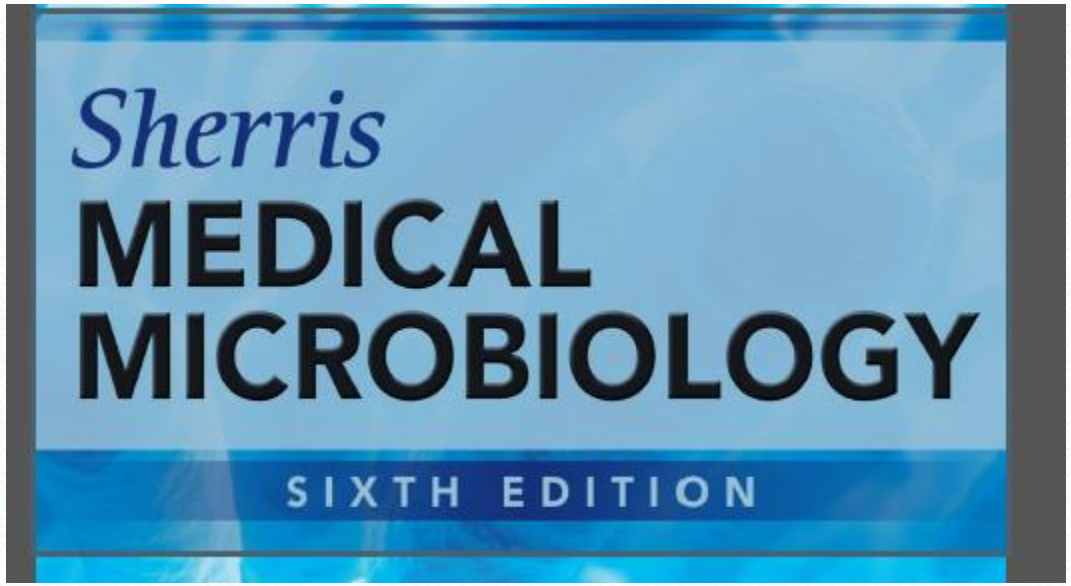
Enterobacteriaceae

Chapter 33
579-605



- Understand the definition of Enterobacteriaceae and its related genera and species
- Describe the epidemiology, general characteristics, clinical presentation, laboratory diagnosis and treatment of *Salmonella* and *Shigella*
- Describe the epidemiology, general characteristics, clinical presentation, laboratory diagnosis and treatment of *E. coli*
- Describe the epidemiology, general characteristics, clinical presentation, laboratory diagnosis and treatment of ***Klebsiella***
- Describe the epidemiology, general characteristics, clinical presentation, laboratory diagnosis and treatment of ***Proteus***

Enterobacteraceae

- Enterobacteraceae or enteric bacteria are a group of bacteria that commonly colonize and infect the alimentary tract (intestine)
- Enterobacteraceae include a large number of bacterial Genera/species some of them are pathogenic to human including:

1. *Citrobacter*
2. *Edwardsiella*
3. *Enterobacter*
4. *Esherishia*
5. *Klebsiella*
6. *Morganella*
7. *Proteus*
8. *Salmonella*
9. *Shigella*
10. *Serratia*
11. *Yersinia*
12. *Hania*

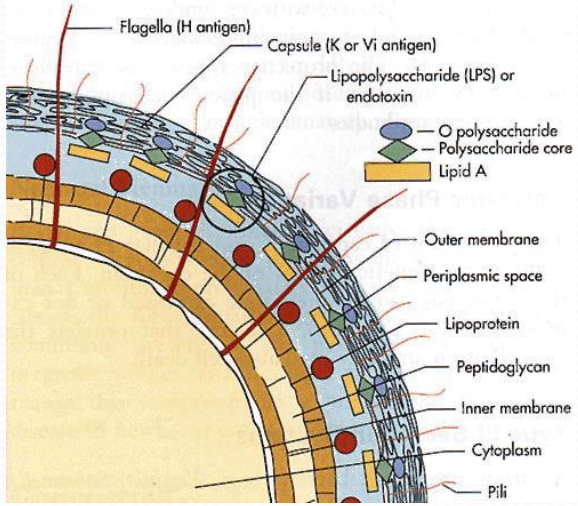
	Salmonella	Shigella	E. coli	Klebsiella	Proteus
Gram	G-	G-	G-	G-	G-
Normal flora	**not** part of normal flora	**not** part of normal flora	normal flora	normal flora	normal flora
Oxidase	Oxidase -	Oxidase -	Oxidase -	Oxidase -	Oxidase -
Motility	motile	**Non motile**	Motile	**Non-motile**	Very motile
Capsule	capsule	Capsule	Capsules	Capsulated	**Non-capsulated**
Anaerobes	Facultative anaerobes	Facultative anaerobes	Facultative anaerobes	Facultative anaerobes	Facultative anaerobes
spore	Non-spore forming	Non-spore forming	Non-spore forming	Non-spore forming	Non-spore forming
nitrite	Reduce nitrates to nitrites	Reduce nitrates to nitrites	Reduce nitrates to nitrites	Reduce nitrates to nitrites	Reduce nitrates to nitrites
Lactose	**Non-lactose fermenting**	**Non-lactose fermenting**	Lactose fermenting	Lactose fermenting	**Non-lactose fermenting**
Glucose	Glucose fermentation	Glucose fermentation	Glucose fermentation	Glucose fermentation	Glucose fermentation
Gas production	+	-	+	+	+
H_2S	H_2S positive	**negative**	**negative**	**negative**	H_2S-positive
urease	Urease negative	Urease negative	Urease negative	**Ureaese-positive**	**Ureaese-positive**

