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To: Wisconsin Clinicians, Infection Preventionists, Tribal Health Centers, and Local Health Departments, HERC Directors, Coroners/Medical Examiners

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Clinical and Laboratory Guidance for Suspected Treatment Failure Among Patients Treated for Gonorrhea Infection

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Summary

- As of 2021, the CDC (Centers for Disease Control and Prevention) has updated its sexually transmitted infection (STI) treatment guidelines, recommending that only cephalosporins like cefixime or ceftriaxone be used for uncomplicated gonorrhea.
- Historical emergence of antibiotic resistant gonorrhea necessitates more rigorous monitoring of appropriate treatment for patients who test positive for gonorrhea.
- It is recommended that those providing treatment and case management for individuals diagnosed with gonorrhea monitor for instances of suspect treatment failure and perform test of cure for patients with a suspected treatment failure.
- The Wisconsin Department of Health Services (DHS) has partnered with the Milwaukee Health Department Laboratory Center of Excellence to offer gonorrhea culture for Cephalosporin Antibiotic Susceptibility Testing (AST) at no charge for clinicians and local or Tribal health departments throughout Wisconsin.

Background

Treatment for gonorrhea, which is among the most common STIs diagnosed in the United States, has become more complicated following years of decreasing antibiotic susceptibility to many of the antibiotics used to treat the infection. Per changes recommended in 2021 CDC Treatment Guidelines, gonorrhea infections are now to be treated with a single 500 mg dose of intramuscular injectable ceftriaxone (1,000 mg for people who weigh over 300 pounds). Cephalosporins (Cefixime or Ceftriaxone) are the last of effective antibiotics used for treatment of gonorrhea. If there are complications with the gonorrhea infection, please consult the 2021 CDC STI Treatment Guidelines.

Neisseria gonorrhoeae acquire antibiotic resistance more commonly than other bacteria that cause STIs. Therefore, it is especially important to quickly identify patients for whom treatment is unsuccessful. Detection of antibiotic-resistant *N. gonorrhoeae* is necessary to limit further spread and long-term

consequences of untreated gonorrhea. The widespread move away from culture testing, where bacteria samples are grown on a plate and then exposed to varying concentrations of antibiotic to determine its susceptibility, further complicates treatment efforts. Instead, nucleic acid amplification testing (NAAT) is used. Positive NAATs are useful for determining infection but do not routinely determine susceptibility. Culture testing is the only reliable means of AST. Remnant NAATs may be used to support diagnoses of antibiotic-resistant *N. gonorrhoeae* given proper laboratory capacity for detecting gene mutations implicated in resistance.

Given the emergent threat of antibiotic-resistant *N. gonorrhoeae,* clinicians and those providing STI screening services are advised to monitor for cases of suspected treatment failure, an indication of reduced susceptibility to antibiotic treatment. Through funding from the CDC, DHS is now able to offer access to testing services for Cephalosporin AST at no charge for clinicians and local or Tribal health departments throughout Wisconsin. The Milwaukee Health Department Laboratory (MHDL) serves as a Center of Excellence Reference Laboratory, providing management of AST for suspect cases of antibiotic-resistant *N. gonorrhoeae*. The following sections outline recommendations for responding to cases of suspected treatment failure, along with guidance on requesting AST from MHDL.

Clinical guidance for suspected treatment failure

To verify cases of suspected treatment failure, clinicians are recommended to perform test of cure (TOC) by collecting specimens for culture and NAAT at all anatomic sites of patient reported sexual activity for patients with:

- Suspected treatment failure, further defined below.
- Anogenital *N. gonorrhoeae* whose treatment was not aligned with CDC recommended treatment.
- Pharyngeal *N. gonorrhoeae**.
- Known reduced susceptibility to Ceftriaxone or Cefixime.

Suspected treatment failure may present in different ways. Clinicians are advised to monitor for patients who may fall into the following suspected treatment failure categories:

Category I: Patients with persistent symptoms 3–5 days after treatment

Category II: Patients with positive TOC by culture and/or NAAT who report no sexual contact since treatment

Category III: Patients meeting any criteria for suspected treatment failure after initial treatment with an alternative regimen

*Note: The CDC recommends all pharyngeal *N. gonorrhoeae* have a test of cure to ensure clearance due to increased difficulty of adequate antibiotic penetrance at this site.

TOC, where a patient treated for *N. gonorrhoeae* returns to the clinic to ensure the antibiotic regimen has successfully treated the infection, should be performed for any patients with *N. gonorrhoeae* isolates with known reduced susceptibility, patients with suspected treatment failure, patients with anogenital *N. gonorrhoeae* not treated with the recommended CDC regimen or CDC-recommended alternative regimens, and any patient with pharyngeal *N. gonorrhoeae.*

If your patient meets any of the above criteria they should be monitored, and TOC should be implemented greater than 7 days following treatment to avoid false positive results. In case of patients

returning in less than 7 days, clinicians should collect specimens for culture only from each anatomic sites of infection and/or new anatomic sites of sexual activity that occurred following treatment. This patient may be re-treated with the typical regimen if positive. Otherwise, patients returning 8–13 days following treatment should first be interviewed to see if a new behavioral risk for reinfection occurred following treatment.

- If a new behavioral risk for reinfection **did not** occur following treatment, and the site of original infection was anogenital, samples should be collected for NAAT and culture.
- If a new behavioral risk for reinfection **did not** occur following treatment, and the site of original infection was oropharyngeal, the patient should return more than 13 days following treatment. At that point, samples should be collected for NAAT and culture.
- If a new behavioral risk for reinfection **did** occur following treatment, specimens for NAAT and culture testing should be collected from all anatomic sites of infection and/or new anatomic sites of sexual activity following treatment.
    - Those at significant risk for reinfection should be re-treated prior to results.
    - Those with samples exhibiting reduced antibiotic susceptibility or suspected treatment failure should be re-treated if the results of either test are positive.
    - Oropharyngeal NAAT testing should be interpreted with caution prior to 14 days due to the typical prolonged time for clearance at this site after adequate treatment.
    - Patients returning more than 13 days after treatment should have samples collected from all anatomic sites of infection so that NAATs and culture testing may be performed. If either test is positive, the patient should be re-treated.

What to do in case of a suspected treatment failure

Clinicians must report any cases of suspected treatment failure to the clinician's state or local public health department within 24 hours. Consultation for specimen collection for TOC and alternative treatment decisions can be accessed through the DHS STI Unit SURRG Project epidemiology coordinator for emerging antibiotic-resistant *N. gonorrhoeae* at DHSDPHARGC@dhs.wisconsin.gov.

Resources for AST testing services

AST can be accessed at the Milwaukee Health Department Laboratory & Center of Excellence Reference laboratory for antibiotic-resistant *N. gonorrhoeae*, **after** consultation for specimen collection and alternative treatment decisions with the DHS STI Unit SURRG Project Epidemiology Coordinator at DHSDPHARGC@dhs.wisconsin.gov. Eligible testing will be at **no cost** and will **not** be billed back to the requesting laboratory, clinical provider, or patient.

For assistance with acquiring specimen collection, transport materials, and courier services as needed to pick up and drop off specimens, contact MHDL by phone at 414-286-3526 or by e-mail at MHDLab@milwaukee.gov.

For patient eligibility and program questions, contact the DHS Division of Public Health STI Unit: SURRG Project Epidemiology Coordinator for emerging antibiotic resistant gonorrhea (ARGC) at DHSDPHARGC@dhs.wisconsin.gov.

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