

SHIGELLOSIS

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Shigellosis or bacterial dysentery is an acute infectious enteritis of humans due to *Shigella*.

Shigellae are Gram-negative rods of the Enterobacteriaceae family, closely related to *E.coli*. *Shigella* are divided into four major O antigenic groups:

- 1) *S.dysenteriae*
- 2) *S.flexneri*
- 3) *S.boydii*
- 4) *S.sonnei*

Within each group there are several serotypes.

Epidemiology

Transmission:

The transmission is fecal-oral. Person-to-person transmission is the most frequent route. Stool concentrations may be very high: 100,000 to 100 million bacteria per gram. As few as 10 to 100 organisms can cause infection, enabling person-to-person transmission where hygienic conditions are compromised.

Reservoir:

Humans are the only natural hosts for *Shigella*.

Carriers:

Long-term carriage is rare in industrialized countries: 1% to 2% of the population excrete the organisms for more than three months (UK study). In developing countries, particularly among children, the rates of carriage are higher: 20% excrete for greater than or equal to one month, 10% for greater than or equal to two months.

Communicability:

The source is a symptomatic individual or a short-term post-recovery individual. Communicability occurs during acute infection and short-term carriage after recovery (four weeks).

Common source outbreak...

... may also occur. *Shigella* find their way in water or food and can be spread through this vehicle. Food borne epidemics are usually traced to infected foodhandlers, and are associated with food eaten raw, or handled after preparation.

Invasiveness:

Shigella are able to penetrate cells; this property is extremely important for virulence. It provides the bacteria a safer environment to continue multiplying, away from antibodies, complement and phagocytes. This allows *Shigella* to be infectious with doses as low as 10 to 200 bacteria ingested by mouth. This low infective dose allows the infection to spread from person-to-person without having the need for enrichment through water or food. The bacteria are included in a vesicle bound by a membrane; cells survive this invasion pretty well. Eventually, after bacterial multiplication, the invaded cells suffer and die.

Endemic shigellosis appears during infancy but becomes more common among toddlers and young children. Shigellosis has become a significant problem in childcare centers. Secondary attack rates in household contacts range from 10% to 40%.

Institutions:

Shigella infection is a high risk for some institutions: day care centers and adult care homes. In the United States, *S. sonnei* primarily infects young children and is a common cause of diarrheal outbreaks in childcare centers. In Houston, a 19-month prospective study of children in day care centers showed an incidence rate of 6.6 per 100 children per year with secondary cases occurring in 25% of families. Attack rates are higher in younger children than in adults. Breast-fed neonates seem to be protected, but bottle-fed neonates are not. Shigellosis spreads easily among closed populations such as army barracks and ships.

About 25% of *S.flexneri* infections in the U.S. are occurring among young adult males, resulting from sexual transmission among men who have sex with men (MSM).

The incubation period...

... is usually one to three days, with a range of 12 hours to four days; and up to one week for *S. dysenteriae*.

Clinical Description

Toxigenicity:

All *Shigella* produce cytotoxins, particularly, the more virulent *S.dysenteriae*. This toxin was found in 80% of stools of Bangladeshi infected with *S.dysenteriae* versus 20% with *S.flexneri*. The toxin causes: (1) secretion of isotonic fluid; (2) damage to the intestinal epithelial cells by apoptosis; (3) epithelial cell death; (4) microulcer formation; (5) inflammatory response; and (6) exudation of leukocytes in the bowel lumen.

Shigella dysenteriae produces a neurotoxin (causing limb paralysis and death if injected to rabbit or mouse). This toxin does not play a role in human pathogenesis.

Asymptomatic infections...

... result from low inoculum infections and preexisting immunity. Most infections in infants result in symptomatic disease. In common source outbreaks, attack rates range from 10% to 85% (mean 40%).

