

Review Article

Epidemiology and Clinical Features of Typhoid Fever: Burden in Bangladesh

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ABSTRACT

Typhoid fever is a systemic infection caused by *Salmonella typhi* or by the related but less virulent *Salmonella paratyphi*. The provision of clean water and good sewage systems led to a dramatic decrease in the incidence of typhoid in these regions. Early antibiotic therapy has transformed a previously life-threatening illness of several weeks' duration with an overall mortality rate approaching 20.0% into a short-term febrile illness with negligible mortality. Case fatality rates of 10.0-50.0% have been reported from endemic countries when diagnosis is delayed. Attack rates are highest in persons younger than 20 years or older than 70 years; however, the highest rate is found in infants. Neonates are at a greater risk to fecal-oral transmission secondary to relative decreased stomach acidity and buffering of ingested breast milk and formula. Elderly persons are at a relative greater risk to infection secondary to chronic underlying illness and weakened immunity. In endemic areas, children aged 1-5 years are at the highest risk of infection, morbidity, and mortality because of waning of passively acquired maternal antibody and a lack of acquired immunity. In young children, the clinical syndrome is often a nonspecific febrile illness that is not recognized as typhoid fever. Typhoid is usually contracted by ingestion of food or water contaminated by fecal or urinary carriers excreting *S. enterica* serotype *typhi*. It is a sporadic disease in developed countries that occurs mainly in returning traveler, with occasional point-source epidemics. In endemic areas, identified risk factors for disease include eating food prepared outside the home, such as ice cream or flavored iced drinks from street vendors, drinking contaminated water, having a close contact or relative with recent typhoid fever, poor housing with inadequate facilities for personal hygiene, and recent use of antimicrobial drugs. The infectious dose of *S. enterica* serotype *typhi* in volunteers varies between 1000 and 1 million organisms. Vi-negative strains of *S. enterica* serotype *typhi* are less infectious and less virulent than Vi-positive strains. *S. enterica* serotype *typhi* must survive the gastric acid barrier to reach the small intestine, and a low gastric pH is an important defense mechanism.

Keywords: epidemiology, clinical features, typhoid fever, enteric fever, *Salmonella typhi*

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Introduction

Typhoid fever is an acute, generalized infection of the reticulo-endothelial system, intestinal lymphoid tissues and gallbladder caused by *Salmonella typhi* (Myron et al, 1999). This highly adapted, human-specific pathogen has evolved remarkable mechanisms for persistence in its host that help to ensure its survival and transmission.

History of Typhoid Fever

Typhoid fever, also known as enteric fever, is a systemic infection by *Salmonella typhi* or by the related but less virulent *Salmonella paratyphi* (Parry et al, 2002). Since ancient times, these bacteria have thrived during wartime and during the breakdown of basic sanitation. Archeologists have found *Salmonella typhi* in Athenian mass graves from the era of the Peloponnesian Wars, implicating it as the cause of the Great Plague of Athens. Hippocrates described a fever which probably was typhoid and it is said that Antonius Musa, a Roman Physician became famous by treating Emperor Augustus with cold baths when he felt ill with typhoid. Thomas Willis was regarded as the pioneer in typhoid fever. He gave a classic description of typhoid fever in 1659. He described the typically variable onset with step-ladder rise of temperature during first week, its maintenance during the second and third week and falls by lysis rather than crisis. Prior to the early decade of the 19th century, typhoid fever was not recognized as a distinct clinical entity and often confused with other prolonged febrile syndromes, particularly typhoid fever (Mirza et al, 1996).

Incidence of Typhoid Fever

Typhoid fever was an important cause of illness and death in the overcrowded and unsanitary urban conditions of the United States and Europe in the 19th century (Osler, 1912). The provision of clean water and good sewage systems led to a dramatic decrease in the incidence of typhoid in these regions. Today most of the burden of the disease occurs in the developing world, where sanitary conditions remain poor. Reliable data from which to estimate the burden of disease in these areas are difficult to obtain, since many hospitals lack facilities for blood culture and up to 90 percent of patients with typhoid are treated as outpatients. Community based studies have consistently shown higher levels of typhoid than public health figures suggest (Parry et al, 2002). Annual incidence rates of 198 per 100,000 in the Mekong Delta region of Vietnam (Lin et al, 2000) and 980 per 100,000 in Delhi, India (Sinha et al, 1999) have recently been reported. According to the best global estimates, there are at least 16 million new cases of typhoid fever each year, with 600,000 deaths (Ivanoff, 1995). The introduction of chloramphenicol for the treatment of typhoid fever in 1948 transformed a severe, debilitating, and often fatal disease into a readily treatable condition (Woodward et al, 1948). The emergence of resistance to chloramphenicol and other antimicrobial agents has been a major setback (Mirza et al, 1996). We now face the very real prospect that untreatable typhoid fever will re-emerge (Parry et al, 2002).

