



# Microbiology

Subject :

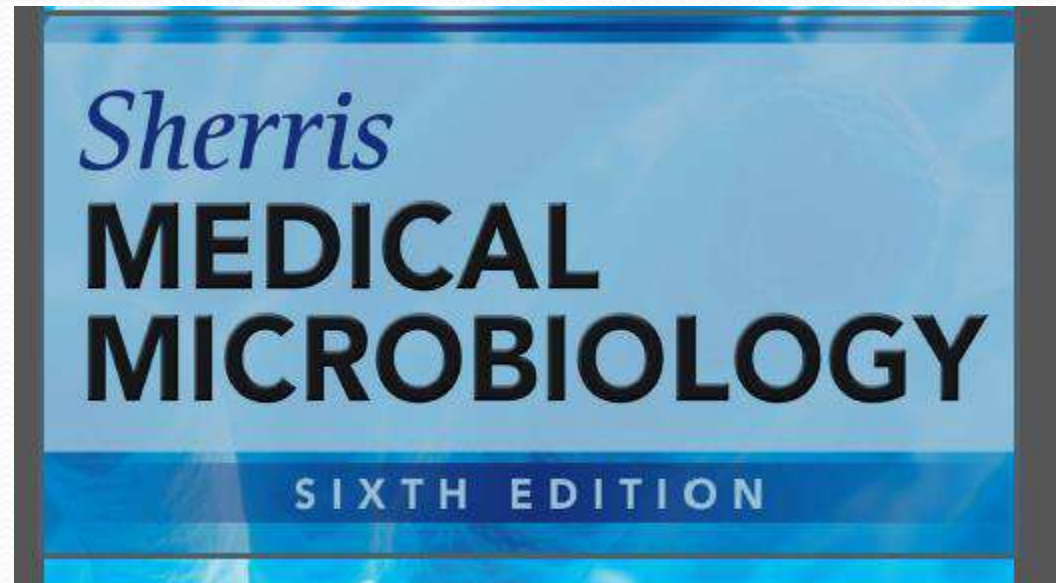
Lec no : 14

Done By : Tabark Aldaboubi

وقار رجب زرنى علما

# 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

Family group of the gram negative  
Sever infection مسؤوله عن 30% من ال  
related of urinary tract infection ← 70%

- 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*
- 1 4. *Esherishia*
5. *Klebsiella*
6. *Morganella*
- 2 7. *Proteus*

- 3 8. *Salmonella*
- 4 9. *Shigella*
10. *Serratia*
11. *Yersinia*
12. *Hania*

الدلهم  
والاكثر  
انتشاراً ←

كانت موجودة و Very common  
كانت لسبب مهاعون و بعدها  
اختفت



	Salmonella	Shigella	E. coli	Klebsiella	Proteus
Gram	Gram <sup>كدهم</sup> negative G-	G-	G-	G-	G-
Normal flora	<b>not</b> part of normal flora	<b>not</b> part of normal flora	normal flora	normal flora	normal flora
Oxidase	Oxidase -	Oxidase -	Oxidase -	Oxidase -	Oxidase -
Motility	motile	<b>Non</b> motile	Motile	<b>Non</b> motile	Very motile
Capsule	capsule	Capsule	Capsules	Capsulated	<b>Non</b> 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	<b>Non</b> lactose fermenting	<b>Non</b> lactose fermenting	Lactose fermenting	Lactose fermenting	<b>Non</b> lactose fermenting
Glucose	Glucose fermentation	Glucose fermentation	Glucose fermentation	Glucose fermentation	Glucose fermentation
Gas production	+	-	+	+	+
H <sub>2</sub> S	H <sub>2</sub> S positive	<b>negative</b>	<b>negative</b>	<b>negative</b>	H <sub>2</sub> S-positive
urease	Urease negative	Urease negative	Urease negative	<b>Ureaese-positive</b>	<b>Ureaese-positive</b>



	Salmonella	Shigella	E. coli	Klebsiella	Proteus
<b>Gram</b>	G-	G-	G-	G-	G-
<b>Normal flora</b>	not part of normal flora	not part of normal flora	normal flora	normal flora	normal flora
<b>Oxidase</b>	Oxidase -	Oxidase -	Oxidase -	Oxidase -	Oxidase -
<b>Motility</b>	motile	<b>Non motile</b>	Motile	<b>Non-motile</b>	Very motile
<b>Capsule</b>	capsule	Capsule	Capsules	Capsulated	<b>Non-capsulated</b>
<b>Anaerobes</b>	Facultative anaerobes	Facultative anaerobes	Facultative anaerobes	Facultative anaerobes	Facultative anaerobes
<b>spore</b>	Non-spore forming	Non-spore forming	Non-spore forming	Non-spore forming	Non-spore forming
<b>nitrite</b>	Reduce nitrates to nitrites	Reduce nitrates to nitrites	Reduce nitrates to nitrites	Reduce nitrates to nitrites	Reduce nitrates to nitrites
<b>Lactose</b>	<b>Non-lactose fermenting</b>	<b>Non-lactose fermenting</b>	Lactose fermenting	Lactose fermenting	<b>Non-lactose fermenting</b>
<b>Glucose</b>	Glucose fermentation	Glucose fermentation	Glucose fermentation	Glucose fermentation	Glucose fermentation
<b>Gas production</b>	+	-	+	+	+
<b>H<sub>2</sub>S</b>	H <sub>2</sub> S positive	<b>negative</b>	<b>negative</b>	<b>negative</b>	H <sub>2</sub> S-positive
<b>urease</b>	Urease negative	Urease negative	Urease negative	<b>Ureaese-positive</b>	<b>Ureaese-positive</b>
<b>IMViC</b>	+++ <span style="color:red">●</span>	+++	+++	---++	+++

