

The Salmonella-group

- Salmonellae are often pathogenic for humans or animals when acquired by the oral route.
- They are transmitted from animals and animal products to humans, where they cause enteric fever ,gastro- enteritis and systemic infection.
- Most isolates are motile with peritrichous flagella. They almost never ferment lactose or sucrose. They form acid and sometimes gas from glucose and mannose. They usually produce H₂S.
- They survive freezing in water for long periods. Salmonellae are resistant to certain chemicals (eg, brilliant green, sodium tetrathionate, sodium deoxycholate) that inhibit other enteric bacteria; such compounds are therefore useful for inclusion in media to isolate salmonellae from feces.
- Salmonellae are named by genus (Salmonella), species (enterica), and subspecies (e.g., typhi or enteritidis) .

Serovars of Medical Importance

- *S. enterica* subsp. Typhi.
- *S. enterica* subsp. Enteritidis
- *S. enterica* subsp. Typhimurium
- *S. enterica* subsp. Choleraesuis
- *S. enterica* subsp. Paratyphi
- *S. enterica* subsp. Dublin

The “Enteric Fevers” (Typhoid Fever)

- Four serotypes of salmonellae that cause enteric fever can be identified in the clinical laboratory by biochemical and serologic tests. These serotypes should be routinely identified because of their clinical significance.
- Salmonella Paratyphi A (serogroup A), Salmonella Paratyphi B (serogroup B), Salmonella Choleraesuis (serogroup C1), and S Typhi (serogroup D).
- Salmonella serotypes Enteritidis and Typhimurium are the two most common serotypes reported in developed world.

Epidemiology

- Typhoid fever is severe systemic disease.
- Incidence differs significantly between developing vs developed countries 0.2-4 cases to up to 500 /10⁵ population.
- Humans are the natural reservoir. The feces of persons who have unsuspected subclinical disease or are carriers are a more important source of contamination than frank clinical cases that are promptly isolated, such as when carriers working as food handlers are “shedding” organisms.
- Many animals, including cattle, rodents, and fowl, are naturally infected with a variety of salmonellae and have the bacteria in their tissues (meat), excreta, or eggs.
- Food, water contaminated with human faeces, vertical transmission (trans-placental).

Pathogenesis

- The vast majority of salmonellae, however, are chiefly pathogenic in animals that constitute the reservoir for human infection; these include poultry, pigs, rodents, cattle, pets (from turtles to parrots), and many others
- Stomach acidity and normal intestinal microbiota are important determinants of susceptibility.
- The salmonella invades peyer patches and transported to other intestinal L.N. where they multiply in Mononuclear cells to mesenteric L.N. to blood through thoracic duct (transient bacteraemia).
- Circulating organism reach reticulo-endothelial cells in liver ,spleen and bone marrow and circulating endo -toxin cause prolonged fever.
- Inflamed mucosa and lymphatics .Necrosis and sloughing of overlying epithelium producing ulcer that may bleed. Ulcers heal without scarring.
- Cell mediated immunity is important

Clinical manifestations

- Incubation 7-14 days. Onset is insidious.
- 1st week
 - Fever malaise ,anorexia myalgia headache, abdominal pain ,diarrhoea early and later constipation.
 - Temp. increase in a stepwise fashion become unremitting and high (a high plateau).
- 2nd week
 - High fever, fatigue, cough ,epistaxis. abdominal symptoms more severe, rose spots and rash.
- 3-4 weeks
 - If no complications, symptoms & signs gradually resolve.
 - In the pre-antibiotic era, the chief complications of enteric fever were intestinal hemorrhage and perforation, and the mortality rate was 10–15%.

Enterocolitis

- This is the most common manifestation of salmonella infection.
- In the United States, *S* Typhimurium and *Salmonella* Enteritidis are prominent, but enterocolitis can be caused by any of the more than 1400 group I serotypes of salmonellae.
- Eight to 48 hours after ingestion of salmonellae, there is nausea, headache, vomiting, and profuse diarrhea, with few leukocytes in the stools. Low-grade fever is common, but the episode usually resolves in 2–3 days. Inflammatory lesions of the small and large intestine are present.
- Bacteremia is rare (2–4%) except in immunodeficient persons.
- Blood culture results are usually negative, but stool culture results are positive for salmonellae and may remain positive for several weeks after clinical recovery.

Bacteremia with Focal Lesions

- This is associated commonly with *S choleraesuis* but may be caused by any salmonella serotype. After oral infection, there is early invasion of the bloodstream (with possible focal lesions in lungs, bones, meninges, and so on), but intestinal manifestations are often absent.
- Blood culture results are positive.

Diagnostic Laboratory Tests

- A. Specimens
- culture : positive in Blood, Bone marrow, Stool & Urine culture results may be positive after the second week.
- In enteric fevers, the stools yield positive results from the second or third week on; in enterocolitis, the stools yield positive results during the first week. A positive culture of duodenal drainage establishes the presence of salmonellae in the biliary tract in carriers.

