

Typhoid Fever

(*Salmonella* serotype Typhi)

PROTOCOL CHECKLIST

- Enter available information into Merlin upon receipt of initial report
- Review background on the disease and its epidemiology (see page 2), case definition (see page 4), and laboratory testing (see page 5)
- Contact provider, if necessary (see page 6)
- Interview patient
 - Review disease facts (see page 2)
 - Modes of transmission
 - Incubation period
 - Symptoms
 - Ask about exposure to relevant risk factors (see page 7)
 - Travel outside of the U.S.
 - Source of drinking water
 - Restaurant meals
 - Food at public gatherings
 - If patient did not travel to a typhoid endemic area during the incubation period, consider culturing contacts who may be carriers in an attempt to determine the source of infection
 - Identify contacts
 - Determine if an infected patient or contact is in sensitive situation (see page 9)
 - Exclude patient or contact from sensitive situations until follow-up cultures are negative (see page 9)
 - Provide education on controlling further spread (see page 10)
 - Do practice proper hand hygiene
 - Do not use recreational water venues
 - Do not prepare food for others
 - Address patient's questions or concerns
- Conduct routine follow-up cultures for all people diagnosed with typhoid fever (see page 9)
- Coordinate follow up with regulatory agencies as appropriate
- Enter additional data obtained from interview into Merlin (see page 8)

Typhoid Fever

1. DISEASE REPORTING

A. Purpose of reporting and surveillance

1. To determine if there is a source of infection of public health concern (e.g., a food handler or commercially distributed food product) and to stop transmission from such a source.
2. To assess the risk of the case transmitting infection to others, and to prevent such transmission.
3. To identify other undiagnosed cases.

B. Legal reporting requirements

Laboratories and physicians are required to report cases of typhoid fever by phone to the county health department (CHD) immediately (24 hours a day, 7 days a week) following laboratory identification or diagnosis. Laboratories must submit *Salmonella* serotype Typhi (*S. Typhi*) isolates to the Florida Department of Health (FDOH) Bureau of Public Health Laboratories (BPHL) for confirmation.

C. County health department investigation responsibilities

1. Begin the investigation as soon as possible, but no longer than one business day, after receiving report from a provider or laboratory.
2. Interview patient to:
 - a. Determine whether the person with the reported case may have put or be putting others at risk in a sensitive situation,
 - b. Determine whether the person with the reported case may be part of a recognized or unrecognized outbreak,
 - c. Conduct contact and environmental investigations as appropriate for symptomatic and asymptomatic *S. Typhi* carriers, and
 - d. Provide education to a person who is infectious, or their parent or guardian, about how to avoid infecting others.
3. Take measures to control further spread. See **Section 6** for recommendations on controlling further spread.
4. Report all confirmed and probable cases in Merlin.
 - a. A person must be symptomatic to meet the confirmed or probable case definition. Asymptomatic infections should not be reported in Merlin.
 - b. A Typhoid Fever Case Report Form is available to assist in follow up and investigation: <http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/index.html#T>
5. Assure that laboratories forward *S. Typhi* isolates to BPHL for confirmation.

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic agent

Typhoid fever is a life-threatening illness caused by the bacterium *S. enterica* subsp. *enterica* serovar Typhi (commonly referred to as *S. Typhi*) a gram-negative bacillus. It is a group D1 *Salmonella*, as are many of those that cause non-typhoidal salmonellosis.

In the United States, about 400 cases occur each year, and 75% of these are acquired while traveling internationally. Typhoid fever is still common in the developing world, where it affects about 21.5 million persons each year.

B. Description of illness

People with typhoid fever usually have a sustained fever as high as 103° to 104° F (39° to 40° C). Additional symptoms may include headache, muscle pain, stomach pain, loss of appetite, and weakness. Constipation is more likely to be a result of infection in adults, since diarrhea is uncommon. In some cases, patients have a rash of flat, rose-colored spots. Severe infections may result in confusion, delirium, intestinal perforation, or death. Laboratory testing is required to confirm infection with *S. Typhi*.

C. Reservoirs

S. Typhi lives only in humans. People with typhoid fever carry the bacteria in their bloodstream and intestinal tract. In addition, a small number of people, called carriers, recover from typhoid fever but continue to carry the bacteria. Both ill persons and carriers shed *S. Typhi* in their stool.