Bacterial Challenge	Percent With Disease	
	<i>S.flexneri</i>	<i>S.dysenteriae</i>
100,000	58%	
10,000	59%	83%
200	22%	50%
10		10%

Most clinical shigellosis is **gastrointestinal illness:**

- Watery diarrhea, abdominal pain, fever
- Dysenteric syndrome: frequent passage of small volume bloody mucoid stools, abdominal cramps and tenesmus. More virulent strains (*dysenteriae* > *flexneri* > *sonnei*) cause a more intense dysenteric syndrome. In well-nourished people, the disease is self-limiting in about seven days. Malnourished children develop a chronic relapsing disease with a 10% fatality rate.

Postdysenteric **Reiter’s syndrome** (oculo-urethro synovial syndrome) is associated with *S.flexneri* and people with HLA –B27 antigen.

Serious complications are usually from *S. dysenteriae* infections: **toxic megacolon; hemolytic uremic syndrome; and toxic encephalopathy (Ekiri Sx).**

Immunity:

Epidemiologic observations suggest an acquired immunity to specific strains of *Shigella*. Usually *Shigella* is endemic among children, and adults have much lower incidence; when a new strain is introduced, the epidemic affects all age groups. Experiments for live oral vaccines have also demonstrated a serotype specific protection.

Laboratory Tests

The diagnosis is made by identifying *Shigella* in the stools or detecting *Shigella* using a non-culture based method. In patients with dysenteric disease, presumptive treatment should be started immediately after collecting the samples, without waiting for the results. Amebic dysentery is the main other cause of dysenteric syndrome in developing countries.

Isolation from the stools...

... where numerous microorganisms are growing, is enhanced by the use of specific selective media to suppress the growth of usually non-pathogenic bacteria, to increase the contrast between *Shigella* and other bacteria so that *Shigella* colonies are easier to pick up. This is done by incorporating a dye, which tags the rapid fermentors of lactose (*Shigella* are not rapid fermentors). Mac Conkey, Hektoen enteric, TTC media are used. SS media is too inhibitory for *Shigella*, particularly *S.dysenteriae*.

Stool samples will yield better results than swabs. If swabs are performed, they should go past the anal canal. The best swabs are those of an ulcer collected under endoscopy.

Stool specimens should be collected on cotton-tipped swabs and these swabs placed in a tube of Cary-Blair culture medium. (These tubes can be obtained from regional laboratories.) Specimens in Cary-Blair should be refrigerated and transported to the lab under refrigerated conditions as soon as possible. (If it is necessary to hold 48 hours or longer, freeze sample at -7°C and transport to lab in a frozen state.) Complete Bacteriology Lab Slip (Lab 93).

Food samples that are sent in should be handled by the sanitarian. In the absence of a sanitarian, submit at least 100 grams (approx. 4 to 5 oz.) of each suspected food item (in separate containers). Be sure to keep food refrigerated (not frozen). Complete Food and Drug Lab Slip (Lab 47).

It will take more than 72 hours for the results to be available. In order to adequately investigate and identify the cause of the outbreak, it is very important to obtain samples of the suspected food and several stool specimens. Confirmation of the causative organism(s) cannot be made with just one of these components.

- Order stool culture for patients suspected of having a *Shigella* infection to obtain isolates for antimicrobial susceptibility testing.
- Culture-independent diagnostic testing does not provide an isolate and therefore cannot be used to assess susceptibility.
- Order antimicrobial susceptibility testing when ordering stool culture for *Shigella*.
 - When antimicrobial susceptibility testing is performed by broth microdilution, request ciprofloxacin testing that includes dilutions of 0.12 µg/mL or lower.
 - Even when treatment is not indicated, identifying patients with drug-resistant infections (i.e., ordering susceptibility testing) will help to inform public health management, such as when to return to work, school, and group settings.

Shigella can also be detected in clinical specimens using a non-culture based method such as multiplex GI pathogen panels.

Treatment

Fluid and electrolyte replacement if diarrhea is abundant and dehydration apparent.

Antibiotics

Unnecessary treatment with antibiotics promotes resistance.

