ENTERIC FEVER
INTRODUCTION

Fever (Caused) by Infection in Intestine

An Acute Generalized Infection of Intestinal Lymphoid Tissues, RES, Gall Bladder

Typhoid – 90 % cases
Paratyphoid – 10 % cases
HISTORICAL BACKGROUND

- Typhoid = Typhus (Rickettsial) like

- Typhos (Gk) = Smoke (cause), Cloudy (sensorium)

- Phytos (Gk) = Putrefaction (of food as cause)

- Identified as a separate identity by: Huxlam(1972), Louis(1829), Gerhardt(1837), Shoenlein(1839), Jenner(1850), Budd(1873), Gaffkey(1884)
THE ORGANISM

- Gram Negative, Nonacid fast, Noncapsulated, Nonsporing bacilli
- A Very Die hard Organism - Life Long Carriers
- Types:
  - Salmonella typhi
  - Salmonella paratyphoid A
  - Salmonella paratyphoid B
  - Salmonella paratyphoid C
THE ORGANISM - ANTIGENIC STRUCTURE

- O – Cell Wall Polysaccharide – Heat Stable
- H – Flagellar – Heat Labile
- Vi – Surface – Virulence – Heat Labile
- (Useful in Serodiagnoses e.g. Widal Test)
EPIDEMIOLOGY

Occurs Exclusively in Humans

Spread – Contaminated Food, Milk, Water
  - By Flies from Human Excreta to Food
  - Poor Personal Hygiene
  - Poor Sanitation

Age  – Older Children, Young Adults
  <5 Years = only 10 %
  <2 Years = only 2 %

Gender - Equal
EPIDEMIOLOGY – CONT..

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Areas</strong></td>
<td>Underdeveloped, Poor</td>
</tr>
<tr>
<td><strong>Annual Occurrence</strong></td>
<td>Throughout the year</td>
</tr>
<tr>
<td><strong>Peak Time</strong></td>
<td>July to August (Summer/Early Rains)</td>
</tr>
<tr>
<td><strong>Incubation Period</strong></td>
<td>1 to 2 weeks (3-60 days)</td>
</tr>
<tr>
<td><strong>Dose of Inoculation</strong></td>
<td>∞</td>
</tr>
<tr>
<td><strong>Infectivity Period</strong></td>
<td>Long (&gt;2 to 3 m)</td>
</tr>
<tr>
<td><strong>Carriers (5%)</strong></td>
<td>20-50 years; Females more</td>
</tr>
</tbody>
</table>
EPIDEMIOLOGY - GLOBAL DISTRIBUTION

- Endemic or hyperendemic mode
- Endemo-epidemic mode
- Sporadic or local outbreak mode
** ROUTES OF TRANSMISSION **

- **Patient**
  - **Chronic Carrier**
  - **Dissemination**
    - **Stool**
    - **Vomit**
    - **Urine**

  - **Indirect Infection** > 90%
    - **Infected Water**
      - **Healthy Subject**
        - **Typhoid Fever**

  - **Direct Infection** < 10%

- **Infected Water**
- **Food**
PATHOGENESIS OF TYPHOID FEVER

S. Typhi

Ingestion

Intraluminal Multiplication

Intestinal Lymphoid Tissue

Release of Endotoxins

Liver, Spleen

Multiply

Reinfect Blood, Alimentary Tract (Excreted in stool)

Blood Stream

Toxemia

Damage other systems e.g. CNS

Infects Bones, Skin, CNS
INTESTINAL LESIONS

Typhoid Bacilli

Intestinal Villi

To Liver and Spleen

Blood Vessels

Perforation Ulcers
MULTI - ORGAN EFFECTS

Peyer’s Patches

Liver and Gallbladder

Spleen

Typhoid Fever

Bones and Bone marrow

Solid Viscera

Heart and Major Vessels
CLINICAL FEATURES

• Fever :
  – Acute Onset
  – Continuous (+ Morning Remission )
  – Moderate To High Grade
  – Persisting since 6-7 Days
  – Classic Step Ladder Pattern Not Seen in children
## Classic Step Ladder Fever of Typhoid

