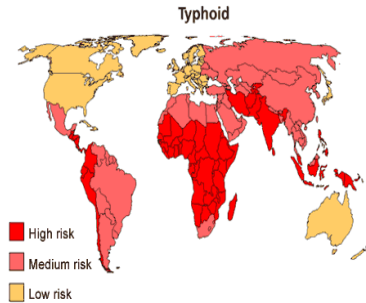




Typhoid fever



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Definition

- An infectious feverish disease caused by the bacterium *Salmonella typhi* (*Salmonella enterica* Serovar Typhi) and less commonly by *Salmonella paratyphi*.
- Acute generalized infection of the reticulo endothelial system, intestinal lymphoid tissue, and the gall bladder.
- The infection always comes from another human, either an ill person or a healthy carrier of the bacterium. The bacterium is passed on with water and foods and can withstand both drying and refrigeration.



History

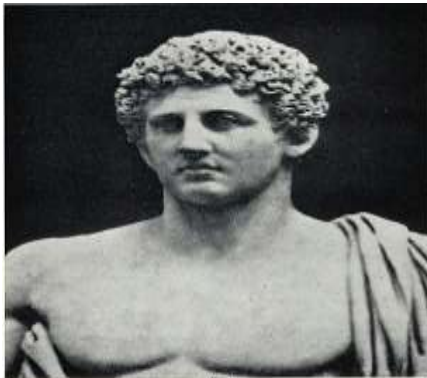


FIG. 6.
Antonius Musa
A Roman physician who achieved fame by treating the Emperor Augustus with cold baths when he fell ill with typhoid.

Antonius Musa, a Roman physician who achieved fame by treating the Emperor Augustus 2,000 year ago, with cold baths when he fell ill with typhoid.

Thomas Willis who is credited with the first description of typhoid fever in 1659.



FIG. 7.
Thomas Willis (1621-1670)
The first description of epidemic typhoid in 1659.



French physician **Pierre Charles Alexandre Louis** first proposed the name “**typhoid fever**”

William Wood Gerhard who was the first to differentiate clearly between typhus fever and typhoid in 1837.





Carl Joseph Eberth who discovered the typhoid bacillus in 1880.

Georges Widal who described the 'Widal agglutination reaction' of the blood in 1896.





1. The best known carrier was "**Typhoid Mary**"; Mary Mallon was a cook in Oyster Bay, New York in 1906 who is known to have infected 53 people, 5 of whom died.
2. Later returned with false name but detained and quarantined after another typhoid outbreak.
3. She died of pneumonia after 26 years in quarantine.

Causes

1. Caused by the bacterium *Salmonella Typhi* .
2. Ingestion of contaminated food or water.
3. Contact with an acute case of typhoid fever.
4. Water is contaminated where inadequate sewerage systems and poor sanitation.
5. Contact with a chronic asymptomatic carrier.
6. Eating food or drinking beverages that handled by a person carrying the bacteria.
7. *Salmonella enteritidis* and *Salmonella typhimurium* are other salmonella bacteria, cause food poisoning and diarrhoea.



Salmonella Entrica

- Member of the **genus *Salmonella***.
- Rod shaped, **flagellated**, aerobic, Gram negative bacterium.
- Large number of **fimbrial** and non-fimbrial **adhesins** are present, mediate **biofilm** formation and contact to host cells.
- Secreted proteins involved in host cell invasion and intracellular proliferation.
- Infects **cattle**, poultry, domestic **cats**, hamsters, humans etc.
- Refrigeration and freezing substantially slow or halt their growth.
- **Pasteurizing** and **food irradiation** kill *Salmonella* for commercially-produced foodstuffs containing raw eggs such as ice cream.
- Foods prepared in the home from raw eggs can spread salmonella if not properly cooked before consumption.



Symptoms

- No symptoms - if only a mild exposure; some people become "carriers" of typhoid.
- Poor appetite,
- Headaches,
- Generalized aches and pains,
- Fever, Lethargy, Lethargy,
- Lethargy,
- Diarrhea,
- Have a sustained fever as high as 103 to 104 degrees Fahrenheit (39 to 40 degrees Celsius),
- Chest congestion develops in many patients, and abdominal pain and discomfort are common,
- Constipation, mild vomiting, slow heartbeat.





Time frame

- Occurs gradually over a few weeks after exposure to the bacteria. Sometimes children suddenly become sick.
- The condition may last for weeks or even a month or longer without treatment.

