

Salmonella

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Introduction

- Salmonellae are ubiquitous human and animal pathogens
- Based on DNA homology and host range, the genus *Salmonella* is classified into two species: *Salmonella enterica* and *Salmonella bongori*
- Most of the salmonellae that are pathogenic to human beings belong to *S. enterica* subsp. *enterica*
- Presently more than 2479 serotypes are described

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- Classified broadly into:
 - ❖ Typhoidal salmonella: *S. Typhi* is responsible for typhoid fever while *S. Paratyphi* A, B, C responsible for paratyphoid fever
- Non-typhoidal salmonella: Salmonellosis is caused by non-typhoidal salmonellae (NTS) which include the pathogenic salmonellae other than *S. Typhi* and *S. Paratyphi* A, B and C

Typhoidal salmonella

Characteristics

- ❖ Gram-negative, nonsporing, non capsulated bacillus measuring 2-4 μm x 0.6 μm
- ❖ facultative anaerobes
- ❖ Catalase positive
- ❖ Oxidase negative
- ❖ Most serotypes are motile by peritrichous flagella
- ❖ Most produce hydrogen sulphide

VIRULENCE FACTORS

Virulence factors	Biological functions
Endotoxin	Causes many systemic manifestations of salmonellosis
Type III secretion systems	Mediate secretion of virulence factors of <i>Salmonella</i> into host cells
Fimbriae	Mediate binding of <i>Salmonella</i> to M (microfold) cells present in Peyer patches of the terminal part of the small intestine
Acid tolerance response (ATR) gene	Protects <i>Salmonella</i> spp. from stomach acids and the acid pH of the phagosome
Catalase	Protects the bacteria from intracellular killing in macrophages
Superoxide dismutase	Protects the bacteria from intracellular killing in macrophages

Epidemiology

- ❖ Reservoir of infection: Humans are the only reservoir ie case and carrier
- ❖ Source of infection:
 - Primary sources are faeces and urine of cases or carriers
 - Secondary sources contaminated water, food, fingers and flies
- ❖ Age: more common among young children and adolescents than adults
- ❖ Sex: More common among males but carrier rate higher among female
- ❖ Carrier: fecal carriers are common. Urinary carriers are rare
- ❖ Chronic carriers excrete bacilli for >1yr, seen in 2-5% cases

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- More common in urban than rural area
- Poor sanitation and hygiene
- Observed throughout the year
- ❖ Mode of transmission:
 - Faeco-oral route or urine-oral route
 - Directly through contaminated hands
 - Ingestion of contaminated water, milk and food or by flies

Pathogenesis

- Transmitted by oral route through contaminated food and water
- Infective dose: 10^3 – 10^6 bacilli
- Adherence: On reaching the intestine, the salmonellae attach themselves by fimbriae or pili to cells lining the ileal mucosa
- Entry into epithelial cells(M-cells): Type III secretory system helps in entry to M-cells in Peyer's patches which is called bacteria-mediated endocytosis. Bacteria remains in vacuoles of cytoplasm
- Entry into macrophages: Salmonellae containing vacuoles cross the epithelial layer to reach submucosa, where they are phagocytosed by the macrophages

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- Survival inside macrophages: Another type of type III secretory system helps for intracellular survival
- Primary bacteremia: Salmonellae contained inside the macrophages spread via the lymphatics to enter the blood stream (transient primary bacteremia)
- Spread: bacilli disseminate throughout the reticuloendothelial tissues (liver, spleen, lymph nodes and bone marrow) and other organs, such as gallbladder, kidneys and lungs where further multiplication takes place
- Secondary bacteremia occurs from the seeded organs, which leads to the onset of clinical disease

Clinical features

- Incubation period is about 10-14 days
- Fever, Headache, chills, sweating, myalgia
- Rashes or rose spots
- Early intestinal manifestation: abdominal pain, nausea, vomiting
- Important signs: Hepatosplenomegaly, relative bradycardia, epistaxis
- Complications: gastrointestinal bleeding, intestinal perforation

Treatment

- Ceftriaxone is drug of choice for empirical treatment
- Azithromycin as alternative drug
- For treatment of carriers, ampicillin or amoxicillin plus probenecid for 6 weeks
- For carriers, cholecystectomy is considered most effective

Laboratory diagnosis

- Specimen:

- Blood and bone marrow culture in first week of illness
- Serum: antibody detection by Widal test second week
- Stool and urine culture in third and fourth week

- Culture:

- Conventional blood culture(brain heart infusion broth) or automated blood culture(Bact/Alert)
- Subcultured on blood agar and Mac Conkey agar
- BA: nonhemolytic moist colonies
- MA: round, translucent, pale non-lactose fermenting

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❖ Stool and urine culture:

