

Lec14+15- Enterobacteriaceae & Gastrointestinal Gram-negative Rods

Enterobacteriaceae is a large family of Gram-negative bacteria found primarily in colon of human and animals many as part of the normal flora.

General properties of members

1. Found in the gastrointestinal (GI), facultative anaerobes, non spore forming, some spp. has capsulate, some motile.
2. catalase positive, oxidase negative except *Vibrio* and *Pseudomonas*.
3. Reduce nitrates to nitrite. Major spp and related disease in following table.

Pathogenesis

They contain lipopolysaccharide (LPS) in their cell wall, which is both antigenic and a potential virulence factor (endotoxin). In addition several exotoxins are produce by *E. coli* and *V. cholerae*, these exotoxins are called enterotoxines that activate adenylate cyclase within the cells of the small intestine, causing diarrhea.

Antigenic structure: Three surface antigens:

1. Cell wall antigen or somatic Ag (O Ag).
2. The flagellar antigen (H Ag).
3. The capsular or antigen or (K Ag) polysaccharide Ag in encapsulated bacteria.

Diagnosis of Enterobacteriaceae

-culture: Blood agar, Macconkey, eosine- methylen blue (EMB), detection of lactose fermentation on macconkey agar; lactose fermenter such as *E. coli* and *Klebsiella* forms pink colonies, while non lactose fermenter such as *Shigella*, *Salmonella*, *Proteus*, *Enterobacter*, *Providencia*, *Morganella*, *Serratia* and forms pale or colorless colonies.

Major pathogens	Representative Diseases
<i>Escherichia coli</i>	Urinary tract infection, travelers diarrhea, neonatal meningitis
<i>Shigella</i>	Dysentery diarrhea
<i>Salmonella, Citrobacter</i>	Typhoid fever, Enterocolitis
<i>Klebsiella</i>	Pneumonia, Urinary tract infection, colonize hospitalized patients
<i>Enterobacter</i>	Pneumonia, Urinary tract infection colonize hospitalized patients
<i>Proteus, Providencia, Morganella</i>	Urinary tract infection (nosocomial UTIs)
<i>Serratia</i>	Pneumonia, Urinary tract infection
<i>Helicobacter</i>	gastric ulcers
<i>Campylobacter</i>	food poisoning
<i>Yersinia</i>	Plague, Enterocolitis, mesenteric adenitis

The selective effect of the media in suppressing Gram+ bacteria. *Proteus* and *S. typhi* produce H₂S from sulfur-containing amino acids.

Enterobacter and *Klebsiella* have capsule.

-**Serological** test depending on the presence or absence of anti-H or anti-K or anti-O antibodies.

- **Molecular techniques** by using PCR specific for selected bacterial genes.

Table (5) show the Major pathogens& Representative Diseases

1. E. coli

- **Diseases:** Urinary tract infection, traveler's diarrhea, neonatal meningitis, and sepsis. Nosocomial (hospital-acquired) infections: These include sepsis/bacteremia, endotoxic shock, and pneumonia.
Habitat: human colon, vagina, urethra. From the urethra, it ascends and causes UTI acquired during birth neonatal meningitis and by fecal –oral route in diarrhea.

Pathogenesis

1. Endotoxin in cell wall cause septic shock.
2. Also enterotoxin (heat labile toxin LT) which stimulates adenylate cyclase by ADP-ribosylation resulting in the increasing in cyclic AMP (cAMP) that causes out flow of chloride ions and water resulting in diarrhea.
3. Enterotoxin (heat stable ST) causes diarrhea by stimulating guanylate cyclase.
4. Vero toxin (Shiga-like toxin) is an enterotoxin, it causes bloody diarrhea and hemolytic uremic syndrome associated with eating undercooked meat. Verotoxin inhibits the proteins synthesis. Following table shows strains of *E. coli* and disease.

Predisposing factors to UTI in women include the proximity of the anus to the vagina and urethra, as well as a short urethra. This leads to colonization of the urethra and vagina by the fecal flora. Colonization of vagina leads to neonatal meningitis acquired during birth.

Virulence factors: pili for attachment, and capsule that suppress phagocytosis.

