

**Gastrointestinal Tract Module**  
**Bacterial infections**

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# Bacterial infections of GIT

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## Introduction

### Classification

#### Gastroenteritis/Food poisoning

*S. aureus*

*B. cereus*

*C. botulinum*

*C. perfringens*

#### Watery (secretory) diarrhea

*V. cholera*

ETEC

EPEC

#### Cell invasion

*Shigella*

*Salmonella enteritidis*

EHEC

EIEC

#### Antibiotic associated diarrhea

*C. difficile*

#### Cell invasion and bacteremia

*C. Jejuni*

*Salmonella typhi*

#### Gastritis and ulcers

*H. pylori*

# *Escherichia coli*

Enteropathogenic *E. coli* (EPEC)

Enterotoxigenic *E. coli* (ETEC)

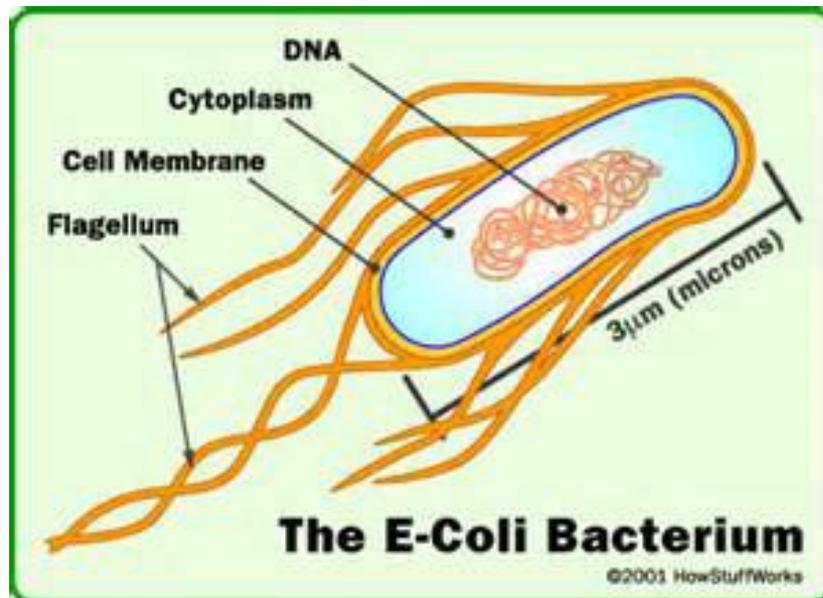
Enterohemorrhagic *E. coli* (EHEC)

Enteroinvasive *E. coli* (EIEC)

# *Escherichia coli*

## Morphology, culture, and antigen structure.

- Gram-negative rods
- Peritrichous flagella
- The complex antigen structure of these bacteria is based on O, K, and H antigens
- Specific numbers have been assigned to the antigens, e.g., serovar O18:K1:H7.



# *Escherichia coli*

## Associated infections

### 1. Extraintestinal infections

- Urinary tract infection
- Sepsis
- Wound infections
- infections of the gallbladder and bile ducts
- Appendicitis
- meningitis

### 2. Intestinal infections: associated with virulence factors

# Escherichia coli

## Virulence factors

➤ Pili: attachment

➤ Toxins:

### 1. Shiga-like toxin (Stx) E. coli O157 : H7 is the main serotype of EHEC

- A & B subunit toxin
- B subunit (binding)
- A subunit is released into cytoplasm: binds to and inactivated the ribosome
- The net result is the inhibition of eukaryotic protein synthesis and death

### Inhibit protein synthesis

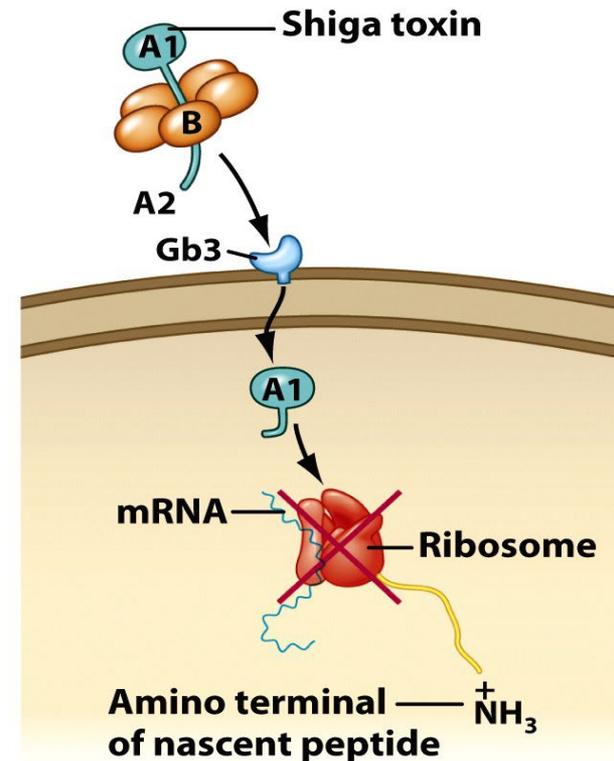


Figure 25.15b Microbiology: An Evolving Science  
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# Escherichia coli