ركزوا على هياي النقطة مش موجودة بالسلايدات الي نازلة  
على التيمز بس بالملف الي شرح عنه الدكتور موجودة

هون نفس القصة  
تاعة السلاب الماخين

## BIOCHEMICAL REACTIONS OF E.coli



بنصحنه  
بالسلايب الكائن



# *E. coli*

The most cause urinary tract infection

Part of normal flora of colone human and other animal but can be bathogenic both inside or outside GI tract

بثقل اراض داخل  
gastrointestinal tract and urinary tract





# Antigenic Structure

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

## 1. O antigen

- Somatic (on LPS) *lipopolysaccharides*
- 171 antigens

## 2. H antigen

- Flagella
- 56 antigens

## 3. K antigen

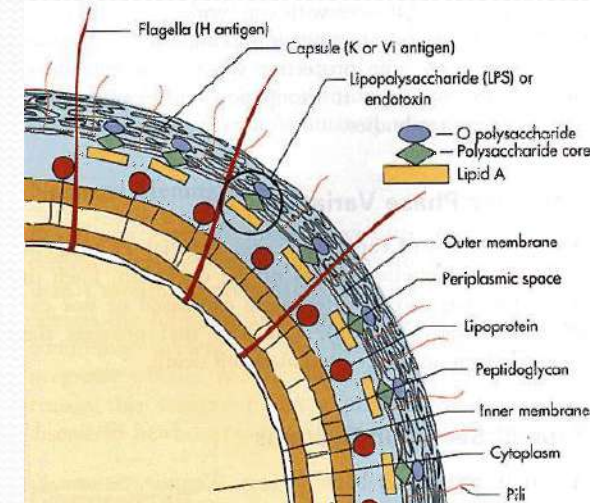
- Capsule and or fimbrial antigen
- 80 antigens

