



## TYPHOID FEVER AND PARATYPHOID FEVER

*Salmonella enterica* serotype Typhi and *Salmonella enterica* serotype Paratyphi

### BACKGROUND

Typhoidal *Salmonella* refers to the specific *Salmonella enterica* serotypes which cause typhoid fever or paratyphoid fever, including Typhi, Paratyphi A, Paratyphi B (see note below), and Paratyphi C.

- Serotype Paratyphi B (tartrate negative, i.e., unable to ferment tartrate) causes typhoidal disease.
- Serotype Paratyphi B (tartrate positive, i.e., able to ferment tartrate) typically causes nontyphoidal disease (uncomplicated gastroenteritis).
- Nontyphoidal *Salmonella* refers to all other *Salmonella* serotypes<sup>13</sup>.
- *S. Typhimurium* does not cause typhoid fever.

*Salmonella* Typhi (*S. Typhi*) and *Salmonella* Paratyphi (*S. Paratyphi*) are bacteria that often cause a potentially severe and occasionally life-threatening bacteremic illness. Typhoid fever and paratyphoid fever are not common in the US, Canada, Western Europe, Australia, or Japan, but they are common in many other countries. In the United States, approximately 300 cases of typhoid fever are reported each year, 85% of which are acquired during international travel to countries such as India, Bangladesh, and Pakistan. Typhoid fever and paratyphoid fever are more common in areas of the world where water is more likely to be contaminated with sewage. Ongoing surveillance of *S. Typhi* and *S. Paratyphi* infections is essential to detect and control outbreaks, determine public health priorities, monitor trends in illness, and assess effectiveness of public health interventions.

### CLINICAL DESCRIPTION

Infections caused by *S. Typhi* and *S. Paratyphi* are often characterized by insidious onset of sustained fever (one that does not come and go) that can be as high as 103–104° F (39–40° C), headache, malaise, loss of appetite, relative bradycardia, constipation or diarrhea, and non-productive cough. However, mild and atypical infections may occur. Some people with typhoid fever or paratyphoid fever develop a rash of flat, rose-colored spots on the trunk. Carriage of *S. Typhi* and *S. Paratyphi* may be prolonged. The incubation period of typhoid fever is typically 6-30 days and for paratyphoid fever, 1-10 days. People who do not get treatment can continue to have fever for weeks or months and can develop complications. In some cases, diarrhea may be so severe that the patient needs to be hospitalized. In these patients, the infection may spread from the intestines to the blood stream, and then to other body sites. In these cases, illness can cause death unless the person is treated promptly with antibiotics. The elderly, infants, and those with impaired immune systems are more likely to have a severe illness.

### CASE DEFINITION

#### Clinical Criteria

One or more of the following:

- Fever
- Diarrhea
- Abdominal cramps
- Constipation
- Anorexia
- Relative bradycardia

## Laboratory Criteria for Diagnosis

### Salmonella Typhi Diagnosis

- **Confirmatory laboratory evidence:** Isolation of *S. Typhi* from a clinical specimen.
- **Presumptive laboratory evidence:** Detection of *S. Typhi* in a clinical specimen using a culture-independent diagnostic test (CIDT).

### Salmonella Paratyphi Diagnosis

- **Confirmatory laboratory evidence:** Isolation of *S. Paratyphi* A, B (tartrate negative), or C from a clinical specimen
- **Presumptive laboratory evidence:** Detection of *S. Paratyphi* A, B (Tartrate negative), or C in a clinical specimen using a CIDT.

*Note: Serologic testing (i.e., detection of antibodies to S. Typhi) should not be utilized for case classification. Also, serologic testing (i.e., detection of antibodies to S. Paratyphi A, B, or C) should not be used for case classification.*

### Epidemiologic Linkage

- Epidemiological linkage to a confirmed *S. Typhi* or *S. Paratyphi* infection case, OR
- Epidemiological linkage to a probable *S. Typhi* or *S. Paratyphi* infection case with laboratory evidence, OR
- Member of a risk group as defined by public health authorities during an outbreak.

A new case should be created when a positive laboratory result is received more than 365 days after the most recent positive laboratory result associated with a previously reported case in the same person.

### Case Classification: 2019 Case Definitions

- **Probable:** A clinically compatible illness in a person with presumptive laboratory evidence  
OR A clinically compatible illness in a person with an epidemiological linkage.
- **Confirmed:** A person with confirmatory laboratory evidence

### Comments

Several serological tests have been developed to detect antibodies to *S. Typhi* and to *S. Paratyphi* A, B, and C. However, no current serological test is sufficiently sensitive or specific to replace culture-based tests for the identification of *S. Typhi* or *S. Paratyphi* infections. Whether public health follow-up for positive serologic testing is conducted and how is at the discretion of the jurisdiction.

It is estimated that approximately 2-5% of persons infected with *S. Typhi* become chronic intestinal carriers who continue to shed *S. Typhi* for more than one year. These people are typically referred to as chronic carriers. The percentage of persons with *S. Paratyphi* A, B, (tartrate negative), or C infections that become chronic carriers is not known.

Differentiating whether a person is a chronic carrier or is experiencing a new infection often relies on a variety of factors, including advanced laboratory testing (e.g., pulsed-field gel electrophoresis [PFGE], whole genome sequencing [WGS]) to compare the isolate from the previous infection to the new isolate. While these methodologies can provide detailed information about the genetic make-up of the organisms, there is still significant variability in how two organisms can be defined as different. Given the potential for inconsistent application of the label “different” across jurisdictions, this case definition does not exclude persons with a previously reported *S. Typhi* Infection case from being counted as a new case if the subsequent positive laboratory result is more than 365 days from the most recent positive laboratory result associated with the existing case.