B. Bacteriologic culturing for Isolation of Salmonellae

1. Enrichment cultures— The specimen (usually stool) also is put into selenite F or tetrathionate broth, both of which inhibit replication of normal intestinal bacteria and permit multiplication of salmonellae.
2. Differential and Selective medium cultures—EMB, MacConkey, or deoxycholate medium. salmonella-shigella (SS) agar, Hektoen enteric agar and xylose-lysine decarboxylase (XLD) agar.
3. Final identification— Suspect colonies from solid media are identified by biochemical reaction patterns and slide agglutination tests with specific sera.

C. Serologic Methods

- 1. Agglutination test— In this test, known sera and unknown culture are mixed on a slide. Clumping, when it occurs, can be observed within a few minutes. This test is particularly useful for rapid preliminary identification of cultures. There are commercial kits available to agglutinate and serogroup salmonellae by their O antigens: A, B, C1 , C2 ,D, and E.

Serologic Methods

- 2. Tube dilution agglutination test (Widal test)—
- Serum agglutinins rise sharply during the second and third weeks of S Typhi infection. The Widal test to detect these antibodies against the O and H antigens has been in use for decades.
- At least two serum specimens, obtained at intervals of 7–10 days, are needed to prove a rise in antibody titer.
- Serial dilutions of unknown sera are tested against antigens from representative salmonellae. False-positive and false-negative results occur. The interpretive criteria when single serum specimens are tested vary, but a titer against the O antigen of greater than **1:320** and against the H antigen of greater than **1:640** is considered positive.
- High titer of antibody to the Vi antigen occurs in some carriers. Alternatives to the Widal test include rapid colorimetric and EIA methods.
- Results of serologic tests for Salmonella infection cannot be relied upon to establish a definitive diagnosis of typhoid fever and are most often used in resource poor areas of the world where blood cultures are not readily available .

Immunity

- Infections with *S Typhi* or *Salmonella Paratyphi* usually confer a certain degree of immunity.
- Reinfection may occur but is often milder than the first infection. Circulating antibodies to O and Vi are related to resistance to infection and disease. However, relapses may occur in 2–3 weeks after recovery despite antibodies.
- Secretory IgA antibodies may prevent attachment of salmonellae to intestinal epithelium.
- Persons with S/S hemoglobin (sickle cell disease) are exceedingly susceptible to *Salmonella* infections, particularly osteomyelitis. Persons with A/S hemoglobin (sickle cell trait) may be more susceptible than normal individuals (those with A/A hemoglobin).

Treatment

- Although enteric fevers and bacteremias with focal lesions require antimicrobial treatment, the vast majority of cases of enterocolitis do not.
- Antimicrobial treatment of Salmonella enteritis in neonates is important. In enterocolitis, clinical symptoms and excretion of the salmonellae may be prolonged by antimicrobial therapy. In severe diarrhea, replacement of fluids and electrolytes is essential.
- Antimicrobial therapy of invasive Salmonella infections is with fluoroquinolones, ampicillin, trimethoprim–sulfamethoxazole, or a third-generation cephalosporin.
- Multiple drug resistance transmitted genetically by plasmids among enteric bacteria is a problem in Salmonella infections.
- Susceptibility testing is an important adjunct to selecting a proper antibiotic. In most carriers, the organisms persist in the gallbladder (particularly if gallstones are present) and in the biliary tract. Some chronic carriers have been cured by ampicillin alone, but in most cases cholecystectomy must be combined with drug treatment.

Prevention and Control

- Three percent of survivors of typhoid become healthy permanent carriers, harboring the organisms in the gallbladder; biliary tract; or, rarely, the intestine or urinary tract.
- Sanitary measures must be taken to prevent contamination of food and water by rodents or other animals that excrete salmonellae.
- Infected poultry, meats, and eggs must be thoroughly cooked.
- Carriers must not be allowed to work as food handlers and should observe strict hygienic precautions.
- Two typhoid vaccines are currently available : an oral live, attenuated vaccine and a Vi capsular polysaccharide vaccine for intramuscular use.
- Vaccination is recommended for travelers to endemic regions, especially if the traveler visits rural areas or small villages where food choices are limited, efficacy of 50–80%.

Yersinia

- The genus *Yersinia* comprises gram-negative bacteria of the family Enterobacteriaceae (gamma proteobacteria).
- They grow best at 25°C and are motile at 25°C but nonmotile at 37°C.
- *Y. pestis* –plague- is transmitted to humans usually through the bite of an infected flea, although inhalation is another potential route.
- Yersiniosis is a zoonotic infection with an enteropathogenic *Yersinia* species, usually *Yersinia enterocolitica* or *Y. pseudotuberculosis*.
- *Y. enterocolitica* is more closely associated with terminal ileitis and *Y. pseudotuberculosis* with mesenteric adenitis, but both organisms may cause mesenteric adenitis and symptoms of abdominal pain and tenderness that result in pseudoappendicitis, with the surgical removal of a normal appendix

- *Y. enterocolitica* is found worldwide and has been isolated from a wide variety of wild and domestic animals and environmental samples, including samples of food and water.
- Most clinical infections are associated with serogroups O:3, O:9, and O:5,27, with a declining number of O:8 infections.
- Consumption or preparation of raw meat , products milk (pasteurized, unpasteurized, and chocolate-flavored) and various foods contaminated with spring water products are linked with infection.
- *Y. pseudotuberculosis* is less frequently reported as a cause of human disease than *Y. enterocolitica*.