Typhoid fever is common in most parts of the world except in industrialized regions such as the United States, Canada, Western Europe, Australia, and Japan.

D. Modes of transmission

Typhoid fever is acquired by ingestion of food or water contaminated with the stool or urine of a person infected with *S. Typhi*. This can occur when a person shedding *S. Typhi* handles food or drink or when contaminated sewage gets into water used for drinking or washing food. Despite frequent suggestions to the contrary, floods or other disasters in non-endemic countries, such as the United States, do not precipitate typhoid fever outbreaks.

E. Incubation period

The incubation period for typhoid fever is typically 8-14 days with a range of 3-60 days.

F. Period of communicability

The period of communicability extends as long as organisms are excreted, typically beginning during the first week after onset and continuing through convalescence

and for a variable period thereafter. Up to 10% of untreated patients may excrete the organisms for three months following onset of symptoms. A chronic carrier state (excretion for more than one year) occurs in approximately 5% of those infected.

G. Treatment

Many patients with uncomplicated disease may be treated on an outpatient basis. Patients with more severe illness may require hospitalization and supportive care or surgery. Antibiotic therapy is the mainstay of treatment and should not be delayed while waiting for culture results. Multi-drug resistant *S. Typhi* is increasingly common so empiric antibiotic choice should be partly based on the antibiogram of the organism in the country of origin. Empiric treatment regimens may require subsequent modification based on the results of susceptibility testing. Relapses can occur and should be treated in the same way as the initial infection. Prolonged courses of antibiotics may successfully treat chronic carriers.

H. Prophylaxis

Two vaccines are currently licensed in the U.S. for the prevention of typhoid fever: live oral Ty21a (Vivotif) and Typhoid Vi polysaccharide vaccine (Typhim Vi). Vaccination for typhoid, while not routinely recommended in the United States, is recommended for the following groups:

- Travelers to areas in which there is a recognized risk of exposure to *S. Typhi*;
- Persons with ongoing exposure (e.g., household contact) to a documented *S. Typhi* carrier;
- Microbiology laboratorians who work frequently with *S. Typhi*.

The efficacy of these two vaccines ranges from 50% to 80%. Therefore, vaccination should not be a substitute for careful selection of food and drink while traveling or proper handling of specimens and cultures in the laboratory. For additional information regarding typhoid fever vaccines, please see the most recent *Red Book* or the Immunization Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1994;43 (No. RR-14).

I. *S. Typhi* in Florida

The Florida Department of Health (FDOH) receives approximately 20 reports of typhoid fever each year. The majority (75% to 95%) of these cases are sporadic and are acquired outside of the U.S., most commonly India and Haiti, but 5% to 25% of cases are acquired in Florida. Cases of apparently sporadic locally-acquired typhoid fever are of greater public health importance, as they indicate local transmission of a disease that is not endemic to Florida.

3. CASE DEFINITION

A. Clinical description

An illness caused by *S. Typhi* that is often characterized by insidious onset of sustained fever, headache, malaise, anorexia, relative bradycardia, constipation or

diarrhea, and nonproductive cough; however, many mild and atypical infections occur. Carriage of *S. Typhi* may be prolonged.

B. Laboratory criteria for diagnosis

Isolation of *S. Typhi* from blood, stool, or other clinical specimen.

C. Case classification

Confirmed: A clinically compatible case that is laboratory confirmed.

Probable: A clinically compatible case that is epidemiologically-linked to a confirmed case in an outbreak.

D. Comment

Isolation of the organism is required for confirmation. Serologic evidence alone is not sufficient for diagnosis. Asymptomatic carriage should not be reported as typhoid fever. Infection with *S. Typhi* should only be reported under the Typhoid Fever disease (code=00200) and not as salmonellosis (code=00300).

Isolates from all cases must be submitted to the Bureau of Public Health Laboratories for confirmation.

4. LABORATORY TESTING

A. Criteria for diagnosis

The diagnosis of typhoid fever is made by isolation of *S. Typhi* from a clinical specimen that can be serotyped and biochemically identified at the BPHL. Serological testing for *S. Typhi* is performed by some laboratories, but is generally considered to be an unreliable diagnostic test in the U.S. and does not meet the surveillance case definition laboratory criteria for diagnosis.