Table (6) the strains of *E. coli*

STRAIN	ABBREVIATION	SYNDROME	THERAPY ¹
Enterotoxigenic <i>E. coli</i>	ETEC	Watery diarrhea	Antibiotics may be useful. ²
Enteropathogenic <i>E. coli</i>	EPEC	Watery diarrhea of long duration, mostly in infants, often in developing countries	Antibiotics may be useful. ²
Enterohemorrhagic <i>E. coli</i>	EHEC	Bloody diarrhea; Hemorrhagic colitis and hemolytic uremic syndrome (HUS)	Avoid antibiotics because of the possible risk of potentiating HUS.
Enteroinvasive <i>E. coli</i>	EIEC	Bloody diarrhea	Rehydration and correction of electrolyte abnormalities.
Enteroadherent <i>E. coli</i>	EAEC	Persistent watery diarrhea in children and patients infected with HIV	Rehydration and correction of electrolyte abnormalities.

Prevention & Treatment

- Eating cooked meat and drinking boiled water, Doxycycline may be preventing traveler diarrhea. Maintenance of fluid and electrolyte balance is of primary importance in treatment.
- Prevention of UTI involves limiting the frequency and duration of urinary catheters.
- Prevention of sepsis involves removing or switching sites of I.V. catheters.
- There is no vaccine against *E. coli* infection.

2. *Salmonella typhi*

Disease: Typhoid fever. **Habitat** human colon only. **Transmission** by fecal-oral route.

Pathogenesis

Salmonella invade epithelial cells of the small intestine and reticuloendothelial cells system (liver and spleen). Endotoxine causes fever. Disease may remain localized or become systemic, sometimes with disseminated foci. The organisms are facultative, intracellular parasites that survive in phagocytic cells

Clinical significance

Salmonella infection can cause both intestinal and extraintestinal diseases.

Gastroenteritis: This localized disease (also called salmonellosis) is caused by *S. enteritidis* and *S. typhimurium* (nontyphoidal salmonella). It is characterized by nausea, vomiting, and diarrhea (usually nonbloody), which develop generally within 48 hours of ingesting contaminated food or water. Fever and abdominal cramping are common.

- **Enteric (typhoid) fever:** This is a severe, life-threatening systemic illness, characterized by fever and, frequently, abdominal symptoms. It is caused *S. typhi*. Nonspecific symptoms may include chills, sweats, headache, anorexia, weakness, sore throat, cough, myalgia, and either diarrhea or constipation. A small percentage of patients become chronic carriers.
- **Other sites of *Salmonella* infection:** *Salmonella* can also cause abdominal infections (often of the hepatobiliary tract and spleen), osteomyelitis, bacteremia, septic arthritis.

Treatment and prevention

For enteric fever, appropriate antibiotics include beta-lactams and fluoroquinolones. Prevention of salmonella infection is accomplished by proper sewage disposal; correct handling of food, and good personal hygiene.

3-*Shigella dysenteriae*

Habitat: human colon only. **Transmission** by fecal-oral route.

Shigella species cause shigellosis or dysentery enterocolitis (bacillary dysentery) a human intestinal disease that occurs most commonly among young children

Pathogenesis and clinical significance

Shigella invades and destroys the mucosa of the large intestine. Infection rarely penetrates to deeper layers of the intestine. *Shigella* has exotoxin (Shiga toxin), enterotoxic and cytotoxic. *Shigella* cause classic bacillary dysentery, characterized by diarrhea with blood, mucus, and painful abdominal cramping.

Treatment and prevention

ciprofloxacin or azithromycin can reduce the duration of illness. Protection of the water and food supply, and personal hygiene are crucial for preventing shigella infections.

4-Campylobacter jejuni

C. jejuni are curved, spiral, or S-shaped organisms that microscopically resemble vibrios. Motile by single, polar flagellum

Pathogenesis and clinical significance

Campylobacter may cause both intestinal and extraintestinal disease. Causes food poisoning. Symptoms (abdominal cramping and diarrhea, which may or may not be bloody). *C. jejuni* is a cause of both traveler's diarrhea.

5-Pseudomonas

P. aeruginosa, the primary human pathogen, is widely distributed in nature (soil, water, plants, and animals). It may colonize healthy humans without causing disease, it is also a significant opportunistic pathogen and a major cause of nosocomial (hospital-acquired) infections. It is motile by polar flagella, catalase and oxidase positive and obligatory aerobic. Nutritional requirements are minimal, can grow on a wide variety of organic substrates. This explains why the organism is responsible for many nosocomial infections.

Pathogenesis & clinical significance

P. aeruginosa produces numerous toxins and extracellular products that promote local invasion and dissemination of the organism. These may cause keratitis and endophthalmitis, external otitis or swimmer's ear wound sepsis, UTI, pneumonia or cystic fibrosis, GTI, CNS; meningitis and brain abscesses. it can cause severe hospital-acquired infections, especially in immunocompromised hosts; it is often antibiotic resistant.