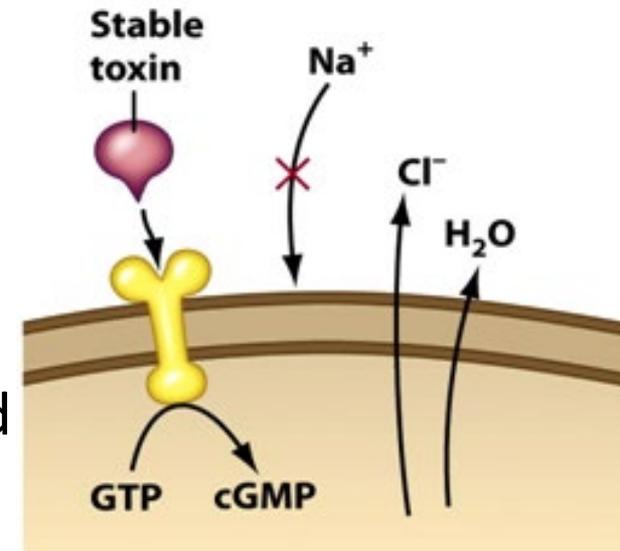
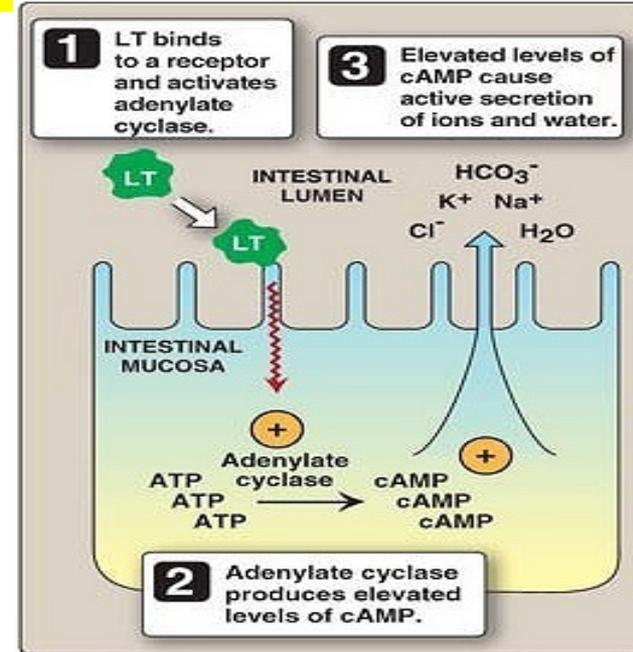
## Virulence factors

2. heat-Labile toxin (LT) (inactivation at 60C for 30 minutes)

- A & B toxin
- B-subunit (binding)
- A-subunit is released into cytoplasm
- Activation of adenylate cyclase
- Increase CL secretion which follows by Na and H<sub>2</sub>O leading to diarrhea
- Similar but less potent than cholera toxin

3. heat-Stable toxin

Mediates the inhibition of Na<sup>+</sup> absorption and stimulates chloride secretion by enterocytes.



# Enterotoxigenic *E. coli* (ETEC)

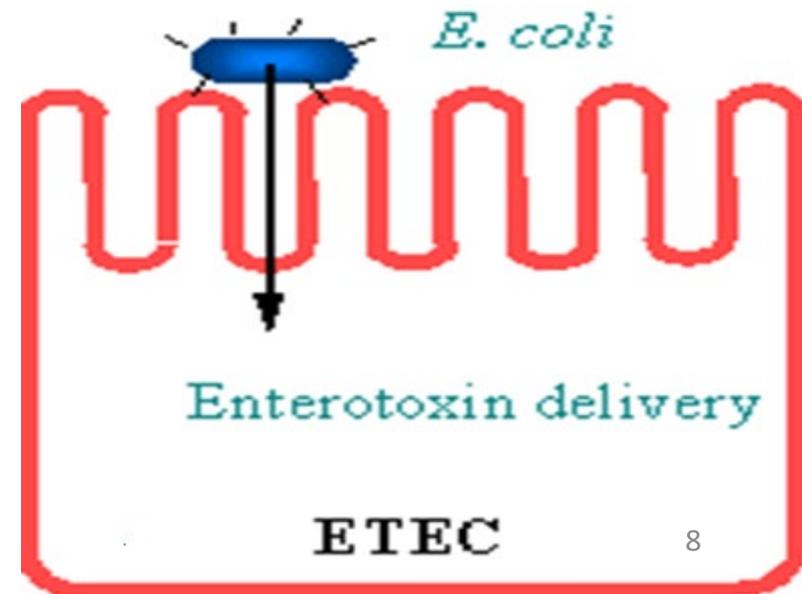
## Epidemiology

- Endemic in low resource countries
- ETEC is the leading cause of diarrhea in travelers from developed regions returning from vacations (**travelers diarrhea**)

## Types of toxins and pathogenesis

- A heat-stable toxin and a heat-labile toxins
- The organism attaches to the intestinal mucosa via colonization factors and then liberates enterotoxin

Entero**T**oxigenic = **T**ravelers



# Enterotoxigenic *E. coli* (ETEC)

## Transmission

- Transmitted when a person eats food, or drinks water contaminated with ETEC bacteria
- Human or animal wastes (e.g., feces) are the main source of ETEC contamination.