Prevalence of Typhoid Fever

In the US: From 1900-1960, the incidence of typhoid fever declined steadily and has remained low in the United States. Improved sanitation and successful antibiotic treatment led to this decline. Averages of 245 cases have been reported annually, with an incidence of 0.2 per 100,000 populations since 1985 compared with 35,994 reported cases in 1920 (Parry et al, 2002). More than 70% of cases occurred within 30 days of returning from international

travel, mostly to the Indian subcontinent and Latin America. The rare outbreaks of typhoid fever due to transmission within the United States are generally traceable to imported food or a food handler from an endemic region (Parry et al, 2002). **Internationally:** *S typhi* and *S paratyphi* infections occur worldwide but primarily in developing nations where sanitary conditions are poor. Typhoid and paratyphoid fevers are endemic in Asia, Africa, Latin America, the Caribbean, and Oceania. Typhoid fever affects 13-17 million people yearly and kills an estimated 600,000 (Parry et al, 2002).

Mortality and Morbidity

Early antibiotic therapy has transformed a previously life-threatening illness of several weeks' duration with an overall mortality rate approaching 20.0% into a short-term febrile illness with negligible mortality. Case fatality rates of 10.0-50.0% have been reported from endemic countries when diagnosis is delayed (Parry et al, 2002).

Race

No racial predilection exists (Parry et al, 2002).

Sex

No sex-related predilection exists (Parry et al, 2002).

Age

Attack rates are highest in persons younger than 20 years or older than 70 years; however, the highest rate is found in infants (130 isolates per 100,000) (Parry et al, 2002). Neonates are at a greater risk to fecal-oral transmission secondary to relative decreased stomach acidity and buffering of ingested breast milk and formula. Elderly persons are at a relative greater risk to infection secondary to chronic underlying illness and weakened immunity. Nursing home residents have a particularly higher risk (Owens, 2008). In endemic areas, children aged 1-5 years are at the highest risk of infection, morbidity, and mortality because of waning of passively acquired maternal antibody and a lack of acquired immunity. In young children, the clinical syndrome is often a nonspecific febrile illness that is not recognized as typhoid fever (Parry et al, 2002). In more recent years, prospective studies have shown that, although the incidence of classic typhoid fever in patients is highest in adolescents and young adults, the overall incidence of blood culture–confirmed disease is generally highest in children aged 3-9 years and declines significantly in late adolescence (Parry et al, 2002).

Sources of Infection

Typhoid is usually contracted by ingestion of food or water contaminated by fecal or urinary carriers excreting *S. enterica* serotype *typhi* (Parry et al, 2002). It is a sporadic disease in developed countries that occurs mainly in returning traveler, with occasional point-source epidemics (Ackers et al, 2000). In endemic areas, identified risk factors for disease include eating food prepared outside the home, such as ice cream or flavored iced drinks from street vendors (Black et al, 1995; Luby et al, 1998), drinking contaminated water (Mermin et al, 1999), having a close contact or relative with recent typhoid fever (Black et al, 1995; Luxemburger et al, 2001), poor housing with inadequate facilities for personal hygiene (Gasem et al, 2001), and recent use of antimicrobial drugs (Luby et al, 1998).

Risk Factors

Salmonella has mechanisms against acidic environments, but a pH level of 1.5 or less kills most of the bacilli (Parry et al, 2002). People who continually ingest antacids, histamine-2 receptor antagonists (H₂ blockers), or proton pump inhibitors; who have undergone gastrectomy; or who have achlorhydria due to aging or other factors require fewer bacilli to produce clinical disease. Acquired immune deficiencies or hereditary deficiencies in immune modulars (such as IL-12 and IL-23) are the increased risk factors for infection, complications, and death (Parry et al, 2002).

Pathogenesis

Infectious Dose: The infectious dose of *S. enterica* serotype *typhi* in volunteers varies between 1000 and 1 million organisms (Wain et al, 1998). Vi-negative strains of *S. enterica* serotype *typhi* are less infectious and less virulent than Vi-positive strains. *S. enterica* serotype *typhi* must survive the gastric acid barrier to reach the small intestine, and a low gastric pH is an important defense mechanism. Achlorhydria as a result of aging, previous gastrectomy, or treatment with histamine H₂-receptor antagonists, proton-pump inhibitors, or large amounts of antacids lowers the infective dose (Wain et al, 1998).

