



Enteric Gram-Negative Bacterial Infections of the Gastrointestinal Tract

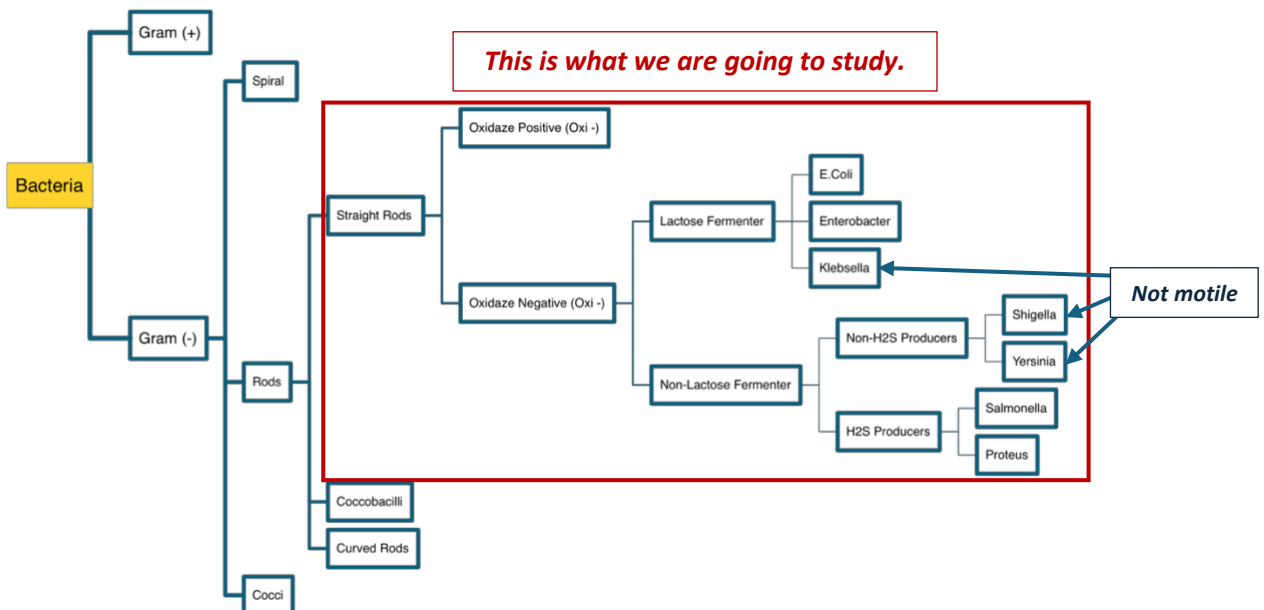
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Gram-Negative Enterobacteriecea – Overview

Overview

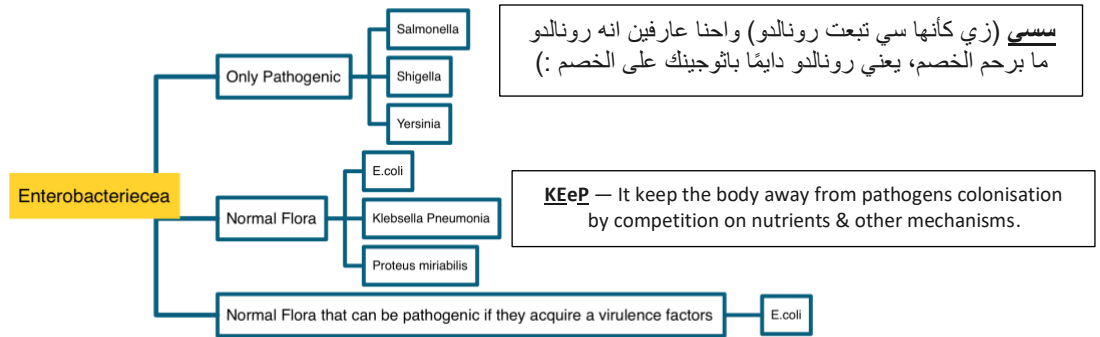
➤ *What are Enterobacteiecea ?*

*Enterobacteriecea are group of bacterial families that Shares the characteristics of being **Straight rods**, **Gram (-)** & **Related to the GI**.*



- Enterobacteriaceae family are **ubiquitous** (group of bacterial families) organisms and part of normal intestinal flora of most animals, including humans.
- Some species are **always associated with human disease**: ex. :**Salmonella** serotype Typhi, **Shigella** spp., **Yersinia pestis**.
- Others (*E. coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*) are commensal flora that cause **opportunistic infections** (they establish an infection when your immunity get suppressed).

