# Typhoid Fever and Paratyphoid Fever

**Please note:** While this protocol primarily references typhoid fever (infection with *Salmonella* Typhi), this protocol can be used to investigate cases of paratyphoid fever (infection with *Salmonella* Paratyphi A, B (tartrate negative), and C) as well. This is due to typhoid fever and paratyphoid fever having very similar clinical descriptions, modes of transmission, incubation periods, and periods of communicability. *During various sections of this protocol, the differences between paratyphoid fever and typhoid fever will be noted.*

## A. Agent:

Typhoid fever

Typhoid fever is a life-threatening illness caused by the bacterium *Salmonella* Typhi[1].

Paratyphoid fever

Paratyphoid fever is a life-threatening illness caused by the bacterium *Salmonella* Paratyphi A, B (tartrate negative), and C[9].

## B. Clinical Description:

Typhoid fever

An illness caused by *Salmonella* Typhi that is often characterized by insidious onset of sustained fever[2-4], headache[2-4], malaise[2-4] , anorexia[2-4], relative bradycardia[2,3], constipation or diarrhea[2,3], and nonproductive cough[2]. However, many mild and atypical infections occur[2]. Carriage of *Salmonella* Typhi may be prolonged[2].

Paratyphoid fever

An illness caused by *Salmonella enterica* serotypes Paratyphi A, Paratyphi B (tartrate negative), and Paratyphi C that is often characterized by insidious onset of sustained fever, headache, malaise, anorexia, relative bradycardia, constipation or diarrhea, and nonproductive cough[9]. However, mild and atypical infections may occur. Carriage of paratyphoidal *Salmonella* may be prolonged[9].

## C. Reservoirs:

*Salmonella* Typhi has no known natural reservoir outside of humans[1-3]. *Salmonella* Paratyphi A, B, and C also do not have any known natural reservoir outside of humans[14].

## D. Mode of Transmission:

*Salmonella* Typhi[1-3] and Salmonella Paratyphi[14] are only known to live in humans[1-3]. Persons with typhoid fever carry the bacteria in their bloodstream and intestinal tract[1]. In addition, a small number of persons, called carriers, recover from typhoid fever but continue to carry the bacteria[1,2]. Both ill persons and carriers shed *Salmonella* Typhi in their feces (stool) [1].

Typhoid and paratyphoid fever are most often acquired through consumption of water or food that has been contaminated by feces of an acutely infected or convalescent person or a chronic, asymptomatic carrier[2]. Transmission through sexual contact, in particular among men who have sex with men, has been documented rarely[2].

**E. Incubation Period:**

The incubation period of typhoid and paratyphoid fever is usually 7-14 days with a range of 3-60 days[3].

**F. Period of Communicability:**

*Salmonella* Typhi and *Salmonella* Paratyphi can continue to spread as long as the bacteria are present in the stool. A chronic carrier state--excretion of the organism for more than 1 year--occurs in approximately 2-5% of infected persons with typhoid fever[6].

**G. Susceptibility and Resistance:**

All humans are susceptible. Risk is very low in the U.S, higher among international travelers, and highest among people living in places with poor sanitation and hygiene[6]. Lifelong immunity usually follows natural infection; reinfections are rare[7]. Immunization with *S.* Typhi vaccine confers protection against *S.* Typhi for two to three years or longer[13]. There is currently no vaccine available to prevent paratyphoid fever[15].

**H. Treatment:**

Typhoid and paratyphoid fever can both be treated with antibiotics[4]. As resistance to antibiotics has emerged including to fluoroquinolones, newer antibiotics such as cephalosporins and azithromycin are used in the regions affected by typhoid fever; resistance to azithromycin has been reported sporadically but it is not common as of yet[8]. Even when the symptoms of typhoid fever go away, people may still be carrying typhoid bacteria, meaning they can spread it to others through their faeces[8].

**I. Clinical Case Definition[9]:**



Typhoid fever

An illness caused by *Salmonella enterica* serotype Typhi (*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.

