Management of Gonorrhea Treatment Failure

Introduction

The U.S. Centers for Disease Control and Prevention (CDC) has declared drug-resistant gonorrhea an urgent public health threat. Gonorrhea is the second most common reportable sexually transmitted disease (STD) in Texas. It is caused by *Neisseria gonorrhoeae*, a bacterium that has progressively acquired resistance to multiple classes of antibiotics. Currently, the U.S. only has one recommended gonorrhea treatment option remaining – cephalosporins, (i.e., ceftriaxone). Reported cases of cephalosporin resistance have occurred in Europe, Asia, Australia, and Canada. To date, there has not been a confirmed case of gonorrhea in the United States that was not successfully treated because of resistance to the currently recommended treatment. This guidance outlines current CDC gonorrhea treatment guidelines, when to consider possible ceftriaxone treatment failure, and steps for clinicians to follow to ensure appropriate evaluation and management.

CDC Gonorrhea Treatment Guidelines

The CDC recommended treatment for gonorrhea is ceftriaxone 500 mg IM (1 gm if weight 330 lbs. or more). There are alternative treatments that may be used for urogenital/rectal infection, but no reliable alternative treatments are available for pharyngeal gonorrhea. Because gonorrhea is more difficult to eradicate from the pharynx than other sites, a test-of-cure should be done after treatment for pharyngeal infection but is not recommended after treatment of uncomplicated urogenital/rectal infections. If urogenital/rectal symptoms do not resolve after treatment, it is important to remember that reinfections are much more common than true ceftriaxone treatment failures. If reinfection is suspected, the client should be retreated with ceftriaxone.[1] If an alternative treatment was used initially, then the client should be retreated with ceftriaxone (unless allergic).

Identification of Possible Treatment Failure

Ceftriaxone treatment failure is the persistence of laboratory-confirmed *N. gonorrhoeae* infection despite appropriate ceftriaxone treatment when the client has not been re-infected.

Consider possible ceftriaxone treatment failure when:

- Symptoms do not resolve in 3-5 days after appropriate ceftriaxone treatment and no reported sexual contact after treatment, or
- Pharyngeal test-of-cure (in asymptomatic client) is positive after appropriate ceftriaxone treatment and no reported sexual contact after treatment. Any person with pharyngeal gonorrhea should return 7-14 days after initial treatment for a test-of-cure by using either culture or nucleic acid amplification test (NAAT); however testing at 7 days might result in an increased likelihood of false positive tests. NAATs are very sensitive and can detect non-viable *N. gonorrhoeae* genetic material.[2]

Evaluation and Management of Possible Treatment Failure

Follow these steps to ensure adequate evaluation and management of possible ceftriaxone treatment failure when a client was appropriately treated for lab-confirmed *N. gonorrhoeae* infection with ceftriaxone and reinfection is unlikely.

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1. Obtain a detailed sexual history including signs and symptoms of STDs, dates and types of recent gonorrhea testing across exposed anatomic sites (including types of gonorrhea NAATs performed), treatment, possible re-exposure, and recent travel of client and partners.
2. Test for other STDs which can cause persistent symptoms.
3. Order test-of-cure with NAAT and culture for antibiotic sensitivity testing (AST) of relevant clinical sites of exposure/infection prior to retreatment. If the site of possible persistent gonorrhea infection is the penile urethra, also obtain a urethral Gram stain, if available.
4. Await test results prior to retreatment unless the client is symptomatic.
5. Report cases with positive test-of-cure result(s) to the health department within 24 hours.
6. Consult with the STD Clinician Consultation Network at Denver Prevention Training Center (PTC) or CDC Gonorrhea Treatment Failure Team (gcfailure@cdc.gov or 404-718-5447) for guidance on clinical management and retreat as indicated.

- NAATs can produce false positive results due to cross reactivity with commensal *Neisseria* in extragenital sites. Additional testing with a NAAT that detects a different *N. gonorrhoeae* target can help exclude these false positive results.[3]
- Criteria for resistance to cefixime and ceftriaxone have not been defined by the Clinical and Laboratory Standards Institute. However, isolates with cefixime mean inhibitory concentration (MIC) of ≥0.25 ug/ml or ceftriaxone MICs ≥0.125 µg/mL are considered to have decreased susceptibility by the CDC.[4]
- If there is any possibility of reinfection, retreatment with standard therapy of ceftriaxone dosed based on weight is preferred. If reinfection is deemed unlikely, for treatment failure at urogenital sites, dual treatment with single doses of IM gentamicin 240 mg plus oral azithromycin 2 gm can be considered, particularly when isolates are identified as having elevated cephalosporin MICs.[5] For pharyngeal sites initially treated with ceftriaxone 500mg IM once and deemed unlikely to be reinfection, retreatment with ceftriaxone 1g IM once can be considered. Counsel the client to refrain from oral, vaginal, and rectal sex after retreatment and return for another test-of-cure.

7. Counsel the client to refrain from deep kissing, oral, vaginal, and rectal sex after retreatment and return for another test-of-cure (NAAT and culture for AST).
8. Encourage the client to cooperate with health department partner services.
9. Test (NAAT and culture for AST) all partners in the last 60 days at all sites of exposure and empirically treat with the same treatment as the client. If the effective treatment regimen for the index case has not yet been determined, empirically treat the partners with the recommended ceftriaxone regimen. If test results are positive, the partner returns for a test-of-cure (NAAT and culture for AST). Retreatment may be indicated based on test results or new information from the index case in consultation with experts at the CDC or Denver PTC.

TESTING RESOURCES

Laboratories (Gonorrhea Culture for AST)

Lab Corp

Quest Diagnostics

Center for Disease Detection

Texas Department of State Health Services Lab

CDC's AR Lab Network

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DSHS HIV/STD Program

737-255-4300
dshs.texas.gov/hivstd

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Additional Information

Drug-Resistant Gonorrhea - CDC

2021 CDC STI Treatment Guidelines

Sources:

[1] *Source: 2021 CDC STI Treatment Guidelines p.73-75.*

[2] *Sources: 2021 CDC STI Treatment Guidelines p. 75. Bissessor M et al. Clinical Infectious Diseases 2015; (60(4): 557-63. Barbee, et. al., Journal of Clinical Microbiology 2021; 60(6):1-8.*

[3] *Sources: 2021 CDC STI Treatment Guidelines p.71. Meyer et al. Pathogens 2020: 9(8): 647.*

[4] *Source: 2021 CDC STI Treatment Guidelines p.73*

[5] *Source: 2021 CDC STI Treatment Guidelines p.76*

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