- Commensal organisms can become pathogenic by acquiring **virulence genes (genes that give them extra virulence properties that allows them to establish an infection and overcome the immunity barrier)** e.g., E. coli



General Properties (Mnemonic: FROG-MAN 🐸👤)

Mnemonic: FROGMAN
General Characteristics of Enterobacteriaceae

F		Ferments glucose (يُخَمَّر الجلوکوز)	✓ They ferment glucose
R		Rods (عصيات)	✓ Rod-shaped bacteria
O		Oxidase Negative	✗ Oxidase negative
G		Gram Negative	✓ Gram-negative bacteria
M		MacConkey agar (ينمو عليه)	✓ Grows on MacConkey agar
A		Anaerobic facultative (يعيش مع/بدون أكسجين)	✓ Facultative anaerobe (with or without oxygen)
N		Nitrate reducer	✓ Reduces nitrate to nitrite

FROGMAN – Easy to remember, hard to forget! 🐸
سهل التذکر، صعب النسيان! 🐸

- Moderate-sized, **non-spore-forming, Gram-negative, facultative anaerobic rods (can live in aerobic & anaerobic environments).**
- All members: **ferment glucose, reduce nitrate, catalase positive, oxidase negative.**
- Grow on **nonselective (blood agar)** and **selective (MacConkey agar)** media — important for stool/blood culture diagnosis.
 - Non-selective means that it allows bacteria to grow **without giving a marker about it being Enterobacteriaceae or not.**
 - **Selective media gives an indicator.**
- MacConkey agar differentiates **lactose fermenters** from **non-lactose fermenters**.
 - **Lactose fermenters:** E. coli, Klebsiella, Enterobacter.
 - **Non-lactose fermenters:** Salmonella, Shigella, Yersinia, Proteus.
- Most are motile (flagella), except: **Klebsiella, Shigella, Yersinia.**
- Modern ID: automated systems, **MALDI-TOF MS**, molecular assays, culture-based susceptibility testing (بس أتطلع عليهم، هذول طرائق حديثة للتعرف على الإنيتيرو بكتيريشا).

MacConkeys Agar



LACTOSE FERMENTOR COLONIES / NON-LACTOSE FERMENTOR COLONIES

Selective & Differential Media

It only allows **Gram Negative** to grow on **(Selective)**, and it **distinguishes the Lactose Fermenters from non lactose fermenters (Differential).**

Antigenic Structure (O, K & H)

- **O antigen (somatic):** outer polysaccharide of LPS — useful for serologic classification.
- **K antigen:** capsular polysaccharide — contributes to immune evasion and virulence.
- **H antigen:** flagellar antigen — present in motile organisms.
- Serotyping is important for **Salmonella, Shigella, and diarrheagenic E. coli.**
- *Antigenic variation helps organisms evade host immunity and complicates epidemiologic classification.*

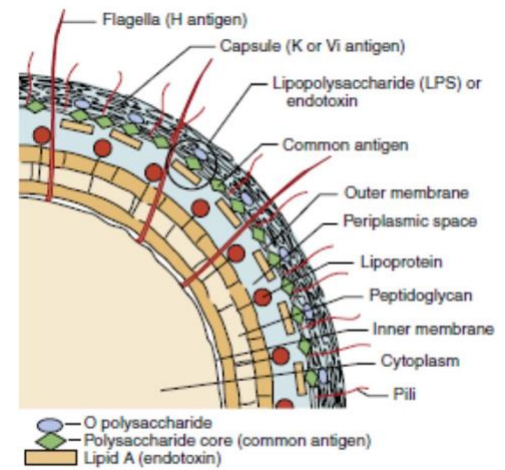


Fig. 25.2 Antigenic structure of Enterobacteriaceae cell wall.

