**Typhoid and Paratyphoid Fever**

**Definition**

- Acute enteric infectious disease
- Caused by Salmonella typhi (S. Typhi)
- Prolonged fever, Relative bradycardia, apathetic facial expressions, roseola, splenomegaly, hepatomegaly, leukopenia.
- *Intestinal perforation, intestinal hemorrhage*

**Etiology**

- Serotype: D group of Salmonella
- Gram-negative rod
- Non-sporing flagella
- Culture characteristics

- Antigens: located in the cell capsule
  - H (flagellar antigen)
  - O (Somatic or cell wall antigen)
  - Vi (polysaccharide virulence)
  - "widel test"

A schematic diagram of a single Salmonella typhi cell showing the locations of the H (flagellar), O (somatic), and Vi (K envelope) antigens.
Epidemiology

- continues to be a global health problem
- areas with a high incidence include Asia, Africa and Latin America
- sporadic occur usually, sometimes have epidemic outbreaks.

Transmission

- fecal-oral route
- close contact with patients or carriers
- contaminated water and food
- flies and cockroaches.

Susceptibility and immunity

- All seasons, usually in summer and autumn.
- Most cases in school-age children and young adults.
- both sexes equally susceptible.

Pathogenesis

- gastrointestinal tract host-pathogen interactions
- The amount of bacilli infection (>10^5 bacteria).

Pathogenesis

- ingested orally
  - Stomach barrier (some Eliminated)
  - enters the small intestine
  - → Penetrate the mucus layer
  - → enter mononuclear phagocytes of ileal peyer's patches and mesenteric lymph nodes
  - → proliferate in mononuclear phagocytes spread to blood. initial bacteremia (Incubation period).
Pathogenesis

- enter spleen, liver and bone marrow (reticulo-endothelial system)  
  further proliferation occurs  
- A lot of bacteria enter blood again. (second bacteremia).  
- Recovery

Pathology

- essential lesion:
  proliferation of RES (reticuloendothelial system )
  specific changes in lymphoid tissues and mesenteric lymph nodes.
  “typhoid nodules”
- Most characteristic lesion:
  ulceration of mucous in the region of the Peyer’s patches of the small intestine

Major findings in lower ileum

- Ulceration stage (3rd week):
  shedding of necrosis tissue and formation of ulcer — intestinal hemorrhage, perforation.
- Stage of healing (from 4th week):
  healing of ulcer, no cicatrices and no contraction

Clinical manifestations

- Often atypical
- sudden onset with high fever, but the classic stepladder rise of fever is relatively rare
- Respiratory symptoms and diarrhea may be followed by constipation, dominant.
- Convulsion common in below 3.
- relative bradycardia rare.
- abdominal pain, and anorexia.
- 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
Common Clinical Features of Typhoid Fever in Children

- High-grade fever
- Coated tongue
- Anorexia
- Vomiting
- Hepatomegaly
- Jaundice
- Abdominal pain
- Tachypnea
- Spleomegaly
- Headache
- Constipation
- Fever
- Diarrhea
- Toxicity
- Pallor
- Splenomegaly
- Constipation
- Headache
- Jaundice
- Obstructed
- Suck

COMPLICATIONS.

- Although altered liver function is found in many patients with enteric fever, clinically significant hepatitis, jaundice, and cholecystitis are relatively rare.
- Rare complications include toxic myocarditis, which may manifest by arrhythmias, sinoatrial block, or cardiogenic shock.
- Neurologic complications are also relatively uncommon among children and may include delirium, psychosis, increased intracranial pressure, acute cerebellar ataxia, chorea, deafness, and Guillain-Barré syndrome. Although case fatality rates may be higher with neurologic manifestations, recovery usually occurs with no sequelae.
- Other reported complications include fatal bone marrow necrosis, disseminated intravascular coagulation (DIC), hemolytic uremic syndrome, pyelonephritis, nephrotic syndrome, meningitis, endocarditis, parotitis, orchitis, and suppurative lymphadenitis.

Intestinal hemorrhage

- Commonly appear during the second-third week of illness
- Difference between mild and greater bleeding often caused by unsuitable food, diarrhea et al serious bleeding in about 2~8% a sudden drop in temperature, rise in pulse, and signs of shock followed by dark or fresh blood in the stool.