E. coli

Antigenic Structure

- More than 700 different serotypes
- Distinguished by different surface proteins and polysaccharides

1. O antigen
   - Somatic (on LPS)
   - 171 antigens
2. H antigen
   - Flagella
   - 56 antigens
3. K antigen
   - Capsule and or fimbrial antigen
   - 80 antigens



O18ac:H7:K1

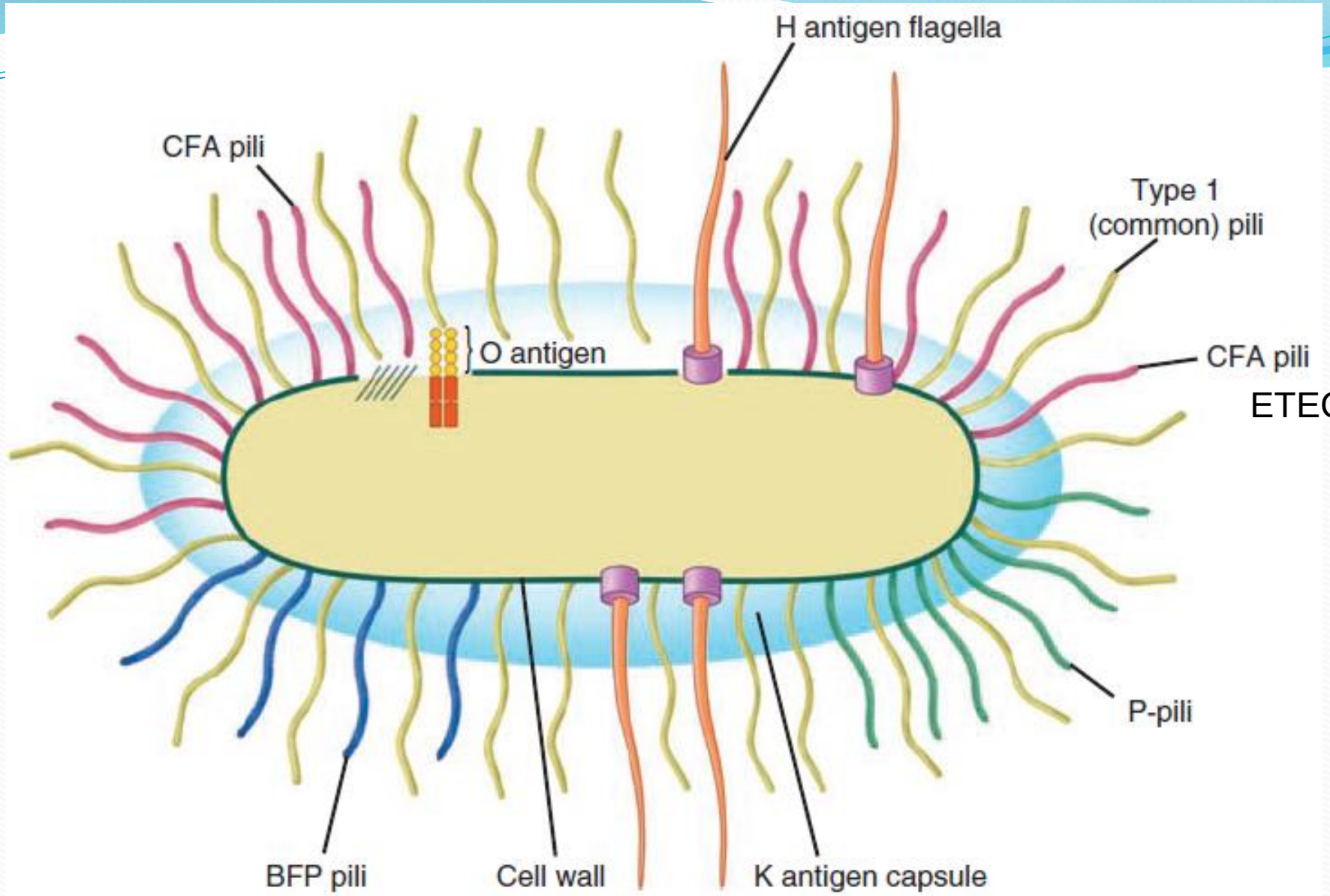
18th O antigen

7th H antigen

1st K antigen

Virulence Factors

- Fimbriae (Pili)
- Hemolysins
- Flagella
- Toxins (α-hemolysin, shiga toxin, labile toxin, and stable toxin)
- Endotoxin (LPS)
- Capsules (K antigens)
- Antigenic variation
- Drug resistance plasmids
- Other virulence plasmids



EPEC

long polar fimbriae [Lpf](EHEC)

aggregative adherence fimbriae (AAF) (EAEC)

Pili

- Attachment
  - Type 1 or common pili.
  - P pili

Toxins

1-A pore-forming cytotoxin,

- The α-hemolysin

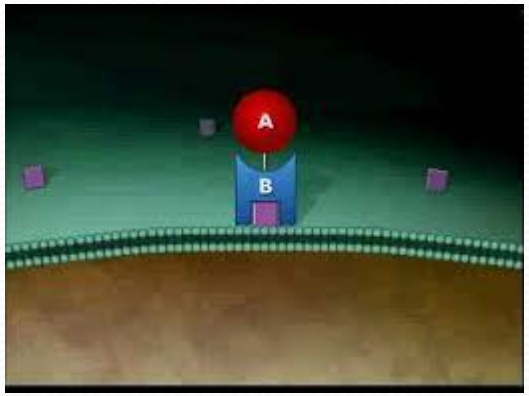
2-Inhibitors of protein synthesis,

3-A number of toxins that alter messenger pathways in host cells.