<table>
<thead>
<tr>
<th>Incubation Phase</th>
<th>Invasion Phase</th>
<th>Status Period</th>
<th>Evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>Oscillating fever</td>
<td>Constant Typhoid state</td>
<td>Long period of convalescence even with suitable and early therapy</td>
</tr>
<tr>
<td></td>
<td>Dissociated pulse</td>
<td>Intestinal disturbances</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Asthenia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Graph

- **98.4°F**
- **104°F**

- **D0**
- **D7**
- **D21**
OTHER SYMPTOMS

- Myalgia
- Anorexia, Vomiting
- Diarrhea / Constipation
- Toxic Look
- Pain in Abdomen
- Headache
- Cough
CLINICAL EXAMINATION

• Coated (Typhoid V) Tongue
• Tympanitis of Abdomen
• Soft Splenomegaly (≥ 1 week fever)
• Hepatomegaly ±
• Chest: Rhonchi / Crepts
• Skin: Rosy Spots - Chest / Paraumblicus - not seen in Indian Children
• Mild / Moderate Anemia
• Meningismus ±
• Jaundice (Rare)
## COMPLICATIONS IN TYPHOID

<table>
<thead>
<tr>
<th>System</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>Encephalopathy (Altered Sensorium),</td>
</tr>
<tr>
<td></td>
<td>Convulsions (Toxic Cases), Meningism, Psychoses</td>
</tr>
<tr>
<td>GIT</td>
<td>Hemorrhage 1-2%, Perforation 0.5%, (Shock,</td>
</tr>
<tr>
<td></td>
<td>Distension of Abdomen) Peritonitis, Hepatitis,</td>
</tr>
<tr>
<td></td>
<td>Cholangitis</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Early – Bronchitis</td>
</tr>
<tr>
<td></td>
<td>Late – Secondary Pneumococcal</td>
</tr>
<tr>
<td></td>
<td>Bronchopneumonia</td>
</tr>
<tr>
<td>CVS</td>
<td>Myocarditis (Bradycardia, systolic murmur)</td>
</tr>
<tr>
<td>Skeletal</td>
<td>Chronic Osteomyelitis, Arthritis</td>
</tr>
<tr>
<td>Skin</td>
<td>Alopecia, Furuncles</td>
</tr>
<tr>
<td>Renal</td>
<td>UTI in 20 to 25 % cases</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Otitis Media, Unilateral Parotitis, Purpuric</td>
</tr>
<tr>
<td></td>
<td>Eruptions/Epistaxis, Thrombosis</td>
</tr>
</tbody>
</table>
DIAGNOSIS

• Mainly Clinical

• Fever of more than seven days
  With/Without

  Toxemia
  Abdominal Pain/ Typanitis
  Altered Sensorium
  Mild Hepatosplenomegaly
## INVESTIGATIONS

<table>
<thead>
<tr>
<th>Week</th>
<th>Code</th>
<th>Test and Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Week</td>
<td>B</td>
<td>Blood / Clot Culture (Bone Marrow Culture, rarely)</td>
</tr>
<tr>
<td>2nd Week</td>
<td>A</td>
<td>Agglutination Test (Widal)</td>
</tr>
<tr>
<td>3rd Week</td>
<td>S</td>
<td>Stool Culture</td>
</tr>
<tr>
<td>4th Week</td>
<td>U</td>
<td>Urine Culture</td>
</tr>
</tbody>
</table>

“BASU”
AGGLUTINATION (WIDAL) TEST

• Agglutinins appear in blood by end of 1st week
• O agglutinin: Rises Rapidly (4 fold in 10-14 days)  
  Persists for months  
  Disappears in a year
• H agglutinin: Rises Slowly  
  Persists for years
• Hence, O agglutinin is important in recent infection
• Diagnostic levels: >1/80 or 1/160 or Rising Titers (7-10 days apart)
• H agglutinin indicates past infection/immunization
FALSE POSITIVES AND NEGATIVES IN WIDAL TEST

False Positives
- Immunization with Typhoid Vaccine
- Repeated Sub clinical Infections
- Past Clinical Infection
- Healthy Carriers of S. Typhi
- Anamnestic Response
- Patients of Cirrhosis and Hepatitis

False Negatives
- Too Early collection of blood sample
- Patients on Antibiotics
- 5 to 10 % do not respond by antibody formation
NON SPECIFIC LAB FINDINGS IN TYPHOID FEVER

