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CDC HEALTH UPDATE

Update – CDC Recommendations for Managing and Reporting *Shigella* Infections with Possible Reduced Susceptibility to Ciprofloxacin

*****Missouri healthcare providers and public health practitioners: Please contact your local public health agency or the Missouri Department of Health and Senior Services (DHSS) Bureau of Communicable Disease Control and Prevention at 573-751-6113 or 800-392-0272 (24/7) with questions regarding this Advisory.*****

Distributed via the CDC Health Alert Network

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Summary

This Health Alert Network (HAN) Update provides current recommendations on management and reporting of *Shigella* infections that have been treated with ciprofloxacin or azithromycin and resulted in possible clinical treatment failure. This is a follow-up to HAN 401: CDC Recommendations for Diagnosing and Managing *Shigella* Strains with Possible Reduced Susceptibility to Ciprofloxacin.

The Centers for Disease Control and Prevention (CDC) continues to identify an increasing number of *Shigella* isolates that test within the susceptible range for the fluoroquinolone antibiotic ciprofloxacin (minimum inhibitory concentration [MIC] values of 0.12-1 µg/mL), but harbor one or more resistance mechanisms. CDC remains concerned about potential clinical failures with fluoroquinolone treatment.

Clinicians should carefully monitor patients with *Shigella* infections who require fluoroquinolone treatment and report any possible treatment failures. If treatment failure is suspected, clinicians should submit a stool specimen for antimicrobial susceptibility testing, and consider consulting an infectious disease specialist to identify best treatment options.

CDC has also identified an increasing number of *Shigella* isolates with azithromycin MICs that exceed the epidemiological cutoff value (ECV), and is requesting reports of any possible treatment failures occurring among patients with *Shigella* infections treated with azithromycin (see below).

Shigellosis is a nationally notifiable condition; all cases should be reported to local health departments.

Recommendations for Clinicians

1. If antibiotic treatment is necessary, monitor patients carefully.
2. If you identify or receive a report of a patient with *Shigella* infection and possible fluoroquinolone or azithromycin treatment failure:

    - Consider consulting an infectious disease specialist to identify other treatment options, because some *Shigella* isolates with susceptible ciprofloxacin MICs may harbor one or more quinolone resistance mechanisms.
    - Contact your local health department to coordinate reporting treatment failure information. This information should be reported to CDC at EntericBacteria@cdc.gov.
    - Collect a stool specimen for culture, and work with your clinical microbiology laboratory to submit for additional antimicrobial susceptibility testing.
    - Request that your laboratory expedite submission of the *Shigella* isolate to your state public health laboratory. Your state laboratory should notify CDC at EntericBacteria@cdc.gov to coordinate additional laboratory testing and/or shipment of the isolate to CDC.

Background

In April 2017, CDC identified an increase in the percentage of *Shigella* isolates in the United States with MIC values of 0.12–1 µg/mL for the fluoroquinolone antibiotic ciprofloxacin; this percentage continues to rise. Preliminary surveillance data from 2016 show that 8.2% of *Shigella* isolates tested by the National Antimicrobial Resistance Monitoring System laboratory (https://www.cdc.gov/narms) had a ciprofloxacin MIC in the 0.12–1 µg/mL range, and 9.5% had an azithromycin MIC greater than the ECV (i.e., non-wild-type; reduced susceptibility). Testing of 2017 surveillance isolates is ongoing. Among those tested, 16.5% have a ciprofloxacin MIC in the 0.12–1 µg/mL range, and 22.1% have reduced susceptibility to azithromycin. Molecular data indicate that most *Shigella* isolates with ciprofloxacin MICs in the noted range harbor at least one quinolone resistance mechanism. *Shigella* isolates without a quinolone resistance mechanism typically have a ciprofloxacin MIC of ≤0.015 µg/mL. Clinical and Laboratory Standards Institute (CLSI) criteria categorize *Shigella* isolates with a ciprofloxacin MIC of ≤1 µg/mL as susceptible to ciprofloxacin. Currently, clinical laboratories have limited ability to differentiate the ciprofloxacin MIC values within the reduced susceptibility range, ≤1 µg/mL. Additionally, CLSI does not have established azithromycin clinical breakpoints for *Shigella* isolates, only ECVs, which do not predict clinical outcome (2).

CDC is particularly concerned about people who are at high risk for multidrug-resistant *Shigella* infections and are more likely to require antibiotic treatment, such as men who have sex with men, patients who are homeless, and immunocompromised patients. These patients often have more severe disease, prolonged shedding, and recurrent infections.

In response to data and concerns presented by CDC, CLSI formed an *ad hoc* working group in June 2017 to assess any available and relevant clinical, pharmacologic, and microbiologic data. The workgroup found that no data are available on the high-risk populations of concern. CDC has not received any reports of clinical treatment failures in patients with *Shigella* infections. Therefore, it is unclear whether fluoroquinolone treatment of a *Shigella* infection with a ciprofloxacin MIC of 0.12–1 µg/mL is associated with a worse clinical outcome or whether such treatment increases the risk of transmission. At this time, CLSI ciprofloxacin MIC breakpoints for the *Enterobacteriaceae* family (excluding *Salmonella*) will continue to apply to *Shigella* isolates.

CDC is working with CLSI and other partners to collect isolates and clinical information from people with *Shigella* infection and possible clinical treatment failure occurring after treatment with a fluoroquinolone or azithromycin. If treatment failure is suspected, clinicians should consider consulting an infectious disease specialist to identify best treatment options, and submit a stool specimen for antimicrobial susceptibility testing. Clinicians should monitor patients carefully and report cases of possible clinical treatment failure to CDC.

For More Information

1. For general information about *Shigella* or shigellosis, visit https://www.cdc.gov/shigella/index.html.
2. For general information about *Shigella* or shigellosis in Spanish, visit https://www.cdc.gov/shigella/esp/index.html
3. For technical information about *Shigella* or shigellosis, including information about national surveillance and other educational resources for medical and public health professionals, visit https://www.cdc.gov/shigella/resources.html.
4. For information about prevention and control of shigellosis, including recommendations for men who have sex with men, visit https://www.cdc.gov/shigella/audience-sexually-active.html.
5. For more information about the serious public health threat posed by antimicrobial-resistant *Shigella*, refer to “Antibiotic Resistance Threats in the United States, 2013” available at https://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf.
6. For specific inquiries related to this HAN Update, email EntericBacteria@cdc.gov.

References

1. HAN 401: CDC Recommendations for Diagnosing and Managing Shigella Strains with Possible Reduced Susceptibility to Ciprofloxacin
2. *Performance Standards for Antimicrobial Susceptibility Testing*. 28th ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.

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issues; and promotes healthy living through strong partnerships with local, national and international organizations.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

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This message was distributed to state and local health officers, state and local epidemiologists, state and local laboratory directors, public information officers, HAN coordinators, and clinician organizations.

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