Paratyphoid fever

An illness caused by *Salmonella enterica* serotypes Paratyphi A, Paratyphi B (tartrate negative), and Paratyphi C that is often characterized by insidious onset of sustained fever, headache, malaise, anorexia, relative bradycardia, constipation or diarrhea, and nonproductive cough. However, mild and atypical infections may occur. Carriage of paratyphoidal *Salmonella* may be prolonged.

**J. Laboratory Criteria for Diagnosis[9]:**

Typhoid fever

- Isolation of *Salmonella* Typhi from a clinical specimen.
- Detection of *S*. Typhi in a clinical specimen using a culture-independent diagnostic test (CIDT).

Paratyphoid fever

- Isolation of *Salmonella* Paratyphi A, Paratyphi B (tartrate negative) or Paratyphi C from a clinical specimen.
- Detection of *Salmonella* Paratyphi A, Paratyphi B (tartrate negative) or Paratyphi C in a clinical specimen using a culture-independent diagnostic test (CIDT).

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

*S. *Paratyphi B variant L(+) tartrate(+) causes salmonellosis, not paratyphoid fever.*

| Case Classification | |
|---|---|
| **Confirmed** | A person with confirmatory laboratory criteria. |
| **Probable** | A clinically compatible illness in a person with presumptive laboratory evidence, or a clinically compatible illness in a person with an epidemiological linkage. |

**K. Classification of Import Status:**

Import status reflects where the *Salmonella* Typhi and Paratyphi infection was acquired: in county, in state, international, out of county but in Arizona, out of state but in U.S., or location of infection is unknown. Mark as *bi-national* if infection was acquired in Canada or Mexico or food was consumed from Canada or Mexico and was not purchased in a U.S. store during the exposure period. For more information, please refer to the MEDSIS User Guide. You can find the guide in MEDSIS under: Resources → MEDSIS Documentation → User Guides.

**L. Laboratory Testing:**

Gold standard is culture. Testing for *Salmonella* is typically included in clinical laboratories' routine stool culture. Stool, blood, or urine samples are preferred. For health departments to facilitate stool specimen submission for testing at ASPHL, instructions for collecting stool specimens are available at: https://azdhs.gov/preparedness/epidemiology-disease-control/index.php#reporting-labs

| TEST[10] | SPECIMEN & TRANSPORT[10] | TESTING AVAILABILITY[10] |
|---|---|---|
| **Culture** | Feces (Cary-Blair transport medium), blood, or urine | Routine stool culture for enteric pathogens |
| ***Salmonella* Serotyping** | Pure culture of isolate in a culture plate/slant (TSI or nutrient agar slant) | ASPHL. Performed for epidemiological purposes using whole genome sequencing. Results available 14 days after submission |
| ***Salmonella* isolation (food)** | Food product (200 grams of a solid product or about 100 ml of a liquid) collected in a sterile container and packed in a leak-proof shipping container | ASPHL. Rapid tests take 1-2 days. Preliminary results available in 48-72 hours. Confirmatory |

| | | |
|---|---|---|
| | with sealed ice packs (must be kept cold <10°C during transport) | results available in 3-11 days. |
| **Serotyping and Whole Genome Sequencing (WGS)** | Pure culture of isolate in a culture plate/slant (TSI or nutrient agar slant) | ASPHL |

See Arizona Department of Health Services (ADHS) Guide to Laboratory Services: Microbiology: https://www.azdhs.gov/preparedness/state-laboratory/public-health-microbiology/index.php

**M. Assessing Laboratory Results:**

A new case of typhoid fever or paratyphoid fever 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.

Paratyphi B (tartrate negative) is categorized as salmonellosis instead of an *S.* Paratyphi Infection. The *Salmonella* serotype Paratyphi B var L(+) tartrate (+) causes salmonellosis, not paratyphoid fever.