- Treatment can shorten the duration of some illnesses, though typically only by one to two days.
- Empiric treatment with an antibiotic to which the organism is resistant may worsen symptoms or prolong the duration of shedding of the organism. Administer for five days.

Do not routinely prescribe antibiotic therapy for *Shigella* infection. Instead, reserve antibiotic therapy for patients for whom it is clinically indicated or when public health officials advise treatment in an outbreak setting.

Antibiotic treatment is recommended for patients who are immunocompromised or who develop severe illness (e.g., patients requiring hospitalization, those with invasive disease, or those with complications).

- Fluoroquinolone: ciprofloxacin, norfloxacin
- Alternative antibiotics: ceftriaxone or cefixime or trimethoprim-sulfamethoxazole

When antibiotic treatment is indicated, tailor antibiotic choice to antimicrobial susceptibility results as soon as possible with special attention given to the MIC for fluoroquinolone antibiotics. Avoid prescribing fluoroquinolones if the ciprofloxacin MIC is 0.12 µg/mL or higher even if the laboratory report identifies the isolate as susceptible. Know the potential risks of fluoroquinolone treatment of *Shigella* infections with ciprofloxacin MICs in this range, including possible treatment failure and increased risk of secondary transmission. The interpretation of MIC values varies for the different fluoroquinolone antibiotics; if susceptibility results are reported for a fluoroquinolone other than ciprofloxacin, contact the microbiology laboratory for assistance with interpretation. If MIC values are not reported to the clinician with susceptibility results, consider contacting the microbiology laboratory where the susceptibility testing was performed to determine the ciprofloxacin MIC value before treating a patient with a fluoroquinolone agent. Some susceptibility testing methods do not produce a MIC value; the impact of a quinolone resistance gene on test results by other methods (e.g., disk diffusion) is not yet known. Consult an infectious disease specialist for cases where the *Shigella* isolate is resistant to multiple antibiotics and appropriate treatment is unclear.

Obtain follow-up stool cultures in shigellosis patients who have continued or worsening symptoms despite antibiotic therapy.

Antimotility agents are not recommended as they may prolong the symptomatic period. They should be limited to one or two doses and should not be administered with the antibiotics.

Fluoroquinolone resistance is of particular concern given that data from the National Antimicrobial Resistance Monitoring System indicate that many *Shigella* isolates with a quinolone resistance gene also are resistant to many other commonly used treatment agents, such as azithromycin, trimethoprim-sulfamethoxazole, amoxicillin-clavulanic acid, and ampicillin. This susceptibility profile may encourage clinicians to prescribe fluoroquinolone antibiotics to patients who require treatment.

Rising fluoroquinolone MIC values among *Shigella* isolates may be related to the emergence of plasmid-mediated quinolone resistance (PMQR) genes in *Shigella* species in the United States. *Shigella* strains harboring PMQR genes were identified earlier this year following whole genome sequencing of isolates from a multistate outbreak of multidrug-resistant *S. flexneri* infections predominantly affecting adult men, many of whom identify as men who have sex with men, according to epidemiologic data collected by the Centers for Disease Control and Prevention's *Shigella* program as part of outbreak response. PMQR genes have also been identified in sporadic cases of *S. sonnei*. Plasmid-mediated resistance genes are of particular concern because of their ability to spread between bacteria and their ability to promote chromosomal mutations conferring quinolone resistance, potentially resulting in rapid spread of fluoroquinolone resistance within or between populations of bacteria. The prevalence of PMQR genes among all U.S. *Shigella* isolates is currently unknown.

Any patient with a *Shigella* infection could carry a strain harboring a quinolone resistance gene with a ciprofloxacin MIC of 0.12–1 µg/mL. The emergence of *Shigella* species with ciprofloxacin MICs of 0.12–1 µg/mL and their association with quinolone resistance genes raises the following concerns:

- Fluoroquinolone treatment of *Shigella* infection with a strain harboring a quinolone resistance gene may be less effective and may increase the risk of a more severe clinical course for the individual (e.g., increased duration or severity of symptoms, increased need for hospitalization or admission to an intensive care unit, increased length of hospitalization, or increased risk of death).