First-Stage Typhoid Fever

The beginning stage is characterized by high fever, fatigue, weakness, headache, sore throat, diarrhea, constipation, stomach pain and a skin rash on the chest and abdominal area. According to the Mayo Clinic, adults are most likely to experience constipation, while children usually experience diarrhea.



Second stage

Second-stage typhoid fever is characterized by weight loss, high fever, severe diarrhea and severe constipation. Also, the abdominal region may appear severely distended.

Typhoid State

When typhoid fever continues untreated for more than two or three weeks, the effected individual may be delirious or unable to stand and move, and the eyes may be partially open during this time. At this point fatal complications may emerge.



Diagnosis

Diagnosis of typhoid fever is made by

- Blood, bone marrow, or stool cultures test
- Widal test
- Slide agglutination
- Antimicrobial susceptibility testing



Widal test

" A test involving agglutination of typhoid bacilli when they are mixed with serum containing typhoid antibodies from an individual having typhoid fever; used to detect the presence of *Salmonella typhi* and *S. paratyphi*."



Standard test tube method

Take four sets of 8 test tubes and label them 1 to 8 for O,H,AH and BH antibody detection.



Pipette in to the tube No.1 of all sets 1.9 ml of isotonic saline.



To each of the remaining tubes (2 to 8) add 1.0 ml of isotonic saline.



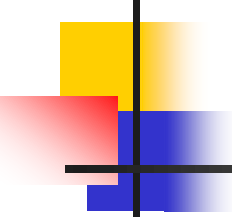
To the tube No. 1 tube in each row add 0.1 ml of the serum sample to be tested and mix well.



Transfer 1ml of the diluted serum from tube no.1 to tube no.2 and mix well.



Discard the 1ml of the diluted serum from tube no.7 of each set.



Tube no.8 in all sets, serves as a saline control. Now the dilution of the serum sample achieved in each set is as follows:

↓

Tube no. 1 2 3 4 5 6 7 8 (control)

↓

Dilutions 1:20 1:40 1:80 1:160 1:320 1:640 1:1280 –

↓

To all tubes (1 to 8) of each set add one drop of the respective WIDAL TEST antigen suspension (O,H,AH,BH) from reagent vials and mix well.

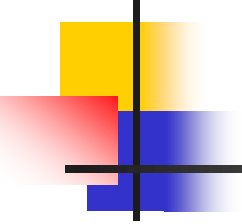
↓

Cover the tubes and incubate at 37 C overnight (approx. 18 hrs).

↓

Dislodge the sedimented button gently and observe.





How do you read Widal test results for typhoid fever?

- The highest dilution of the patients serum in which agglutinations occurs is noted, ex. if the dilution is 1 in 160 then the titer is 169.
- Agglutination in dilution up to $<1:60$ is seen in normal individuals . Agglutination in dilution 1:160 is suggestive of Salmonella infection.
- Agglutination in dilution of and more than 1:320 is confirmatory of Enteric fever .

Prevention

Two main typhoid fever prevention strategies:

1. Vaccination

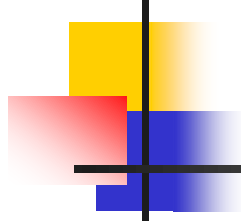
First type of vaccine:

- Contains killed *Salmonella typhi* bacteria.
- Administered by a shot.

Second type of vaccine:

- Contains a live but weakened strain of the *Salmonella* bacteria that causes typhoid fever.
- Taken by mouth.





- ✓ Be vaccinated against typhoid while traveling to a country where typhoid is common.
- ✓ Need to complete your vaccination at least one week before travel.
- ✓ Typhoid vaccines lose their effectiveness after several years so check with your doctor to see if it is time for a booster vaccination.

2. Avoid risky food and drinks

- Buy bottled drinking water or bring it to a rolling boil for one minute before drinking it.
- Ask for drinks without ice, unless the ice is made from bottled or boiled water. Avoid Popsicles and flavored ices.
- Eat food that have been thoroughly cooked and that are still hot and steaming.
- Avoid raw vegetables and food that cannot be peeled like lettuce.
- When eat raw fruit and vegetables that can be peeled, peel yourself. Don't eat the peelings.
- Avoid foods and beverages from street vendors.



Treatment

Consultations

- An infectious disease specialist or surgeon should be consulted.

Surgical Care

- Usually indicated in cases of intestinal perforation.
- Most surgeons prefer simple closure of the perforation with drainage of the peritoneum.
- Small-bowel resection is indicated for patients with multiple perforations.
- If antibiotic treatment fails to eradicate the hepatobiliary carriage, the gallbladder should be resected.
- Cholecystectomy is not always successful in eradicating the carrier state because of persisting hepatic infection.