## Clinically

- Diarrhea caused by ETEC is a self-limiting illness of moderate severity with watery stools and abdominal cramps
- Illness develops 1-5 days after exposure, lasts 3-4 days.
- Some infections may take a week or longer to resolve

## Treatment

- Recovery within a few days, without specific treatment
- Liquids are recommended to prevent dehydration and loss of electrolytes

# Enterotoxigenic *E. coli* (ETEC)

## How is infection with ETEC diagnosed?

- Diagnosis based on a patient's history and symptoms
- The techniques necessary to identify ETEC are not widely available

# Enteropathogenic E. coli (EPEC)

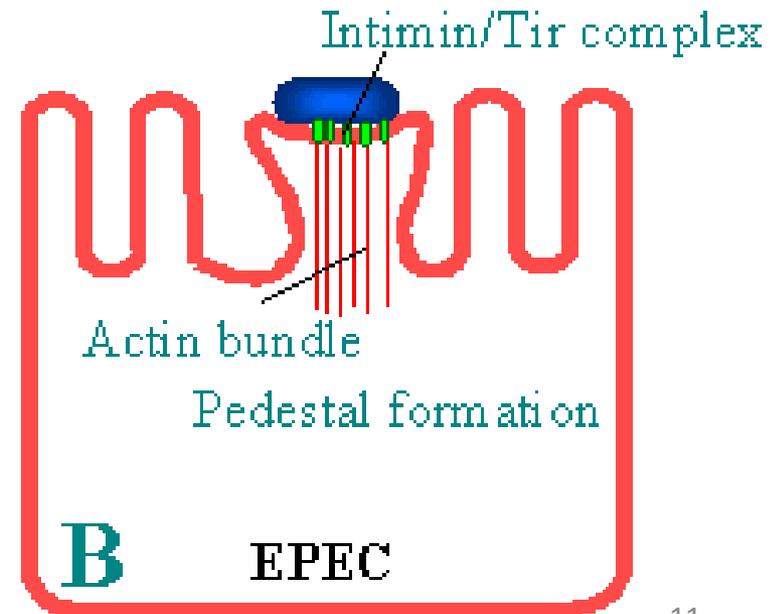
## Epidemiology

- Contaminated drinking water and sometimes meat products
- Contact with domestic animals
- EPEC infection typically occurs in neonates and children  $\leq 2$  years of age (mostly  $\leq 6$  months)
- Outbreaks Occurred in hospital nurseries, why?

During hospital outbreaks, EPEC is isolated from asymptomatic carriers including nursing and family members (1% -30%)

- 20% in bottle-fed infants
- Intimin and its translocated intimin receptor (Tir) are bacterial proteins that mediate adhesion between mammalian cells and attaching and effacing pathogens.

(**p**athogenic=**p**ediatrics)



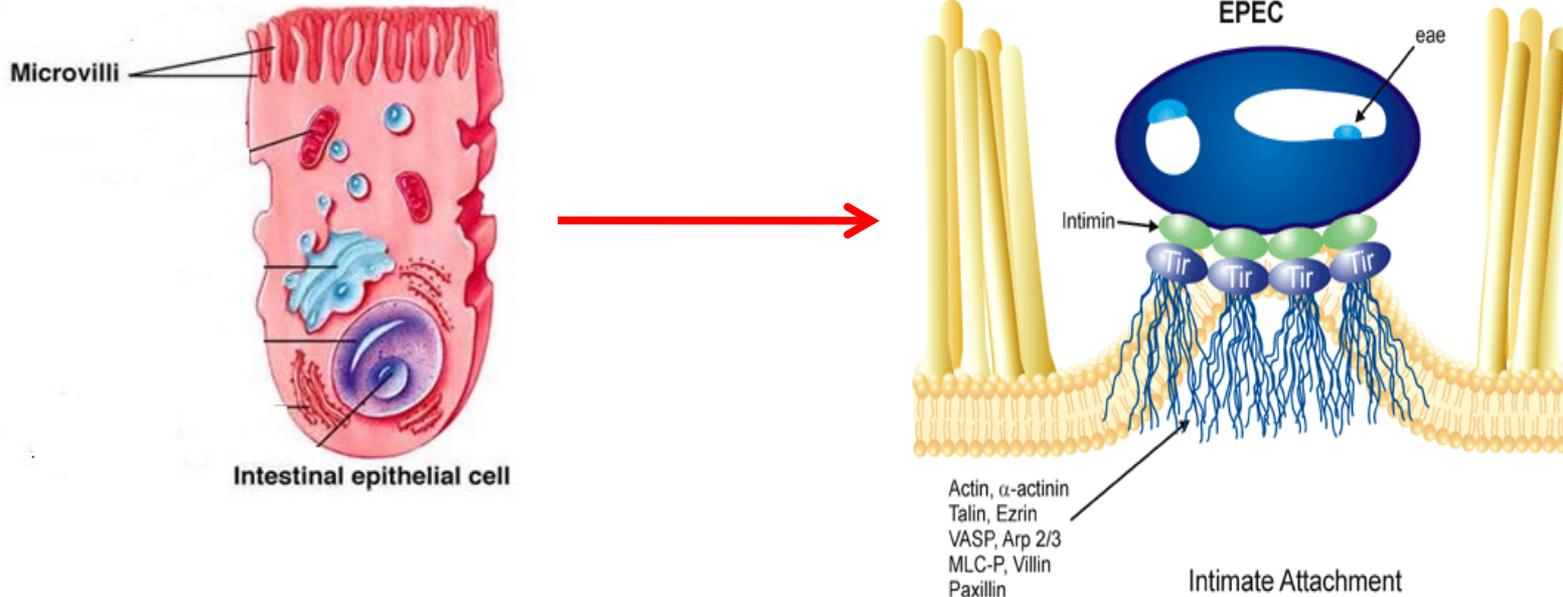
# Enteropathogenic E. coli (EPEC)

