PATHOGENESIS & CLINICAL FINDINGS of Enteric FEVER

Prof WWMaw
• *Salmonella* Typhi,
• *Salmonella* Paratyphi A and
• *Salmonella* Paratyphi B are
• primarily infective for humans and
• infection with these organisms implies acquisition from a human source
• There is **no animal reservoir**
PATHOGENESIS & CLINICAL FINDINGS

• The infectious dose is low
• \((10^3 \text{ Salmonella Typhi})\)
• So person-to-person spread is common
• The host factors that contribute to resistance to salmonella infection are

  » 1. gastric acidity,
  » 2. normal intestinal microbial flora,
  » 3. local intestinal immunity
Causal organisms

- *Salmonella* Typhi
- *Salmonella* Paratyphi A
- *Salmonella* Paratyphi B - Europe
- *(S. schottmuelleri)*
- *Salmonella* Paratyphi C *(S. hirschfeldii)* – Far east
MOT

• Fecal-oral route, 5 Fs
• usually with contaminated food or drink
• Organisms in water - carried through the stomach relatively rapidly,
• evade the effect of gastric acids
• Organisms within food would
• also evade gastric acid
The ingested salmonellae pass through the stomach, reach the small intestine, attach to the mucosa of the small intestine and invade into the M (microfold) cells located in Peyer patches, as well as into enterocytes.
Salmonella typhimurium (red) invading cultured human cells

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• The bacteria replicate in an endocytic vacuole or
• can also be transported across the cytoplasm and
• released into the blood or (Blood culture)
PATHOGENESIS & CLINICAL FINDINGS

- They are **carried by the blood** to many organs,
- including the intestine
- The organisms **multiply in intestinal lymphoid tissue and**
- are **excreted in stools** (stool culture)
- also excreted in urine (Urine culture)
"S. typhi" enters M cell

Tight junction

First exposure of Peyer's patch to S. typhi

Peyer's patch ulcer

S. typhi re-enters GI tract

2nd exposure of Peyer's patch to S. typhi

Mesenteric lymph node

Blood

Liver

Spleen

Blood via gall bladder

Key:
- Peyer's patch
- Red blood cells
- S. typhi
- Necrotic Peyer's patch
- Macrophage
- T cells
- Lymph node

TRENDS in Microbiology
• Incubation period of 10-14 days
• Fever, malaise, headache, Step ladder rise
• Fever step ladder rise to high plateau
• constipation,
• Pea soup diarrhoea
• , malaise, head-ache, on and myalgia
• Rose spots, usually appear on the skin of the abdomen or chest, are seen briefly in rare cases 30%

• Relative bradycardia

• bradycardia and myalgia occur

• Spleen & liver become enlarged

• White blood cell count is normal or low
Typhoid

- Rose spots at 7-10 days
- Relative bradycardia
- Distended, doughy uncomfortable abdomen
- Constipated in older
- Palpable spleen
- Confused

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Coated tongue, rose spot
Pea soup diarrhoea
Complications

- intestinal hemorrhage and perforation
- hyperplasia and necrosis of lymphoid tissue (e.g. Peyer's patches)
- hepatitis, focal necrosis of the liver and
- inflammation of the gallbladder, periosteum, lungs
  and other organs
• The mortality rate was 10-15%

• Treatment with antibiotics has reduced the mortality rate to less than 1%
The gut immune system comprises effector sites and inductive sites.
Salmonella Typhimurium entering a HEp-2 cell through bacteria-mediated endocytosis
M cells are interspersed between enterocytes and in close contact with subepithelial lymphocytes and dendritic cells.

M cells take up antigens from the gut lumen by endocytosis.
M cells are interspersed between enterocytes and in close contact with subepithelial lymphocytes and dendritic cells.

M cells take up antigens from the gut lumen by endocytosis.

Antigens are released beneath M cells and taken up by antigen-presenting dendritic cells.
Salmonellae enter and kill M cells and then infect macrophages and epithelial cells.

Salmonellae invade the luminal surface of epithelial cells.

Salmonellae enter dendrites of dendritic cells that are sampling the gut luminal contents.
Figure 10-27 Immunobiology, 6/e. (© Garland Science 2005)
Mucosal immune system