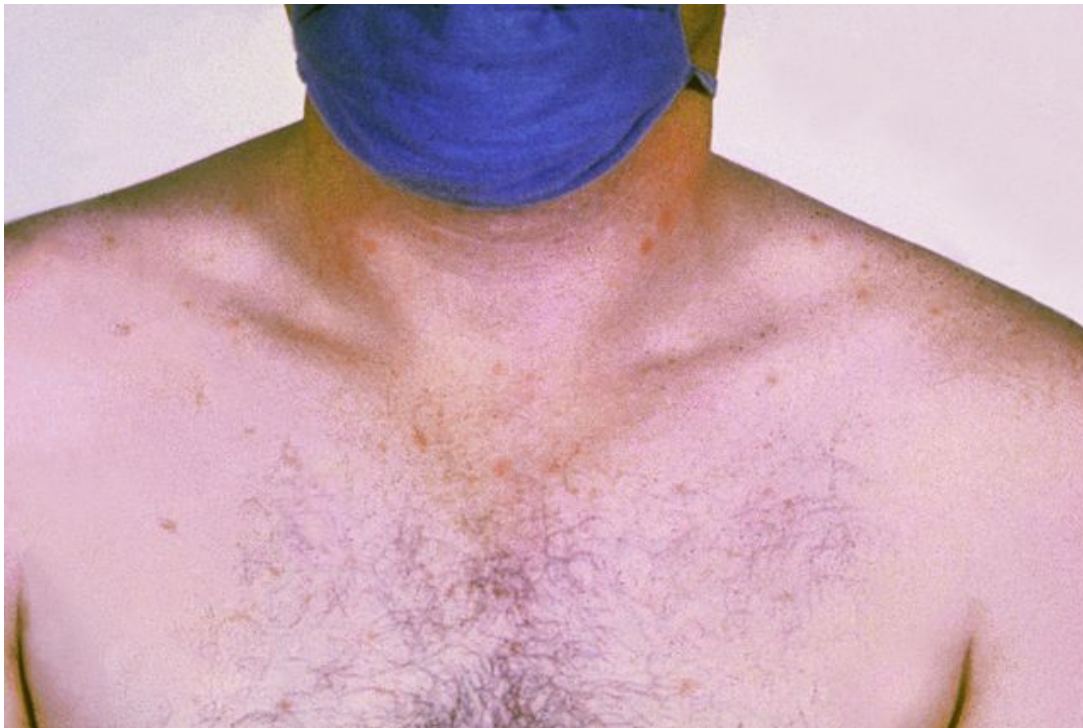


Enteric Fever (Typhoid Fever) — Definition and Diagnosis

[See online here](#)

Enteric fever is caused by the *Salmonella Typhi* species. Affected individuals present with a high-grade fever that is cyclic, abdominal pain, headaches, and constipation. Recent travel history to endemic areas is usually positive in most cases. The clinical picture should be enough to start empirical antibiotic therapy with ceftriaxone and ciprofloxacin. Once culture and sensitivity results are available, the patient should be switched to a more specific narrow-spectrum antibiotic.



Definition of Enteric Fever

Enteric fever, also known as **typhoid fever**, is a **systemic illness** caused by ***Salmonella enterica*** which presents with high fever, abdominal pain, [headaches](#) and sometimes a skin rash. The most commonly implicated subspecies is known as ***enterica* serovar Typhi** and to a lesser extent serovars **Paratyphi A, B, and C**. **the organisms will be** simplified as *Salmonella Typhi* and *Paratyphi* for easier reference in this article.

Epidemiology of Enteric Fever

Salmonella infections are related to **sanitation** and the **use of antibiotics** in the society. Since the introduction of antibiotics in the United States and the improved sanitation conditions, the cases of Salmonella typhi have decreased dramatically. The most recent report shows only **314 cases** of Salmonella Typhi infection in 2006 in the United States. In the developing world salmonella, outbreaks are seen during war times and other periods where there is a breakdown in sanitation and the availability of medications.

Salmonella Typhi is transmitted by the **inadequate handling of infected food products**, especially imported food from endemic areas.