Major Virulence Factors

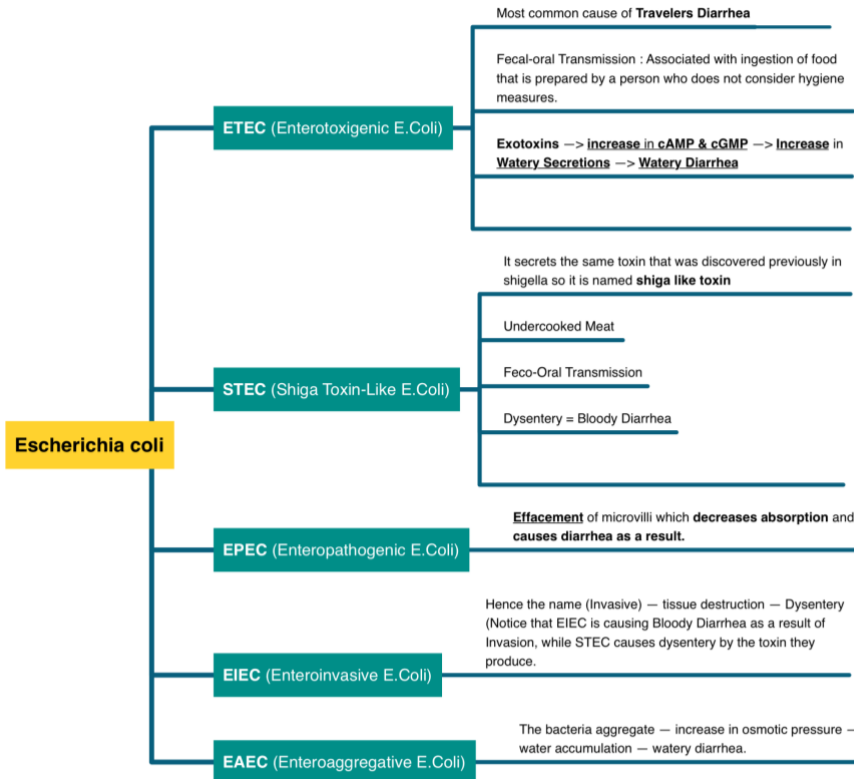
Mnemonic: “Very Evil Bacteria Can Always Escape”

- **V** → Virulence genes
 - **E** → Endotoxin
 - **B** → Biofilm / binding (Adhesins)
 - **C** → Capsule
 - **A** → Adhesins
 - **E** → Exotoxins
- Pathogenic strains **acquire virulence genes** → ability to attach, invade, produce toxins, or survive host defenses.
 - some strains become dangerous because they **gain special genes called virulence genes.** These genes are often acquired through mechanisms like plasmids, bacteriophages, or transposons.
 - These virulence genes give the bacteria new abilities, such as:
 - **Attachment (adhesion):** stick to intestinal cells instead of being washed away
 - **Invasion:** enter and damage host cells
 - **Toxin production:** release harmful substances (e.g., enterotoxins, Shiga toxin)
 - **Immune evasion:** survive despite the body’s defenses.
 - **Endotoxin (Lipid A of LPS):** shared by aerobic gram-negative rods **triggers fever, inflammation, shock, and DIC.**
 - **Capsules:** **protect from phagocytosis; interfere with complement-mediated killing** (mechanism where the complement system (part of innate immunity) kills bacteria directly in the blood).
 - **Adhesins:** **allow binding to host epithelial surfaces** — essential for intestinal colonization.
 - **Exotoxins** (enterotoxins, Shiga toxins): **explain many diarrheal syndromes.**
 - **Antimicrobial resistance and resistance to serum killing.**
 -

Escherichia coli (E.coli)

Overview

- Most common and important member of genus *Escherichia*.
- Associated with **gastroenteritis** and extraintestinal infections.
- Gastroenteritis strains subdivided into: **ETEC, EPEC, EAEC, STEC, EIEC**.
- Key virulence factors: **adhesins and exotoxins**.



Sketchy Video : [Click Here](#)

Osmosis: [Click Here](#)

يا وردة يا وردة يا وردة في البستان... يا مسكن
الفراشة... يا زينة الأغصان...



Note : most of infos in this videos aren't mentioned in the slides, but its important to know them as a doctor.