Invasion: In the small intestine, the bacteria adhere to mucosal cells and then invade the mucosa. The M cells, specialized epithelial cells overlying Peyer's patches, are probably the site of the internalization of *S. enterica* serotype *typhi* and its transport to the underlying lymphoid tissue (Wain et al, 1998). After penetration, the invading microorganisms translocate to the intestinal lymphoid follicles and the draining mesenteric lymph nodes, and some pass on to the reticulo-endothelial cells of the liver and spleen. *Salmonella* organisms are able to survive and multiply within the mononuclear phagocytic cells of the lymphoid follicles, liver, and spleen (House et al, 2001). At a critical point that is probably determined by the number of bacteria, their virulence, and the host response, bacteria are released from this sequestered intracellular habitat into the bloodstream.

Incubation period: The incubation period of typhoid fever varies with the size of the infecting dose and averages 7-14 (range, 3-60) days (Wain et al, 1998). In paratyphoid infection, the incubation period ranges from 1-10 days. In the bacteremic phase, the organism is widely disseminated (Wain et al, 2001).

Sites of infections

The most common sites of secondary infection are the liver, spleen, bone marrow, gallbladder and Peyer's patches of the terminal ileum. Gallbladder invasion occurs either directly from the blood or by retrograde spread from the bile. Organisms excreted in the bile either reinvade the intestinal wall or are excreted in the feces. Counts of bacteria in patients with acute typhoid fever indicate a median concentration of 1 bacterium per milliliter of blood about 66.0% of which are inside phagocytic cells and about 10 bacteria per milliliter of bone marrow (Wain et al, 2001). Even though *S. enterica* serotype *typhi* produces a potent endotoxin, mortality from treated typhoid fever for patients at this stage is less than 1 percent. Studies have shown increased levels of circulating pro-inflammatory and anti-inflammatory cytokines in patients with typhoid and a reduced capacity of whole blood to produce inflammatory cytokines in patients with severe disease (Bhutta et al, 1997; Keuter et al, 1994; Butler et al, 1993). Typhoid induces systemic and local humoral and cellular immune

responses, but these confer incomplete protection against relapse and re-infection. The interaction of host immunologic mediators and bacterial factors in infected tissue may contribute to the necrosis of Peyer's patches in severe disease (Everest et al, 2001). The evidence for an association between typhoid and infection with the human immunodeficiency virus (HIV) is conflicting, whereas there is a large increase in the incidence of non-typhi salmonella bacteremia in HIV infection (Gotuzzo et al, 1991; Crewe-Brown et al, 1998). Major-histocompatibility-complex class II and class III alleles have been shown to be associated with typhoid fever in Vietnam. HLA-DRB1*0301/ 6/8, HLA-DQBI*0201-3, and TNFA*2(-308) were found to be associated with susceptibility to typhoid fever, whereas HLA-DRBI*04, HLA-DQBI*0401/2, and TNFA* 1(-308) were associated with disease resistance (Dunstan et al, 2001). Polymorphisms in the genes encoding the natural-resistance-associated macrophage protein were not associated with resistance to typhoid, in contrast to the importance of this allele in the murine model (Dunstan et al, 2001).