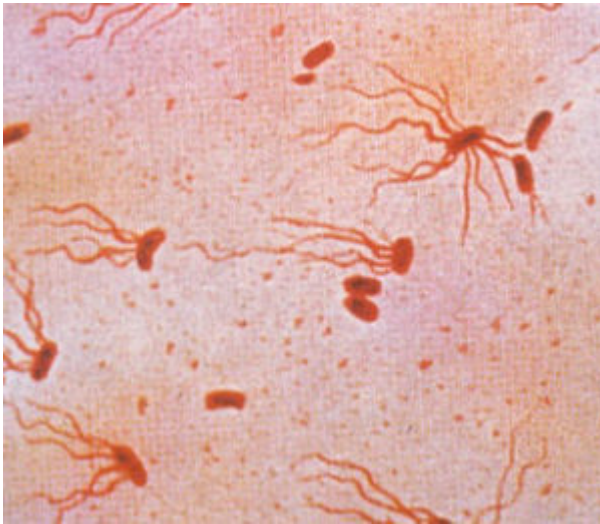


Image: "Salmonella Typhi." by Roinujs - Own Work. License: [CC BY-SA 4.0](#)

The estimated incidence of typhoid fever in the United States is less than 1 per million. On the other hand, approximately 7.6 per million are affected by enteric fever per year in Africa. India has the highest incidence of enteric fever - 122 per million per year.

Nowadays, **mortality** from enteric fever is **very unlikely**. The median duration of hospitalization for patients diagnosed with enteric fever is around 6 days. If left untreated, most patients develop **serious central nervous system complications**. The mortality rate without prompt antibiotic therapy is approximately 13%.

The most commonly affected age group with enteric fever are **school-aged children**. Infants might also develop enteric fever, but the presentation is usually atypical and difficult to identify.

Pathophysiology of Enteric Fever

Salmonella non-Typhi species, when present in the gut, are first engulfed by **phagocytes**. Once this happens, the phagocytes present the bacteria to the **macrophages** found in the **lamina propria**. Macrophages identify the organism and produce **inflammatory mediators** such as interleukin-8 which attracts T cells and neutrophils.

It is currently believed that salmonella Typhi gets **entry to the bloodstream** via specialized fimbriae attachment to the epithelium over the **Peyer patches**, which are

specialized clusters of lymphoid tissue in the **ileum**. Once there, the bacteria are able to travel through the **lymphatic system**.

Salmonella Typhi has a **specialized Vi capsular antigen** that makes it difficult for neutrophils to identify the organism and produce an appropriate inflammatory response. This important virulence feature is hypothesized to be responsible for the increased invasiveness of Salmonella Typhi compared to other salmonella species.

Salmonella Typhi can also cause a **chronic carrier state** that is usually asymptomatic. These individuals are usually responsible for **typhoid fever outbreaks** and, with adequate epidemiological studies, one can trace typhoid fever endemics to certain carriers.

The most important risk factors for typhoid fever are related to **poor hygiene, poor handling of food items** and **drinking sewage-contaminated water**. Therefore, education about good food handling practices and improving sanitation are known to lower the risk of acquiring Salmonella typhi significantly.

Clinical Presentation of Enteric Fever

The typical **incubation period** is usually one to two weeks. **Fever** builds up gradually during the day and then drops down the next morning. This cyclic pattern is usually evident in most patients.

Patients develop **severe abdominal pain, abdominal tenderness**, and **constipation**. Constipation is thought to result from the **enlargement of the Peyer patches** in the bowel. This gastrointestinal stage usually lasts for one week and is then followed by a **dry cough, frontal headaches**, and **delirium**. Once the patient develops these late symptoms, they become very **tired** and develop **malaise**.

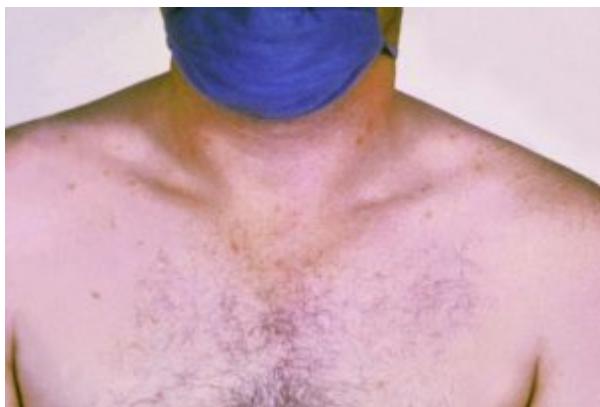


Image: "Rose spots as seen in enteric fever." by CDC/Armed Forces Institute of Pathology, Charles N. Farmer - This media comes from the Centers for Disease Control and Prevention's Public Health Image Library (PHIL), with identification number #2215. License: Public Domain

After one week, the **fever** becomes constant at 39 to 40 Celsius degrees. The patients, at this stage, also develop a characteristic **skin rash** that has rose spots and **blanching truncal maculopapules**.