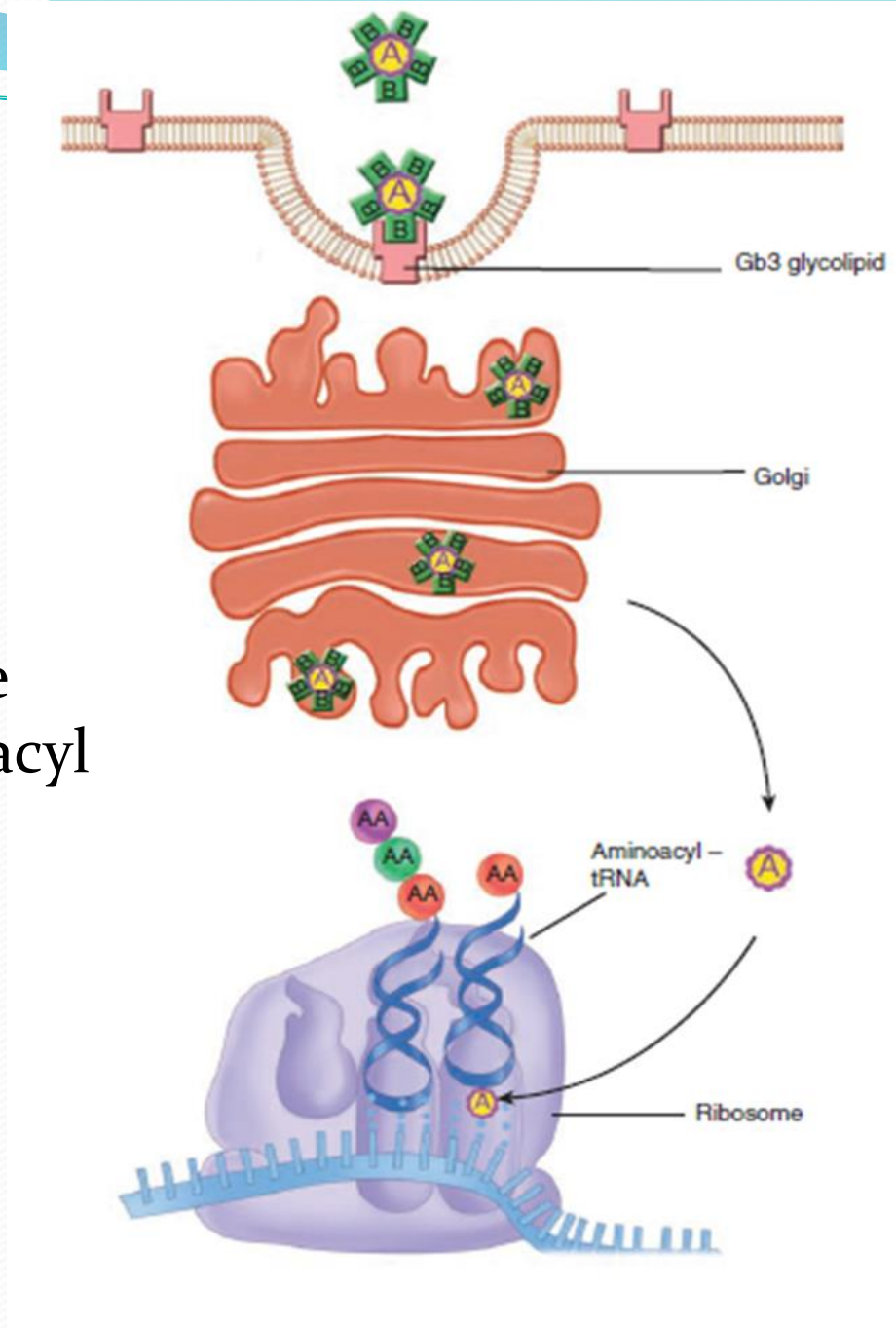
Toxins

4-Cytotoxic necrotizing factor (CNF)

- Often produced inconcert with α-hemolysin.
- **A-B toxin** that disrupts G proteins regulating signaling pathways in the cell cytoplasm
- multiple effects including cytoskeleton rearrangement and apoptosis.



- 5-Shiga toxin (Stx)
  - The B unit directs binding to a specific glycolipid receptor (Gb3)
  - internalized in an endocytotic vacuole.
  - enzymatically modifies the ribosome site (28S-RNA of 60S subunit) where amino acyl tRNA binds.
  - This alteration blocks protein synthesis, leading to cell death.