Clinical Features

The clinical manifestations and severity of typhoid fever vary with the patient and the population studied. Most patients who present to hospitals with typhoid fever are children or young adults from 5 to 25 years of age (Stuart and Pullen, 1946; Huckstep, 1962). However, community-based studies in areas of endemic disease indicate that many patients with typhoid, particularly children under five years of age, may have a nonspecific illness that is not recognized clinically as typhoid (Lin et al, 2000; Ferreccio et al, 1984). Between 60 and 90 percent of people with typhoid do not receive medical attention or are treated as outpatients (Lin et al, 2000). After a person ingests *S. enterica* serotype *typhi*, an asymptomatic period follows that usually lasts 7 to 14 days (range, 3 to 60). The onset of bacteremia is marked by fever and malaise. Patients typically present to the hospital towards the end of the first week after the onset of symptoms (Stuart and Pullen, 1946). A coated tongue, tender abdomen, hepatomegaly, and splenomegaly are common. A relative bradycardia is considered common in typhoid, although in many geographic areas this has not been a consistent feature. Adults often have constipation, but in young children and in adults with HIV infection, diarrhea is more common (Vinh et al, 1996). It is unusual for a patient hospitalized with typhoid to have no abdominal symptoms and normal bowel movements. Initially the fever is low grade, but it rises progressively, and by the second week it is often high and sustained (39⁰ to 40⁰ C). A few rose spots, blanching erythematous maculopapular lesions approximately 2 to 4 mm in diameter, are reported in 5 to 30 percent of cases (McClelland et al, 2001). They usually occur on the abdomen and chest and more rarely on the back, arms, and legs. These lesions are easily missed in dark-skinned patients. There may be a history of intermittent confusion, and many patients have a characteristic apathetic affect. Convulsions may occur in children under five years of age (Butler et al, 1991). The hemoglobin level, white-cell count, and platelet count are usually normal or reduced. Disseminated intravascular coagulation may be revealed by laboratory tests, but it is very rarely of clinical significance. The levels of liver enzymes are usually two to three times the upper limit of normal. Complications occur in 10.0% to 15.0% of patients and are particularly likely in patients who have been ill for more than two weeks (Bhutta, 1996). Typhoid causes many complications of which gastrointestinal bleeding, intestinal perforation, and typhoid encephalopathy are the most important. Gastrointestinal bleeding is the most common, occurring in up to 10.0% of patients (Punjabi et al, 1988). It results from erosion of a necrotic Peyer's patch through the wall of an enteric vessel. In the majority of cases, the bleeding is slight and resolves without the need for blood transfusion, but in 2.0% of cases, bleeding is clinically significant and can be rapidly fatal if a large vessel is involved. Intestinal

perforation is the most serious complication, occurring in 1 to 3.0% of hospitalized patients (Parkhill et al, 2001). Perforation may be manifested by an acute abdomen or, more covertly, by simple worsening of abdominal pain, rising pulse, and falling blood pressure in an already sick patient. A reduced level of consciousness or encephalopathy, often accompanied by shock, is associated with high mortality (Hoffman et al, 1984; Rogerson et al, 1991). The patient is commonly apathetic although rousable. Patients can be severely agitated, delirious, or obtunded, but complete stupor or coma is infrequent. The incidence of these neuropsychiatric presentations varies among countries. It ranges from 10.0% to 40.0% among hospitalized patients with typhoid in Indonesia (Hoffman et al, 1984; Punjabi et al, 1988) and Papua New Guinea (Rogerson et al, 1991) but is less than 2.0 percent in Pakistan (Bhutta, 1996) and Vietnam (Hoa et al, 1998). This geographic variation is unexplained. Typhoid fever during pregnancy may be complicated by miscarriage, although antimicrobial treatment has made this outcome less common (Seoud et al, 1988). Vertical intrauterine transmission from an infected mother may lead to neonatal typhoid, a rare but severe and life-threatening illness (Reed and Klugman, 1994). It can cause septicemia and meningitis in neonates at very early stage by transmitting through birth canal during passage of baby from infected mother, baby cot and also from utensil. This study was done in India (Mulay et al, 2004), in Pakistan (Khan et al, 1991), in Hong Kong (Cheng et al, 1991) and also in Bangladesh (Begum et al, 2007). Relapse occurs in 5 to 10 percent of patients, usually two to three weeks after the resolution of fever. The relapse is usually milder than the original attack, and the *S. enterica* serotype *typhi* isolate from a patient in relapse usually has the same antibiotic-susceptibility pattern as the isolate obtained from the patient during the original episode. Re-infection may also occur and can be distinguished from relapse by molecular typing (Hermans et al, 1996). Up to 10.0% of convalescing patients with untreated typhoid excrete *S. enterica* serotype *typhi* in the feces for up to three months; 1 to 4.0% becomes long-term carriers, excreting the organism for more than one year. Up to 25 percent of long-term carriers have no history of typhoid. Chronic carriage is more common among women and the elderly and in patients with cholelithiasis (Levine et al, 1982). Most carriers are asymptomatic. Patients with an abnormal urinary tract, such as those who have schistosomiasis, may excrete the organism in the urine for long periods. The average case fatality rate is less than 1 percent, but the rate varies considerably among different regions of the world. Among hospitalized patients, the case fatality rate varies from less than 2 percent in Pakistan (Bhutta, 1996) and Vietnam (Hoa et al, 1998) to 30.0 to 50.0% in some areas of Papua New Guinea (Rogerson et al, 1991) and Indonesia (Hoffman et al, 1984). The case fatality rates are highest among children under one year of age and among the elderly (Bhutta, 1991). However, the most important contributor to a poor outcome is probably a delay in instituting effective antibiotic treatment (Butler et al, 1991).

