TYPHOID AND PARATYPHOID FEVER

BY: DR. A. SEIKH

DATE: 18/8/2016

OUTLINE

- Definition and historical background
- Epidemiology
- Microbiology and pathogenesis
- Clinical manifestations
- Diagnostic evaluation
- Treatment and prognosis
- Complications
- Prevention

INTRODUCTION

- Typhoid is a febrile systemic illness with abdominal symptoms caused by *Salmonella typhi* & *Salmonella paratyphi*
  - *S. paratyphi* has subtypes A, B, C
  - *S. typhi* has serovars; serovar *enterica* is pathogenic

- Typhi meaning ;typhus-like' according to one source. From Greek '*typhos*' – an ethereal smoke or cloud that was believed to cause illness and madness

SHORT HISTORY

- The best known carrier was **Typhoid Mary**.
- She was a cook and an asymptomatic carrier.
- She died of pneumonia after 26 years in quarantine.

EPIDEMIOLOGY

- Typhoid is common in areas with **poor infrastructure in terms of hygiene and disposal of waste** esp. in developing countries with low socioeconomic statuses.
- Overcrowding is also a risk factor for typhoid infection.
- In the developed countries, most infections are due to travelling.
- 200-300 cases/year in the USA
- Mortality is 9-13% pre-antibiotics – now < 1%
- Children are at a greater risk of getting the disease.
- Tose who work in or travel to endemic area/
- Those who have close contact with infected people are susceptible.
- Immunosuppression is also a risk factor

ETIOLOGY

- Typhoid fever is cause by a gram –ve bacilli in the family of *enterobacteriaceae*, flagellated, facultatively anaerobic, non-spore forming, glucose fermentor, reduces nitrates but does not produce cytochrome oxidase.
- All salmonellae are motile except *S. gallinarium-pullorium*
- All produce H_2S except *S. typhi*
- Only 1% of clinical isolates ferments lactose
- Antigens located in the cell capsule:
  - H (flagellar antigen)
  - Vi (Polysaccharide virulence Ag)
  - O (Somatic antigen)

PATHOPHYSIOLOGY

- Greater dose – higher attack rate, shorter incubation. About 30% of volunteers given 10^5 CFU (Colony Forming Units), 10-20% with 10^3 CFU develop illness
- Most cases get low dose with low attack rate and long incubation of 2-3 weeks
- Ingested – pass to stomach to SB. Doesn't tend to cause fulminant enteritis as do non-typhi Salmonella; 10-20% get it at some point.
- Phagocytic cells in the Peyer's patches take to sub-mucosal region and proliferate – primary terminal ileum; In the Peyer's patches, hypertrophy takes place, necrosis occurs resulting in ulceration.
  - There are regulatory genes and secretory mechanisms within the bacilli that enable it to survive within the macrophage.
  - The infected macrophage moves around the RES disseminating the bacilli. Further replication takes place and secondary bacteremia occurs. At this point dissemination can occur to any organ hence typhoid is a systemic disease.
  - The macrophage also produces pro-inflammatory cytokines (IL-1, IL-6, TNF) resulting in fever.
- Protective factors:
  - Low Gastric pH
- Those at increased risk:
  - Achlorhydria
    - Pernicious anemia
    - Previous gastric resection
    - PPI use
  - Extremes of age
- Fe is needed for its growth.

CLINICAL

- Common tropical diseases that is difficult to diagnose early and accurately
- Non-specific prodrome. Many organs can be affected, Can mimic many other diseases,
- Fever predominates in the first week (**Step-ladder pyrexia)**
  - Not seen lately due to early medication
- Abdominal symptoms predominate in the second week
  - Abdominal crampy pain, constipation, diarrhea, dysentery (due to sloughing of enterocytes, with tenesmus)
  - Toxemia
  - All clinical spectra depending on the dissemination of the bacilli can be seen during te 2nd week e.g. myocarditis, osteomyelitis
- Bowel perforations, tachycardia week 3
- Resolution and slow recovery – week 4

CLINICAL HISTORY

- Fever
- Weakness
- Anorexia
- Headache
- Dizziness

PHYSICAL FINDINGS

- Fever
- Coated tongue
- Apathy
- Pink maculopapular rash that blanches easily – **rose spots**
- Apathetic look – typhoid facies
- Abdominal tenderness
- Faget's sign: relative bradycardia

ENDEMIC AREA

- Must have a high index of suspicion
- Consider if > 3 days of fever

LAB DIAGNOSIS

- Normocytic anemia
- WBC normal or decrease (15-30%); Tends to be increased in children or if perforation
- Increased ESR
- Thrombocytopenia

DIAGNOSIS: CULTURES

- Bone marrow culture is most sensitive
- Blood sensitivity initially is good but goes down
- Puncture biopsy from the rose spots
- Urine and stool – when abdominal symptoms predominate
- Widal test is not sensitive or specific and is no longer considered acceptable for diagnosis
  - Measures agglutinating antibodies to H. O antigens of *S. typhi*
  - Positive if prior infection or immunization
  - O titer more specific, H more sensitive

COMPLICATIONS

- Gross intestinal hemorrhage
- Pneumonia and encephalopathy
- Intestinal perforation
  - More common in adults than in children
  - Classically in 3rd week
  - Worsening, sudden onset increased RLQ pain
  - Usually in terminal ileum
- Relapse
- Pancreatitis

DIFFERENTIALS

- Malaria
- Influenza
- Dengue

PROGNOSIS

- Higher if antibiotics like chloramphenicol are delayed

- Causes of death
  - Early shock

TREATMENT - RESISTANCE

- 3rd Generation cephalosporins (Ceftriaxone or cefixime)
  - High initial response rate but high relapse rates
- Nalidixic acid and other quinolones (Beware! NARST < Nalidixic Acid Resistance>)
  - Outpatient
- Azithromycin
- Chloramphenicol (there has been plasmid-mediated resistance)
- In children:
  - Quinolones
  - Beta lactams: Ceftriaxone, cefixime
  - Azithromycin

RELAPSE

- Common
- 2-3 weeks after resolution
- Use same drug but for longer

CARRIER STATE

- Can shed normally up to 3 months
- Chronic carriers are given quinolones for a longer duration (up to a month)

- Predisposing factors to becoming a chronic carrier:
  - Female
  - Biliary tract abnormalities
  - GI malignancies
  - Schistomiasis in the urinary tract

PREVENTION

- 4 vaccines
  - viCPS
  - VirEPA
  - Heat killed phenol extracted whole cell vaccine – highest efficacy
  - Oral S/ typhi vaccine strain Ty21a

- Given to people travelling to endemic areas.

TYPED BY DR. E. NAILA