- Fluoroquinolone treatment of *Shigella* infection with a strain harboring a quinolone resistance gene also may increase the risk of secondary cases, if the treatment prolongs the duration or increases the quantity of organisms shed in the stool, given the very low infectious dose required for transmission of *Shigella* bacteria.

Surveillance

Shigellosis is a condition reportable within one business day from diagnosis.

Clinical Description

An illness of variable severity characterized by diarrhea, fever, nausea, cramps, and tenesmus. Asymptomatic infections may occur.

Laboratory Criteria for Diagnosis

Confirmatory

- Isolation of *Shigella* from a clinical specimen.

Supportive

- Detection of *Shigella* spp. or *Shigella*/enteroinvasive *E. coli* (EIEC) in a clinical specimen using a culture-independent diagnostic testing (CIDT).

Case Definition

Confirmed

- A case that meets the confirmed laboratory criteria for diagnosis. When available, O antigen serotype characterization should be reported.

Probable

- A case that meets the supportive laboratory criteria for diagnosis; **OR**
- A clinically compatible case that is epidemiologically linked, i.e., is a contact of a confirmed case or a member of a risk group defined by public health authorities during an outbreak.

Investigation / Intervention

The purpose of investigation is to identify cases, to differentiate *Shigella* from other bacterial infections, to determine the mode of transmission (whether from person-to-person or by common vehicle), to identify the population exposed to increased risk of infection, and to institute disease control measures.

- Upon receipt of a report of a case of shigellosis, confirm the diagnosis.
- Request the private physician or hospital to submit a *Shigella* isolate to the nearest public health laboratory for serotyping.
- Determine if the person with shigellosis (or any ill contacts) is in a high-risk setting (such as a childcare or foodhandler). If no high-risk setting is identified, then no further action is necessary.

Child care center, institution, nursing home, etc.

- Determine if any of the staff or attendees/residents are symptomatic

- Refer symptomatic persons for testing (exclude these persons from child care if the diarrhea cannot be contained in a diaper); if a large number of stool samples will be sent to the state lab for testing, notify the lab prior to submitting the specimens.
- Discuss routes of transmission and recommended control measures with the staff (use the shigellosis fact sheet as necessary), and stress the importance of thorough handwashing after toilet use/assistance, between diaper changes, before eating, and before handling/preparing food.
- Ask the director to monitor attendees/residents and staff for additional cases.
- Monitor/review reported shigellosis cases for a connection to the case in the childcare center, institution, nursing home, etc.
- The child should be excluded until the diarrhea is gone, or the diarrhea can be contained in a diaper, and one negative culture is obtained, or the child has been cleared by the child's physician or health department.

Foodhandlers

- Determine if any of the staff or patrons are symptomatic.
- Refer symptomatic persons for testing (exclude from food handling any symptomatic persons); if a large number of stool samples will be sent to the state lab for testing, notify the lab prior to submitting the specimens.
- Determine the food handling role of the person with shigellosis and assess his or her hygiene habits (such as handwashing, personal cleanliness, not working while ill, etc.)
- Discuss routes of transmission and recommended control measures with the staff (use the shigellosis fact sheet as necessary); stress the importance of thorough handwashing after toilet use/assistance, before eating, and before handling/preparing food, and the need to not work while ill (especially with vomiting and/or diarrhea)
- Exclude symptomatic individuals from foodhandling, and from direct care of hospitalized and institutionalized patients.

Other circumstances in which further evaluation may be necessary:

- If a physician requests that family members be tested.
- If follow-up is requested by the Infectious Disease Epidemiology Section.
- If the case is suspected to be part of an outbreak.
- Determine the possible source(s) of the infection: collect information on the recent food history [such as date and time of suspected event; list of food items served; list of participants; symptoms reported; the onset date and time; etc.]. Recover all suspected foods for appropriate testing.