Clinical History

Untreated typhoid fever lasts at least 4 weeks. Most of the classic signs and symptoms of typhoid fever are prevented with prompt treatment. Clinical response begins about 2 days after starting antibiotics, and the patient's condition markedly improves within 4-5 days (Wain et al., 1999). During the incubation period, 10.0-20.0% of patients have transient diarrhea (enterocolitis) that usually resolves before the onset of the full-fledged disease (Wain et al., 1999). As bacteremia develops, the incubation period ends. Patients often experience with fever, influenza-like symptoms with chills (although rigors are rare), a dull frontal headache, malaise, anorexia, nausea, poorly localized abdominal discomfort, a dry cough, diaphoresis and myalgia, but with few physical signs and these appears before the onset of a high fever. About 20.0-40.0% of patients present with abdominal pain (Wain et al., 1999). In

immunocompetent adults, constipation is common and is most likely due to hypertrophy of Peyer's patches. Young children and individuals with AIDS are more likely to have diarrhea that is probably due to blunted secondary immunity. The incidence of constipation versus diarrhea varies geographically, perhaps because of local differences in diet or *S. typhi* strains or genetic variation (Wain et al., 1999). Unusual modes of onset include isolated severe headaches that may mimic meningitis. *S. typhi* infection may cause an acute lobar pneumonia. In the early stages of the disease, rigors are rare unless the person also has malaria. This is not an unusual pairing of diseases. Patients may present with arthritis only, urinary symptoms, severe jaundice, or fever. Some patients, especially in India and Africa, may present with confusion and delirium or report parkinsonian symptoms or spastic rigidity (Wain et al., 1999). This regional variety in neuropsychiatric presentation may be due to the same factors that cause the variation in gastrointestinal symptoms (Wain et al., 1999).

Physical findings

The classic signs of enteric fever include fever, toxemia, delirium, abdominal pain, constipation, and hepatosplenomegaly (Punjabi et al, 1988).

First week: Fever occurs in 75-85% of patients in the first week and is often initially remittent but becomes steady. The individual's temperature often rises to as high as 103-104°F (39-40°C). Constipation often develops early and is likely due to obstruction at the ileocecal valve by swollen Payer patches. It may last for the entire duration of illness (Punjabi et al, 1988). **End of first week:** At approximately the end of the first week of illness, about a third of patients develop bacterial emboli to the skin known as rose spots. These are considered a classic symptom in typhoid fever, but they occasionally appear in shigellosis and non-typhoidal Salmonellosis. Rose spots constitute a subtle, extremely sparse (often ≤ 5 spots), salmon-colored, blanching, truncal, maculopapular rash with 1 to 4 mm lesions that generally resolve within 2-5 days; however, relative bradycardia and a dicrotic pulse are also common during this stage of illness (Parry et al, 2002).

Second week: During the second week of illness, the patient is toxic-appearing and apathetic with sustained fever. The abdomen is slightly distended, and soft splenomegaly is common (Parry et al, 2002).

Third week: In the third week, the patient grows more toxic and anorexic with significant weight loss. The patient may have a thready pulse, tachypnea, conjunctivitis, and crackles over the lung bases (Parry et al, 2002). Pyrexia persists. The patient may enter into a typhoid state of apathy, confusion, and even psychosis. Patients may develop polyneuropathy. Abnormal cerebrospinal fluid should prompt a search for a different cause. Meanwhile, the patient commonly has pronounced abdominal distension. Some individuals may produce liquid, foul, green-yellow diarrhea (pea soup diarrhea). At this stage, the patient may die from overwhelming toxemia, myocarditis, intestinal hemorrhage, or perforation due to necrotic Peyer patches (Parry et al, 2002). Rare complications of enteric fever include pancreatitis, meningitis, orchitis, and osteomyelitis.

Fourth week: During the fourth week, the fever, mental state, and abdominal distension slowly improve over a few days, but intestinal complications may still occur in surviving untreated individuals. Weight loss and debilitating weakness persist last months. Relapses occur in 10% of patients, mostly during the first 2-3 weeks of convalescence (Parry et al, 2002).