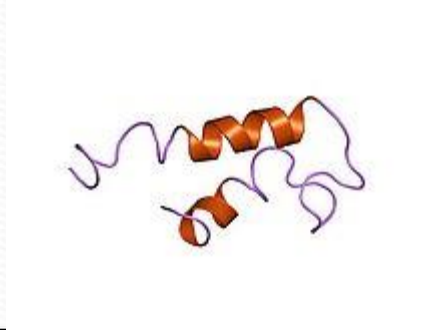


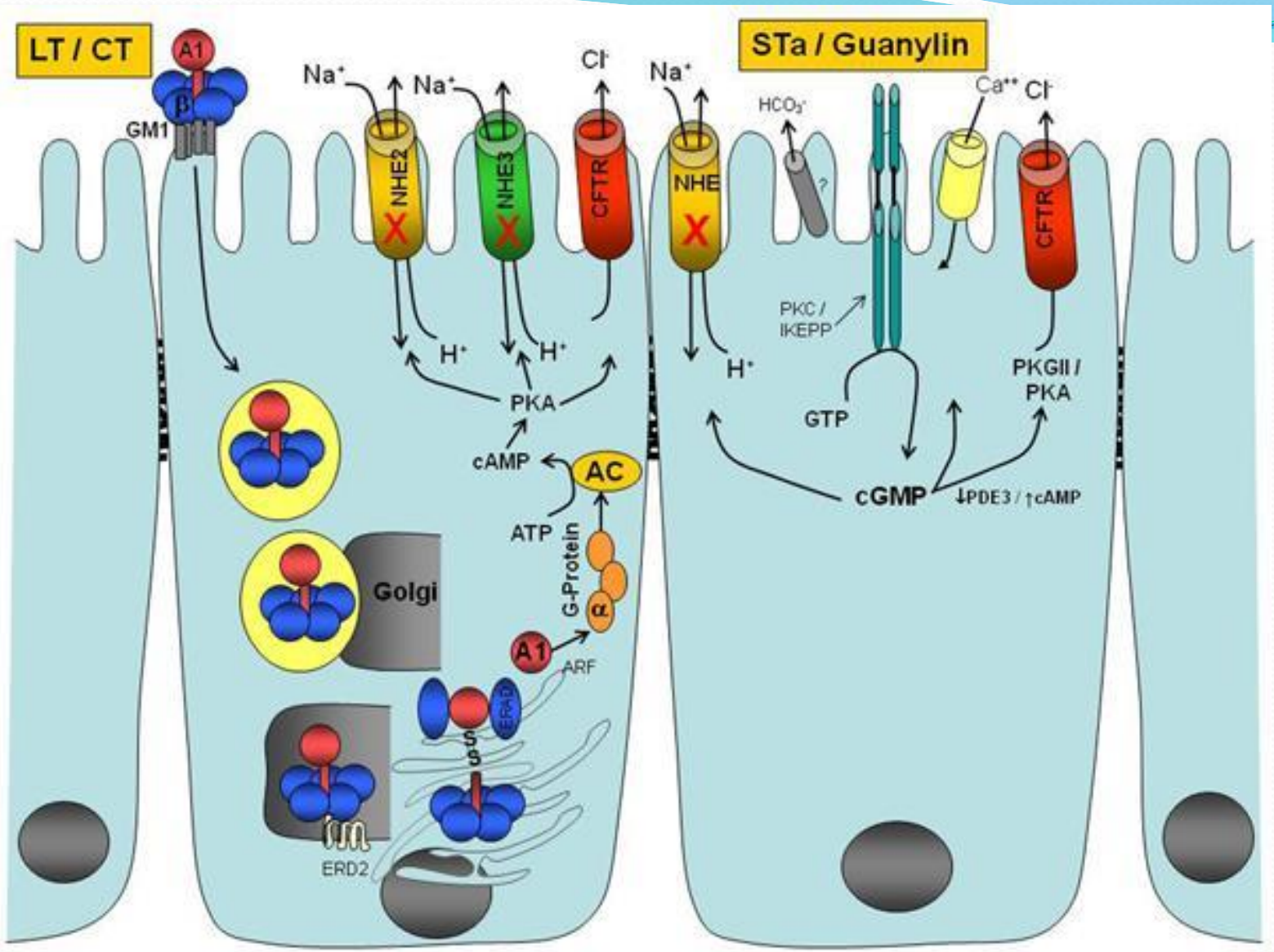
6- Heat-labile toxin (LT) is also an **A–B toxin**.

- Catalyzes the ADP-ribosylation of a regulatory G protein
- Permanent activation of the membrane-associated adenylate cyclase system (changes ATP into cAMP)
- stimulation of chloride secretion out of the cell and the blockage of NaCl absorption. The net effect is the secretion of water and electrolytes into the bowel lumen.
- LT is less potent than CT.

7-Heat-stable toxin

- **small peptide** that binds to a glycoprotein receptor,
- resulting in the activation of a membrane-bound guanylate cyclase. (converts guanosine triphosphate (GTP) to cyclic guanosine monophosphate (cGMP)
- The subsequent increase in cyclic GMP concentration causes an LT-like net secretion of fluid and electrolytes into the bowel