**N. Outbreak Definition:**

Since we do not expect to see any locally acquired typhoid or paratyphoid fever cases, any 1 case with suspected exposure within Arizona should be treated and investigated as an outbreak.

- Diagnosis or detection of two or more cases from different households and families who experience an illness clinically compatible with *Salmonella* Typhi or *Salmonella* Paratyphi A, B (tartrate negative), or C infection, at least one with laboratory-confirmed *S.* Typhi or *S.* Paratyphi A, B (tartrate negative), or C infection, after exposure to a common food or a shared experience; **OR**
- An unexplained, unexpected increase in cases of laboratory-confirmed *Salmonella* Typhi of *Salmonella* Paratyphi infections that is clustered by time, place, or person.
- An outbreak investigation is triggered when *Salmonella* Typhi or Paratyphi A, B (tartrate negative), or C isolates from two or more individuals collected within 60 days of each other are determined to be highly related by WGS.

**O. Time Frame[11]:**

All confirmed and probable cases of typhoid fever are to be reported within 24 hours to the Local Health Department. Outbreaks should be entered into the MEDSIS Outbreak Module within 24 hours of receipt of report. *Typhoid and paratyphoid fever report form (shown in section P) should be sent to CDC within 30 days after specimen obtained.*



**P. Forms:**

- Please refer to the Department-provided formats for submitting Epidemiologic Investigation Reports for guidance on the required fields and forms for each morbidity.

- ADHS Reporting & Investigation Forms: https://www.azdhs.gov/preparedness/epidemiology-disease-control/index.php#investigations-forms

**Q. Investigation Steps:**

**Confirm Diagnosis**

i. Contact health care provider/facility to obtain demographic and clinical information.
ii. If case was hospitalized, obtain medical records including admission notes, progress notes, lab report, and discharge summary.
iii. Facilitate forwarding of specimens to the Arizona State Public Health Laboratory.

**Conduct Case Investigation**

i. Cases should be entered into MEDSIS as soon as possible and contacted by the investigator.
    a. The investigator will attempt three phone calls, or text messages following unreturned voicemails, before sending a letter to the patient's address (depending upon local health department's protocols and capacity).
    b. All interview attempts, even if unsuccessful (i.e., leaving a voicemail or text message), should be entered into the Case Contacted & Interviews table in MEDSIS as close to real time as possible.
    c. If phone numbers appear invalid or non-functioning, contact food@azdhs.gov to request a LexisNexis search. This can be conducted for individuals 18 years and older. For those younger than 18, a parent/guardian name must be used to search in LexisNexis; otherwise, a search can be conducted in ASIIS for the individual under 18 years of age.
ii. Report electronically through MEDSIS; and use the CDC Typhoid and Paratyphoid Fever Surveillance Report Form (see link to forms in section P, above) to conduct your investigation. Attach form to MEDSIS case once it is complete.
    a. Ask questions about international travel, sick contacts, and country of origin.
    b. Inquire about where the case may volunteer or be employed. Food handlers, those in daycare or caring for children, and those providing patient care will require exclusion per A.A.C. R9-6-311.
    c. Educate case on transmission routes and the importance of handwashing.
iii. The ADHS Foodborne Disease Epidemiologist, Environmental Health Food Safety Program Manager, and Medical Director are available as resources.

**Conduct Contact Investigation**

- Inquire about case's activities and occupations since their symptoms began.
- Record any food handling, healthcare (providing direct patient contact) and child care association (including nursery school, preschool, or baby-sitting group), either as attendee, employee, or household contact to attendee or employee. Include dates, location, and activities.
- Consider case's occupation and activities; identify the following contacts:
    a. Close personal contacts:
        i. Household and sexual contacts.
        ii. Persons who have shared illicit drugs with an infectious case.
        iii. Person with other types of ongoing, close personal contact evaluated on a case-by-case basis (e.g. regular babysitting of infectious child).
    b. High-risk contacts: those more likely to experience adverse outcomes from infection (people with blood clotting disorder or chronic liver disease) and whose child care

association, occupation, or personal activities could result in further transmission of the virus.

c. Child care facility contacts.
d. Hospital/long-term care facility contacts.
e. Food service contacts:
    i. Co-workers who work the same shift as the infected food handler.
    ii. Patrons of the establishment of an infected food handler if:
        1. The food handler worked while infectious AND
        2. The food handler had diarrhea while working AND
        3. The food handler had the opportunity to have bare-hand contact with ready-to-eat food or if the facility's sanitation practices are deficient.