Intestinal perforation:

- Commonly appear during 2-3 weeks.
- Take place at the lower end of ileum.
- Before perforation, abdominal pain or diarrhea, intestinal bleeding.
- When perforation, abdominal pain, sweating, drop in temperature, and increase in pulse rate, then, rebound tenderness when press abdomen, abdomen muscle entasia, reduce or disappear in the sonant extent of liver, leukocytosis.
- celiac free air under x-ray.

fatal complications:

- Intestinal hemorrhage is infrequent among children
- Intestinal perforation
- Severe toxemia
Extraintestinal Infectious Complications of Typhoid Fever Caused by *Salmonella enterica* Serotype Typhi

<table>
<thead>
<tr>
<th>ORGAN SYSTEM INVOLVED</th>
<th>PREVALENCE</th>
<th>RISK FACTORS</th>
<th>COMPLICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central nervous system</td>
<td>3–35%</td>
<td>Residence in endemic region, malignancy, endocarditis, congenital heart disease, paranasal sinus infections, pulmonary infections, meningitis, trauma, surgery, and osteomyelitis of the skull</td>
<td>Encephalopathy, cerebral edema, subdural empyema, cerebral abscess, meningitis, ventriculitis, transient parkinsonism, motor neuron disorders, ataxia, psychosis, Guillain-Barré syndrome, myelopathy</td>
</tr>
<tr>
<td>Cardiovascular system</td>
<td>1–5%</td>
<td>Cardiac abnormalities—e.g., existing valvular abnormalities, rheumatic heart disease, congenital heart defects</td>
<td>Endocarditis, myocarditis, pericarditis, arteritis, congestive heart failure</td>
</tr>
<tr>
<td>Pulmonary system</td>
<td>1–6%</td>
<td>Residence in endemic region, past pulmonary infection, sickle cell anaemia, alcohol abuse, diabetes, HIV infection</td>
<td>Pneumonia, empyema, bronchopleural fistula, bronchial obstruction, chronic lung disease, respiratory failure</td>
</tr>
<tr>
<td>Bone and joint</td>
<td>&lt;1%</td>
<td>Sickle cell anaemia, diabetes, systemic lupus erythematosus, lymphoma, liver disease, previous surgery or trauma, those at extremes of age, and steroid use</td>
<td>Osteomyelitis, septic arthritis</td>
</tr>
<tr>
<td>Hepatobiliary system</td>
<td>1–26%</td>
<td>Residence in endemic region, pyogenic infections, intravenous drug use, splenic trauma, HIV, haemoglobinopathy</td>
<td>Cholecystitis, hepatitis, hepatic abscesses, splenic abscesses, peritonitis, paralytic ileus</td>
</tr>
<tr>
<td>Genitourinary system</td>
<td>&lt;1%</td>
<td>Urinary tract, pelvic pathology, and systemic abnormalities</td>
<td>Urinary tract infection, renal abscess, pelvic infections, testicular abscess, epididymitis</td>
</tr>
<tr>
<td>Soft tissue infections</td>
<td>At least 17 cases reported in the English-language literature</td>
<td>Diabetes, haemoglobinopathy, osteomyelitis, septic arthritis</td>
<td></td>
</tr>
<tr>
<td>Haematologic</td>
<td>At least 5 cases reported in the English-language literature</td>
<td>Haemophagocytosis syndrome</td>
<td></td>
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</table>

**Laboratory findings**

**Routine examinations:**
- white blood cell count is normal or decreased.
- Leukocytopenia (specially eosinophilic leukocytopenia).
- recovery with improvement of diseases decreased in relapse

**Bacteriological examinations:**

- **Blood culture:**
  - the most common use
  - 40–60% positive during the first 1 weeks of illness
  - not easy in 4th week
  - re-positive when relapse and recrudescence
  - attention to the use of antibiotics

- **The bone marrow culture**
  - Although bone marrow cultures may increase the likelihood of bacteriologic confirmation of typhoid, these are difficult to obtain and relatively invasive.
  - (single most sensitive method of diagnosis)
- **Urine and stool cultures**
  - increase the diagnostic yield
  - positive less frequently
  - stool culture better in 3–4 week
Serological tests (Widal test):

- **five types of antigens:**
  - somatic antigen (O), flagella (H) antigen, and paratyphoid fever flagella (A, B, C) antigen.
  - Antibody reaction appear during 2\textsuperscript{nd} week
  - 70% positive in 3~4 weeks and can prolong to several months
  - In some cases, antibodies appear slowly, or remain at a low level,
  - Some (10~30%) not appear at all.