## Mechanism of diarrhea

### 1- Attachment and effacing

- Attachment to enterocytes
- Formation of microcolonies
- Rearrangement of enterocytes cytoskeleton
- The net result is the loss of microvilli (effacing)

### 2- Injection of protein (actin bundles) that mediate electrolyte imbalance



# Enteropathogenic E. coli (EPEC)

## Clinically

- Fever (60%)
- Watery diarrhea that is often severe and can result in dehydration (30%)
- Abdominal distension
- Symptoms usually last for one week

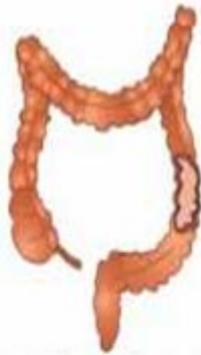
## Diagnosis

- Diarrhea, commonly lasting for **as long as two weeks**
- Detection of EPEC pili by specific antibodies or PCR amplification for pili encoded gene (not widely available)

**Antibiotic associated diarrhea**  
***C. Difficile***



# *Clostridium difficile*



The intestines have hundreds of bacteria, many of which have useful functions, such as helping to stimulate the immune system and produce vitamins. When *C. diff* spores exist in the colon, the other bacteria do not allow them to grow and thrive.

[www.patedu.com](http://www.patedu.com)

**+ Antibiotic treatment = Diarrhea**

**Because of *C. difficile* it becomes very difficile (difficult) to give a patient antibiotics**

# *Clostridium difficile*

## **Distribution**

- Spores are wide spread in environment
- Particular isolation from hospitals (the spores can be cultured from the floor, bedpan, and toilet rooms occupied by patients , hand and clothing of health care workers (therefore it is the major cause of diarrhea acquired in hospitals)

# *Clostridium difficile*

## Risk factors

### ➤ Antimicrobial exposure

- ✓ A remarkable feature of *C. difficile* diarrhea is its association with antimicrobial drugs
- ✓ The resistant spores to antibiotics start germination and toxin production at a certain time after antibiotic treatment

### ➤ Advanced age

### ➤ Immunosuppression

#### Frequently associated

Ampicillin  
Amoxicillin  
Cephalosporins  
Clindamycin

#### Occasionally associated

Penicillins other than ampicillin  
Sulfonamides  
Erythromycin  
Trimethoprim  
Quinolones

#### Rarely or never associated

Parenteral aminoglycoside  
Tetracyclines  
Chloramphenicol  
Metronidazole  
Vancomycin

# *Clostridium difficile*

## **Associated toxins**

Pathogenic strains produce two toxins:

- Toxin A is an enterotoxin that causes excessive fluid secretion, but also stimulates an inflammatory response
- Toxin B is a cytotoxin; in tissue culture, it disrupts protein synthesis and causes disorganization of the cytoskeleton

