

LIVESAY EXPEDITIONS & ADVENTURES

Typhoid and Paratyphoid Fever

Eric Mintz

Infectious Agent

Typhoid fever is an acute, life-threatening febrile illness caused by the bacterium *Salmonella enterica* serotype Typhi. Paratyphoid fever is a similar illness caused by *S. Paratyphi* A, B, or C.

Mode of Transmission

- Humans are the only source. No animal or environmental reservoirs have been identified.
- Typhoid and paratyphoid fever are most often acquired through consumption of water or food that have been contaminated by feces of an acutely infected or convalescent individual or a chronic asymptomatic carrier.
- Transmission through sexual contact, especially among men who have sex with men, has rarely been documented.

Occurrence

- An estimated 22 million cases of typhoid fever and 200,000 related deaths occur worldwide each year; an additional 6 million cases of paratyphoid fever are estimated to occur annually.
- Approximately 400 cases of typhoid fever and 150 cases of paratyphoid fever are reported to CDC each year among persons with onset of illness in the United States, most of whom are recent travelers.

Risk for Travelers

- Risk is greatest for travelers to South Asia (6 to 30 times higher than all other destinations). Other areas of risk include East and Southeast Asia, Africa, the Caribbean, and Central and South America.
- Travelers to South Asia are at highest risk for infections that are nalidixic acid-resistant or multidrug-resistant (i.e., resistant to ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole).
- Travelers who are visiting friends or relatives are at increased risk (see the [VFR](#) section in Chapter 8).
- Although the risk of acquiring typhoid or paratyphoid fever increases with the duration of stay, travelers have acquired typhoid fever even during visits of less than 1 week to countries where the disease is endemic.

Clinical Presentation

- The incubation period of typhoid and paratyphoid infections is 6–30 days. The onset of illness is insidious, with gradually increasing fatigue and a fever that increases daily from low-grade to as high as 102° F–104° F (38.5° C–40° C) by the third to fourth day of illness. Headache, malaise,

and anorexia are nearly universal. Hepatosplenomegaly can often be detected. A transient, macular rash of rose-colored spots can occasionally be seen on the trunk.

- Fever is commonly lowest in the morning, reaching a peak in late afternoon or evening. Untreated, the disease can last for a month. The serious complications of typhoid fever generally occur only after 2–3 weeks of illness, mainly intestinal hemorrhage or perforation, which can be life threatening.

Diagnosis

- Infection with typhoid or paratyphoid fever results in a very low-grade septicemia. Blood culture is usually positive in only half the cases. Stool culture is not usually positive during the acute phase of the disease. Bone-marrow culture increases the diagnostic yield to about 80% of cases.
- The Widal test is an old serologic assay for detecting IgM and IgG antibodies to the O and H antigens of *Salmonella*. The test is unreliable, but is widely used in developing countries because of its low cost. Newer serologic assays are somewhat more sensitive and specific than the Widal test, but are infrequently available.
- Because there is no definitive test for typhoid or paratyphoid fever, the diagnosis often has to be made clinically. The combination of a history of being at risk for infection and a gradual onset of fever that increases in severity over several days should raise suspicion of typhoid or paratyphoid fever.

Treatment

- Specific antimicrobial therapy shortens the clinical course of typhoid fever and reduces the risk for death.
- Empiric treatment of typhoid or paratyphoid fever in most parts of the world would utilize a fluoroquinolone, most often ciprofloxacin. However, resistance to fluoroquinolones is highest in the Indian subcontinent and increasing in other areas. Injectable third-generation cephalosporins are often the empiric drug of choice when the possibility of fluoroquinolone resistance is high.
- Patients treated with an appropriate antibiotic still require 3–5 days to defervesce completely, although the height of the fever decreases each day. Patients may actually feel worse during the time that the fever is starting to go away. If fever does not subside within 5 days, alternative antimicrobial agents or other foci of infection should be considered.

