Subject Line: AMR Gonorrhea: Two Cases of Concern Identified

Preheader Text: Following CDC's STI Tx Guidelines remains essential

January 19, 2023

Dear Colleagues,

We are writing to inform you of two gonococcal infections with concerning lab results identified in Massachusetts (see clinical alert). The first case had a cultured isolate which showed decreased susceptibility to ceftriaxone, cefixime and azithromycin, as well as resistance to ciprofloxacin, tetracycline, and penicillin. Molecular testing confirmed that the reduced susceptibility to ceftriaxone was caused by a mutation in the *penA60* allele and a second case was found to have the *penA60* allele through molecular surveillance. Although both cases were successfully clinically and microbiologically cured following treatment with ceftriaxone, these findings are concerning.

Background

A patient presented to a primary care clinic with symptoms of urethritis. *N. gonorrhoeae* was isolated from a clinical specimen. The Massachusetts State Laboratory identified a concerning susceptibility pattern through culture testing and sent isolates to CDC for further testing (see box).

Box 1: Minimum Inhibitory Concentrations (MIC) by Agar Dilution of the Massachusetts Gonococcal Isolate of Concern

Drug	MIC	Susceptible	Intermediate Resistance
Ceftriaxone	1.0 µg/mL	≤ 0.25 µg/mL	UD^
Cefixime	> 1.0 µg/mL	≤ 0.25 µg/mL	UD^
Azithromycin	2.0 µg/mL	≤ 1.0 µg/mL	UD^
Ciprofloxacin	16.0 µg/mL	≤ 0.06 µg/mL	0.12–0.5 µg/mL
Tetracycline	2.0 µg/mL	≤ 0.25 µg/mL	0.5–1.0 µg/mL
Gentamicin	8 µg/mL	UD^	UD^
Penicillin	32.0 µg/mL	≤ 0.06 µg/mL	0.12–1.0 µg/mL

^UD: undefined

Follow-up testing performed by the Centers for Disease Control and Prevention's Sexually Transmitted Disease (STD) Laboratory identified the *penA60* allele, previously associated with ceftriaxone non-susceptible cases, as well as an additional case with the *penA60* allele as part of molecular surveillance.

This is the first case of documented resistance to 6 of the 7 drugs tested on the standard GISP (Gonococcal Isolate Surveillance Project) panel, and these are the second and third identified gonococcal cases in the US with the *penA60* allele. The first *penA60* allele was identified in Las Vegas, Nevada in December 2019. The United Kingdom (UK) also recently published a case series of ten ceftriaxone-resistant cases, nine carrying the *penA60* allele. All isolates were identified in the first six months of 2022 and most reported travel to Asia. All were cured with UK's recommended gonorrhea treatment – a single injection of ceftriaxone 1g intramuscularly. In the United States, the **recommended regimen is a single injection of ceftriaxone 500 mg intramuscularly.** CDC also recommends routine test of cure for all known pharyngeal infections.

What to do if treatment failure is suspected

There are specific actions you can take if there is suspicion of a gonococcal treatment failure in any patient at any anatomic site:

- Conduct a thorough sexual history to evaluate for possible reinfection.

- If reinfection has been ruled out, repeat NAAT testing at all exposed anatomic sites, along with collection of specimens for gonococcal culture and antimicrobial susceptibility testing (AST). Clinics that do not have access to culture and AST can reach out to two regional laboratories.
- Treating clinicians should consult a STD Clinical Prevention Training Center clinical expert or CDC for advice on obtaining cultures, antimicrobial susceptibility testing, and treatment.
- **Presumptive treatment failures, where re-infection has been ruled out, should be reported to CDC through the local or state health department within 24 hours of diagnosis.**

This case is a reminder that antimicrobial-resistant gonorrhea remains an urgent public health threat nationally and internationally; all providers in all clinical settings need to remain vigilant. Timely identification and treatment, as well as rapid public health response, are essential to keeping patients safe and reducing the risk of community transmission. We must all remain alert for potential gonococcal treatment failures as we combat the growing threat of antimicrobial resistance in the US.

Thank you for your ongoing commitment to STI prevention.

Regards,

Laura Hinkle Bachmann, MD, MPH, FIDSA, FACP
Chief Medical Officer
Division of STD Prevention
National Center for HIV, Viral Hepatitis, STD and TB Prevention
Centers for Disease Control and Prevention