# *Clostridium difficile*

## **Diagnosis**

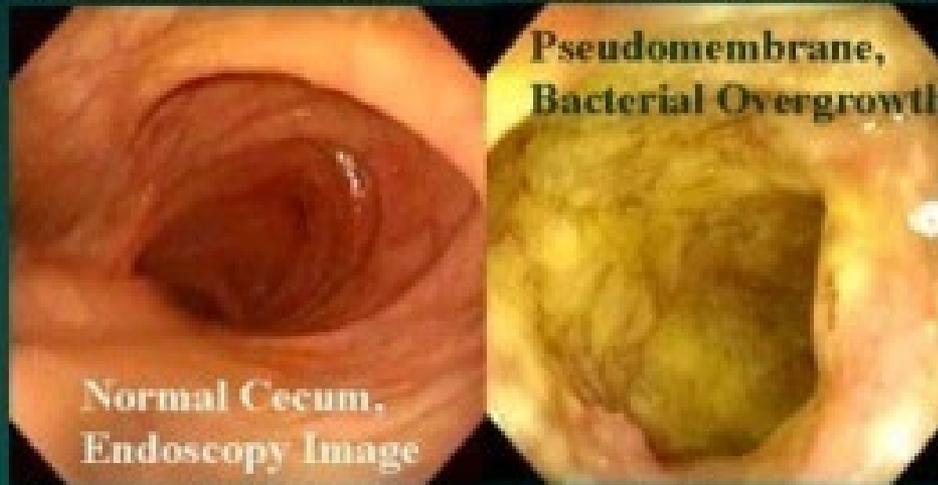
### **A. Clinical diagnosis**

- Diarrhea occurring  $\geq 3$  times a day for at least 2 days
- Abdominal cramping, fever, and dehydration
- Peripheral leukocytosis
- Pseudomembranes : The membrane composed of mucus, fibrin, inflammatory cells and cell debris overlying an ulcerated epithelium, is best demonstrated by lower GI endoscopy
- Toxic megacolon (Infrequently)
- Colonic perforation/peritonitis

### **B. Laboratory identification**

- *C. difficile* can be cultured from stools and identified by routine anaerobic procedures
- the more rapid and useful tests are directed at demonstrating toxin production in stool extracts by real-time PCR and ELISA
- Latex agglutination to detect **antigen** in stools

# Pseudomembranous Ulcerative Colitis



*C. difficile*  
overgrowth

# *Clostridium difficile*

## Treatment

- Stop all non-essential antimicrobial agents.
- Consider anti- *C. difficile* therapy as recommended
- Discontinue all antiperistaltic, stool softeners, laxative medications

## Infection Control

- Requires gowns and gloves for room entry before contact and hand washing with antiseptic soap after contact
- When *C. difficile* is suspected, the patient should be placed on presumptive Isolation immediately
- Presumptive isolation may be discontinued after patient is without symptoms for  $\geq 72$  hours or a negative PCR result

Cell invasion

*Shigella*

*Salmonella enteritidis*

EHEC

EIEC



# Shigella

## Characteristics

- Gram-negative bacteria
- facultative anaerobic bacteria
- fragile, easily killed by heat during cooking or processing.

## Sources of infection

- Fecally contaminated water
- Any food contaminated by a food handler with poor hygiene
- Raw vegetables

## Species

- *S. dysenteriae* (Group A, the most pathogenic)
- *S. flexneri* (Group B)
- *S. boydii* (Group C)
- *S. sonnei* (Group D)

# pathogenesis

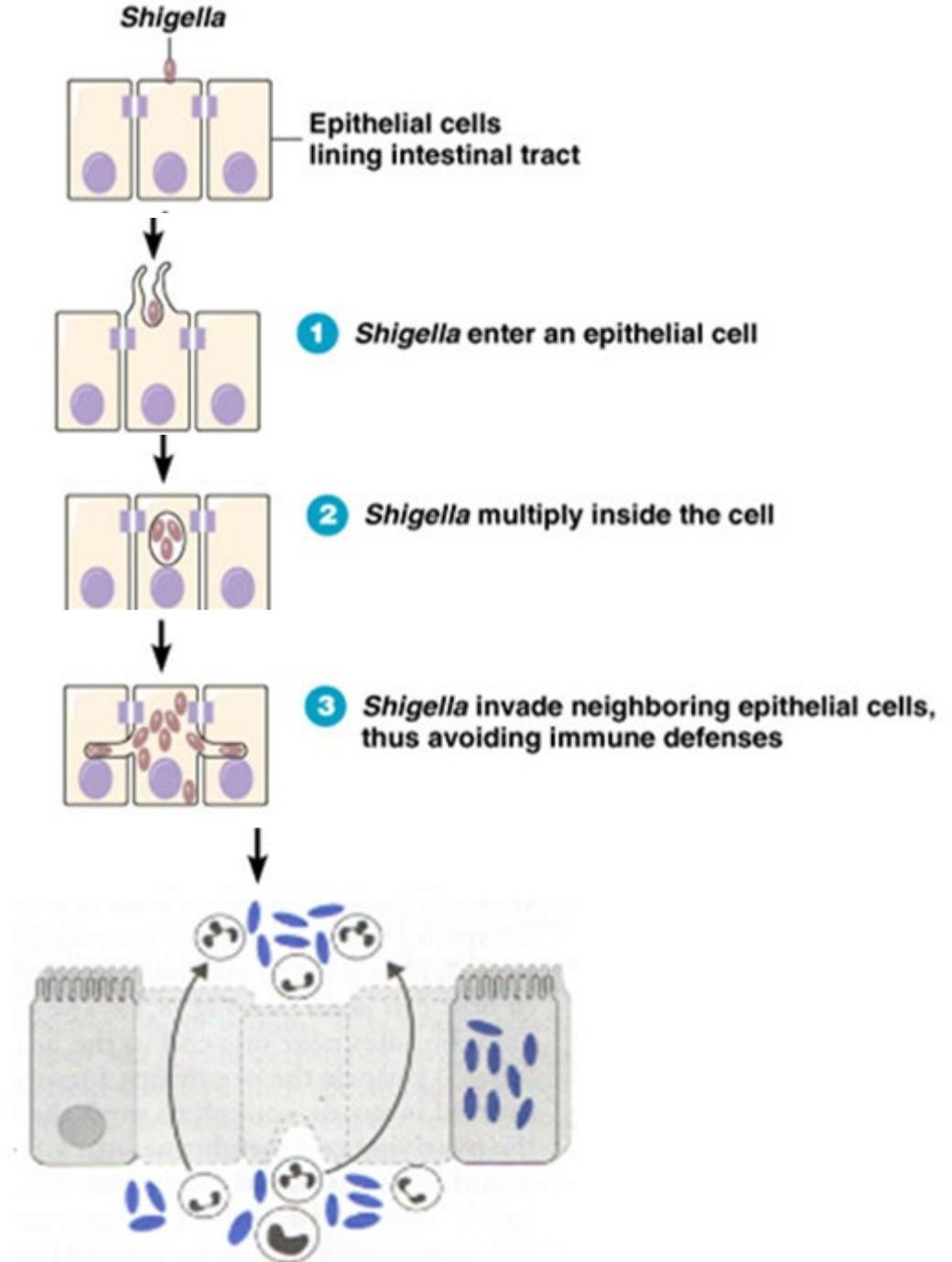
- Destruction of endothelial cells causing hemorrhage

