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Enteric Fever (Typhoid Fever)

ETIOLOGY

Typhoid fever is mainly caused by ***Salmonella* Typhi** (also called *Salmonella enterica* serovar Typhi) a Gramnegative bacterium.. Less commonly it caused by ***Salmonella* Paratyphi** (A, B, & C) which cause similar but less severe disease.

One of the most specific gene products is the polysaccharide capsule Vi(virulence), which is present in approximately 90% of all freshly isolated *S.* Typhi and has a protective effect against the bactericidal action of the serum of infected patients.

EPIDEMIOLOGY

Typhoid fever is **endemic in developing countries**, especially Asia. *S.* Typhi is highly adapted to infect human beings; transmission occurs after (direct or indirect) **contact with infected person** (sick or chronic carrier) through ingestion of contaminated foods or water.

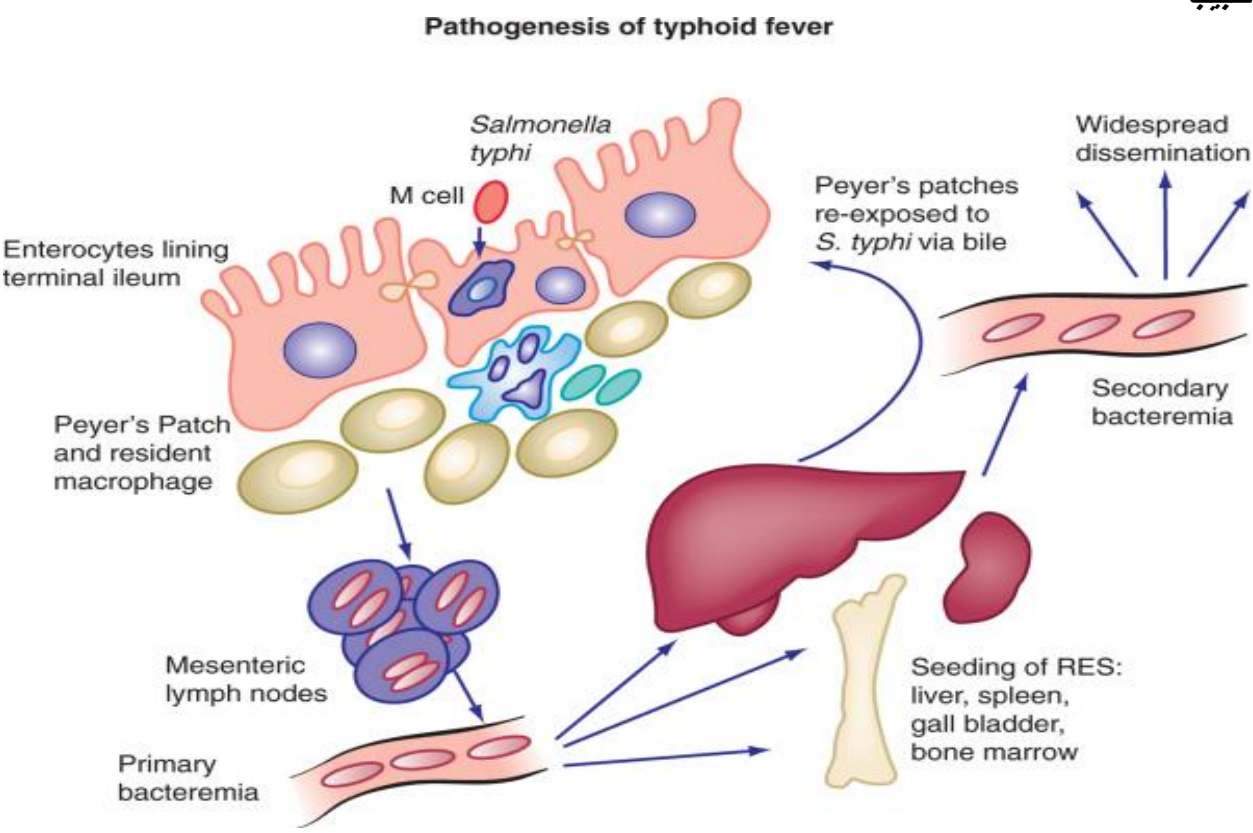
PATHOGENESIS

Enteric fever occurs through the ingestion of the organism, and a variety of sources of fecal contamination have been reported, including street foods and contamination of water reservoirs. Human volunteer experiments established an infecting dose of about 105-109 organisms, with an incubation period ranging from 4-14 days, depending on the inoculating dose of viable bacteria.