In the second week of the illness, patients develop **abdominal distension** and **splenomegaly**. **Bradycardia** is also common in the second week.

If still untreated, patients develop **severe confusion, altered mental state, severe**

abdominal distension, and **green-yellow diarrhea** in the third week. Patients can also develop **bowel perforation** due to Peyer patches necrosis. **Weight loss** is evident by this stage.

Patients who survive the disease without treatment are likely to develop **permanent neurological sequelae**. Treated patients do not show this typical picture. Instead, their illness usually subsides within four days and they markedly improve without the development of constant fever, neurological symptoms or other complications.

Diagnostic Workup for Enteric Fever

The diagnostic of enteric fever is a clinical one; still, many laboratory investigations can be helpful to confirm the diagnosis. The best diagnostic modality is **culturing of the organism**.

Bone marrow cultures are helpful in the confirmation of the diagnosis, even after starting antibiotic therapy, but this procedure is too painful to be considered in every patient presenting with enteric fever. Instead, **blood and intestinal secretions or stool cultures** are usually sufficient to confirm the diagnosis. They can yield a positive result in approximately 90% of the cases. **Multiple blood cultures**, usually more than three blood samples, can increase the sensitivity to approximately 97%.

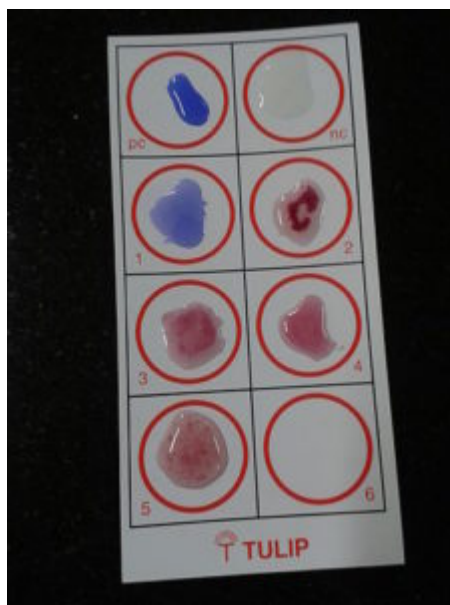


Image: "A Widal Test slide showing agglutinations in reactions of corresponding O and H antigens." by Sujith - Own work. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

Polymerase chain reaction testing is available as a research tool to identify *Salmonella typhi* from blood and urine samples. This technique has a sensitivity of about 82.7% and a specificity of 100%. Unfortunately, these tests are not available for clinical practice, but they are rarely needed as the clinical picture and history of exposure are usually evident.

The Widal serological test can help support the diagnosis of *Salmonella typhi*, but should not be considered as a confirmatory test. Instead, patients who have a positive Widal test should undergo a culture or a DNA confirmatory test to confirm the diagnosis.

IgM and IgG antibodies can be detected using **indirect enzyme-linked**

immunosorbent assay (ELISA) and the results are promising.

Because enteric fever is a systemic condition, the **erythrocyte sedimentation rate** is usually elevated. Patients can also develop **thrombocytopenia** and **lymphopenia**. **Elevated prothrombin** and **activated partial thromboplastin time**, combined with **low fibrinogen levels**, are also commonly seen in patients with typhoid fever.

People suspected to have **intraabdominal abscesses** should undergo computed tomography scanning or magnetic resonance imaging.

Treatment of Enteric Fever

Any patient presenting with the pattern of fever described above, which is also associated with **severe abdominal pain** and **constipation**, should be questioned about **recent travel history to endemic areas**. If travel history is positive, **antibiotic treatment** should be started immediately and the previously mentioned laboratory investigations should not delay the treatment.

Empirical therapy for typhoid fever consists of **ceftriaxone** combined with **ciprofloxacin**. This empirical antibiotic regimen should be used temporarily until confirmatory tests and culture results are back with sensitivity profiles. Once the sensitivity profile of the infecting *Salmonella typhi* is known, **narrow-spectrum antibiotic therapy** should be switched to.

References

Bhan MK, Bahl R, Bhatnagar S. Typhoid and paratyphoid fever. *Lancet*. 2005 Aug 27-Sep 2;366(9487):749-62. PubMed PMID: 16125594.

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