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**CLINICAL ALERT**

**January 19, 2023**

**MULTI-DRUG NON-SUSCEPTIBLE GONORRHEA IN MASSACHUSETTS**

* A novel strain of multidrug-non-susceptible *Neisseria gonorrhoeae* with reduced susceptibility to ceftriaxone, cefixime, and azithromycin, and resistance to ciprofloxacin, penicillin, and tetracycline, has been identified in a Massachusetts resident. Although ceftriaxone 500 mg IM was effective at clearing infection for this case, this is the first isolate identified in the United States to demonstrate resistance or reduced susceptibility to all drugs that are recommended for treatment.
* Enhanced surveillance has identified a second isolate that, based on its genome, likely has similarly reduced susceptibility to ceftriaxone and cefixime.
* Identification of this strain, the same as what was recently reported in the United Kingdom[[1]](#endnote-2) and previously reported as circulating in Asia-Pacific countries, is a warning that *N. gonorrhoeae* is becoming less responsive to a limited arsenal of antibiotics.

**MDPH recommends that clinicians take the following action:**

* Ensure compliance with recommended treatment of ceftriaxone 500 mg IM as a single dose for persons weighing <150 kg, (1 gram IM for persons weighing ≥150 kg), per 2020-21 CDC guidelines.[[2]](#endnote-3)

* Perform gonococcal culture from genital and extragenital sites for symptomatic patients, in addition to routine nucleic acid amplification testing (NAAT). Clinicians should consult with local clinical microbiology laboratories to determine how best to optimize gonococcal culture, for example by using non-nutritive swab transport systems (e.g., Amies agar gel).
* Obtain risk history, including travel history, for all gonorrhea-positive cases, and perform test of cure using NAAT or culture, 14 days after initial treatment, at all previously positive mucosal sites. Test of cure following treatment is already recommended for all patients with known or suspected pharyngeal infection.2
* Perform test of reinfection with NAAT 3 months after treatment for patients previously treated for gonorrhea. Scheduling the follow-up visit for test of reinfection at the time of treatment is encouraged. If retesting at 3 months is not possible, clinicians should retest whenever persons next seek medical care <12 months after initial treatment.

**Background**

The case presented to primary care with urethritis, without known exposure to gonococcal infection or initial disclosure of risk factors. Acquisition likely occurred within Massachusetts, as history of recent travel was not reported, however, recent travel by sex partners could not be ruled out. The patient was successfully treated with ceftriaxone 500 mg IM, the currently recommended treatment for gonorrhea, with documented subsequent negative testing at urethral, pharyngeal, and rectal sites. The isolate displayed reduced *in vitro* susceptibility to cephalosporins (ceftriaxone, cefixime, cefoxitin) and azithromycin; and resistance to ciprofloxacin, penicillin and tetracycline, via E-test and agar dilution methods. The isolate is of a multilocus sequence type, MLST 8123, which was originally identified in the Asia-Pacific region. Sequencing has confirmed the presence of a mosaic penA60 allele conferring reduced ceftriaxone susceptibility. Eight cases of the same sequence type, also with reduced ceftriaxone susceptibility, have been identified in the United Kingdom between December 2021 and June 2022. All individuals in the U.K. were successfully treated with ceftriaxone. However, emergence of this strain indicates *N. gonorrhoeae*’s continued evolution and ability to develop resistance to antimicrobial treatment.

Gonorrhea is the second-most-reported sexually transmitted infection (STI) in the United States. In Massachusetts, laboratory-confirmed cases more than quadrupled since a nadir of 1,976 in 2009, to 8,133 in 2021. With rising case numbers, proportional increases have been observed in reports of uncomplicated disease ranging from asymptomatic carriage to urethritis, cervicitis, pharyngitis, and proctitis; reports of complicated locally invasive disease such as penile abscess, pharyngeal abscess, epididymitis, pelvic inflammatory disease, and gonococcal conjunctivitis including ophthalmia neonatorum; and disseminated gonococcal infection including endocarditis and meningitis.

**Diagnosis**

The CDC and U.S. Preventive Services Task Force recommend routine gonorrhea screening for sexually active women ≤24 years and women 25 years or older who are at increased risk.2,[[3]](#endnote-4) CDC further recommends screening sexually active men who have sex with men, at least annually but up to every 3 months if at increased risk. Screening recommendations should be adapted based on anatomy and reported sites of sexual exposure.

NAAT and/or culture are available for detecting urogenital (urine, urethral, vaginal, cervical) and extragenital (rectal, oropharyngeal, conjunctival) infection with *N. gonorrhoeae*. NAAT sensitivity and specificity for detecting *N. gonorrhoeae* from urogenital and extragenital anatomic sites are superior to culture but vary by NAAT type. However, NAAT is not approved for sequencing or antimicrobial susceptibility testing for clinical purposes. Because *N. gonorrhoeae* has demanding laboratory growth requirements, optimal culture recovery rates are achieved when swab specimens are inoculated directly and when growth medium is promptly incubated in a carbon dioxide (CO2)-enriched environment. Non-nutritive swab transport systems (e.g., Amies agar gel) that may maintain gonococcal viability for <24 hours in ambient temperatures, are available for sample transport to clinical microbiology laboratories. Please consult with your clinical microbiology laboratory to determine how best to optimize gonococcal culture.