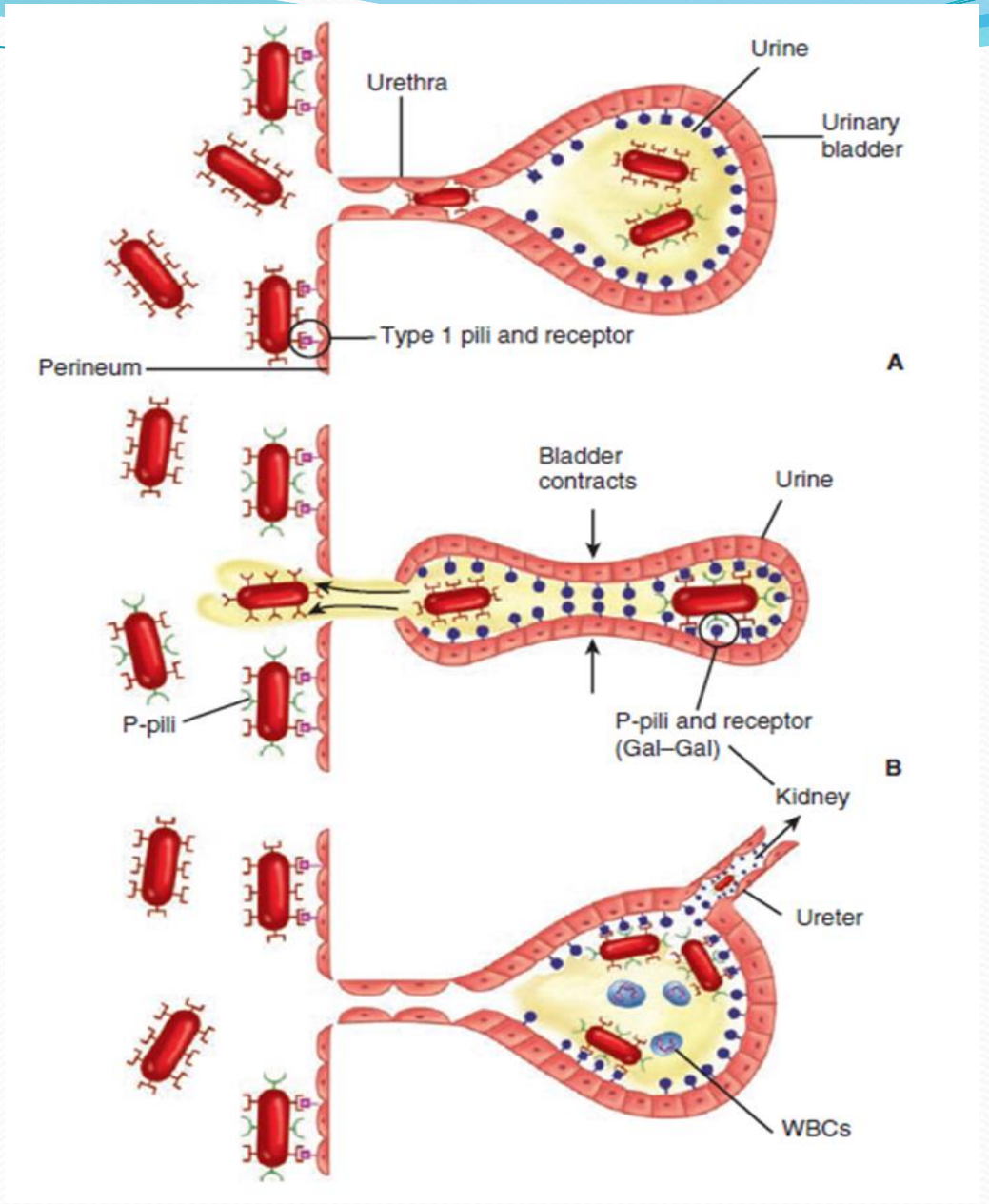

LT / CT
A1
β
GM1
Na+
Na+
NHE2
NHE3
Cl-
CFTR
H+
H+
PKA
cAMP
AC
ATP
G-Protein
α
A1
ARF
Golgi
ERD2
STa / Guanylin
Na+
NHE
H+
HCO3-
?
Ca++
Cl-
CFTR
PKC /
IKEPP
GTP
PKGII /
PKA
cGMP
↓PDE3 / ↑cAMP

Uropathogenic E coli (UPEC)

- Minor trauma or mechanical disruptions can allow bacteria colonizing the periurethral area brief access to the urinary bladder.
- E coli is the prototype UTI pathogen.

Pili

- Attachment
  - Type 1 or common pili.
  - P pili