Escherichia coli

1. Red Theme – Gram Neg.
2. Milk Container - Ferments lactose - Grow pink on MacConkey's Agar.
3. Capsule - Encapsulated - Facultative Anaerobic, Oxidase negative, green sheen on EMB.
4. K Cake - Main Virulence Factor - Capsular K antigen and Flagellar H Antigens.
5. Green Coasters - Metallic green sheen on EMB Agar.
6. Cat - Catalase Positive.
7. #1 UTI Bladder Drink with long fimbriae bow off girls head - Fimbriae that will lead to UTI's #1 cause of UTI's.
8. Red Strawberry Milkshake - E.coli leading cause of gram neg sepsis by LPS endotoxin in outer cell membrane.
9. Meningitis Helmet - Causes neonatal meningitis only if have the K antigen.
10. STEC - Severe Hemorrhagic Colitis caused by O157 H7
 - a. Burger - Most Commonly caused by eating undercooked meat.
 - b. Red Stool and bloody Ketchup- Causes bloody diarrhea, red stool symbol
 - c. Sorbitol Free Coke - Only E.coli that does not ferment sorbitol
 - d. Gorilla toy, Blown up balloon - Toxin: inhibits ribosomes at the 60s position. Shiga like Toxin can cause hemolytic uretic syndrome. Shiga like toxin damages endothelial cells of capillaries in the glomerulus. Damaged endothelial lining causes platelets to adhere decreasing platelet count causing thrombocytopenia and these platelet clumps will hemolysis RBCs. Little to no fever but mucosal inflammation or invasion.
 - e. "E. Coli Burger only \$1.57" - O157:H7 Antigen is associated with outbreaks.
11. ETEC - travelers' Diarrhea
 - a. Water Truck - Transmitted via water sources.
 - b. It's in Spanish - Recent travel to Mexico where they drank the water, called Montezuma's revenge.
 - c. "eL Agua" - Heat labile toxin produces cAMP.
 - d. "San Gabriel" - Stable produces cGMP.
 - e. Brown Stool with water above it - Watery Diarrhea.
12. Treatment :
 - a. TMP/SMX or fluoroquinolones. (Antibiotics).

Enterotoxigenic E.coli (ETEC)

- One of the most common causes of **bacterial diarrheal disease in developing countries** and **traveler's diarrhea** (remember the truck from the window in e, cola fountain in sketchy video)
- Acquired by ingestion of **contaminated food or water**.
- **Pathogenesis: bacterial attachment** to small bowel via colonization factors → **enterotoxin production**.
- **Diarrhea: watery, non-bloody**; abdominal cramps, nausea, sometimes low-grade fever.
- **No tissue invasion** → absence of **dysentery (bloody diarrhea)**.

ETEC Toxins

- Produces **heat-labile toxin (LT), heat-stable toxin (ST), or both**.
- **LT**: similar to cholera toxin → increases intracellular **cAMP**.
- **ST**: increases **cGMP** → promotes intestinal fluid secretion; more responsible for severe disease.
- **Both mechanisms** → impaired **absorption + increased secretion of water and electrolytes into the intestinal lumen**.
- Clinical result: **watery diarrhea** resembling mild cholera but usually **self-limited**.

Enteropathogenic E.coli (EPEC)

- Important cause of **diarrhea in infants** in developing countries.
- Virulence genes on chromosomal pathogenicity island: **Locus of Enterocyte Effacement (LEE)**.
- Mechanism: attaches to enterocytes → **attaching and effacing (A/E) lesions** → loss of microvilli → disrupted absorption.
- **Transmission: fecal-oral** (contaminated surfaces or food).
- Diarrhea: watery, may be prolonged in infants; may require hospitalization.
- Unlike ETEC: disease is due to **epithelial injury and altered absorption**, not classic enterotoxin.