Chronic carrier state

One to four percent of untreated patients become chronic carriers, defined as individuals who excrete *Salmonella* for more than 1 year (Parry et al, 2002). Some individuals may continue to excrete the bacterium for decades. Bladder infection with *Schistosoma haematobium* predisposes to urinary carriage. The parasite itself becomes a carrier. Stool carriage is more frequent in people with preexisting biliary abnormalities, perhaps because *S enterica* survives in gallstones, and these people have a greater incidence of cholecystitis (Parry et al, 2002). Chronic carriers have a greater risk for carcinoma of the gallbladder and other gastrointestinal malignancies; chronic carriers had a 6-fold increase in the risk of death due to hepatobiliary cancer. This may be due to chronic inflammation caused by the bacterium (Parry et al, 2002).

Table: Important Complications of Typhoid Fever (Parry et al, 2002)

Abdominal	Respiratory
Gastrointestinal perforation Gastrointestinal hemorrhage Hepatitis Cholecystitis (usually subclinical)	Bronchitis Pneumonia (<i>Salmonella enterica</i> serotype typhi, <i>Streptococcus pneumoniae</i>)
Cardiovascular	Hematologic
Asymptomatic electrocardiographic changes Myocarditis Shock	Anemia Disseminated intravascular coagulation (usually subclinical)
Neuropsychiatric	Other
Encephalopathy Delirium Psychotic states Meningitis Impairment of coordination	Focal abscess Pharyngitis Miscarriage Relapse Chronic carriage

Laboratory Diagnosis

The absence of specific symptoms or signs makes the clinical diagnosis of typhoid difficult (Vallenas et al., 1985). In areas of endemic disease, a fever without evident cause that lasts more than one week should be considered typhoid until proved otherwise. Blood cultures are the standard diagnostic method; provided a large volume of blood is cultured (15 ml in adults), they are positive in 60 to 80.0% of patients with typhoid (Parry et al., 2002). Culture of bone marrow is more sensitive. The result is positive in 80.0 to 95.0% of patients with typhoid, even patients who have been taking antibiotics for several days, regardless of the duration of illness (Wain et al., 2001). Blood cultures are less sensitive than bone marrow cultures because of the lower numbers of microorganisms in blood as compared with bone marrow (Wain et al., 2001). The sensitivity of blood culture is higher in the first week of the illness, is reduced by prior use of antibiotics, and increases with the volume of blood cultured and the ratio of blood to broth (Hoffman et al., 1986). Cultures have also been made from the buffy coat of blood (Rubin et al., 1990), streptokinase-treated blood clots (Hoffman et al., 1986), intestinal secretions with the use of a duodenal string capsule (Vallenas et al., 1985), and skin snips of rose spots (Gilman et al., 1975). The sensitivity of stool culture depends on the amount of feces cultured, and the positivity rate increases with the duration of the illness.

Stool cultures are positive in 30 percent of patients with acute typhoid fever. For the detection of carriers, several samples should be examined because of the irregular nature of shedding (Wain et al., 1998). The role of Widal's test is controversial, because the sensitivity, specificity, and predictive values of this widely used test vary considerably among geographic areas (Parry et al., 1999). The test detects agglutinating antibodies to the O and H antigens of *S. enterica* serotype typhi. Unfortunately, *S. enterica* serotype typhi shares these antigens with other salmonella serotypes and shares cross-reacting epitopes with other Enterobacteriaceae. Furthermore, patients with typhoid may mount no detectable antibody response or have no demonstrable rise in antibody titer. Despite this, some centers have found Widal's test helpful when it is used with locally determined cutoff points (Clegg et al., 1990). A Vi agglutination reaction has been used to screen for *S. enterica* serotype typhi carriers. Its reported sensitivity is 70 to 80 percent, with a specificity of 80.0 to 95.0% (Lanata et al., 1983). Newer serologic tests are being developed but do not yet perform well enough to ensure their widespread adoption (Bhutta et al., 1999). DNA probes and polymerase-chain-reaction protocols have been developed to detect *S. enterica* serotype typhi directly in the blood (Song et al., 1993). The methods are not yet widely used and are impractical in many areas where typhoid is common. Typhoid must be distinguished from other endemic acute and subacute febrile illnesses (House et al., 2001). Malaria, deep abscesses, tuberculosis, amebic liver abscess, encephalitis, influenza, dengue, leptospirosis, infectious mononucleosis, endocarditis, brucellosis, typhus, visceral leishmaniasis, toxoplasmosis, lymphoproliferative disease, and connective-tissue diseases should be considered.

Conclusion

Typhoid fever is a great problem to the local community as well as society. The prevention is a better option for resist this disease. The proper treatment can cure this disease. Drastic measures should be implemented to prevent this disease.

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