After ingestion, ***S.* Typhi invade the gut mucosa** through "M cells" in the terminal ileum to the mesenteric lymphoid system, then to blood- stream via the lymphatics. This **primary bacteremia** is usually asymptomatic, and blood cultures are frequently negative at this stage. Bacteria then disseminated throughout the body and colonize organs of the reticulo-endothelial system, where they may **replicate within macrophages**, then shed back to blood, causing **secondary bacteremia**, which coincides with the onset of clinical symptoms.

In addition to enteritis, *S.* Typhi can cause inflammation, ulceration or perforation of the Peyer patches of terminal ileum, but more commonly they heal without scar or stricture formation.

Predisposition to infection is depend on many factors including: surface Vi (virulence) polysaccharide capsular antigen found in *S.* Typhi (which interferes with phagocytosis), dose of inoculums, state of immunity & nutrition, HLA of the host as well as infection with *H. pylori have anincreased risk of acquiring typhoid fever*..



CLINICAL FEATURES

The incubation period of typhoid fever is usually 7-14 days but depends on the infecting dose and ranges between 3 and 30 days. The clinical presentation varies from a mild illness with low-grade fever, malaise, and slight, dry cough to a severe clinical picture with abdominal discomfort and multiple complications.

Typhoid fever usually manifests as high-grade fever with a wide variety of associated features, such as generalized myalgia, abdominal pain, hepatosplenomegaly, abdominal pain, and anorexia (Table 198-5). In children, diarrhea may occur in the earlier stages of the illness and may be followed by constipation.

The fever may rise gradually, but the classic stepladder rise of fever is relatively rare(rarely associated with relative bradycardia). In approximately 25% of cases, a macular or maculopapular rash (rose spots) may be visible around the 7th-10th day of the illness, and lesions may appear in crops of 10-15 on the lower chest and abdomen and last 2-3 days (Fig. 198-5). These lesions may be difficult to see in dark-skinned children. Patients managed as outpatients present with fever (99%) but have less emesis, diarrhea, hepatomegaly, splenomegaly, and myalgias than patients who require admission to the hospital.

If no complications occur, the symptoms and physical findings gradually resolve within 2-4 wk; however, the illness may be associated with malnutrition in a number of affected children.

COMPLICATIONS

GIT; *intestinal hemorrhage or perforation (with features of peritonitis), hepatitis (with jaundice), & cholecystitis.*

Neurologic; *delirium, psychosis, ↑ ICP, acute cerebellar ataxia, chorea, deafness, & Guillain-Barre syndrome.*

Others; *fatal BM necrosis, DIC, HUS, nephrotic syndrome, pyelonephritis, meningitis, endocarditis, parotitis, orchitis, & suppurative lymphadenitis.*

DIAGNOSIS

1. CBP; usually there is leukopenia (although leucocytosis may occur in young children); thrombocytopenia may be a marker of severe disease.
2. Serology; The classic Widal test measures antibodies against O and H antigens of S. Typhi but it lacks sensitivity and specificity in the endemic areas. Because many false-positive and false-negative results occur, diagnosis of typhoid fever by Widal test alone is prone to error Therefore, now it has been replaced with Monoclonal Antibodies that directly detect S. Typhi–specific antigens in serum or S. Typhi Vi antigen in urine.
3. Culture is the gold standard for Dx.. The mainstay of the diagnosis of typhoid fever is a positive result of culture from the blood or another anatomic site. Results of blood cultures are positive in 40-60% of the patients seen early in the course of the disease, and stool and urine culture results become positive after the 1st wk. The stool culture result is also occasionally positive during the incubation period then also become +ve after the 1st wk of illness.
4. PCR.

DIFFERENTIAL DIAGNOSIS

AGE , bronchitis, or bronchopneumonia. malaria; sepsis with other bacterial pathogens; infections caused by intracellular microorganisms, such as TB , brucellosis, tularemia, leptospirosis, & rickettsial diseases; & viral infections such as Dengue fever, acute hepatitis, & EBV **.**