• Mild Normochromic Anemia
• Mild Thrombocytopenia
• Leucopenia / Leucocytosis
• Eosinopenia – Presence heralds recovery
• An Increased ESR
• Laboratory Evidence of Mild DIC
• Hyponatremia and Hypokalemia
• Elevation of Liver Enzymes
• Urine : Some Proteins and White Cells
• Stool : Leucocytes and Blood common
DIFFERENTIAL DIAGNOSIS

- Infective Diarrhea: Stool Examination
- Viral Fever: Self limiting (< 7 days)
- UTI: Urinalysis
- Malaria: Blood smear examination
- Miliary TB: F/H, CXR, Mantoux
- Appendicitis: White cell count
- Bacterial Endocarditis: Blood Culture
- Viral Hepatitis: LFTs
- Kala – Azar: Double rise temperature, good appetite, no toxemia
TREATMENT - GENERAL

• Tepid Sponging
• Paracetamol
• Adequate water and food intake
• Hospitalize if: Toxemic / Complications
  - Needs Fluids/ Therapy by IV Route
TREATMENT - MEDICAL

Uncomplicated Typhoid fever
• Fully sensitive:
  - Chloramphenicol or Amoxicillin as first line
  - Fluoroquinolone as second line
• MDR:
  - Fluoroquinolone or Cefixime as first line
  - Azithromycin as second line
• Quinolone resistant:
  - Azithromycin or Ceftriaxone as first line
  - Cefixime as second line
TREATMENT - MEDICAL

Complicated/Severe Typhoid fever
• Fully sensitive:
  - Ceftriaxone as first line
  - Fluoroquinolone as second line
• MDR:
  - Fluoroquinolone as first line
  - Ceftriaxone/Cefotaxime as second line
• Quinolone resistant:
  - Ceftriaxone as first line
  - Azithromycin or Gatifloxacin as second line
TREATMENT – MEDICAL – CONT..

- Chloramphenicol: 50-75mg/kg/day for 14-21 days
- Cefixime: 15-20 mg / kg/day/O in 2 doses x 7-14 days
- Ceftriaxone: 80-100 mg/kg/day/IV in 2 doses x 10-14 days
- Cefotaxime: 100mg/kg/day/IV in two doses x 10-14 days
- Azithromycin: 20mg/kg/day/O single dose x 7 days
- Ofloxacin/Ciprofloxacin: 15mg/kg/day for 10-14 days
- Gatifloxacin: 10mg/kg/day for 7 days
TREATMENT OF COMPLICATIONS

• INTESTINAL HAEMORRHAGE
  – Bed rest / foot end raised
  – Nothing orally
  – Repeated blood transfusions
  – Morphine sc.

• ENCEPHALOPATHY
  – Anticonvulsants
  – Dexamethasone

• PNEUMONIA
  – ↑ Antimicrobial spectrum

• ANAEMIA: Blood replacement

• INTESTINAL PERFORATION
  – Surgical intervention
  – Clindamycin / Metronidazole
PREVENTION

• Personal Hygiene
• Safe drinking water and food habits
• Avoid unpasteurized dairy products
• Public health measures for
  – Disposal of Excreta
  – Ban on sale of contaminated food
• Tracing & Treatment of Carriers
• Active immunization with vaccine
CARRIERS

• Convalescent carrier: Patients who continue to shed bacilli in feaces for 3 weeks to 3 months after cure
• Temporary carrier: Those who shed for 3 months to 1 year
• Chronic Carrier: Those who shed more than 1 year (2 – 4% patients become chronic carrier)
• Healthy carrier / Intermittent carrier:
  – Harbours infection without suffering from the disease
  – Bacilli persists in gall bladder or kidney
• Treatment:
  – Prolonged treatment with quinolones or Cephalosporins
  – May require gall bladder removal
TYPHOID VACCINES

• Two Typhoid conjugate vaccines currently available (Typbar-TCV, PedaTyph)
  - PedaTyph not yet approved
  - First does at 9-12 months of age with at least 4 wks. interval with MMR vaccine
  - Booster dose at 2yrs of age

• Booster dose can be either conjugate vaccine or Vi-Polysaccharide vaccine
TYPHOID VACCINES

• Those receiving booster Vi-PS vaccine need revaccination every 3yrs
• Need for further boosters after conjugate vaccine is not yet determined
THANK YOU