Enterobacteriaceae

a bacterial family with larger medical importance than any other

genus	representative species
• *Escherichia*	• *E. coli*
• *Salmonella*	• *S. enterica*
• *Shigella*	• *S. dysenteriae*
• *Klebsiella*	• *K. pneumoniae*
• *Enterobacter*	• *E. cloaceae*
• *Proteus*	• *P. vulgaris*
• *Serratia*	• *S. marcescens*
• *Yersinia*	• *Y. pestis*

etc.

- **Gram-negative rods**
- **Facultative anaerobes (sugar fermentation)**
- **Oxidase negative, nitrate reduction (to nitrite)**
- **Habitat**
  - human and animal intestines
  - environment
- Medical role
  - **some** are intestinal pathogens (e.g. *Salmonella spp.*)
  - **some** form the resident intestinal microflora but are extraintestinal pathogens (e.g. *Proteus spp.*)
  - **some** (*from the environment*) occasionally cause opportunistic infections (*only extraintestinal*) i.e. are facultative pathogens (e.g. *Serratia marcescens*)

Salmonella genus

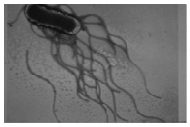
- *S. enterica* and *S. bongori*
- *S. enterica* species has 7 subspecies (I, II, IIIa, IIIb, IV, VI, VII)
- *S. enterica subspecies I* (~1700 serovariants)

  Most human pathogenic strains belong to here
- Most serovariants have *species like* names:

e.g. S. Typhi = *S. enterica subspecies I serovar* Typhi

Molecular background of serotype diversity

- O antigen (mosaic type – high diversity)
- H antigen (biphasic, mosaic type – high diversity)
- Vi antigen (capsule – certain strains)

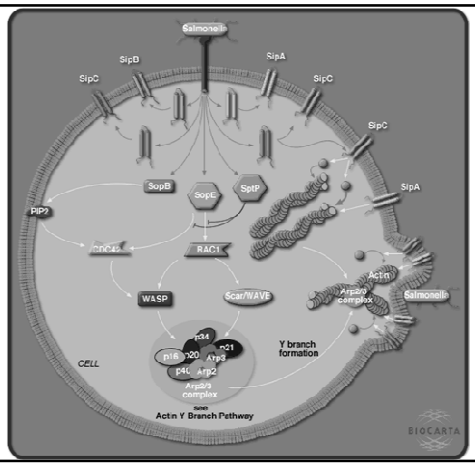


Virulence factors

- Salmonella Pathogenicity Island 1 (SPI-1)
  - entry into intestinal epithelium
  - Enables pathogen to exploit host intestinal environment
- Salmonella Pathogenicity Island 2 (SPI-2)
  - intracellular bacterial replication and initiation of systemic infection
  - Do not influence enteropathogenesis to any great extent

SPI-1 effector proteins

- SipA
  - binds actin and stabilizes filaments
  - allows actin to polymerize more easily
  - maximizes efficiency of Salmonella invasion
- SipC
  - aides in entry of other SPI-1 effector proteins
  - activtes G-actin to form F-actin, then polymerize
  - aides in cytoskeleton rearrangements in membrane ruffling



Salmonellae causing human diseases

	strictly human adapted	of broad host range	primarily animal adapted
	S. typhi S. paratyphi A, B, C	many strains, e.g. S. typhimurium S. enteritidis	certain strains, e.g. S. choleraesuis
disease	enteric fever	enterocolitis septicemia in immuno-compromised.	bacteremia, septicemia
infectious dose	moderate	high	probably high
infectious source	infected humans	human & zoonotic	zoonotic
transmission	food (enrichment) direct contact	food (enrichment)	food (enrichment)
prevention by proper food handling	+	+	+
vaccine	+	-	-

Enteric fever

- source of infection: symptomless (recovery) or sick people
- transmission: direct contact, or contaminated food/water (fecal-oral)
- infective dose: 10^3 - 10^4
- incubation period: 2 weeks

Enteric fever

- Infection begins in the small intestines but few enteric symptoms occur
- Bacterial invasion of blood stream,
  secondary infection of RES followed by high infectious dose, severe, secondary bacteremia resulting in continuously high fever
  - **no diarrhea at this stage**
- Bacteria circulate back into the intestines via bile
  - Late complications at this stage:
    - intestinal hemorrhage leading to bloody diarrhea
    - intestinal perforation
- Bacterial shedding via stool

Symptoms of enteric fever

- high fever (continua type, 41 C)
- relative bradycardia
- hepato-splenomegaly
- skin rashes („roseola")
- leukopenia with relative lymphocytosis
- profound mental status („typhoid")

History

- Prince Albert, the consort of Queen Victoria, died of a Salmonella infection in 1861. During the Victorian era, an estimated 50,000 cases per year occurred in England.
- typhoid epidemic in the Spanish-American War (1898)
  - in all, 20,738 recruits contracted the disease (82% of all sick soldiers), 1,590 died (yielding a mortality rate of 7.7%)
  - it accounted for 87% of the total deaths from disease.
  - a significant number of these deaths actually occurred at training areas in the southeastern United States.

Chronic carrier state

- chronic carriers shed viable, pathogenic bacteria
- chronic carriers serve as sources for subsequent outbreaks
- chronic carriers harbor the bacteria in the gallbladder
- chronic carriers require longterm therapy and follow-up cultures and occasionally surgery for eradication of the bacteria

History: Mary Mallon (Typhoid Mary)

- Mary Mallon caused several typhoid outbreaks, moving from household to household, always disappearing before an epidemic could be traced back to the particular household Mary was working in. All together, she had worked for 7 families, with 22 cases of typhoid and one death.
- She was finally overtaken by the authorities in 1907 and committed to an isolation center on North Brother Island, NY. There she stayed until she was released in 1910, on the condition that she never accept employment involving food handling.
- But: She was found to work as a cook and to cause typhoid outbreaks again. She was admitted back to North Brother Island, where she lived until her death in 1938.