People who are actively ill with typhoid fever or paratyphoid fever and people who are carriers of *Salmonella Typhi* or *Salmonella Paratyphi* bacteria can both spread the bacteria to other people. Carriers are people who have recovered from typhoid fever or paratyphoid fever but continue to carry the bacteria. About 1 in 20 people remain carriers after they’ve recovered. A chronic carrier state, in which stool or urine cultures for *Salmonella Typhi*

remain positive for more than 1 year, occurs in up to approximately 5% of infected persons. Both groups of people shed (excrete) *Salmonella* Typhi or *Salmonella* Paratyphi in their feces (poop).

Because people can remain carriers for a long time and still spread the disease, extra precautions should be taken by people potentially exposed to a confirmed case of disease.

## CASE MANAGEMENT

### S. Typhi and S. Paratyphi Case

The infected *S. Typhi* or *S. Paratyphi* case must have at least 3 consecutive negative cultures of feces at least 24 hours apart, at least 48 hours after any antimicrobials, and not earlier than one month after onset. If any of these are positive, repeat cultures at monthly intervals during the 12 months following onset until at least 3 consecutive negative cultures are obtained.

### S. Typhi and S. Paratyphi Contact

For close contacts and family members of a case, consideration should be given to obtaining 2 negative stool cultures, taken at least 24 hours apart. If the close contact or family member works in a sensitive occupation (like food handlers, patient care or care of young children or elderly persons), they should remain off work until obtaining the 2 negative stool cultures, taken at least 24 hours apart.

Additional considerations:

- **Travel Companions:** All members of a group who travelled with a case should be identified and assessed. The risk of a co-traveler developing infection is higher for anyone who is likely to have been exposed to the same source of infection as the case. It may be helpful to contact the trip organizer to gather names and contact information for every travel companion. Consider using the Outbreak Management System (OMS) for contact tracing.
- **Food handlers:** If the case works as a food handler, coordinate efforts with environmental health and communicable disease sections until clearance testing and exclusions/restrictions are complete. Notify MDARD and MDHHS as mandatory exclusions/restrictions (per the Michigan Food Code) will apply to the case.
- **Healthcare Worker:** If the case works as a healthcare provider, coordinate with occupational or employee health to ensure clearance testing and exclusions/restrictions are completed.
- **Childcare Center Worker or Attendee:** Coordinate with the facility until clearance testing and exclusions/restrictions are completed. Monitoring facility staff and attendees for development of symptoms may be indicated. Consider using OMS for contact tracing.
- **Drug-Resistant Strains (MDR or XDR):** If a case traveled to areas of the world where there are antibiotic-resistant strains of typhoid/paratyphoid infection (such as [Pakistan](#)), susceptibility testing will need to be performed to ensure that the proper antibiotic treatments is given to the case. Be aware that relapses can occur in these patients after initial clinical improvement and the timeline for public health supervision may need to be adjusted.
- **Cases Without an Identified Source of Infection:** Cases with an unknown source of infection (e.g. no recent travel history, or those for whom travel is an unlikely source) should be further assessed and may include contact tracing. Investigations should focus on household members or other close contacts and the possibility of a contaminated food source. This may include testing of immediate and extended family members who have had prior travel to an endemic area or were born in an endemic area, to look for carriage.
- **Cases and Contact that are Lost to Follow-Up:** Consider working with the primary care provider to ensure completion of clearance testing.

## PREVENTION

### Vaccination

Typhoid fever and paratyphoid fever can be prevented. If you are planning to travel outside the US, you should get vaccinated against typhoid fever (there is no vaccine against paratyphoid fever). You should complete the vaccinations at least 1-2 weeks before you travel so that vaccine has time to take effect. Typhoid vaccines lose effectiveness after several years so if you were vaccinated in the past, ask your doctor if it is time for a booster vaccination.

### Food and Water Safety

Contaminated food or drinks can cause diseases. Travelers to developing countries are especially at risk. Reduce your risk by sticking to safe eating and drinking habits from CDC at <https://wwwnc.cdc.gov/travel/page/food-water-safety>

## RESOURCES

Salmonella CDC Website: <https://www.cdc.gov/salmonella/index.html>

Typhoid Fever and Paratyphoid Fever CDC Website: <https://www.cdc.gov/typhoid-fever/index.html>

Travelers' Health Food and Water Safety: <https://wwwnc.cdc.gov/travel/page/food-water-safety>

WHO Guidance for the Management of Typhoid Fever:

<http://apps.who.int/medicinedocs/documents/s20994en/s20994en.pdf>

Heymann, DL. Control of Communicable Diseases Manual – 20<sup>th</sup> Edition. 2015.

Extensively Drug-Resistant Typhoid Fever in Pakistan: <https://wwwnc.cdc.gov/travel/notices/watch/xdr-typhoid-fever-pakistan>

Recognition and Management of Drug-Resistant Typhoid Fever:

[https://www.medscape.com/viewarticle/902953?src=par\\_cdc\\_stm\\_mscpedt&faf=1](https://www.medscape.com/viewarticle/902953?src=par_cdc_stm_mscpedt&faf=1)