Typhoid Fever
(Enteric Fevers)

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Enteric Fevers

- Salmonella Typhi
- Salmonella Paratyphi A, B, C
**Historical landmarks in Typhoid**

- In 1880s, the typhoid bacillus was first observed by Eberth in
  - Spleen sections
  - **Mesenteric lymph nodes** from a patient who died from typhoid.
Typhoid Mary

- A famous example is "Typhoid" Mary Mallon, who was a food handler
- Responsible for infecting 78 people, killing 5.
Typhoid Mary

• "Typhoid Mary," real name Mary Mallon, worked as a cook in New York City in the early 1900s.
• After discovering that she was the common link among many people who had become ill from typhoid fever, she was traced to typhoid outbreaks a second time.
• So she was put in prison again where she lived until she died.
Etiology of Typhoid fever

• Typhoid fever is a bacterial disease, caused by *Salmonella typhi*.

• Transmitted through
  – Ingestion contaminated food & drink by the faeces or urine of infected people.

• Para typhoid fevers are produced by other species named Paratyphi A, B, C
Bacteriology – Typhoid fever

- Salmonella belong to Enterobactericiiae
- Gram negative bacilli
- Antigen on structure
Antigenic structure of Salmonella

- Two sets of antigens
- Detection by serotyping

1 Somatic or O Antigens
   - Contain long chain polysaccharides

2 Flagellar or H Antigens
   - Strongly immunogenic
   - Induces antibody formation rapidly
   - High titers following infection or immunization.
How a Typhoid fever spreads

- *Salmonella* Typhi lives only in humans.
- Persons with typhoid fever carry the bacteria in their bloodstream and intestinal tract.
- In addition, a small number of persons, called carriers, recover from typhoid fever but continue to carry the bacteria.
- Both ill persons and carriers shed *S. Typhi* in their feces (stool).
Pathogenesis of Enteric fever

• Caused by S. Typhi & S. Paratyphi A, B or C
• The organisms penetrate ileal mucosa
• Reach mesentric lymph nodes via Lymphatics
• Multiply in lymph nodes
• Invade Blood stream via thoracic duct
• In 7 – 10 days through blood stream infect Liver, Gall Bladder, spleen, Kidney, Bone marrow.
• After multiplication bacilli pass into blood causing secondary and heavier bacteremia
• Through the blood, it reaches to liver & gall bladder
• From Gall bladder further invasion occurs in intestines
• Involvement of peyr’s patches, gut lymphoid tissue
• Lead to inflammatory reaction & infiltration.
• Leads to Necrosis, Sloughing and formation of characteristic typhoid ulcers intestine
Clinical feature

• Incubation Period: Ingestion to onset of fever varies from 3 – 50 days. (2 weeks)
• Insidious start, early symptoms are vague
• Dull continuous head ache
• Abdominal tenderness
• Abdominal discomfort
• *May progress and present with step ladder pattern temperature*
Clinical features

- Typhoid fever (enteric fever) is a septicemia
- Characterized initially by
  - Fever – High Grade
  - Relative Bradycardia,
  - Hepatomegaly
  - Splenomegaly
  - Abdominal symptoms like Pain in abdomen, Nausea, Vomiting
  - ‘Rose spots' which are clusters of pink patches on the skin.

Complications

- intestinal hemorrhage or perforation can develop in untreated patients or when treatment is delayed.
Events in a Typical typhoid Fever

*CHART 23. — Course of typhoid fever of a previously immunized American patient in Vietnam*

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Rashes in Typhoid

- Rash
- Rose spots 2 - 4 mm in diameter
- Raised discrete irregular
- Found in front of chest
- Fade after 3 – 4 days
Complication in Typhoid

- Intestinal perforation
- Severe intestinal hemorrhage
- Severe bacteremia
Relapse

- 5 – 10 % of untreated patients
- On few occasions relapses can be severe and may be fatal.
Immune Response in Typhoid

![Graph showing immune response over days with IgG and IgM antibodies]
Typhoid carriers

• 1 per 30 of the survivors become carriers.
• In carriers the bacteria remain
  – Inside the gall bladder
  – Spread bacteria to environment through stool
  – causing new infections to healthy through contaminated water & food.
Diagnosis of Enteric Fever
Blood Cultures in Typhoid Fevers

- Blood culture in Bile broth
- Bacteremia occurs early in the disease
- Blood Cultures are positive in
  - 1\textsuperscript{st} week in 90%
  - 2\textsuperscript{nd} week in 75%
  - 3\textsuperscript{rd} week in 60%
  - 4\textsuperscript{th} week and later in 25%
Slide agglutination tests

• In slide agglutination tests,
  – known serum and unknown Serum is mixed
  – clumping occurs within few minutes
**Bactek and Radiometric based methods are in recent use**

- Bactek methods
- Isolation of Salmonella
- Rapid and Sensitive method
- In early diagnosis of Enteric fever.
Other methods in Isolation of Enteric Pathogens

- Feces Culture
- Urine Culture
- Bone marrow cultures (Highly Sensitive)
Widal test

- The widal test detects antibodies against O and H antigens
- Serial dilutions
- **Two serum** specimens obtained at intervals of 7 – 10 days to read the raise of antibodies.

- Following Titors of antibodies against the antigens are significant
  
  O > 1 in 160
  
  H > 1 in 320
Management

Antimicrobial Therapy in Typhoid

• With antibiotic therapy, more than 99% are cured.

1. **Chloramphenicol** = Drug of choice and effective
2. **Tromethoprim Sulfamethoxazole**
3. Fluoroquinolones like **Ciprofloxacin**, **Levofloxacin**.
4. 3rd generation cephalosporins, **Ceftriaxone**, **Cefixime**
Vaccines for Typhoid Prevention

Oral – A live oral vaccine (Typhoral)
1, 3, 5 days (three doses)
No antibiotics should be taken during the period of administration of vaccine

The injectable vaccine, (Typhim –vi)

• Given Subcutaneous or Intramuscular injection
• Single dose is adequate.
Vaccines for Typhoid

Both vaccines are given to only > 5 years of age. Immunity lasts for 3 years Need a booster

Vaccines are not effective in prevention of Paratyphoid fevers
Simple hand hygiene and washing can reduce several cases of Typhoid
It is nice to have money and the things that money can buy. But it's important to make sure you haven't lost the things which money can't buy.”