Laboratory diagnosis

- 1-2 weeks: culture from blood or bone marrow sample
- 3-4 weeks: culture from stool or urine and serological reactions (Gruber-Widal tube agglutination, 4x ↑ titer)

Vaccines

- killed *S. typhi* vaccine for travelers to endemic areas and household contacts of infected persons, 55-77 % protection, two injections 4 weeks apart, booster is required every 3 years
- capsular polysaccharide vaccine (ViCPS), single dose enough, fewer side effect, booster is needed every 2 years
- live, attenuated, (Ty21a), booster is needed every 5 years

Gastroenteritis (food poisoning)

- 15 000 cases/year in Hungary
- source of infection: chicken, duck egg, pork meat, poultry
- infective dose: 10^6 -10^8
- incubation period: 1-2 days

Symptoms

- fever
- vomiting
- diarrhea
- malaise
- transient bacteremia

Laboratory diagnosis

- sample: stool, food etc.
- culture on selective-differential media
- PCR
- serotyping

Treatment

- fluid and electrolyte replacament
- antibiotics are not recommended (except in sepsis)

Shigella genus

- Strictly human adapted bacteria
- Very low infectious dose (10^2)
- Feco-oral transmission
  infectious source: water, food contaminated by infectious human feces direct contact
  rule of 4 four Fs: food, finger, feces, flies
- disease: **bacillary dysentery**
- 4 species:
  S. dysenteriae, S. flexneri, S. boydii, S. sonnei

Antigenic structure

O antigen

S. dysenteriae 12 serotypes

S. flexneri 6 serotypes (most frequent in developing countries)

S. boydii 18 serotypes

S. sonnei 1 serotype (most frequent in Europe)

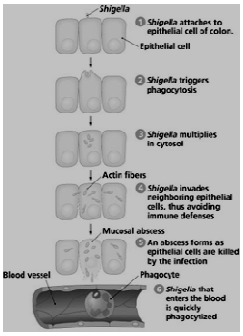
Virulence factors

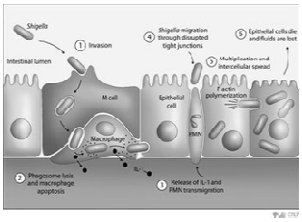
- endotoxin
- Shiga toxin (only *S. dysentaeriae* 1. type)
- invasion plasmid antigen (*Ipa*)

Pathogenesis

- invasion through epithelium of the terminal ileum and the colon
  essential virulence factor: invasion plasmid (also EIEC)
  additional virulence factor:
  Shiga toxin in some strains of S. dysenteriae
- drop shaped subepithelial microabscesses (purulent lesions)
- lesions of mucuous membrane: focal necrosis, superficial exulceration, bleeding, pseudomembrane formation
- Symptoms of dysentery
  - diarrhea containing blood and mucus (pus)
  - tenesmus (painful rectal spasms)

Pathogenezis





Symptoms

– bloody, mucoid diarrhea
– tenesmus
– fever
– complication: HUS

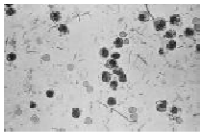
Treatment

•Rehydration
•antibiotics
- Sumetrolim
- fluoroquinolones
- 3. generation cephalosporins

Antimotility agents should not be used!

Laboratory diagnosis

• microscopic examination of native stool (PMNL)
•culture on selective-differential media
•Serotyping
• detection of *Ipa* gene by PCR
•Serény test



Control

•personal hygiene
•good hand washing practices
•fly control
•hygienic food preparations practices

Yersinia genus

Y. enterocolitica

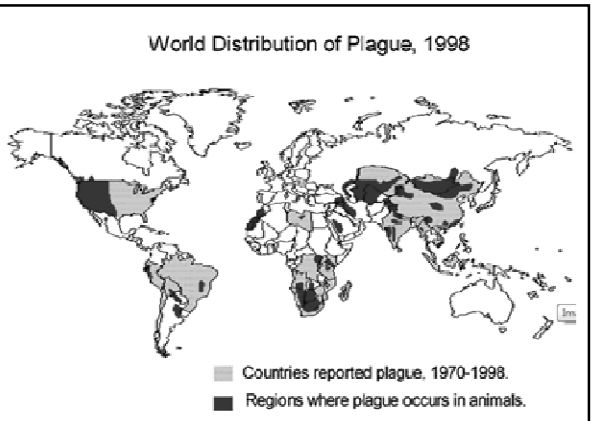
- intestinal infection mostly with zoonotic source (although human to human feco-oral transmission also occurs)
- *enterocolitis* – diarrhea, abdominal pain inflammation, exulceration, fecal leukocytes,
- *mesenteric lymphadenitis* (pseudoappendicitis)

Y. pseudotuberculosis

- intestinal infection from zoonotic source
- *mesenteric lymphadenitis, septicemia*

Yersinia pestis (plague)

- endemic among rodents
- transmission to human by the bite of rat flea
- human to human transmission by inhalation of dried exsudate from bubo and sputum (highly contagious)
- disease manifestation:
  - bubonic plage after flea bite
  - progression into septicemia (high lethality)
  - pulmonic plague (via inhalation – high lethality)
- prevention by killed vaccine and rodent control
- treatment: tetracylin (& streptomycin)



Bubonic plague