- Bacteria enter blood

- entering the cell

destruction of vacuoles to escape into the cytoplasm

Spreading laterally to the neighboring enterocytes



# *Shigella*

## **Virulence factors:**

**Characters of Shiga toxin:** has three effects on the human body

- Neurotoxic effects: fever and abdominal pains.
- Enterotoxic effects blocking of absorption in the intestine by attaching itself to the receptors in the intestine
- Cytotoxic effects attacks the surface of enterocytes and blood vessels inside the GIT causing cell death and hemorrhage

# *Shigella*

## **Clinically**

- The infective dose is between 10-200 organisms
- Incubation of 1-7 days
- Followed by fever, cramping, abdominal pain, and watery diarrhea for 1-3 days (neurotoxic and enterotoxic)
- This may be followed by scant stools with blood, mucous, pus, and tenesmus (cytotoxic effect)

## **Diagnosis**

- Dehydration with fast heart rate and low blood pressure
- Abdominal tenderness
- Elevated white blood cell count
- Stool culture
- White and red blood cells in stool

# Shigella

## Treatment

- Self limiting
- Rehydration
- Antibiotics are usually avoided in mild cases
- Medical treatment should only be used in severe cases or for certain populations with mild symptoms (elderly, immunocompromised, food service industry workers, child care workers)

## Control

- Proper hand washing after using the bathroom.
- Use properly treated water.
- Cook foods to appropriate temperatures

# Enteroinvasive *E. coli* (EIEC)

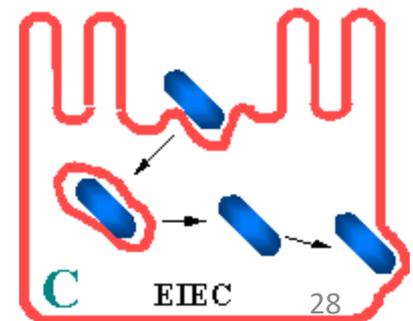
## Pathogenesis

Similar to *Shigella* (They produce no toxins, but severely damage the intestinal wall through mechanical cell destruction.) their ability to induce their entry into epithelial cells and disseminate from cell to cell

## Clinically

Dysentery, similar to that caused by *Shigella*, characterized by:

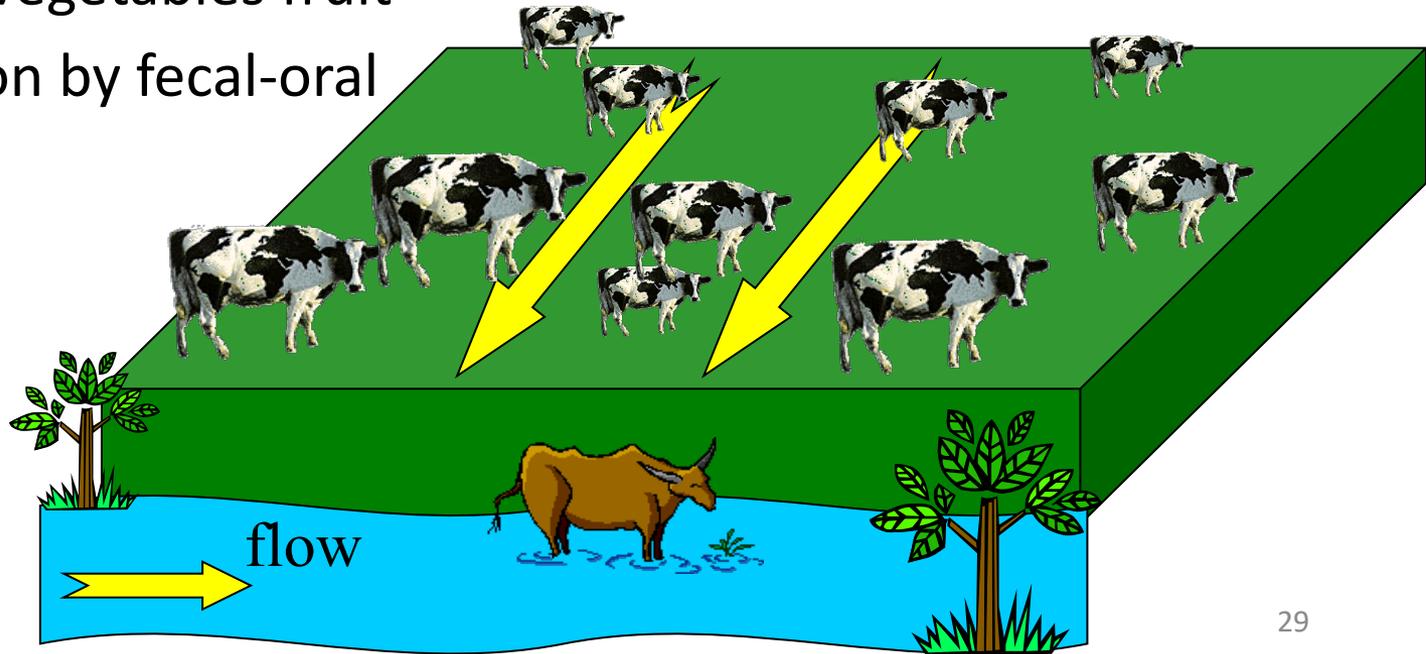
- Fever
- Diarrhea
- Vomiting, crampy abdominal pain and tenesmus
- Stools often contain blood and leukocytes.
- Occurred, usually secondary to ingestion of contaminated food



# Enterohemorrhagic *E. coli* (EHEC)

## Source of EHEC infection

- Consumption of contaminated food and water, or by contact with animals, feces and contaminated soil
- Infected hamburger, salami, and sausages served at fast food chains
- Unpasteurized milk
- Contaminated vegetables fruit
- Person to person by fecal-oral



# Enterohemorrhagic *E. coli* (EHEC)

## Characteristics

- Similar to EPEC (characterised by the production of an outer membrane protein called intimin) but in addition it secretes the powerful **Shiga-like toxin (also called verotoxin) potent cytotoxins that inhibit host cell protein synthesis.**
- Infective dose (50 bacteria per gram hamburger)
- Attachment via pili to the intestinal mucosa and liberates the **shiga-like toxin**
- 3-4 days Incubation period is but can be as long as 8 days

## Symptoms

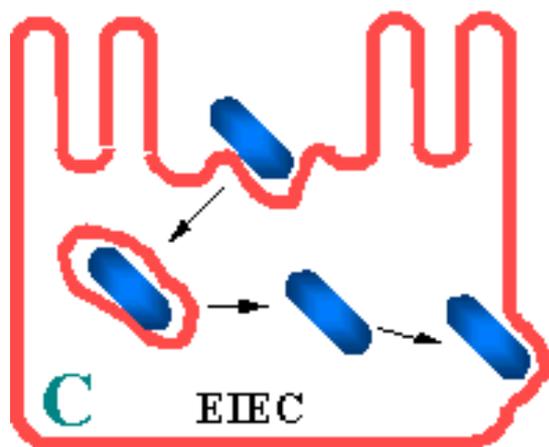
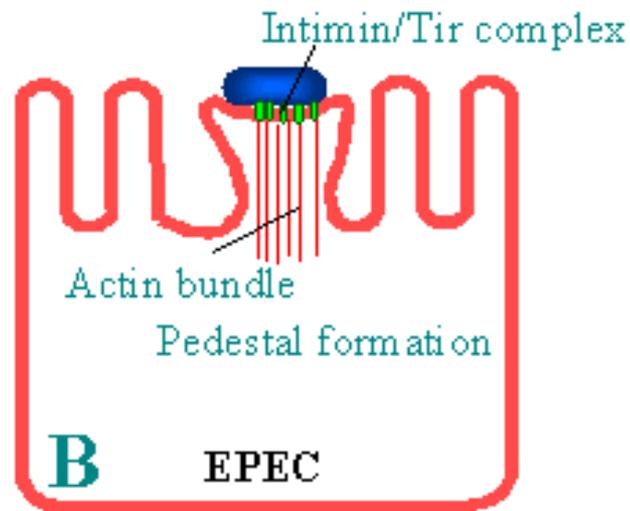
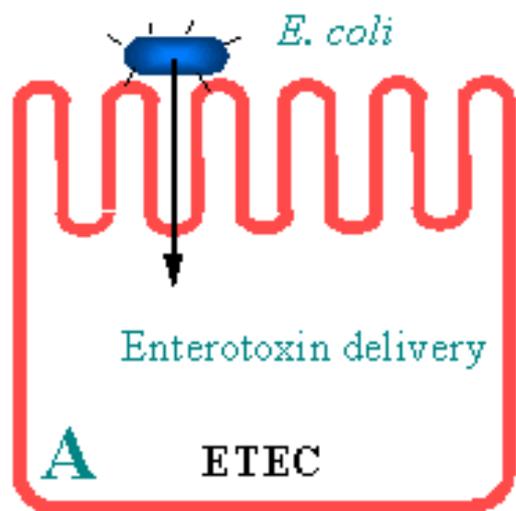
- Start with a watery diarrhea that progresses to bloody diarrhea and the hemolytic uremic syndrome (HUS) (a complication of shiga toxin)
- **No or mild fever**



