CAHAN San Diego
California HEALTH ALERT NETWORK

To: CAHAN San Diego Participants
Date: June 26, 2018
From: Epidemiology Program

**Shigellosis: Updated National Recommendations and Local Case Information**

This health advisory updates local healthcare providers about recent recommendations from the Centers for Disease Control and Prevention (CDC) on the management and reporting of shigellosis and summarizes reported case information in San Diego County. Resources on shigellosis are provided.

**Key messages:**

- CDC is warning about potential clinical failures with ciprofloxacin or azithromycin treatment for shigellosis.
- Most shigellosis cases are self-limited and do not require antibiotic treatment.
- When treatment is needed for shigellosis, it should be guided by culture with antibiotic susceptibility testing (AST).
- Men who have sex with men (MSM), persons experiencing homelessness (PEH), and immunocompromised individuals are at increased risk for shigellosis, especially for illness caused by multidrug-resistant *Shigella.* These individuals are more likely to require antibiotic treatment due to increased severity of disease.
- PEH with shigellosis should not be released from medical care without shelter and access to an unshared restroom.
- All shigellosis, including any suspected drug-resistant or antibiotic failure cases, should be reported within one working day to the County Epidemiology Program.

**Situation**

On June 7, 2018, CDC issued the attached health update entitled, "Recommendations for Managing and Reporting *Shigella* Infections with Possible Reduced Susceptibility to Ciprofloxacin." The advisory provides current recommendations on the management and reporting of shigellosis cases that have been treated with ciprofloxacin or azithromycin and resulted in possible clinical treatment failure. This is an update to the April 2017 CDC health advisory on shigellosis with possible drug resistance.

MSM, PEH, and people who are immune compromised are at higher risk than the general population for shigellosis. These groups are more likely to get infected with *Shigella* that is resistant to commonly used antibiotics, especially trimethoprim/sulfamethoxazole and azithromycin. They are also more likely to require antibiotic treatment due to illness severity. Culture with AST should be a routine part of the evaluation of all individuals with possible shigellosis.

The figure on page three shows reported shigellosis cases in San Diego County from 1993 to date. Reported cases in 2017 were the highest in 20 years. The table on page three summarizes all *Shigella* species cases reported in San Diego County residents from 2016 to date in 2018. Reported cases of shigellosis increased by 38% from 2016 to 2017. Self-identified MSM comprised 16% of cases in 2016, 15% in 2017, and 25% in 2018 year-to-date. PEH accounted for 7% of cases in 2016, 12% in 2017, and 7% in 2018 year-to-date.

**Background**

CDC estimates that 500,000 cases of shigellosis occur each year in the United States, but less than one in 20 is diagnosed and reported. Shigellosis typically causes watery or bloody diarrhea, abdominal pain, tenesmus, fever, and malaise. Bloody diarrhea is more common with *S. flexneri* than other species of *Shigella*. Stools tend to be of small volume, and severe dehydration is rare.

Shigellosis is highly contagious (as few as 10 to 100 organisms can cause infection), and transmission occurs via contaminated food and water or direct person-to-person spread. *Shigella* species are present in the stool of infected persons while they have diarrhea and for up to a few weeks after diarrhea has resolved. Shigellosis is usually self-limited in immunocompetent hosts, although complications may occur, such as post-infectious arthritis, bloodstream infections, seizures, and hemolytic-uremic syndrome. Treatment with antibiotics is common: 75% of cases reported in San Diego County, since 2012, have received antibiotics.

**Recommendations for Providers and Hospitals**

1. **Obtain a sexual history in patients who present with apparent infectious diarrhea and offer HIV testing to sexually active individuals who are not aware of their HIV status.**

2. **Consider shigellosis during the work-up of patients who present with diarrhea or bloody diarrhea, especially MSM, PEH, and people who are immune compromised.**
   - Obtain a stool culture with antimicrobial susceptibility testing (AST) and request ciprofloxacin AST that includes dilutions of 0.12 µg/mL or lower.
   - If a polymerase chain reaction (PCR) test is ordered, order the culture and AST also. PCR does not replace culture, because an isolate is needed for AST and serotyping. If a PCR test is positive for *Shigella*, laboratories **must** attempt to obtain a bacterial culture isolate for submission to the San Diego Public Health Laboratory (SDPHL) per California Code of Regulations Title 17, Section 2505, subsection (m)(3). SDPHL does not perform AST.

3. **Await AST results when possible before treating shigellosis.**
   - Antimicrobial treatment may be warranted based on severe or prolonged illness, hospitalization, and underlying risk factors such as immune-compromising conditions including HIV/AIDS or treatment with immunosuppressive drugs. Clinicians should use AST results to guide therapy and consider consultation with an infectious disease specialist.
   - If the ciprofloxacin MICs are in the 0.12–1.0 µg/mL range, avoid prescribing fluoroquinolones.
   - Obtain follow-up stool cultures and AST in shigellosis patients who have continued or worsening symptoms despite antibiotic therapy.

4. **Advise MSM to avoid sex for at least two weeks after recovery from illness.**
   - When having sex again, MSM should refrain from oral-anal contact or use barriers, such as condoms or dental dams. Washing genitals, anus, sex toys, and hands before and after sexual activity may reduce risk.

