March 2, 2020

Dear Colleagues,

As a sentinel surveillance project, the Gonococcal Isolate Surveillance Project (GISP) has documented rising antimicrobial resistant gonorrhea (ARGC) trends in different antibiotics over the years: ciprofloxacin resistance in the early 2000s, cases of high-level azithromycin "resistance" (minimum inhibitory concentration, MIC $\geq$ 256 µg/mL) and the overall rising prevalence of reduced azithromycin susceptibility since 2013. Now, we would like to inform you of the first GISP *Neisseria gonorrhoeae* isolate with a confirmed ceftriaxone MIC of 1.0 µg/mL. This isolate, identified in Las Vegas, has the highest ceftriaxone MIC identified in GISP to date.

In November 2019, the Texas Department of State Health Services Laboratory, as part of the Antibiotic Resistance Laboratory Network (AR Lab Network), notified CDC of a GISP isolate with a concerning susceptibility pattern. The male urethral isolate was determined to have a reduced susceptible ceftriaxone MIC of 1.0 µg/mL (susceptible is $\leq$ 0.25 µg/mL), a reduced susceptible cefixime MIC of 2.0 µg/mL (susceptible is $\leq$ 0.25 µg/mL), and a susceptible azithromycin MIC of 0.25 µg/mL (susceptible is $\leq$ 1.0 µg/mL) by agar dilution. Additional testing of the isolate and whole genome sequencing was done at CDC. The results confirmed the initial MIC test results from the Texas Laboratory and identified genetic mutations (i.e., *pen*A60 allele) consistent with the ceftriaxone reduced susceptibility results.

The isolate was collected from a male patient seen at the Southern Nevada Health District who reported 3 recent female sexual partners. The patient presented to the GISP participating STD clinic with urethritis symptoms and was treated on the same day with ceftriaxone 250 mg intramuscularly (IM) and azithromycin 1 g orally (PO). The patient responded to treatment with resolution of his symptoms. Repeat testing with nucleic acid amplification tests (NAATs) and culture at three anatomic sites were performed at the clinic and all follow up test results returned negative for gonorrhea. Upon identification of the isolate, CDC worked with the Southern Nevada Health District and the Nevada Department of Health and Human Services to investigate the partners of the index patient and identified possible links to China. All partners were unable to be evaluated, so limited additional NAATs or cultures directly related to the index patient were available for testing. The Southern Nevada Public Health Laboratory provided 257 specimens representing all remnant positive NAATs from September 2019 to November 2019 for additional testing to detect the *pen*A60 allele. Among the 257 NAAT samples tested, no additional specimens containing the *pen*A60 allele were detected. In addition, to date, CDC is not aware of any additional isolates with this susceptibility pattern through our gonorrhea antimicrobial susceptibility testing (AST) projects: GISP, enhanced GISP (eGISP) and Strengthening the US Response to Resistant Gonorrhea (SURRG). These projects, in partnership with the AR Lab Network, have conducted AST by agar dilution for over 9600 gonococcal isolates in 2018 and over 7600 isolates for the first 3 quarters of 2019.

Information of this concerning isolate with reduced ceftriaxone susceptibility but susceptibility to azithromycin which responded with current CDC recommended treatment is for your awareness only. It should be noted that gonococcal isolates with this *pen*A60 allele leading to ceftriaxone reduced susceptibility have already been reported outside the United States, including in Australia, Canada, Japan, United Kingdom, some of which have

been associated with treatment failures. At this time, we recommend the continued use of the **recommended regimen for gonococcal infections: ceftriaxone 250 mg IM x 1 dose and azithromycin 1 g PO x 1 dose**.

This is a reminder that the threat of ARGC remains urgent. In the case of a suspected treatment failure at any anatomic site, NAAT testing at all exposed anatomic sites should be conducted, along with collection of specimens for gonococcal culture and antibiotic susceptibility testing. Treating clinicians should consult an STD/HIV Prevention Training Center clinical expert (https://www.stdccn.org) or CDC GISP (by email: oew3@cdc.gov or telephone: 404-718-5447) 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.

As a community, all our efforts are needed to identify and manage antibiotic resistant gonorrhea in the US. We look forward to continuing our work together as we address this ongoing challenge.

Regards,

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