infection

← Pathogenic

مفيدة

في انواع الـ E-coli



O18ac:H7:K1

18<sup>th</sup>

O antigen

7<sup>th</sup>

H antigen

1<sup>st</sup>

K antigen



\* different strain has different virulence factor

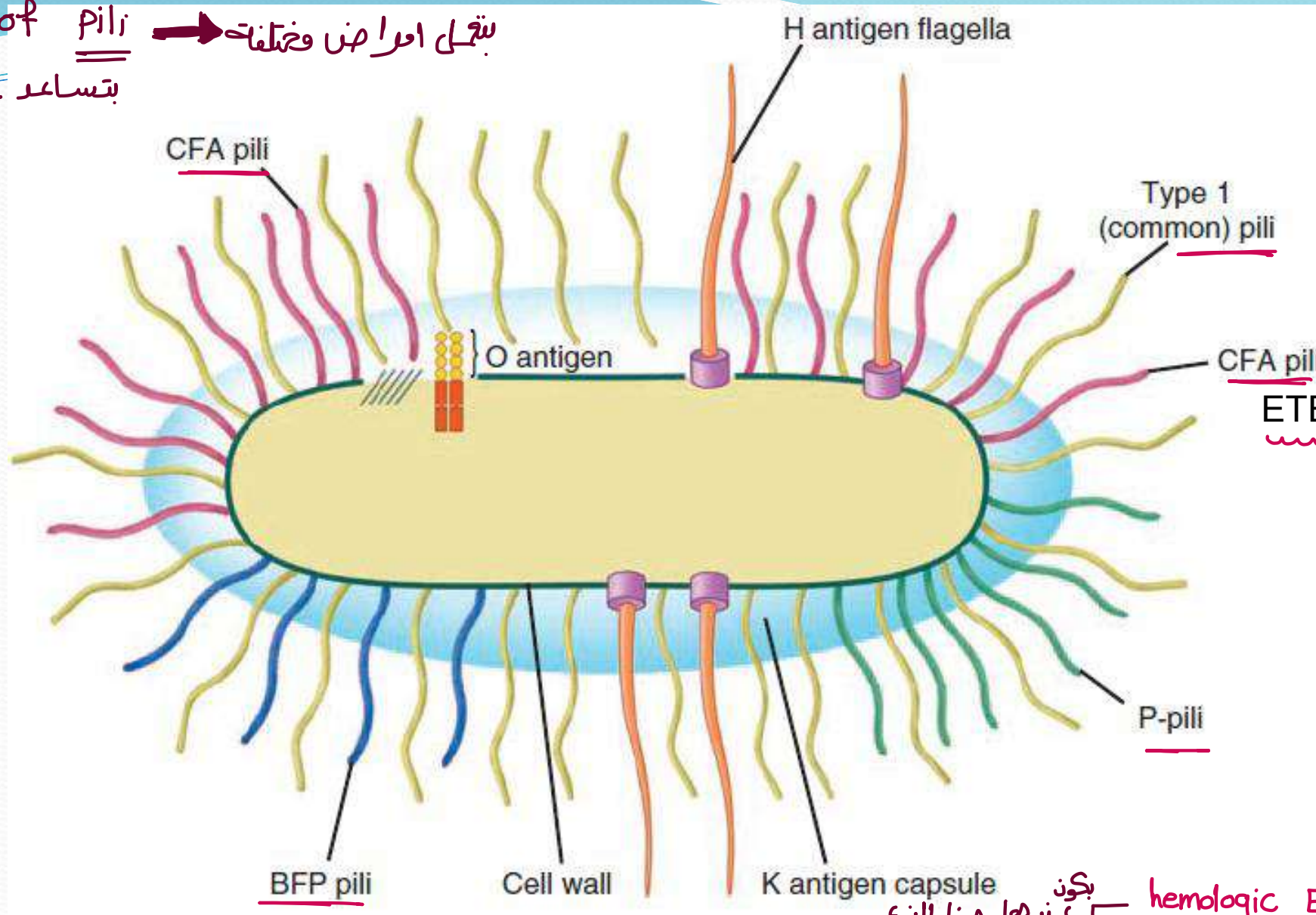
# Virulence Factors

- Fimbriae (Pili) → Attachment *التعلق*
- Hemolysins
- Flagella → Motility
- Toxins ( $\alpha$ -hemolysin, shiga toxin, labile toxin, and stable toxin)
- Endotoxin (LPS)
- Capsules (K antigens)
- Antigenic variation
- Drug resistance plasmids
- Other virulence plasmids



different type of pili → بتقلى اعراس وختلقات

Attachment بتساعد على ال



عندها  
هكذا النوع  
من ال Pili

EPEC

رح تعرفها بعد شوي ← hemologic E-coli يكون عندها هذا النوع .  
long polar fimbriae [Lpf](EHEC)

aggregative adherence fimbriae (AAF) (EAEC)



# Pili

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

↓  
فِي نَقَبَاتِ هَوْن

من الملف الي شرح عنها الدكتور

## Pili

- Attachment
- Type 1 or common pili. الاغلب عندهم هذا النوع
  - d-mannose residues commonly present on epithelial cell surfaces
- P pili → **kidney infection** الها علاقة بال
  - bind to digalactoside (Gal-Gal) moieties on kidney cells and erythrocytes of the P blood group.

# Toxins

عندما عدة انواع من الـ *Toxins* .

1-A pore-forming cytotoxin,

- The  $\alpha$ -hemolysin  $\rightarrow$  damage of plasma membrane and this will lead to cell death

2-Inhibitors of protein synthesis,  $\rightarrow$  بالتالي يهمل cell death و damage

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

يهمل Apoptosis



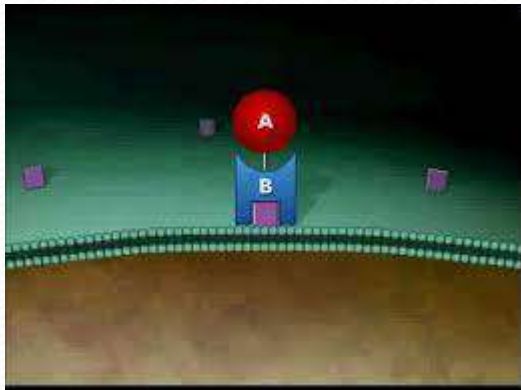
# Toxins

Toxic the cell → Apoptosis and necrosis بطل

## 4-Cytotoxic necrotizing factor (CNF)

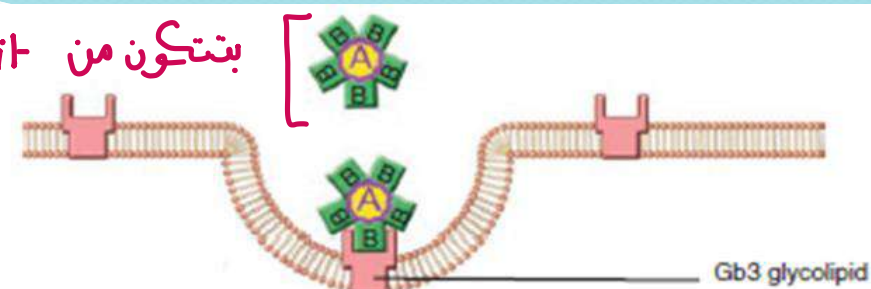
دائماً يكون موجود مع  
Strain  $\alpha$  hemolysin

- Often produced in concert with  $\alpha$ -hemolysin.
- **A-B toxin** that disrupts G proteins regulating signaling pathways in the cell cytoplasm  
شغلة يكون على: ↑
- multiple effects including cytoskeleton rearrangement and apoptosis.