- Also used for detection of carriers
- Urine culture seldom becomes positive
- Stool culture: Enrichment media like selenite F broth used.
Subcultured on selective media like XLD, DCA
- DCA- colorless colonies NLF, XLD- pink colonies with black centres

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❖ Identification:

- Catalase positive, oxidase negative
- Indole negative, sulphide producer, motile
- Citrate and urease test negative
- In TSI alkaline/acid, gas non producer, speck of sulphide produced
- ❖ Slide agglutination: polyvalent O antisera used
- ❖ Widal test: based on principle of agglutination
- Significant titre differs according to place depending on endemicity

Prevention

- Early diagnosis, notification and prompt treatment of case
- Follow up urine and stool culture for detection of carrier
- Effective treatment of carriers
- Protection and purification of drinking water supplies
- Promotion of food hygiene
- Improvement of basic sanitation
- Health education
- Active surveillance
- Typhoid conjugate vaccine: Used in Nepal, Single dose given to children below 15yrs

Non-typhoidal salmonellae

Characteristics

- Non-typhoidal salmonellae(NTS) include the pathogenic salmonellae other than *S. Typhi* and *S. Paratyphi* A, B and C.
- Gram negative bacilli belonging to the family Enterobacteriaceae
- Non fastidious, Fermentative, non sporing
- Facultative anaerobe
- Catalase positive, oxidase negative, motile by peritrichous flagella

Virulence factors

- Endotoxin
- Type III secretion system
- Fimbriae
- Catalase

Epidemiology

- ❖ Majority of infections due to NTS are caused by *S. Typhimurium* and *S. Enteritidis*
- ❖ NTS are widely prevalent in developed as well as developing countries
- ❖ Malaria and malnutrition predispose to invasive disease among children, and HIV does so among both children and young adults
- ❖ The emergence of *Salmonella* with antimicrobial resistance is mainly promoted by the use of antibiotics in animal feed to promote the growth of food animals, and in veterinary medicine to treat bacterial infections in those animals
- ❖ Reservoir and sources of infection :
 - Main reservoir is the intestinal tract of man and animals(cattle, swine, rodents and fowl)
 - Source of the infecting agent could be contaminated food, animals, man or the environment.

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❖ Carrier:

- Carriers occur among both man and animals
- Less than 1% become chronic carriers and may excrete for >1yr

❖ Mode of transmission:

- Ingestion of contaminated food and water
- direct contact with domestic animals especially such as dogs, pigeons, rats, mice
- ❖ Transmission is facilitated by: food handling methods, Sanitary conditions
- ❖ Seasonality: highest during rainy season in tropical climates and during the warmer months in temperate climates

Pathogenesis

- Bacteria enter the digestive tract via contaminated food
- Adhere to epithelial cells by adhesin
- Bacteria mediated endocytosis: mediated by type III secretion system
- Following the engulfment into the host cell, the bacterium is encased in a membrane compartment called a vacuole
- Type III secretion system inject other effector proteins into the vacuole, causing the alteration of the compartment structure.
- The remodelled vacuole blocks the fusion of the lysosomes and this permits the intracellular survival and replication of the bacteria within the host cells
- There is massive neutrophil infiltration into intestinal mucosa

Clinical features

- Incubation period depends on host and inoculum but generally 6–72 hours
- Characterized by:
 - Acute onset of fever and abdominal pain
 - Nausea and Vomiting
 - Diarrhea that can be bloody
 - Approximately 5% of individuals will develop bacteremia
- Other complications: Meningitis, Septic arthritis

Laboratory diagnosis

- Specimen:

- Stool

- Invasive NTS: blood, CSF

- Culture: Conventional blood culture(brain heart infusion broth) or automated blood culture(Bact/Alert)

- Subcultured on blood agar and Mac Conkey agar

- BA: nonhemolytic moist colonies, MA: round, translucent, pale non-lactose fermenting

- Stool culture: Enrichment media like sodium taurocholate broth, selenite F broth used.

- Subcultured on selective media like XLD, DCA, Salmonella shigella agar

- ❖ Identification:

- Catalase positive, oxidase negative

- Serotyping

Treatment

- ❖ In uncomplicated NTS gastroenteritis, the treatment is conservative with fluid replacement
- ❖ Ciprofloxacin is given for preemptive treatment or severe gastroenteritis
- ❖ Ceftriaxone is indicated for bacteremia and invasive infections
- ❖ Management of chronic carriers is generalized from experience with *S. Typhi*, and includes the long-term use of oral antibiotics and consideration of cholecystectomy

Prevention and control

- Proper handling and cooking of food
- Personal hygiene
- Environmental sanitation
- Use of safe water
- Exclusive breastfeeding for 6months
- Health education about how infections spread
- Vaccinate livestock and poultry
- Restrict the inappropriate use of antibiotics in food animals and their feed to prevent development and transmission of resistant strains