Pathogenesis

- The usual route of infection is oral. initial replication in the small intestine is followed by invasion of Peyer's patches of the distal ileum via M cells, with onward spread to mesenteric lymph nodes. The liver and spleen can also be involved after oral infection.
- The characteristic histologic appearance of enteropathogenic yersiniae after invasion of host tissues is as extracellular micro-abscesses surrounded by an epithelioid granulomatous lesion.
- *Y enterocolitica* can produce a heat-stable enterotoxin, but the role of this toxin in diarrhea associated with infection is not well defined
- All yersiniae possess lipopolysaccharides that have endotoxic activity when released.
- They have type III secretion systems that consist of a membrane- spanning complex that allows the bacteria to inject proteins directly into cytoplasm of the host cells
- The pathogenic yersiniae have a pathogenicity island (PAI) that encodes for an iron-scavenging siderophore

Clinical manifestations

- Self-limiting diarrhea is the most common reported presentation in infection with pathogenic *Y. enterocolitica*, especially in children under the age of 4, who form the single largest group in most case series.
- Blood may be detected in diarrheal stool. Older children and adults are more likely than younger children to present with abdominal pain, which can be localized to the right iliac fossa—a situation that often leads to laparotomy for presumed appendicitis (pseudoappendicitis).
- Gastrointestinal complications include granulomatous appendicitis, a chronic inflammatory condition affecting the appendix.
- Post-infective phenomena of reactive arthritis might be developing within 2–4 weeks of a preceding infection.

LABORATORY DIAGNOSIS

➤ Specimens

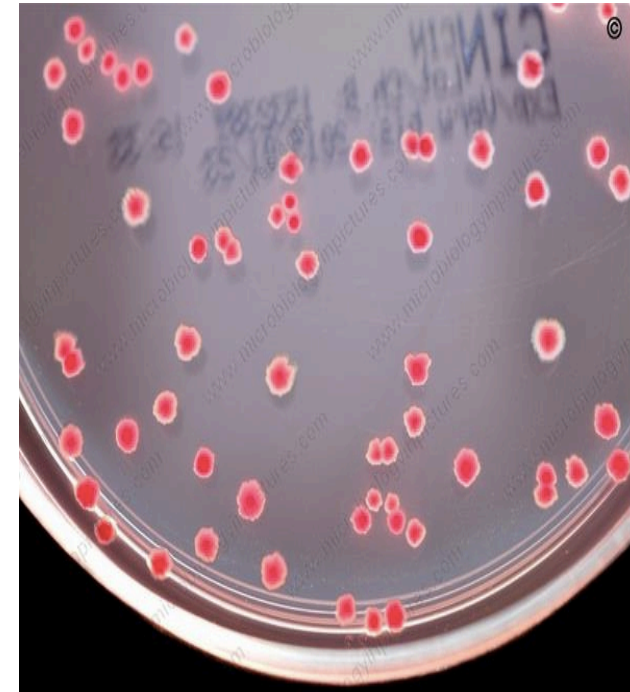
- Specimens may be stool, blood, or material obtained at surgical exploration.

➤ Culture

- The number of yersiniae in stool may be small and can be increased by “cold enrichment”. Subcultures made at intervals on MacConkey agar may yield yersiniae. Alternatively, most clinical laboratories use a Yersinia selective agar such as cefsulodin-Irgasan-novobiocin (**CIN**) agar incubated at room temperature for several days.
- *Y enterocolitica* colonies have a bull’s eye appearance with a red center on CIN agar.

➤ Serology

- serum specimens taken 2 or more weeks apart, a rise in agglutinating antibodies can be shown; however, cross-reactions between yersiniae and other organisms (vibriosis, salmonellae, and brucellae) may confuse the results.



Treatment

- Most cases of diarrhea caused by enteropathogenic *Yersinia* are self-limiting. Data from clinical trials do not support antimicrobial treatment for adults or children with *Y. enterocolitica* diarrhea.
- Systemic infections with bacteremia or focal infections outside the gastrointestinal tract generally require antimicrobial therapy.
- fluoroquinolone therapy is effective for bacteremia in adults; for example, ciprofloxacin, A third-generation cephalosporin is an alternative

PREVENTION AND CONTROL

- Safe handling and processing of food.
- No vaccine is effective in preventing intestinal colonization of food animals by enteropathogenic Yersinia.
- Consumption of food made from raw meat should be discouraged at present because it is not possible to eliminate contamination with the enteropathogenic Yersinia strains found worldwide.

The End