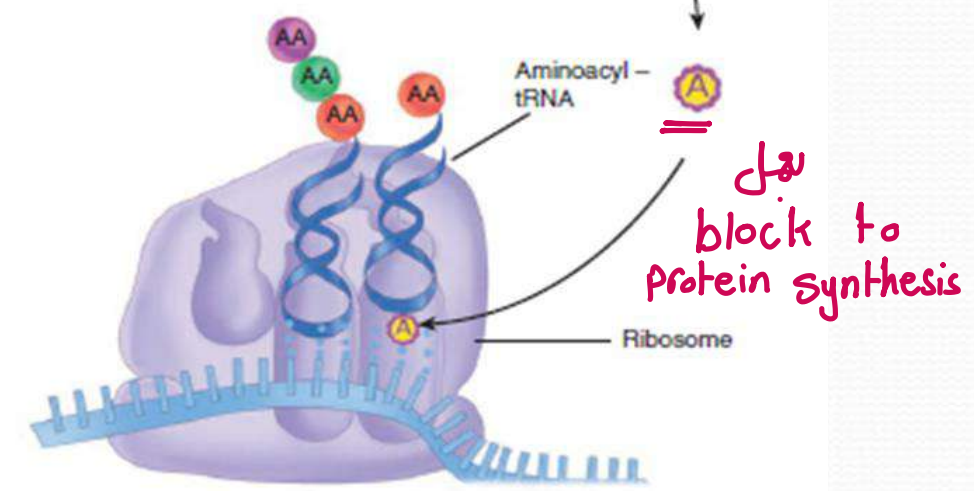
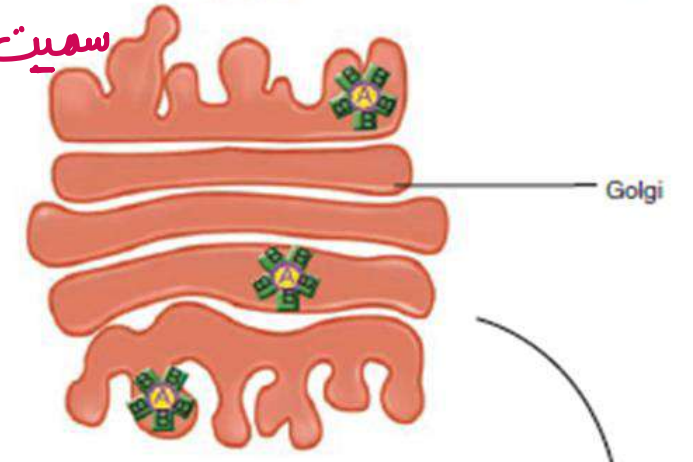
enzymatic Activity // A و B unit بتكون من B بتعمل binding بس الـ A هي الي فيها enzymatic Activity هون بتعمل block to protein synthesis



5-Shiga toxin (Stx)

Shigella infection الحة العالم الي اكتشف سميت لسبخة

- 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.



الـ B بتعمل binding مع reseptore (Gb3) وبدخل لما يصير حوا الـ cell الـ A بتعمل block to protein synthesis

Toxin heat بهذا ال ايشن بتعمل ال

unit unit

B unit bind to cell membrane

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

A unit →

- Catalyzes the ADP-ribosylation of a regulatory G protein → Activation of the adenylate cyclase system
- Permanent activation of the membrane-associated adenylate cyclase system (changes ATP into cAMP)
- stimulation<sup>①</sup> of chloride secretion<sup>②</sup> out of the cell and the blockage<sup>③</sup> of NaCl absorption<sup>④</sup>. The net effect is the secretion of water and electrolytes into the bowel lumen.
- LT is less potent than CT.