- type 1 pili (periurethral and bladder colonization).
- P pili may add to the strength of this attachment
  - P pili are more important for upper urinary tract disease. Their Gal–Gal receptor is most abundant in the **renal pelvis and kidney where P pili facilitate pyelonephritis.**

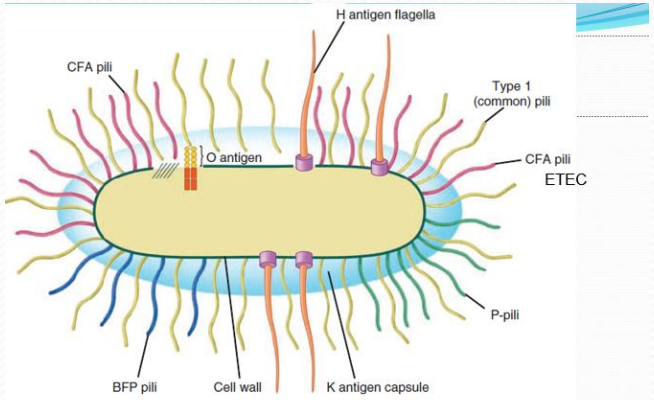
Diarrhea-causing E coli

1. entero**toxigenic** (ETEC),
2. entero**pathogenic** (EPEC),
3. entero**invasive** (EIEC),
4. entero**hemorrhagic** (EHEC),
5. entero**aggregative** (EAEC).