Exclusion

If exclusion is recommended, return to day-care, school, food handling upon cessation of diarrhea, and in case of an outbreak, foodhandlers, healthcare workers, or daycare attendees and staff, one negative stool specimen is recommended.

Prevention

Prevention of fecal-oral transmission relies on:

- Handwashing: Handwashing before meals, after urination and defecation is very effective if done systematically. In day care centers, toddlers who are toilet independent are at the highest risk if not properly watched and prompted to wash their hands.
- Sanitary disposal of feces
- Protection of water supply: Outbreaks of *Shigella* resulting from contaminated water supply are rare, but do occur.
- Food preparation
- Counsel patients with active diarrhea on how they can prevent spreading the infection to others, regardless of whether antibiotic treatment is prescribed.

- Children with active diarrhea should not attend childcare, school, or group activities while they are ill.
- Wait to have sex (vaginal, anal, and oral) for two weeks after you no longer have diarrhea. Use safe sex practices for several weeks after resuming sex, because *Shigella* bacteria may still be in stool for several weeks.
- Control of vectors: Insects, particularly flies may play a small role in spreading the infections. In areas where feces are found in nature, flies are attracted by feces, meat and decaying fruits. They carry *Shigella* from feces to food. In a study, 20% of flies were shown to carry fecal pathogens, 5% being *Shigella*
- Prophylaxis: In endemic settings, exposure occurs very frequently; therefore, prophylaxis would have to be long-term. This would promote the resistance of bacteria and is not recommended. For travelers who visit endemic areas for short periods, prophylaxis against traveler's diarrhea has been recommended by some.

Hospital precaution and isolation:

Contact precautions until one stool culture, at least 48 hours after cessation of antimicrobial therapy, is negative.

Day Care Letter

Dear School/Day Care Director,

The Office of Public Health is investigating a recent rise in the number of cases of Shigellosis in the Central Louisiana area. Shigellosis is a diarrheal illness caused by the *Shigella* group of bacteria. Most who are infected with *Shigella* experience symptoms such as diarrhea, fever, stomach cramps, nausea and vomiting. We strongly recommend that any student who develops these gastrointestinal symptoms be examined by a doctor to obtain a stool culture for diagnosis. Children who have been diagnosed with Shigellosis should not be permitted to return to school until diarrhea has ceased and stool cultures are negative for *Shigella*. If any children in your school are diagnosed with Shigellosis or develop gastrointestinal symptoms, please report the illness to the Office of Public Health.

The single most important measure to prevent transmission of Shigellosis in schools and day care centers is frequent and careful handwashing with soap, especially after going to the bathroom, after changing diapers, and before preparing foods or beverages. Some additional tips for preventing the spread of shigellosis in your facility include the following:

- dispose of soiled diapers properly
- disinfect diaper changing areas after using them
- keep children with diarrhea out of child care settings
- supervise handwashing of toddlers and small children after they use the toilet
- persons with diarrheal illness should not prepare food for others

Please contact the Office of Public Health if you have need for any additional information about Shigellosis, or to report an illness in your facility. Thank you for your cooperation in this matter.

Sincerely,

Physician / Pediatrician Letter

Dear Doctor,

The Office of Public Health is investigating a recent rise in the number of cases of Shigellosis in _____ . We are initiating active surveillance for suspected cases. We are asking physicians within the _____ area to report suspected cases. A form for reporting is provided and we are requesting it be faxed to our local office daily / twice weekly on _____ until further notice. Additionally, we strongly suggest that children diagnosed with Shigellosis not be permitted to return to school until diarrhea has ceased and a stool culture is negative.

If you need any additional information about our active surveillance program, please contact _____, Regional Disease Surveillance Specialist at (555) 555-5555, or by email at jsnow@la.gov. Thank you for your cooperation in this matter.

Sincerely,

Public Health Regional Administrator/Medical Director