg orally PLUS Azithromycin 2g orally
Culture shows decreased AST to relevant antibiotics	Consult Health Department
Allergy precludes regimen	Consult Health Department, local ID specialist, or NYC STD/HIV Prevention Center (www.nycptc.org)

5) Notify the Health Department of suspected (non-reinfection) treatment failures. Contact Julie Schillinger at jschilli@health.nyc.gov or call the Provider Access Line: 866-NYC-DOH1 (866-692-3641).

Sincerely,

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References:
(1) Centers for Disease Control and Prevention. *Sexually Transmitted Disease Treatment Guidelines, 2015*. Gonococcal Infections. MMWR 2015; 60-68.

Resources:
CDC MMWR *Neisseria gonorrhoeae* Antimicrobial Susceptibility Surveillance
https://www.cdc.gov/mmwr/volumes/65/ss/ss6507a1.htm?s_cid=ss6507a1_w
CDC's 2015 STD guidelines for gonococcal infections: https://www.cdc.gov/std/tg2015/gonorrhea.htm
NYC Health Department STD clinic: http://nyc.gov/stdclinics
NY State approved laboratories for anorectal or oropharyngeal GC NAAT testing:
http://www1.nyc.gov/assets/doh/downloads/pdf/std/nys-lab-gc-naat-testing.pdf
For provider training in the diagnosis and management of STDs: http://www.nycptc.org
For assistance with partner notification: http://www.inspot.org/
For tips on preventing antibiotic resistance: http://www.cdc.gov/features/antibioticresistance/