Preventive Measures for Travelers

Vaccine

- CDC recommends typhoid vaccine for travelers to areas where there is a recognized increased risk of exposure to *S. Typhi*.
- The typhoid vaccines currently available do not offer protection against *S. Paratyphi* infection.
- Travelers should be reminded that typhoid immunization is not 100% effective, and typhoid fever could still occur.
- Two typhoid vaccines are currently available in the United States.
 - Oral live, attenuated vaccine (Vivotif vaccine, manufactured from the Ty21a strain of *S. Typhi* by Crucell/Berna) (*Updated July 27, 2009*)
 - Vi capsular polysaccharide vaccine (ViCPS) (Typhim Vi, manufactured by sanofi

pasteur) for intramuscular use

- Both vaccines protect 50%–80% of recipients.
- Table 2-10 provides information on vaccine dosage, administration, and revaccination. The time required for primary vaccination differs for the two vaccines, as do the lower age limits.
- Primary vaccination with oral Ty21a vaccine consists of four capsules, one taken every other day. The capsules should be kept refrigerated (not frozen), and all four doses must be taken to achieve maximum efficacy. Each capsule should be taken with cool liquid no warmer than 37° C (98.6° F), approximately 1 hour before a meal. This regimen should be completed 1 week before potential exposure. The vaccine manufacturer recommends that Ty21a not be administered to infants or children <6 years of age.
- Primary vaccination with ViCPS consists of one 0.5-mL (25-µg) dose administered intramuscularly. One dose of this vaccine should be given at least 2 weeks before expected exposure. The manufacturer does not recommend the vaccine for infants and children <2 years of age.

Vaccine Safety and Adverse Reactions

Information on adverse reactions is presented in Table 2-11. Information is not available on the safety of these vaccines in pregnancy; it is prudent on theoretical grounds to avoid vaccinating pregnant women. Live, attenuated Ty21a vaccine should not be given to immunocompromised travelers, including those infected with HIV. The intramuscular vaccine presents a theoretically safer alternative for this group. The only contraindication to vaccination with ViCPS vaccine is a history of severe local or systemic reactions after a previous dose. Neither of the available vaccines should be given to persons with an acute febrile illness.

Precautions and Contraindications

Theoretical concerns have been raised about the immunogenicity of live, attenuated Ty21a vaccine in persons concurrently receiving antimicrobials (including antimalarial chemoprophylaxis), IG, or viral vaccines. The growth of the live Ty21a strain is inhibited in vitro by various antibacterial agents. Vaccination with Ty21a should be delayed for >72 hours after the administration of any antibacterial agent. Available data do not suggest that simultaneous administration of oral polio or yellow fever vaccine decreases the immunogenicity of Ty21a. If typhoid vaccination is warranted, it should not be delayed because of administration of viral vaccines. Simultaneous administration of Ty21a and IG does not appear to pose a problem.

Table 2-10. Dosage and schedule for typhoid fever vaccination

Vaccination	Age (Years)	Dose/Mode of Administration	No. of Doses	Dosing Interval	Boosting Interval
Oral, live, attenuated Ty21a vaccine (Vivotif)					
Primary series	≥6	1 capsule ¹ , oral	4	48 hrs	Not applicable
Booster	≥6	1 capsule ¹ , oral	4	48 hrs	Every 5 years
Vi Capsular polysaccharide vaccine (Typhim Vi)					
Primary series	≥2	0.50 mL, intramuscular	1	Not applicable	Not applicable
Booster	≥2	0.50 mL, intramuscular	1	Not applicable	Every 2 years

¹Administer with cool liquid no warmer than 98.6°F (37°C).

Table 2-11. Common adverse reactions to typhoid fever vaccines

Vaccine	Reactions		
	Fever	Headache	Local Reactions
Ty21a¹	0%–5%	0%–5%	Not applicable
Vi Capsular polysaccharide	0%–1%	16%–20%	7% erythema or induration 1 cm

¹The side effects of Ty21a are rare and mainly consist of abdominal discomfort, nausea, vomiting, and rash or urticaria.

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