B. Services available at the BPHL

1. BPHL routinely screens stool specimens for *Salmonella*, as well as provides pure isolate confirmation and speciation of *Salmonella* species.
2. BPHL algorithm:
 - a. Stool cultures or referred isolates are identified biochemically as *Salmonella*.
 - b. After biochemical identification, every *Salmonella* isolate is serogrouped and undergoes Pulse-field gel electrophoresis (PFGE).
 - c. In outbreak situations or by physician request, serotyping is also performed.
3. Culturing food items is generally non-productive in sporadic cases; however, implicated food items may be cultured by BPHL during outbreak investigations. Please consult BPHL and your Regional Environmental Epidemiologist (REE) to discuss testing food items.

C. Testing requests

1. Submitting specimens/isolates to BPHL
 - a. All submissions should be accompanied by Clinical Lab Submission Form 1847.



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- b. Electronic Laboratory Ordering (ELO) may also be used by entering request into the HMS State Laboratory System, placing the bar coded label on the Cary-Blair vial, and writing the date collected on the vial.
2. Specimen collection
 - a. A small portion (acorn size) of formed stool or equal portion of liquid stool should be transferred aseptically to a modified Cary-Blair transport vial that is properly labeled (name, date of birth, date collected).

Note: for stool specimens, simply mark test 1900 on the Clinical Lab Submission Form 1847 and all enteric pathogens are automatically screened (*Salmonella*, *Shigella*, *Campylobacter*, *E. coli* O157).

- b. For isolate submission, subculture a pure single colony of your suspect *Salmonella* species on a general purpose bacterial slant (TSA slant, chocolate slant, etc.), properly label (name, date of birth, date collected), and incubate the suspect slant for 18 to 24 hours at 35°C to 37°C before shipping to the laboratory to ensure viable growth.

Note: for isolates, please write, "suspect *Salmonella*" in the comment section of the Clinical Lab Submission Form 1847.

3. Packaging and shipping
 - a. Specimens and isolates for *Salmonella* testing should be sent to the Jacksonville BPHL laboratory.
 - b. Place the labeled vial into the proper inner or outer container (aluminum screw-cap inner container with spill absorber holds the primary vial and is then placed into an outer cardboard screw-cap container). Please place the Clinical Lab Submission Form 1847 in a plastic Ziploc bag between the inner and outer container. Package according to International Air Transport Association (IATA) regulations, labeling the outer shipping container: *UN3373, Biological Substance Category B*.
 - c. Specimens and isolates should be sent at ambient temperature or cooler, but cool packs should not be in direct contact with vials.
 - d.



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3. Contact the regional laboratory with questions:
- | | |
|--------------|--------------|
| Jacksonville | 904-791-1500 |
| Miami | 305-324-2432 |
| Tampa | 813-974-8000 |
| Pensacola | 850-595-8895 |

5. CASE INVESTIGATION

A. Contact the physician or hospital

1. Confirm that typhoid fever has been diagnosed in the reported patient.
2. Obtain the following:
 - a. Date of onset
 - b. Signs and symptoms
 - c. Predisposing conditions (e.g., immunosuppression)
 - d. Tests performed (including cultures, susceptibility testing, EIA, PFGE testing, etc.)
 - e. Treatment (especially antimicrobials)
3. Ask what information has been given to the patient, including whether the patient knows about the diagnosis.
4. Obtain as much demographic information as possible, including contact information (home, cellular, pager and/or work numbers). Ask how and where the patient can be contacted (i.e., at hospital or home).
5. Notify the physician that you will be contacting the patient as FDOH follows up on all cases of typhoid fever to assess risks factors, to better characterize the occurrence of typhoid fever infection in Florida, and to identify potential means for preventing further illness. It may also be appropriate at this point to determine if the physician has any concerns in regards to the CHD contacting the patient.

B. Interview the case

1. Contact the patient to complete an interview as soon as possible after reporting to optimize recall.
 - a. Make at least three phone call attempts to reach the case.
 - b. Calls should be made at different times of the day, with at least one attempt in the evening.
2. **Typhoid Fever Case Report Form (required):**
<http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/index.html#T>. This form can be used to guide the interview and can be completed during the interview.