- Identify and create a line list of primary contacts.
- Follow up symptomatic contacts as probable cases.

### Initiate Control and Prevention Measures

Per **A.A.C. R9-6-388**[11], a local health agency shall exclude a typhoid fever contact from working as a food handler, caring for children in or attending a child care establishment, or caring for patients or residents in a health care institution until:

At least one month after the date of onset of illness; and

After two successive stool specimens, collected from the typhoid fever case at least 24 hours apart and at least 48 hours after cessation of antibiotic therapy, are negative for *Salmonella typhi*.

### Case Management

i. Educate case on measures to avoid future illness and its transmission.
    - In particular, educate on the importance and effectiveness of washing hands with soap and water after using the bathroom and before preparing, serving, or eating food.
ii. To assure compliance with work restrictions, follow-up is indicated if a case handles food or cares for young children, the elderly, or patients or residents in a health care institution.
iii. Refer to A.A.C. R9-6-388 for individuals who continue to test positive following antibiotic therapy.

### Contact Management

i. Symptomatic contact (such as household members, sexual partners and members of a travel party): Considered a probable case; initiate any work or daycare/school restrictions. Encourage to seek medical evaluation.
ii. Follow-up of contacts may be needed to ensure no further transmission of disease occurs.
iii. Make arrangements for specimen collection if necessary.
iv. Immunization of contacts with typhoid fever vaccine is not generally recommended, but should be considered for individuals with ongoing household and intimate exposure to a known *S.* Typhi carrier[2].

### Notifications

i. Cases of typhoid and paratyphoid fever should be reported within 24 hours.
ii. Report data electronically via MEDSIS or by fax if necessary, including:
    - All essential data that was collected during the investigation, especially data that helps to confirm or classify a case. Remember to verify that all key Disease Specific Observation fields are filled out.
    - For epi-linked cases, please include the MEDSIS ID of the related case in the case notes section.

iii. If appropriate, work with Public Information Officer to ensure appropriate and timely dissemination of public information.
iv. ADHS will notify CDC and federal regulatory agencies (FDA, USDA) if needed.

**R. Outbreak Guidelines:**

Refer to the Outbreak Investigation Guide. For complete guidelines to investigating foodborne outbreaks, consult ADHS Foodborne and Waterborne Disease Outbreak Investigation Resource Manual[12].

**S. Special Situations:**

Special Situations

Intentional Contamination:

- If suspected, notify supervisors and preparedness staff.
- Consider ADHS epidemiologic and law enforcement guidance.
- Implement chain-of-custody procedures for all samples collected, as they will be considered evidence in a criminal investigation.
- Refer to the Zebra Manual: A Reference Handbook for Bioterrorism Agents.

## Additional Information & Resources

**Laboratory References:**

- ADHS Guide to Laboratory Services: Microbiology: http://www.azdhs.gov/lab/documents/microbiology/lab-guide.pdf
- Directions for collection of stool specimens: https://azdhs.gov/preparedness/epidemiology-disease-control/index.php#reporting-labs

**Foodborne and Waterborne Disease Outbreak Investigation Resource Manual:**
http://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/disease-investigation-resources/foodborne-waterborne-disease-outbreak-manual.pdf

**ADHS Zebra Manual**:
Division of Public Health Services, Bureau of Public Health Emergency Preparedness.
https://www.azdhs.gov/zebramanual.pdf