5. **Report shigellosis within one working day to the Epidemiology Program.**
   - Healthcare providers should report clinically suspect cases and not wait for culture results.
   - Laboratories should report within one working day any positive stool or blood cultures, or PCR tests for *Shigella* species. Forward culture isolates to SDPHL. AST results should be reported when available.
   - **PEH with shigellosis should not be released from medical care without shelter and access to an unshared restroom,** which in some cases may be arranged through the Epidemiology Program.
   - The Epidemiology Program can be contacted by calling 619-692-8499 during normal business hours (Monday-Friday 8 AM-5 PM), or 858-565-5255 after hours, during weekends, and on County-observed holidays. A confidential morbidity report may also be faxed to 858-715-6458.

**Resources**

- Detailed information for clinicians on shigellosis, including shigellosis among MSM, may be found at the CDC and CDPH shigellosis websites.
- The Los Angeles County Public Health Department has developed information handouts and palm cards with shigellosis prevention messages in English and Spanish tailored to MSM, available here.
- For general guidelines on the management of shigellosis, see the Infectious Diseases Society of America Practice Guidelines for the Management of Infectious Diarrhea.
- For information about the management of shigellosis in HIV-infected persons, see the Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents.

Thank you for your continued participation.

**CAHAN San Diego**
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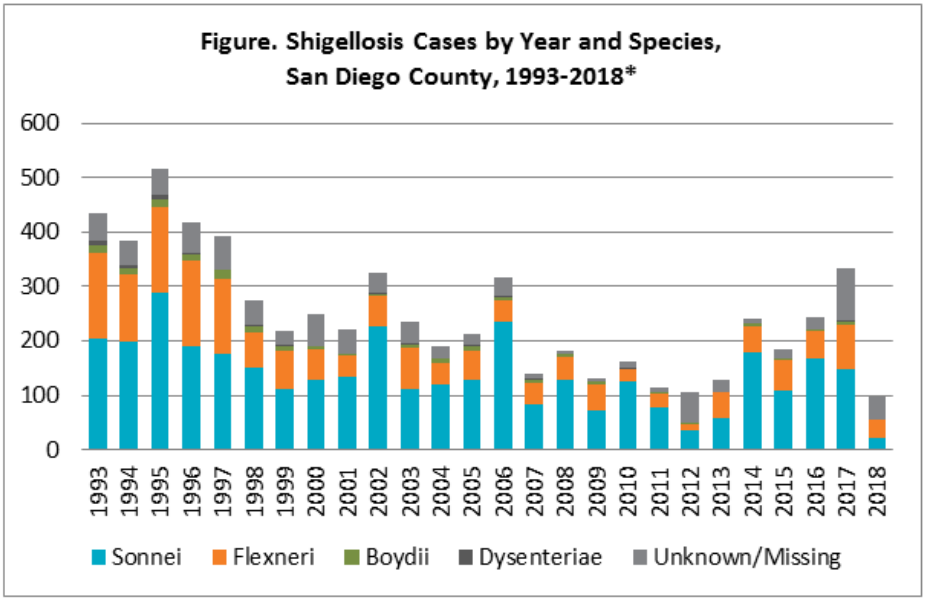


*2018 data are year to date; current as of 6/13/2018. Data are provisional and subject to change as additional information becomes available. Grouped by CDC disease years.

**Table. *Shigella* case reports by species, gender, men who have sex with men (MSM) and persons experiencing homelessness (PEH), San Diego County, 2016-2018 (year-to-date).**

| ***Shigella* species** | **2016** | | | | **2017** | | | | **2018 (year-to-date)** | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Total** | Male (%) | MSM (%) | PEH (%) | **Total** | Male (%) | MSM (%) | PEH (%) | **Total** | Male (%) | MSM (%) | PEH (%) |
| ***S. boydii*** | **1** | 0 (0) | 0 (0) | 0 (0) | **6** | 3 (50) | 0 (0) | 0 (0) | **1** | 1 (100) | 1 (100) | 0 (0) |
| ***S. dysenteriae*** | **1** | 1 (100) | 0 (0) | 0 (0) | **4** | 1 (25) | 0 (0) | 0 (0) | **0** | 0 (0) | 0 (0) | 0 (0) |
| ***S. flexneri*** | **52** | 39 (75) | 11 (21) | 2 (4) | **82** | 62 (76) | 11 (13) | 6 (7) | **33** | 20 (61) | 7 (21) | 2 (6) |
| ***S. sonnei*** | **168** | 108 (64) | 24 (14) | 14 (8) | **147** | 83 (57) | 19 (13) | 22 (15) | **22** | 13 (59) | 3 (14) | 2 (9) |
| **Unknown** | **21** | 14 (67) | 4 (19) | 1 (5) | **95** | 60 (63) | 19 (20) | 12 (13) | **41** | 25 (61) | 13 (32) | 3 (7) |
| **Total** | **243** | 162 (67) | 39 (16) | 17 (7) | **334** | 209 (63) | 49 (15) | 40 (12) | **97** | 59 (61) | 24 (25) | 7 (7) |

**This is an official**

# CDC HEALTH UPDATE

Distributed via the CDC Health Alert Network
June 7, 2018, 1100ET (11:00 AM ET)
CDC HAN-00411

## Update – 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:

    - 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. CLSI. *Performance Standards for Antimicrobial Susceptibility Testing*. 28th ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.

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**Categories of Health Alert Network messages:**

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| **Health Alert** | Requires immediate action or attention; highest level of importance |
| **Health Advisory** | May not require immediate action; provides important information for a specific incident or situation |
| **Health Update** | Unlikely to require immediate action; provides updated information regarding an incident or situation |
| **HAN Info Service** | Does not require immediate action; provides general public health information |

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