الطاقة حوا الخلية بتصير اكبر

②

④

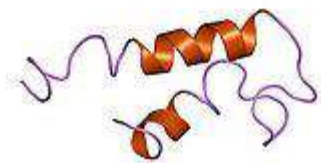
③

①



## 7-Heat-stable toxin *Not A,B*

- 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



Labile  
Toxin  
(LT)

عمل نفس التأثير وينتج نفس الطاقة ناعمة

بس الطرق مختلفة



# Heat labile toxin



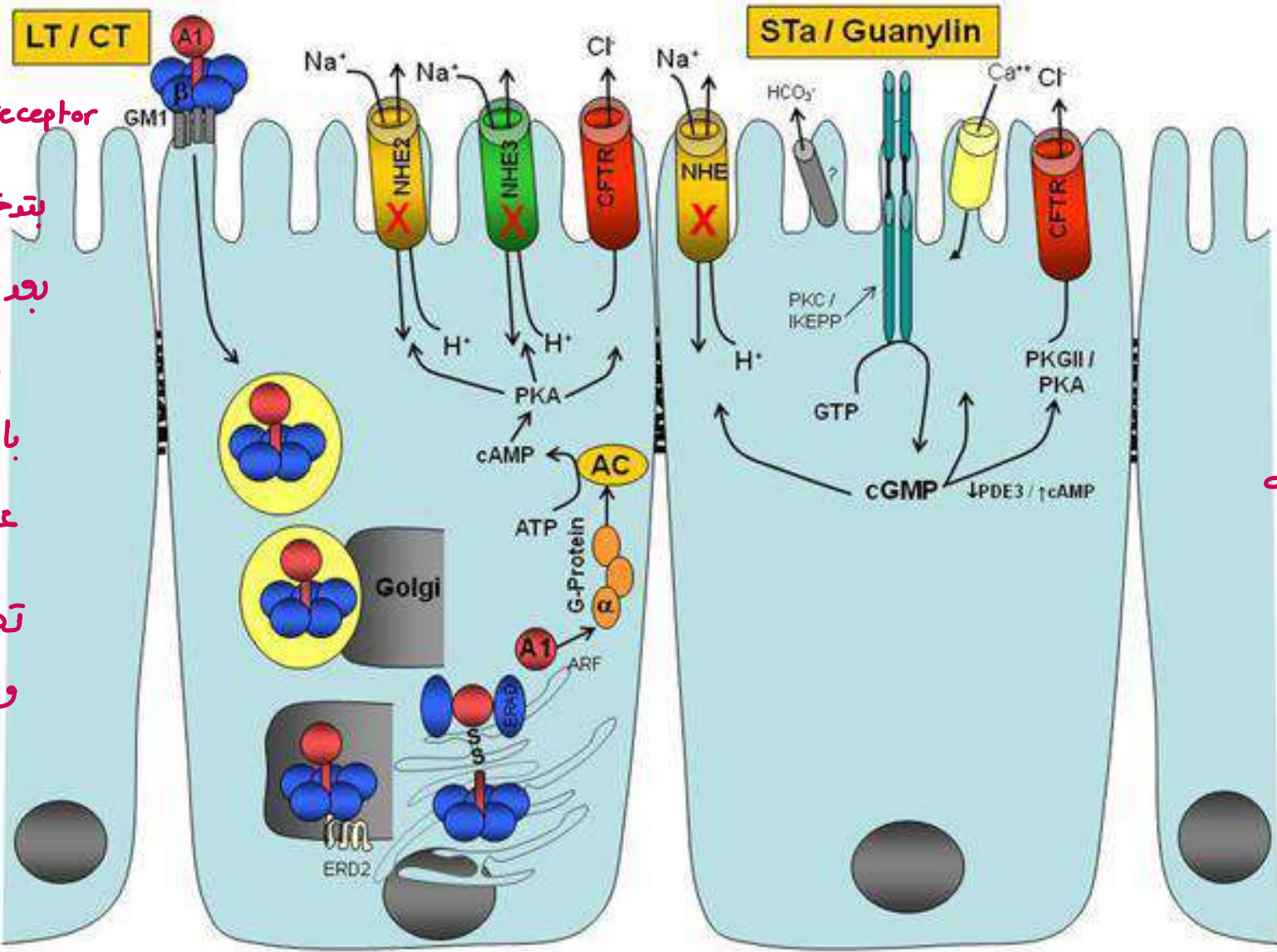
بتدخل A و B جوا بحويصلات  
بعدين بتطلع ال A ليعمل

Activation to cAMP

بالتالي بصير عنا ATP

عالي جوا الخلية وبتصير

تطلع ال fluid و Na و  
ويجلب diarrhea



# Heat stable toxin

Small peptide عبارة عن

لاخل وبتبطل مع GTP

ويحفز cGMP و بصرنو

لنتج طاقة وبتصير كثير

جوا الخلية وبتطلع ال fluid

ولا Na<sup>+</sup> لبرا و بصير diarrhea

# ↓ Uropathogenic E coli (UPEC)

The most common cause of urinary tract infection

- 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.



