Notes from the Field

Shigella with Decreased Susceptibility to Azithromycin Among Men Who Have Sex with Men — United States, 2002–2013

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Bacteria of the genus Shigella cause approximately 500,000 illnesses each year in the United States. Diarrhea (sometimes bloody), fever, and stomach cramps typically start 1-2 days after exposure and usually resolve in 5-7 days.* For patients with severe disease, bloody diarrhea, or compromised immune systems, antibiotic treatment is recommended, but resistance to traditional first-line antibiotics (e.g., ampicillin and trimethoprim-sulfamethoxazole) is common. For multidrugresistant cases, azithromycin, the most frequently prescribed antibiotic in the United States (1), is recommended for both children and adults (2,3). However, not all Shigellae are susceptible to azithromycin (4-6). Nonsusceptible isolates exist but are not usually identified because there are no clinical laboratory guidelines for azithromycin susceptibility testing. However, to monitor susceptibility of Shigellae in the United States, CDC's National Antimicrobial Resistance Monitoring System (NARMS) has, since 2011, routinely measured the azithromycin minimum inhibitory concentration (MIC) for every 20th Shigella isolate submitted from public health laboratories to CDC, as well as outbreak-associated isolates. All known U.S. Shigella isolates with decreased susceptibility to azithromycin (DSA-Shigella), and the illnesses caused by them, are described in this report.

DSA-Shigella is defined as a Shigella isolate with an azithromycin MIC > 16 μ g/mL (4). Twenty-nine DSA-Shigella isolates were identified through routine NARMS testing. Additional isolates from 2002–2013 were identified through a previous NARMS study (n = 3) (4), requests to public health officials (n = 2), and retrospective testing of available isolates with pulsed-field gel electrophoresis (PFGE) patterns indistinguishable from DSA-Shigella isolates (n = 21).

Among 55 patients from 17 states infected with DSA-Shigella (36 S. flexneri, 18 S. sonnei, one S. boydii), age ranged from 1 to 89 years (median: 42 years); 44 (80%) were men, and seven (13%) were children (aged <18 years). Of 35 patients for whom information was available, 23 (66%) were white,

11 (31%) were black, and one (3%) was Asian/Pacific Islander (two patients self-identified as white and Hispanic and one as Hispanic only). All but one patient resided in an urban area; one child and none of 29 adults for whom information was available reported international travel. Four patients were part of a recognized shigellosis outbreak (5). The median duration of illness was 11 days (n = 17). Of patients for whom information was available, 46% (12 of 26) had bloody diarrhea, 50% (16 of 32) had fever, and 45% (19 of 42) were hospitalized. Eighty-one percent (13 of 16) of men for whom information was available were human immunodeficiency virus (HIV)positive, and 79% (11 of 14) identified as gay, bisexual, or other men who have sex with men (collectively referred to as MSM). Four men reported recent high-risk sexual practices, including anonymous sexual contact (n = 1), sexual contact without a barrier (n = 2 anal-genital; n = 1 oral-anal), and many sexual partners (n = 1); five had a history of syphilis.

All isolates harbored *mph*A or *erm*B macrolide resistance genes that are commonly plasmid-encoded. Fifty-three percent (29 of 55) were resistant to five or more classes of antibiotics, and 4% (2 of 55) were resistant to ciprofloxacin. NARMS data indicated that isolates were not susceptible to the drug used for treatment in seven of 19 patients, including three treated with azithromycin.

DSA-Shigella infections are occurring in the United States. Although some of the infections occurred among children, who are often treated with azithromycin for shigellosis, these data suggest that MSM, especially HIV-infected MSM, are currently at greater risk for infection with DSA-Shigella. Shigellosis is more common and can be more severe among HIV-infected persons with CD4 cell counts <200/mm³ (7). Clinical failure of azithromycin was recently reported in a Dutch HIV-infected patient with shigellosis (6). Clinicians should be aware that MSM and HIV-positive persons with shigellosis might be infected with Shigella strains with reduced susceptibility to azithromycin. Clinicians should culture stool specimens of MSM and HIV-infected men experiencing diarrhea and determine antimicrobial susceptibility of Shigella to antibiotics other than azithromycin to help guide treatment, if needed. Meticulous handwashing and reducing fecal-oral exposures during sexual contact can reduce risk for infection (7).

The number of cases presented in this report is likely a substantial underestimate because NARMS routinely tests only 5% of *Shigella* isolates submitted to public health laboratories, and targeted testing using PFGE might miss cases because *Shigella* is highly mutable and plasmid-encoded macrolide

^{*}Additional information available at http://www.cdc.gov/nczved/divisions/dfbmd/diseases/shigellosis.

resistance genes are mobile. Additionally, because NARMS began routinely measuring susceptibility to azithromycin in 2011, and recent isolates were more likely to be available for retrospective analysis, these data provide no information about trends. To better track illnesses and guide patient management, clinical laboratory guidelines for azithromycin susceptibility testing among *Enterobacteriaceae* are urgently needed.

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References

- Hicks L, Taylor T. U.S. outpatient antibiotic prescribing, 2010. N Engl J Med 2013;368:1461–2.
- American Academy of Pediatrics. Shigella infections. In: Red book: 2012 report of the Committee on Infectious Diseases. Pickering LK, ed. 29th edition. Elk Grove Village, IL: American Academy of Pediatrics; 2012:645–7.
- 3. World Health Organization. Guidelines for the control of shigellosis, including epidemics due to *Shigella dysenteriae* type 1. Geneva, Switzerland: World Health Organization; 2005. Available at http://whqlibdoc.who.int/publications/2005/9241592330.pdf.
- Howie RL, Folster JP, Bowen A, Barzilay EJ, Whichard JM. Reduced azithromycin susceptibility in *Shigella sonnei*, United States. Microb Drug Resis 2010;16:245–8.
- Karlsson MS, Bowen A, Reporter R, et al. Outbreak of infections caused by *Shigella sonnei* with reduced susceptibility to azithromycin in the United States. Antimicrob Agents Chemother 2013;57:1559–60.
- Hassing RJ, Melles DC, Goessens WHF, Rijnders BJA. Case of Shigella flexneri infection with treatment failure due to azithromycin resistance in an HIV-positive patient [Letter]. Infection 2014; February 2, 2014 [Epub ahead of print].
- 7. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Atlanta, GA: US Department of Health and Human Services, CDC; 2014. Available at http://aidsinfo.nih.gov/contentfiles/ lvguidelines/adult_oi.pdf.

Announcement

American Heart Month — February 2014

February is American Heart Month. Cardiovascular disease (CVD), including heart disease, stroke, and high blood pressure, is the leading cause of death among women and men in the United States as well as a leading cause of disability (1). CVD costs the United States approximately \$300 billion each year, including the cost of health-care services, medications, and lost productivity from premature death (1).

CVD does not affect all persons in the same way. Factors such as age, race, ethnicity, and sex can affect a person's risk for heart disease. Regardless, CVD and risk factors are largely preventable with changes in health habits, community changes to create healthier living spaces, and improvement of quality of care (2).

In observance of American Heart Month, CDC has published an online feature article focusing on CVD (available at http://www.cdc.gov/features/heartmonth), which includes information to help persons take control of their heart health using the "ABCS": A) take aspirin as directed by your healthcare provider; B) control your blood pressure; C) manage your cholesterol; and S) don't smoke.

Additional information about CVD and heart health is available this month and throughout the year at http://millionhearts.hhs.gov/index.html.

References

- 1. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. Circulation 2014;129:e28—e292.
- Lloyd-Jones DM, Hong Y, Labarthe D. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. Circulation 2010;12:586–613.