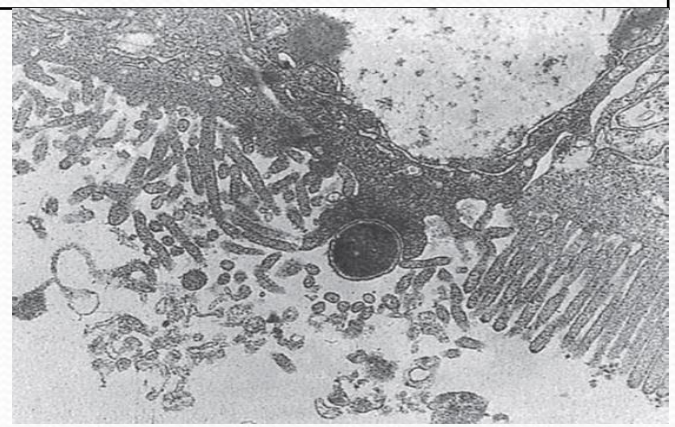
- ETEC and EIEC strains infect only humans.
- Food and water contaminated with human waste and person-to-person contact are the principal means of infection.

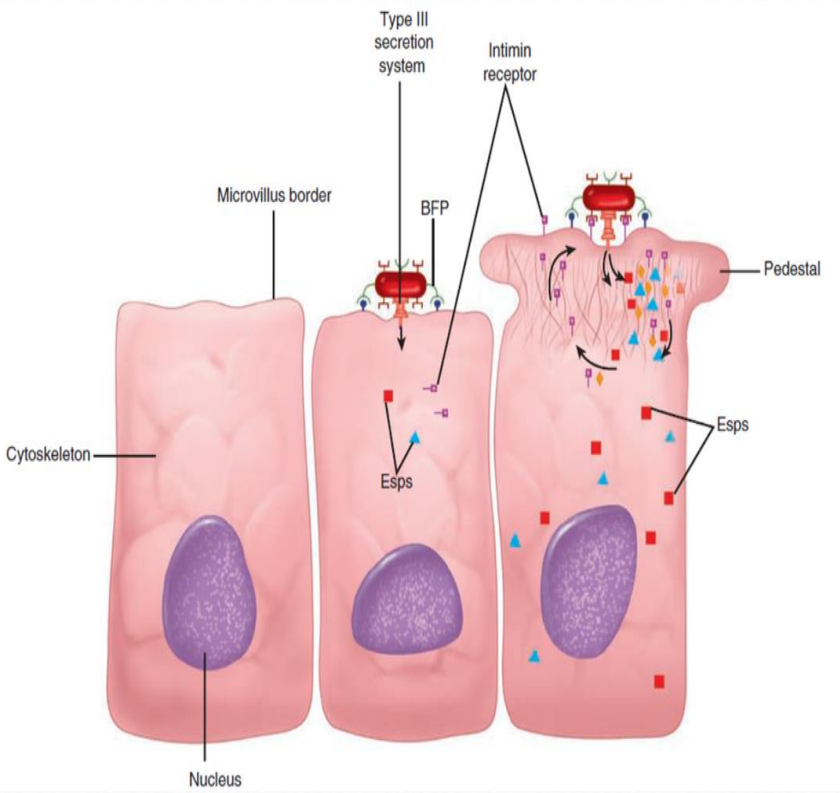
Enterotoxigenic E coli (ETEC)

LT, ST and colonizing factor (CF) pili
Watery diarrhea, not invasive
Traveler diarrhea, diarrhea in infant (developing countries)
Food and water contamination, animals not involved
High infecting dose (p2p is unusual)



EPEC
effacement or loss of microvilli
Acute or chronic diarrhea in infants (20%)
Feco-oral route
Low infecting dose in infant, high infecting dose in adult
Bundle forming (Bfp) pili, microcolnies
degeneration brush border, loss of the microvilli, and changes in the cell morphology (pedestals)
attachment and effacing (A/E) lesion (intimin, and an injection (type III) secretion system)
modifications in enterocyte cytoskeleton proteins (actin-rich A/E lesion)
mitochondrial injury and induction of apoptosis, change electrolyte transport across the luminal membrane