Diet

- Fluids and electrolytes should be monitored and replaced diligently.
- Oral nutrition with a soft digestible diet is preferable in the absence of abdominal distension or ileus.

Activity

- No specific limitations on activity are indicated.
- Rest is helpful, but mobility should be maintained if tolerable.
- The patient should be encouraged to stay home from work until recovery.



Some common home remedies

- Take two grains of Un nab, Munnakka 4, Kuhbkalan 3 gm's. and Misri 10 gm's. grind all of them and mix in 100 ml. of water, preferably boiled and cooled. Strain the water and make the patient drink at four hourly interval.
- Take 4 basil leaves, saffron 7 shreds, 7 grains of black pepper. Grind them to a paste by adding water and form small tablets out of the whole lot. Take each tablet twice or thrice everyday with lukewarm milk. The fever would also subside and the patient would get the desired relief.
- 1 to 2 teaspoons of fresh juice of coriander leaves mixed in 1 cup buttermilk and taken 2-3 times a day.
- Mash a ripe banana along with 1 tablespoon honey and eat twice a day for a few days.



Medication

Antibiotics

- Antibiotics, such as ampicillin, chloramphenicol, fluoroquinolone trimethoprim-sulfamethoxazole, Amoxicillin and ciprofloxacin etc used to treat typhoid fever.
- Prompt treatment of the disease with antibiotics reduces the case-fatality rate to approximately 1%.



Fluoroquinolones

- Optimal for the treatment of typhoid fever
- Relatively inexpensive, well tolerated and more rapidly and reliably effective than the former first-line drugs, viz. chloramphenicol, ampicillin, amoxicillin and trimethoprim-sulfamethoxazole.
- The majority of isolates are still sensitive.
- Attain excellent tissue penetration, kill *S.typhi* in its intracellular stationary stage in monocytes/macrophages and achieve higher active drug levels in the gall bladder than other drugs.
- Rapid therapeutic response, i.e. clearance of fever and symptoms in three to five days, and very low rates of post-treatment carriage.



Chloramphenicol

- Binds to 50S bacterial-ribosomal subunits and inhibits bacterial growth by inhibiting protein synthesis.
- The recommended dosage is 50 - 75 mg per kg per day for 14 days divided into four doses per day, or for at least five to seven days after defervescence.
- Oral administration gives slightly greater bio availability than intramuscular (i.m.) or intravenous (i.v.) administration of the succinate salt.
- The disadvantages of using chloramphenicol include a relatively high rate of relapse (57%), long treatment courses (14 days) and the frequent development of a carrier state in adults.



Cephalosporins

- Ceftriaxone: 50-75 mg per kg per day one or two doses
- Cefotaxime: 40-80 mg per kg per day in two or three doses
- Cefoperazone: 50-100 mg per kg per day



Amoxicillin (Trimox, Amoxil, Biomox)

- Interferes with synthesis of cell wall mucopeptides during active multiplication, resulting in bactericidal activity against susceptible bacteria.
- At least as effective as chloramphenicol in rapidity of defervescence and relapse rate.
- Convalescence carriage occurs less commonly than with other agents when organisms are fully susceptible.
- Usually given PO with a daily dose of 75-100 mg/kg tid (three times a day) for 14 d.

Adult

1 g PO q8h

Pediatric

20-50 mg/kg/d PO divided q8h for 14 d



Trimethoprim and sulfamethoxazole

- Inhibits bacterial growth by inhibiting synthesis of dihydrofolic acid.
- Antibacterial activity of TMP-SMZ includes common urinary tract pathogens, except *Pseudomonas aeruginosa*.
- As effective as chloramphenicol in defervescence and relapse rate.
- Trimethoprim alone has been effective in small groups of patients.
- Dosing

Adult

6.5-10 mg/kg/d PO bid/tid; can be given IV if necessary; 160 mg TMP/800 mg SMZ PO q12h for 10-14 d

Pediatric

<2 months: Do not administer

>2 months: 15-20 mg/kg/d PO, based on TMP, tid/qid for 14 d



Dexamethasone (Decadron)

- Prompt administration of high-dose dexamethasone reduces mortality in patients with **severe typhoid fever** without increasing incidence of complications, carrier states, or relapse among survivors.
- Initial dose of 3 mg/kg by slow i.v. infusion over 30 minutes.
- 1 mg/kg 6 hourly for 2 days.