**Treatment**

In the United States, the regimens listed below are recommended for treatment of gonococcal infection. For alternative regimens and recommendations for treatment of additional clinical syndromes associated with gonococcal infection (e.g., pelvic inflammatory disease, epididymitis, and proctitis), please refer to CDC STI Guidelines.2 For recommendations for treatment of gonococcal infections among neonates, infants and children, please refer to CDC STI Guidelines, and the American Academy of Pediatrics Red Book[[4]](#endnote-5).

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| Recommended Regimen for Uncomplicated Gonococcal Infection of the Cervix, Urethra, Pharynx, or Rectum Among Adults and Adolescents\* |
| **Ceftriaxone** 500 mg\*\* IM in a single dose for persons weighing <150 kg |
| Recommended Regimen for Gonococcal Conjunctivitis Among Adolescents and Adults |
| **Ceftriaxone** 1 g IM in a single dose  Providers should consider one-time lavage of the infected eye with saline solution |
| Recommended Regimen for Gonococcal-Related Arthritis and Arthritis-Dermatitis Syndrome |
| **Ceftriaxone** 1 g IM or IV every 24 hours\*\*\* |
| Recommended Regimen for Gonococcal Meningitis and Endocarditis |
| **Ceftriaxone** 1–2 g IV every 12-24 hours |

\*If chlamydia infection has not been excluded, clinicians should treat for chlamydia with doxycycline 100 mg PO bid for 7 days.

\*\*For persons weighing ≥150 kg, 1 g ceftriaxone should be administered.

\*\*\*When treating for arthritis-dermatitis syndrome, switch to an oral agent can be guided by antimicrobial susceptibility testing 24–48 hours after substantial clinical improvement, for a total treatment course of at least 7 days.

**Patient Counseling and Information for Partners**

Recent sex partners (i.e., persons having sexual exposure to an infected patient <60 days preceding onset of symptoms or gonorrhea diagnosis) should be referred for evaluation and testing at all exposed mucosal sites, and presumptive treatment if symptomatic. If the patient’s last potential sexual exposure was >60 days before onset of symptoms or diagnosis, the most recent sex partner should be tested and treated if symptomatic. To avoid reinfection, sex partners should be instructed to abstain from sexual intercourse for 7 days after they and their sex partners have completed treatment and after resolution of symptoms.

**Reporting**

Health care providers, laboratories, and others as required by regulation, must report all gonorrhea cases to the MDPH within 24 hours. Laboratories must send *N. gonorrhoeae* isolates to the State Public Health Laboratory for further examination.[[5]](#endnote-6)

MDPH Case Report Forms are required for all gonorrhea cases and provide details on clinical characteristics and treatment. These details are not automatically reported, unless your clinical organization participates in **E**lectronic Medical Record **S**upport for **P**ublic Health (ESP) for gonorrhea case reporting. Health care providers should report gonorrhea information via the following form: <https://madss.casetivity.com/process-definition/gonorrhea-brf/start-form>.

**Please continue to contact the MDPH Division of STD Prevention and HIV Surveillance for:**

* **Clinical consultation on complex cases**, available through the MDPH Division of STD Prevention clinical team (Public Health Nurse, Kaitlin Nichols, RN and Medical Director, Katherine Hsu, MD, MPH) or the STD Clinical Consultation Network.[[6]](#endnote-7) CDC treatment and partner management guidelines are available as an app for Apple and Android devices at: <https://www.cdc.gov/std/treatment-guidelines/provider-resources.htm#MobileApp>.
* **Partner services** – contact tracing and notification are automatically performed for new HIV infection, infectious syphilis cases, and cases of ceftriaxone-non-susceptible gonorrhea. For more information, please call the MDPH Reporting and Partner Services Line at 617-983-6999 or review resources at <https://www.mass.gov/service-details/partner-services-program-information-for-healthcare-providers>.

1. Day M, Pitt R, Mody N, *et al.* Detection of 10 cases of ceftriaxone-resistant *Neisseria gonorrhoeae i*n the United Kingdom, December 2021 to June 2022. *Euro Surveill*. 2022 Nov;27(46):2200803. <https://doi.org/10.2807/1560-7917.ES.2022.27.46.2200803> [↑](#endnote-ref-2)
2. CDC STI Treatment Guidelines, 2021. <https://www.cdc.gov/std/treatment-guidelines/toc.htm> [↑](#endnote-ref-3)
3. USPSTF Final Recommendation Statement: Chlamydia and Gonorrhea: Screening. <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/chlamydia-and-gonorrhea-screening> [↑](#endnote-ref-4)
4. Gonococcal Infections. In: Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH, eds. *Red Book: 2021 Report of the Committee on Infectious Diseases.* Itasca. IL: American Academy of Pediatrics: 2021, pages 338 – 44. [↑](#endnote-ref-5)
5. Massachusetts: 105 CMR 300.00: Reportable diseases, surveillance, and isolation and quarantine requirements <https://www.mass.gov/regulations/105-CMR-30000-reportable-diseases-surveillance-and-isolation-and-quarantine-requirements> [↑](#endnote-ref-6)
6. National Network of STD Clinical Prevention Training Centers: STD Clinical Consultation Network. [www.stdccn.org](http://www.stdccn.org) [↑](#endnote-ref-7)