

This is an official
CDC Health Update

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

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:
 - o 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-wildtype; 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.

Resources for Additional 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 <https://emergency.cdc.gov/han/han00401.asp>
2. CLSI. Performance Standards for Antimicrobial Susceptibility Testing. 28th ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2018. <https://clsi.org/standards/products/microbiology/documents/m100/>

The Centers for Disease Control and Prevention (CDC) protects people's health and safety by preventing and controlling diseases and injuries; enhances health decisions by providing credible information on critical health issues; and promotes healthy living through strong partnerships with local, national, and international organizations.

DHEC contact information for reportable diseases and reporting requirements

Reporting of *Shigella* is consistent with South Carolina Law requiring the reporting of diseases and conditions to your state or local public health department. (State Law # 44-29-10 and Regulation # 61-20) as per the DHEC 2018 List of Reportable Conditions available at:

<http://www.scdhec.gov/Library/CR-009025.pdf>

Federal HIPAA legislation allows disclosure of protected health information, without consent of the individual, to public health authorities to collect and receive such information for the purpose of preventing or controlling disease. (HIPAA 45 CFR §164.512).

Regional Public Health Offices – 2018			
Mail or call reports to the Epidemiology Office in each Public Health Region			
MAIL TO:			
Lowcountry 4050 Bridge View Drive, Suite 600 N. Charleston, SC 29405 Fax: (843) 953-0051	Midlands 2000 Hampton Street Columbia, SC 29204 Fax: (803) 576-2993	Pee Dee 145 E. Cheves Street Florence, SC 29506 Fax: (843) 661-4859	Upstate 200 University Ridge Greenville, SC 29602 Fax: (864) 282-4373
CALL TO:			
Lowcountry Berkeley, Charleston, Dorchester Phone: (843) 953-0043 Nights/Weekends: (843) 441-1091 Beaufort, Colleton, Hampton, Jasper Phone: (843) 549-1516 ext. 218 Nights/Weekends: (843) 441-1091 Allendale, Bamberg, Calhoun, Orangeburg Phone: (803) 268-5833 Nights/Weekends: (843) 441-1091	Midlands Kershaw, Lexington, Newberry, Richland Phone: (803) 576-2749 Nights/Weekends: (888) 801-1046 Chester, Fairfield, Lancaster, York Phone: (803) 286-9948 Nights/Weekends: (888) 801-1046 Aiken, Barnwell, Edgefield, Saluda Phone: (803) 642-1618 Nights/Weekends: (888) 801-1046	Pee Dee Chesterfield, Darlington, Dillon, Florence, Marlboro, Marion Phone: (843) 661-4830 Nights/Weekends: (843) 915-8845 Clarendon, Lee, Sumter Phone: (803) 773-5511 Nights/Weekends: (843) 915-8845 Georgetown, Horry, Williamsburg Phone: (843) 915-8804 Nights/Weekends: (843) 915-8845	Upstate Anderson, Oconee Phone: (864) 260-5581 Nights/Weekends: (866) 298-4442 Abbeville, Greenwood, McCormick Phone: (864) 260-5581 Nights/Weekends: (866) 298-4442 Cherokee, Greenville, Laurens Pickens, Spartanburg, Union Phone: (864) 372-3133 Nights/Weekends: (866) 298-4442
For information on reportable conditions, see http://www.scdhec.gov/Health/FHPF/ReportDiseasesAdverseEvents/ReportableConditionsInSC/		DHEC Bureau of Disease Control Division of Acute Disease Epidemiology 2100 Bull St • Columbia, SC 29201 Phone: (803) 898-0861 • Fax: (803) 898-0897 Nights / Weekends: 1-888-847-0902	

Categories of Health Alert messages:

Health Alert	Conveys the highest level of importance; warrants immediate action or attention.
Health Advisory	Provides important information for a specific incident or situation; may not require immediate action.
Health Update	Provides updated information regarding an incident or situation; unlikely to require immediate action.
Info Service	Provides general information that is not necessarily considered to be of an emergent nature.