Extraintestinal Infectious Complications of Typhoid Fever

ORGAN SYSTEM INVOLVED	*PREVALENCE*	*RISK FACTORS*	*COMPLICATIONS*
CNS	*3–35%*	*malignancy, endocarditis, CHD, paranasal sinus infections, pulmonary infections, meningitis, trauma, surgery, & osteomyelitis of the skull*	*Encephalopathy, cerebral edema, subdural empyema, cerebral abscess, meningitis, ventriculitis, transient parkinsonism, MND , ataxia, seizures, GBS, psychosis*
Cardiovascular system	*1–5%*	*Cardiac abnormalities—e.g., existing valvular abnormalities RHD , or CHD*	*Endocarditis, myocarditis, pericarditis, arteritis, CHF*
Pulmonary system	*1–6%*	*, past pulmonary infection, sickle cell anemia, alcohol abuse, diabetes, HIV infection*	*Pneumonia, empyema, bronchopleural fistula*
Bone &joint	*<1%*	*SCA DM, SLE, lymphoma, liver disease, previous surgery or trauma, those at extremes of age, & steroid use*	*Osteomyelitis, septic arthritis*
Hepatobiliary system	*1–26%*	*Residence in endemic region, pyogenic infections, intravenous drug use, splenic trauma, HIV, hemoglobinopathy*	*Cholecystitis, hepatitis, hepatic abscesses, splenic abscess, peritonitis, paralytic ileus*
Genitourinary system	*<1%*	*Urinary tract, pelvic pathology, & systemic abnormalities*	*UTI, renal abscess, pelvic infections, testicular abscess, prostatitis, epididymitis*
Soft tissue infections		*Diabetes*	*Psoas abscess, gluteal abscess, cutaneous vasculitis*

Haematologic			***Hemophagocytosis syndrome***

TREATMENT

The vast majority of children with typhoid fever can be managed at home with oral antibiotics and close medical follow-up for complications or failure of response to therapy. Patients with persistent vomiting, severe diarrhea, and abdominal distention may require hospitalization and parenteral antibiotic therapy.

There are general principles of typhoid fever management (adequate rest, hydration, nutrition (with a bland diet), & antipyretics e.g. acetaminophen every 4–6 hr.)

Antibiotic therapy include: high dose Amoxicillin 75-100 mg/kg/day or Chloramphenicol 50-75 mg/kg/day, both for 2-3 wk (unless the organisms are resistant), or fluoroquinolone e.g. Ciprofloxacin 15 mg/kg/day for only 5-7 days.

Alternative agents include: 3rd generation cephalosporins e.g. Ceftriaxone or Cefixime for 1-2 wk; or Azithromycin for 1 wk (Azithromycin may be an alternative antibiotic for children with uncomplicated typhoid fever)..

Dexamethasone can be given for severely ill patients, but must be done under strict supervision because it may masks the signs of abdominal Cxs; initial dose is 3 mg/kg then 1 mg/kg every 6

hr for 2 days. Note: This dose is higher than that used in meningiti

OPTIMAL THERAPY				ALTERNATIVE EFFECTIVE DRUGS		
SUSCEPTIBILITY	Antibiotic	Daily Dose (mg/kg/day)	Days	Antibiotic	Daily Dose (mg/kg/day)	Days
UNCOMPLICATED TYPHOID FEVER						
Fully sensitive	Chloramphenicol	50–75	14–21	Fluoroquinolone, e.g., ofloxacin or ciprofloxacin	15	5–7
	Amoxicillin	75–100	14			
Multidrug resistant	Fluoroquinolone or cefixime	15	5–7	Azithromycin	8–10	7
		15–20	7–14	Cefixime	15–20	7–14
Quinolone resistant[†]	Azithromycin or ceftriaxone	8–10	7	Cefixime	20	7–14
		75	10–14			
SEVERE TYPHOID FEVER						
Fully sensitive	Ampicillin or ceftriaxone	100	14	Fluoroquinolone, e.g., ofloxacin or ciprofloxacin	15	10–14
		60–75	10–14			
Multidrug resistant	Fluoroquinolone	15	10–14	Ceftriaxone or cefotaxime	60	10–14
					80	
Quinolone resistant	Ceftriaxone	60–75	10–14	Fluoroquinolone	20–30	14

PROGNOSIS

Although there are many factors that affect prognosis, generally uncomplicated disease is usually resolves within 2-4 wk. However, even with antibiotic Rx, relapse may occur due to the emergence of multidrug- resistant strains of S. Typhi, especially to amoxicillin, chloramphenicol, TMP-SMZ as well as fluoroquinolones.

Individuals who excrete S. Typhi for ≥3 mo after infection are regarded as chronic carriers, but the risk increases with age, thus it is low in children.

Children with Schistosomiasis can develop urinary carrier state because S. Typhi can infect the parasite itself.

PREVENTION

Improve sanitation by handwashing & prevention of food contamination, chlorination of water, screening of food handlers, & tracing of chronic carrier. There are 2 vaccines; Oral live-attenuated & IM Vi capsular polysaccharide vaccines.