**CDC Typhoid Fever:**
https://www.cdc.gov/typhoid-fever/index.html

# References


1. Centers of Disease Control and Prevention. Typhoid Fever – General Information [Internet]. Centers of Disease Control and Prevention. Centers for Disease Control and Prevention; 2014 [cited 2022Feb07]. Available from: https://www.cdc.gov/typhoid-fever/about/?CDC_AAref_Val=https://www.cdc.gov/typhoid-fever/sources.html
2. Mintz E, Slayton M, Walters M. Typhoid Fever and Paratyphoid Fevers. In: Heymann DL, editor. Control of communicable diseases manual. 20th ed. Washington, DC: American Public Health Association; 2015. p. 654-660.

3. American Academy of Pediatrics. 2021 Red Book: Report of the Committee on Infectious Disease, 32nd Edition. Illinois, Academy of Pediatrics, 2021.
4. Centers of Disease Control and Prevention. Typhoid Fever – Symptoms & Treatment [Internet]. Centers of Disease Control and Prevention. Centers for Disease Control and Prevention; 2016 [cited 2022Feb07]. Available from: https://www.cdc.gov/typhoid-fever/signs-symptoms/?CDC_AAref_Val=https://www.cdc.gov/typhoid-fever/symptoms.html
5. World Health Organization. Typhoid Fever [Internet]. World Health Organization. World Health Organization; 2018 [cited 2022Feb07]. Available from: https://www.who.int/news-room/fact-sheets/detail/typhoid
6. Centers of Disease Control and Prevention. Typhoid Fever – For Healthcare Professionals [Internet]. Centers of Disease Control and Prevention. Centers for Disease Control and Prevention; 2013 [cited 2022Feb07]. Available from: https://www.cdc.gov/typhoid-fever/hcp/clinical-overview/?CDC_AAref_Val=https://www.cdc.gov/typhoid-fever/health-professional.html
7. WORLD HEALTH ORG. Typhoid vaccines: WHO position paper. *Weekly Epidemiological Record* 2008;83:49-60.
8. BAHN MK, BAHL R, and Bhatnagar S. Typhoid and paratyphoid fever. *Lancet* 2005; 366:749-762.
9. Arizona Department of Health Services. In: Case Definitions for Reportable Communicable Morbidities: 2022. 2022 [cited 2022Feb24]; Available from: https://www.azdhs.gov/documents/preparedness/epidemiology-disease-control/disease-investigation-resources/casedefinitions/case-definitions.pdf
10. Waddell V, Lavine DM, Slanta WM. Guide to Laboratory Services: Microbiology [Internet]. Guide to Laboratory Services: Microbiology. Arizona Department of Health Services; 2019 [cited 2022Feb07]. Available from: http://azdhs.gov/documents/preparedness/state-laboratory/public-health-microbiology/lab-guide.pdf
11. Arizona Administrative Code. 2013Sep30 [cited 2022Feb07]. Available from: http://apps.azsos.gov/public_services/Title_09/9-06.pdf
12. Arizona Department of Health Services. Foodborne and Waterborne Disease Outbreak Investigation Resource Manual [Internet]. Arizona Department of Health Services; 2010 [cited 2017May11]. Available from: http://azdhs.gov/documents/preparedness/epidemiology-disease-control/disease-investigation-resources/outbreak-investigation-resource-manual.pdf
13. CDC. Typhoid Fever and Paratyphoid fever - Vaccination. Available at https://www.cdc.gov/typhoid-fever/typhoid-vaccination.html#:~:text=Typhoid%20vaccines%20are%20not%20100,a%20booster%20every%205%20years
14. CDC. Traveler's Health - Typhoid and Paratyphoid fever. Available at https://www.cdc.gov/yellow-book/hcp/travel-associated-infections-diseases/typhoid-and-paratyphoid-fever.html
15. WHO. Paratyphoid fever. Available at https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/paratyphoid-fever#:~:text=There%20is%20currently%20no%20vaccine,are%20licensed%20vaccines%20for%20S.