3. Currently, there is no Extended Data screen in Merlin to enter data from the Case Report Form. Please scan and attach the form to the case in Merlin.
4. Items to cover during interview include:
 - a. Provide a brief background on the disease, including possible modes of transmission, incubation period, symptoms, etc.
 - b. Activities during exposure period (3 to 60 days before onset):
 - i. Travel outside Florida or the U.S. or contact with others who have traveled outside the U.S. Determine the dates of travel.
 - ii. Source(s) of drinking water at home, work, during trips, and in any vocational or recreational pursuit, including water from streams, rivers or lakes (obtain travel locations and dates).
 - iii. Restaurant meals that were consumed. Obtain the name of the restaurant, and date and location of the meal.
 - iv. Public gathering where the food was consumed. Obtain the date, location, and sponsor of the event.
 - v. **If the patient did not travel to a typhoid endemic area during the incubation period, consider culturing contacts who may be carriers in attempt to determine the source of infection.**
 - c. Determine if others (e.g., family, friends, coworkers, customers, patients, etc.) are known or thought to be ill with similar symptoms. If so, inquire about possible common source exposures. Obtain the name, phone number or address and clinical information of the ill person. Anyone meeting the probable case definition should be reported and investigated in the same manner as a confirmed case.
 - d. Determine if the patient or contacts are associated with sensitive situations (i.e., an attendee or employee of a daycare or childcare setting, a food handler, or an employee in a health care setting with direct patient care). Determine the dates and times they worked to determine the risk of transmission to others. **See Isolation of Contacts and Management of Contacts in Section 6.**
 - e. Provide basic instructions to patients and potentially exposed contacts about hand washing after defecation, diaper changing, and before food preparation. **See Section 6 for recommendations on controlling further spread.**

C. Environmental evaluation

If a particular food or water exposure is suspected as the likely source of infection during routine case investigations of typhoid fever, the CHD investigator should complete the Online Foodborne and Waterborne Illness Complaint Form: <http://www.floridahealth.gov/diseases-and-conditions/food-and-waterborne-disease/online-food-complaint-form.html>. The CHD investigator should record the complaint in their complaint log, and forward it to the appropriate agency with jurisdiction.

For each interviewed locally-acquired sporadic case of typhoid fever with an environmental exposure that could affect many people (e.g., a restaurant, water park, or high-risk commercially distributed food item), review complaint logs and recent typhoid fever cases in Merlin for additional cases that may be linked to the same facility or exposure source. When a community outbreak of typhoid fever is identified, most or all cases will be a high priority for interview and investigation. A

joint investigation or an environmental assessment for single, sporadic cases of locally-acquired typhoid fever should be performed. If additional cases are suspected or an outbreak is detected, the REE should be notified and a joint investigation or environmental assessment will be conducted with the appropriate regulatory authority. Technical assistance is also available from your REE, if needed.
<http://www.foodsafetyflorida.org/Staff.aspx>.

D. Merlin data entry

Create a case in Merlin under disease code **TYPHOID FEVER – 00200**. Enter the data collected into Merlin, being sure to include all required fields on the Basic Data screen, complete the Case Symptoms screen, and attach all relevant laboratory test results. Please attach **ALL** laboratory results received via electronic laboratory reporting (ELR) to the case.

6. CONTROLLING FURTHER SPREAD

A. Patient/household education on prevention recommendations

1. Case reports prioritized for investigation (i.e., part of an outbreak, in a sensitive situation, or still likely to be symptomatic) should be educated on preventing and transmitting infection to others.
 - a. Wash hands after using the toilet, changing diapers, handling soiled clothing or linens.
 - b. People infected with *S. Typhi* should not prepare food for others.
 - c. People infected with *S. Typhi* should not use recreational water venues (e.g., pools, lakes, interactive fountains, water parks) until two weeks after symptoms resolve.
2. General information on preventing disease may also be covered.
 - a. Typhoid fever is common in most parts of the world except in industrialized regions such as the United States, Canada, Western Europe, Australia, and Japan. Therefore, travelers to the developing world should consider taking precautions.
 - b. Over the past ten years, travelers from the United States to Asia, Africa, and Latin America have been especially at risk.
 - c. While traveling in typhoid endemic areas, people should follow the general rule, "Boil it, cook it, peel it, or forget it".
 - d. Other prevention measures:
 - i. Drink bottled water or bring water to a rolling boil for one minute before drinking. Bottled carbonated water is safer than uncarbonated bottled water.
 - ii. Ask for drinks without ice unless the ice is made from bottled or boiled water. Avoid popsicles and flavored ices that may have been made with contaminated water.
 - iii. Eat foods that have been thoroughly cooked and are still hot and steaming.
 - iv. Avoid raw vegetables and fruits that cannot be peeled. Vegetables like lettuce are easily contaminated and are very hard to wash well.