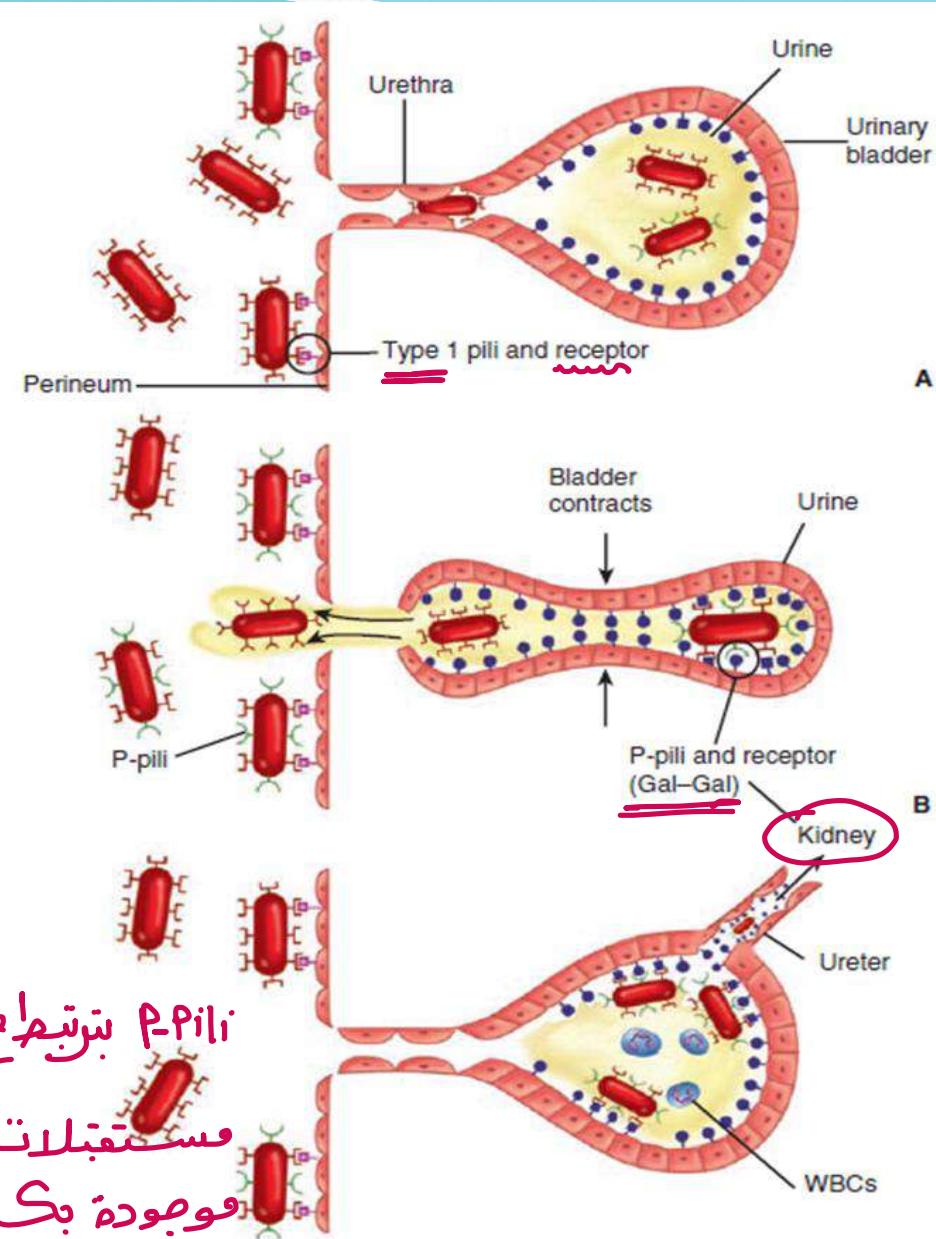
# Pili

- 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.

بال kidney وينقل  
وجوده بكثرة  
مستقبلاتها  
P-Pili يرتبط مع



احد عوامل المشراسية

P-Pili يرتبط مع

مستقبلاتها

وجوده بكثرة

بال kidney وينقل

# Diarrhea-causing E coli

Type of E - coli :

1. enterotoxigenic (ETEC),
  2. enteropathogenic (EPEC),
  3. enteroinvasive (EIEC),
  4. enterohemorrhagic (EHEC),
  5. enteroaggregative (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)

The most common cause of diarrhea

LT, ST and "colonizing factor (CF) pili" Attachment pili لازم يكون موجود هالنوع من ال

Watery diarrhea, not invasive <sup>not damage cell</sup> Acute diarrhea بس يتطلع ال water

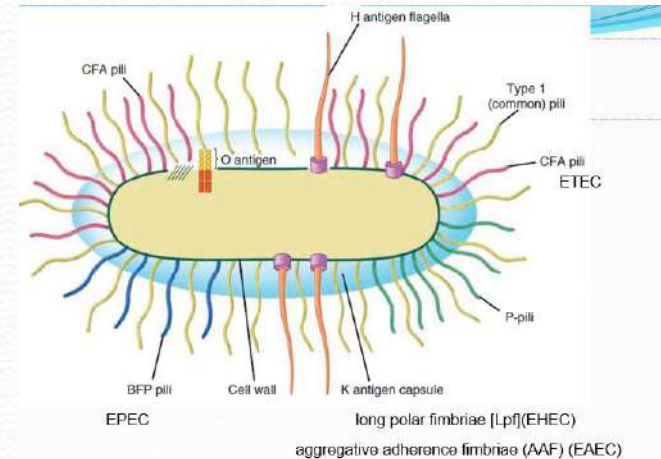
Traveler diarrhea, diarrhea in infant (developing countries)

Food and water contamination, animals not involved

High infecting dose (p2p is unusual) need large number of E-coli to cause this type of infection.

