

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 infection (STI) 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. 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 infection 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
- test-of-cure is positive (culture or urethral Gram stain at least 72 hours after treatment, or nucleic acid amplification test (NAAT) in the timeframes below) after appropriate ceftriaxone treatment and no reported sexual contact after treatment.

NAATs are very sensitive and can detect non-viable *N. gonorrhoeae* genetic material. Data are limited to guide best timing of pharyngeal test-of-cure in asymptomatic clients to avoid false positive NAAT results.² Based on limited data, the following is recommended for test-of-cure collection (in asymptomatic clients):

- 10-14 days after treatment of pharyngeal gonorrhea for RNA-based NAATs, e.g., Aptima Combo 2®.
- 14-28 days after treatment of pharyngeal gonorrhea for DNA-based NAAT, e.g., cobas®.



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.

1. Obtain a detailed sexual history including signs and symptoms of STIs, recent testing across exposed anatomic sites, dates and types of gonorrhea NAATs performed, treatment, possible re-exposure, and recent travel of client and partners.
2. Test for other STIs which can cause persistent symptoms.
3. Order test-of-cure with culture/antibiotic sensitivity testing (AST) and NAAT of relevant clinical sites of exposure/infection (if not already done) 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 for guidance on clinical management and retreat as indicated.
 - 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 μ g/mL are considered to have decreased susceptibility by the CDC.³
 - 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. 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.
7. Counsel the client to refrain from oral, vaginal, and rectal sex after retreatment and return for another test-of-cure.
8. Encourage the client to cooperate with health department partner services.
9. Test all partners in the last 60 days at all sites of exposure and empirically treat with the same treatment as the client.

Additional Information

- [CDC Antibiotic Resistant Gonorrhea](#)
- [2021 CDC STI Treatment Guidelines](#)

TESTING RESOURCES

Get set up to submit culture/AST and order swabs and transport systems.

Lab Corp

Quest Diagnostics

Center for Disease Detection

Texas Department of State Health
Services Lab
culture/AST starting 2022

Maryland Public Health Lab
InTray® culture device requires
24-hour incubation before
transport to lab

DSHS HIV/STD Program

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

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Sources:

1. [2021 CDC STI Treatment Guidelines p.73-75](#)
2. Wind et al. *Clinical Infectious Diseases* 2016;62(11): 1348-1355. Beymer MR et al. *Sex Transm Dis.* 2014 October; 41(10): 595-600. Bissessor M et al. *Clinical Infectious Diseases* 2015; 60(4): 557-63.
3. [2021 CDC STI Treatment Guidelines p.73](#)
4. [2021 CDC STI Treatment Guidelines p.76](#)



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