- v. Peel raw fruits or vegetables themselves (wash hands with soap first). Do not eat the peelings.
- vi. Avoid foods and beverages from street vendors. It is difficult for food to be kept clean on the street, and many travelers get sick from food bought from street vendors.

B. Isolation of cases

Routine follow-up cultures are indicated for all persons diagnosed with typhoid fever.

1. All people infected with *S. Typhi* should be supervised by the CHD until they have three consecutive negative stool cultures beginning at least one month after illness onset, provided the patient has been off antibiotic therapy for a period of one week. If one of the specimens is positive, another set of three specimens taken 24 hours apart are required for release of case. If *S. Typhi* is isolated from any of the three clearance stools, supervision by the CHD should continue until the patient has three consecutive negative stool cultures collected at one-month intervals following onset of symptoms.
2. Each stool specimen should be shipped individually, immediately, to the BPHL location in Jacksonville, Tampa, or Miami for arrival Tuesday through Thursday. Write "typhoid case screening" in the comments section of the lab form.
3. Persons who excrete the organism for a prolonged period can consider antibiotic treatment in attempt to eliminate the carrier state.
4. While under CHD supervision, persons excreting *S. Typhi*:
 - a. Should be excluded from sensitive situations (i.e., an attendee or employee of a daycare or childcare setting, a food handler, or an employee in a health care setting with direct patient care);
 - b. Should notify the CHD at once of any change in address or occupation;
 - c. Should notify the CHD at once of any suggestive illness among household members or other personal contacts.

C. Management of contacts

Symptomatic and asymptomatic household contacts of a typhoid case who may be excreting *S. Typhi* as determined by the CHD director, administrator, or their designee, and who are in a sensitive situation are prohibited from returning to such occupation or situation until no less than three specimens of feces taken at least 24 hours apart are negative for typhoid organisms.

D. Laboratory testing during outbreaks

1. Laboratory testing should be performed to assist in public health decision making and for epidemiologic studies.
2. Symptomatic and asymptomatic contacts may be asked to submit stool specimens to establish the etiology of the outbreak.
3. Once the etiologic agent for the outbreak has been identified (four to six specimens) further testing is usually not required for public health purposes.

E. Food or water is implicated as the source of an outbreak

Contact your REE for investigation assistance and guidance (<http://www.foodsafetyflorida.org/Staff.aspx>).

7. MANAGING SENSITIVE SITUATIONS

See Isolation of Contacts and Management of Contacts in the previous Section.

8. IMPORTANT LINKS

- A. Typhoid Fever Case Report Form:
<http://www.floridahealth.gov/diseases-and-conditions/disease-reporting-and-management/disease-reporting-and-surveillance/index.html#T>
- B. CDC's Typhoid Fever FAQ
http://www.cdc.gov/nczved/divisions/dfbmd/diseases/typhoid_fever/
- C. Online Food and Waterborne Illness Complaint Form
<http://www.floridahealth.gov/diseases-and-conditions/food-and-waterborne-disease/online-food-complaint-form.html>
- D. *Florida Administrative Code* 64D-3.040(6)
<https://www.flrules.org/gateway/ChapterHome.asp?Chapter=64D-3>

9. REFERENCES

- A. Heymann, D.L. (Ed.). (2008). *Control of Communicable Diseases manual* (19th ed.). Washington: American Public Health Association.
- B. American Academy of Pediatrics. (2009). *Red Book: 2009 Report of the Committee on Infectious Diseases* (28th ed.). Grove Village, IL: American Academy of Pediatrics.
- C. Immunization Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1994;43 (No. RR-14).
- D. Red Book or the Immunization Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1994;43 (No. RR-14).