Person to Person

الشخصين سافر تعرضوا لقيح  
الجو والاكل فاول الحم يوم  
بصير عنده diarrhea



## EPEC Change of structure

effacement or loss of microvilli

Acute or chronic diarrhea in infants (20%)

Feco-oral route → *transmission*

Low infecting dose in infant, high infecting dose in adult

Bundle forming (Bfp) pili, microcolonies

degeneration brush border, loss of the microvilli, and changes in the cell morphology (pedestals) *Structure*

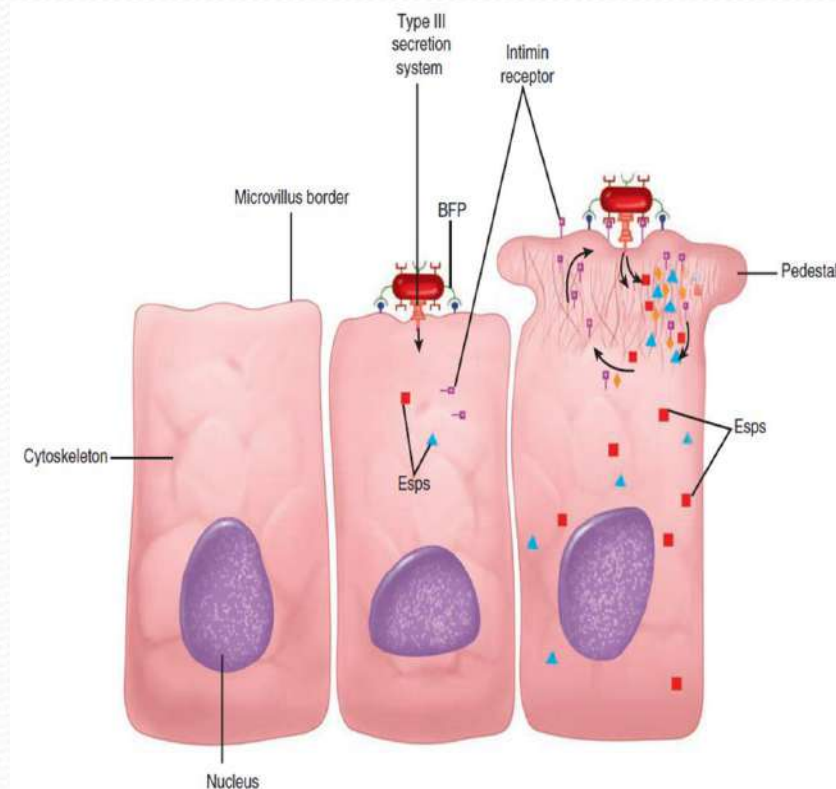
attachment and effacing (A/E) lesion (intimin, and an injection (type III secretion system)

modifications in enterocyte cytoskeleton proteins (actin-rich A/E lesion)

mitochondrial injury and induction of apoptosis, change electrolyte transport across the luminal membrane

*Pathology in intestinal cell*

*الوظيفة تاعتها رح يصير فيها خلل بصير عنده  
diarhea → لوقت حولى*





damage to mucosal cell

# Enteroinvasive e coli

diarrhea with blood  
کونہ بیمار damage cell

Mild version of shigelosis related to Shigella

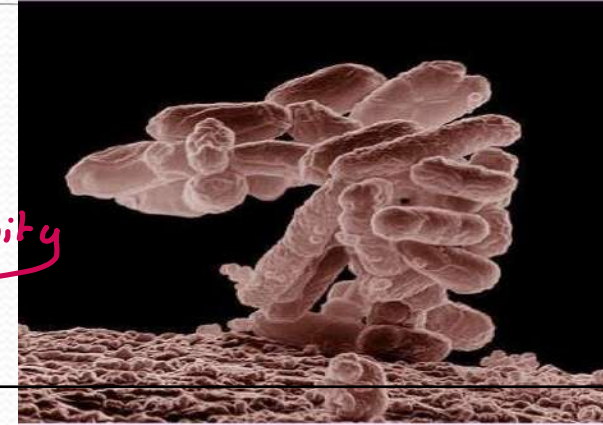
Contaminated food and water, high infection dose (low p2p)

→ Dysentery usually with blood Stool (mucus and blood)

Invade intestinal epithelial cells, lyse the phagosomal vacuole, spread through the cytoplasm and infect adjacent cell similar to shigella