Enteraggregative E.coli (EAEC)

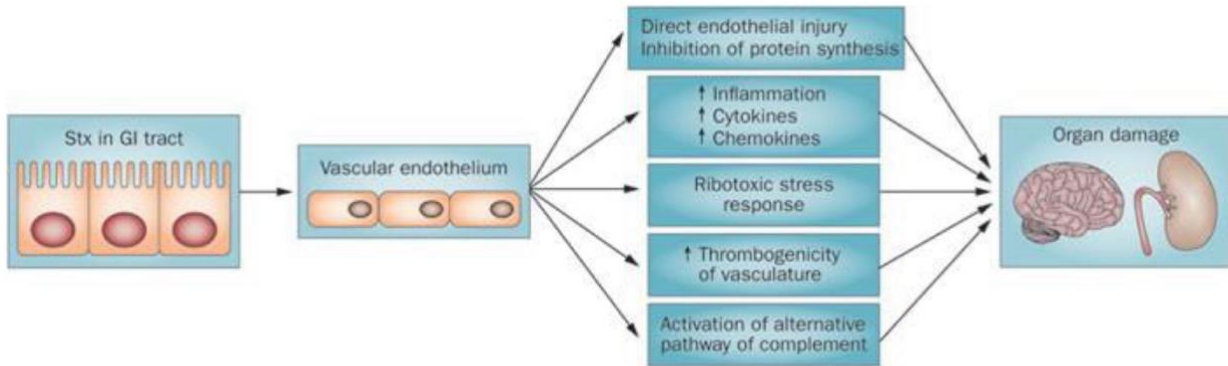
- Associated with **acute or persistent diarrhea** in children and immunocompromised patients.
- Adheres in a characteristic **"stacked-brick" aggregative pattern**.
- **May produce: mucus biofilm, inflammatory injury, toxins** → prolonged disease.
- Clinical: watery diarrhea with fever, nausea, vomiting, abdominal pain.
- Important because chronicity can cause **nutritional compromise and growth effects** in children.

Shiga Toxin Producing E.Coli (STEC/EHEC)

- **Also called VTEC (verocytotoxin-producing) or EHEC (enterohemorrhagic)**.
- Disease strongly associated with **Shiga toxins Stx1 and Stx2**.
- **Reservoirs: cattle**; transmission via undercooked beef, unpasteurized products, contaminated produce, or person-to-person.
- Most common serotype: **O157:H7**.
- Illness: abdominal cramps → watery diarrhea → **bloody diarrhea and hemorrhagic colitis**.
- **Fever may be absent or low-grade** (helps distinguish from invasive dysentery).

STEC Complications & Management

- Most feared complication: **Hemolytic Uremic Syndrome (HUS)** — especially in children <10 (5-10%) and older adults.
- **HUS triad: microangiopathic hemolytic anemia + thrombocytopenia + acute kidney injury.**
- **Outcomes:** self-resolves in 4-10 days; death in 3-5% with HUS; severe sequelae in up to 30% (renal impairment, hypertension, CNS).
- **AVOID: antibiotics and antimotility agents** (may worsen HUS); early IV fluids may reduce renal failure risk.
- **Diagnosis:** detection of Shiga toxin or Shiga toxin genes; stool culture for epidemiology.



Trachtman, H., Austin, C., Lewinski, M. et al. Renal and neurological involvement in typical Shiga toxin-associated HUS. *Nat Rev Nephrol* 8, 658–669 (2012). <https://doi.org/10.1038/nrneph.2012.196>

Enteroinvasive E.Coli (EIEC)

- Causes **invasive diarrheal illness resembling shigellosis.**
- **Invades and replicates within colonic epithelial cells → initially watery diarrhea.**
- Minority progress to dysenteric form: fever, abdominal cramps, tenesmus, bloody/mucoid diarrhea.
- *Less commonly identified in clinical practice than other E. coli pathotypes.*
- Important concept: shows that not all E. coli diarrhea is toxin-mediated or watery.

Summary For E.Coli

Organism	Site	Disease	Pathogenesis	Diarrhea Type
ETEC	Small intestine	Traveler's diarrhea; infant diarrhea	ST/LT enterotoxins → hypersecretion of fluids	Watery, non-bloody
EPEC	Small intestine	Infant diarrhea in developing countries	A/E lesions; loss of microvilli → malabsorption	Watery, non-bloody
EAEC	Small intestine	Persistent diarrhea; traveler's diarrhea	Stacked-brick adherence; decreased fluid absorption	Watery, may be persistent
STEC	Large intestine	Hemorrhagic colitis; HUS	Shiga toxins (Stx1, Stx2) → destroy protein synthesis	Bloody, little/no fever
EIEC	Large intestine	Shigellosis-like; fever + cramping	Invasion and destruction of colonic epithelium	Watery → may progress to bloody