Enteroinvsive e coli

Mild version of shigelosis related to Shigella
Contaminated food and water, high infection dose (low p2p)
Dysentery usually with blood
Invade intestinal epithelial cells, lyse the phagosomal vacuole, spread through the cytoplasm and infect adjacent cell similar to shigella

Enteroaggregative *E. coli* (EAEC)

autoagglutinate
No enterotoxins
prolonged watery diarrhea >14d +_blood mucus
aggregative adherence fimbriae [AAF]), no A/E lesions
thick mucus–bacteria biofilm
Stx toxin

Enterohemorrhagic E. coli (EHEC)

Shiga toxin
O157:H7
Hemorrhagic colitis Crampy abdominal pain, little or no fever, bloody diarrhea, **HUS**
Animal (cattle), p2p, low infection dose (100)
More in developed countries
Hamburger (rare in the middle)
A/E lesion (intimin) and and Stx (extraintestinal features)
long polar fimbriae [Lpf] (colon not intestine)
Stx • production causes capillary thrombosis and inflammation of the colonic mucosa, leading to a hemorrhagic colitis • glomerular swelling and the deposition of fibrin and platelets in the microvasculature

Enterohemorrhagic

- 5%-10% HUS : oliguria, edema, and pallor, progressing to the triad of microangiopathic hemolytic anemia, thrombocytopenia, and renal failure
- Requiring transfusion and hemodialysis for survival.
- The mortality rate is 5%, and up to 30% of
- those who survive suffer sequelae such as renal impairment or hypertension

Enterotoxigenic	Enteropathogenic	Enteroaggregative	Enteroinvasive	Enterohemorrhagic
mild **watery** diarrhea (2-4d) last few days High infecting dose (p2p is unusual)	mild **watery** diarrhea (2-4d) last few days may chronic Low infecting dose in infant, high infecting dose in adult	mild **watery** diarrhea (2-4d) **last for weeks** High infecting dose (p2p is unusual)	mild watery diarrhea (2-4d) last few days. **Dysenteric** **high infection dose (low p2p)**	mild watery diarrhea (2-4d) last few days **dysenteric** vomiting, pain, bloody diarrhea Colonoscopy :edema, hemorrhage, and pseudomembrane formation (3-10)day resolve) low infection dose (100)

TREATMENT

- Acute uncomplicated UTIs are often treated empirically.
- trimethoprim/sulfamethoxazole (TMP-SMX) or fluoroquinolones

Enterotoxigenic	**Enteropathogenic**	**Enteroaggregative**	**Enteroinvasive**	**Enterohemorrhagic**
TMP-SMX or fluoroquinolones Antimotility agents are not helpful	TMP-SMX or fluoroquinolones Antimotility agents are not helpful	TMP-SMX or fluoroquinolones	TMP-SMX or fluoroquinolones **c/I** Antimotility agents	Hemodialysis c/I TMP-SMX or fluoroquinolones **c/I** Antimotility agents

TABLE 33–1 Characteristics of Pathogenic Enterobacteriaceae

	DIAGNOSTIC ANTIGENS	PILI	ADHESIN OR CAPSULE	EXOTOXIN	PATHOGENIC LESIONS	SECRETED PROTEINS[a]	GENETICS	TRANSMISSION	DISEASE
Escherichia coli	**O, H, K**								
Common	>150 types	Type I[b]	K1 polysaccharide	α-Hemolysin	Inflammation			Adjacent flora	Opportunistic
Uropathogenic (UPEC)		Type I[b], P (Gal–Gal)		α-Hemolysin	Inflammation			Fecal flora, ascending	UTI
Enterotoxigenic (ETEC)		CFs		LT, ST	Hypersecretion		Plasmid (CF, LT, ST)	Fecal–oral	Watery diarrhea (travelers)
Enteropathogenic (EPEC)		Bfp	Intimin		A/E, small intestine	Esps	PAI	Fecal–oral	Watery diarrhea
Enteroinvasive (EIEC)			Ipas		Invasion, inflammation, ulcers	Ipas	Large plasmid, PAI	Fecal–oral	Dysentery
Enterohemorrhagic (EHEC)	0157:H7	Lpf	Intimin	Stx	A/E, colon, hemorrhage	Esps	PAI	Fecal–oral direct, low dose, cattle	Bloody diarrhea, HUS
Enteroaggregative (EAEC)		AAFs		Stx	Adherent biofilm				watery or bloody[d] diarrhea, HUS[d]