- "O" agglutinin antibody titer $\geq 1:80$ and "H" $\geq 1:160$ or "O" 4 times higher supports a diagnosis of typhoid fever
- "O" rises alone, not "H", early of the disease. Only "H" positive, but "O" negative, often nonspecifically elevated by immunization or previous infections.
- Antibody level maybe lower when have used antibiotics early.

- False positive in some infectious diseases.
- Some positive in blood culture, but negative in Widal test.

Diagnosis

- Epidemiology data
- Typical symptoms and signs
- Laboratory findings.

Differential diagnosis

**Viral infections:**
- such as upper respiratory tract infection.
- abrupt onset with fever, headache, leucopenia, sore throat, cough, coryza.
- no rose spots, no enlargement of liver & spleen. The course of illness no more than 2 wks.
- differential diagnosis depends on typical manifestations and blood culture.

Malaria

- history of exposure to malaria.
- Paroxysms (often periodic) of sequential chill, high fever and sweating.
- Headache, anorexia, splenomegaly, anemia, leukopenia
- Characteristic parasites in erythrocytes, identified in thick or thin blood smears.
### Tuberculosis
- continuous high or low fever, fatigue, weight loss, night sweats.
- Mild cough
- Pulmonary infiltration on chest radiograph
- Positive tuberculin skin test reaction (most cases)
- Acid-fast bacilli on smear of sputum
- Sputum culture positive for Mycobacterium tuberculosis.

### Septicemia of Gram-negative bacilli
- Abrupt onset, high fever, symptom of toxemia.
- Chill, sweats.
- Shock.
- Positive of gram-negative bacilli from blood culture.

### Prognosis:
- Case fatality 0.5~1%.
- But high in old ages, infant, and serious complications
- Have immunity for ever after diseases
- About 3% of patients become fecal carriers.

### Treatment
- **General treatment**
  - Rest
  - Good nursing care and supportive treatment
  - Close observation T, P, R, BP, abdominal condition and stool.
  - Suitable diet include easy digested food or half-liquid food. Drink more water.
  - Intravenous injection to maintain water and acid-base and electrolyte balance.

- **Symptomatic treatment:**
  - For high fever:
    - Physical measures firstly
    - Antipyretic drugs such as aspirin should be administered with caution
    - Delirium, coma or shock, 2-4mg dexamethasone in addition to antibiotics reduces mortality.

- **Antibiotic therapy**
  - Antibiotic therapy is critical to minimize complications.
  - Choice of empirical therapy is guided by various factors including the severity of illness, inpatient/outpatient therapy, presence of complications, and local sensitivity patterns.
  - For uncomplicated, cefixime 20mg/kg/day, Azithromycin 10-20mg/kg/day.
  - For severe illness and associated with complications, intravenous ceftriaxone or cefotaxim 100mg/kg/day.
### Treatment of complication.

<table>
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<th><strong>Intestinal bleeding:</strong></th>
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<td>bed rest, stop diet, close observation T, P, R, BP.</td>
</tr>
<tr>
<td>intravenous saline and blood transfusion, and attention to acid-base balances.</td>
</tr>
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<td>sometimes, operative.</td>
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<th><strong>Perforation:</strong></th>
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<td>early diagnosis.</td>
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<tr>
<td>stop diet.</td>
</tr>
<tr>
<td>decrease down the stomach pressure.</td>
</tr>
<tr>
<td>intravenous injection to maintain electrolyte and acid-base balances.</td>
</tr>
<tr>
<td>use of antibiotics.</td>
</tr>
<tr>
<td>sometimes operative.</td>
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### Chronic carrier:

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<td>Ofloxacin 0.2 bid or ciprofloxacin 0.5 bid, 4～6 weeks.</td>
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<tr>
<td>Amoxicillin 100mg/kg/day tid plus probenecid 30mg/kg/day, 4～6 weeks.</td>
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<tr>
<td>Cholecystitis may require cholecystectomy.</td>
</tr>
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</table>

### PREVENTION.

- Cut of course of transmission
  - key way
  - avoid drinking untreated water and food.
- Vaccination
  - side-effect more, less use