# Enteroaggregative *E. coli* (EAEC)

تجمع مغطية بـ *E. coli*  
Community



autoagglutinate

No enterotoxins

prolonged watery diarrhea <sup>بفضل أكثر من أسبوعين</sup> >14d <sup>day</sup> + blood mucus → بتخذ وهما شوي من البكتيريا وشوي من الـ Cell

aggregative adherence fimbriae [AAF]), no A/E lesions

thick mucus–bacteria biofilm

Stx toxin



# اللاخطر Enterohemorrhagic E. coli (EHEC)

Shiga toxin damage cell و necrosis

O157:H7 sever infection رقمه مميز لو شفتنا بتوقع الاقوي لهاي الامراض ↓

Hemorrhagic colitis

hemolytic uremic syndrome

Crampy abdominal pain, little or no fever, bloody diarrhea, **HUS**

Animal (cattle), p2p, low infection dose (100)

سرعية الانتقال

More in developed countries

Hamburger (rare in the middle)

A/E lesion (intimin) and Stx (extraintestinal features )

long polar fimbriae [Lpf] (colon not intestine)

Stx اذا وصل الـ Shiga toxin على الدم بمل:

- production causes <sup>①</sup>capillary thrombosis and inflammation of the colonic mucosa, leading to a hemorrhagic colitis  
↓  
hemolysis (تكسير RBC)
- glomerular swelling and the deposition of fibrin and platelets in the microvasculature

# Enterohemorrhagic

hemolytic uremic syndrome

- 5%-10% HUS : oliguria, edema, and pallor, progressing to the triad of microangiopathic hemolytic anemia, thrombocytopenia, and renal failure → *Capillary* بتروح للـ الكليية  
*decreased in number platelet*
- 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
<p>mild <u>watery</u> diarrhea (2-4d)                      last few days                      acute diarrhea</p> <p>High <u>infecting</u> dose                      (p2p is unusual)</p>	<p>mild <u>watery</u> diarrhea (2-4d)                      last few days                      may chronic</p> <p><u>Low</u> infecting dose in infant, <u>high</u> infecting dose in adult</p>	<p>mild <u>watery</u> diarrhea (2-4d)                      last for weeks</p> <p><u>High</u> infecting dose (p2p is unusual)</p>	<p>mild <u>watery</u> diarrhea (2-4d)                      last few days.</p> <p>Dysenteric</p> <p><u>high</u> infection dose (low p2p)</p>	<p>mild <u>watery</u> diarrhea (2-4d)                      last few days                      dysenteric</p> <p>vomiting, pain, bloody diarrhea</p> <p>Colonoscopy :edema, hemorrhage, and pseudomembrane formation (3-10)day resolve)</p> <p><u>low</u> infection dose (100)</p>

# TREATMENT

بس نعرف انه كلهم gram negative بس بدنا نعالجها نعطي مضاد حيوي  
ونعطيه supportive treatment نساعده بحيث نعطيه الاشياء الي خسرها

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

Enterotoxigenic	Enteropathogenic	Enteraggregative	Enteroinvasive	Enterohemorrhagic
TMP-SMX or fluoroquinolones Antimotility agents are not helpful	TMP-SMX or fluoroquinolones Antimotility agents are not helpful  شخص عنده diarrhea بتروح تعطيه دوا بوقف diarrhea هالاشي مت بنصح فيه لانو احنا ما بدنا البكتيريا ترجع بالعكس بدنا اياها تطلع مع ال stool	TMP-SMX or fluoroquinolones	TMP-SMX or fluoroquinolones <b>c/I</b> Antimotility agents	Hemodialysis c/I TMP-SMX or fluoroquinolones  <b>c/I</b> Antimotility agents



**TABLE 33-1** Characteristics of Pathogenic Enterobacteriaceae

	DIAGNOSTIC ANTIGENS	PILI	ADHESIN OR CAPSULE	EXOTOXIN	PATHOGENIC LESIONS	SECRETED PROTEINS <sup>a</sup>	GENETICS	TRANSMISSION	DISEASE
<i>Escherichia coli</i>	O, H, K								
Common	>150 types	Type I <sup>b</sup>	K1 polysaccharide	$\alpha$ -Hemolysin	Inflammation			Adjacent flora	Opportunistic
Uropathogenic (UPEC)		Type I <sup>b</sup> , P (Gal-Gal)		$\alpha$ -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	Esp	PAI	Fecal-oral	Watery diarrhea
Enteroinvasive (EIEC)			Ipa		Invasion, inflammation, ulcers	Ipa	Large plasmid, PAI	Fecal-oral	Dysentery
Enterohemorrhagic (EHEC)	O157:H7	Lpf	Intimin	Stx	A/E, colon, hemorrhage	Esp	PAI	Fecal-oral direct, low dose, cattle	Bloody diarrhea, HUS
Enteraggregative (EAEC)		AAF		Stx	Adherent biofilm				watery or bloody <sup>d</sup> diarrhea, HUS <sup>d</sup>

كن موقفاً  
مادمت تسعى  
للطموح ستسعى