## Diagnosis

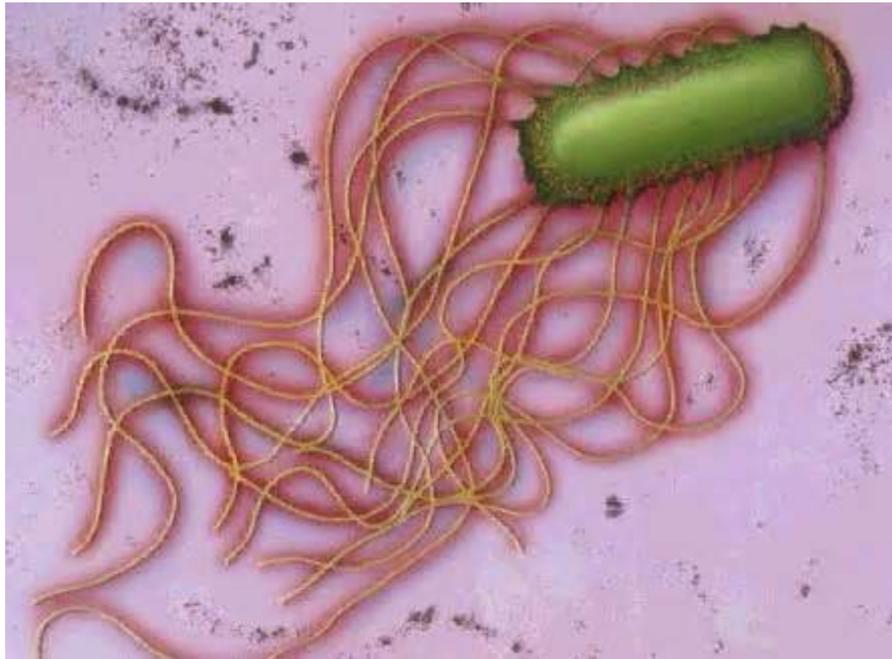
This is most often caused by serotypes O157:H7.

1. This strain of *E. coli* can be differentiated from other strains of *E. coli* by the fact that it does not ferment sorbitol in 48 hours (other strains do)
2. One must confirm that the isolate is *E. coli* O1547:H7 using serological testing
3. Confirm production of the shiga-like toxin by either ELISAs, agglutination, or immunoblotting before reporting out result.
4. Genotyping for shiga toxin gene



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# *Salmonella*



# *Salmonella*

## General characteristics

- Gram negative motile rods
- Facultative anaerobe
- Some serovars are pathogenic
- *Salmonella* (like *Shigella*) is never a part of the intestinal flora ( always pathogenic)
- Different types of the *Salmonella* bacteria can cause the illness. The two most common types are *S. typhimurium* and *S. enteritidis*.

# Salmonella

## **Salmonella associated diseases**

### **Gastroenteritis or salmonellosis (diarrhea)**

- **Reservoir:**
  - Normal flora of domestic animals, especially cattle, chickens, and exotic pets such as turtles
  - Poultry, pork, beef and fish (seafood): if the meat is prepared incorrectly or is infected with the bacteria after preparation
  - Infected eggs, egg products, and milk when not prepared, handled, or refrigerated properly
  - Contaminated fruits and vegetables
- Humans are **infected** when there is contamination of food or water with **animal feces**

# Salmonella

## Pathogenesis

- The bacteria remains restricted to the intestine: The inflammatory response prevents the spread beyond the GI tract and eventually kills the bacteria.

## Manifestations (Gastroenteritis)

- Typically, the episode begins 24 to 48 hours after ingestion
- abdominal cramps and diarrhea
- Diarrhea persists as the predominant symptom for 3 to 4 days and usually resolves spontaneously within 7 days.
- Fever (39°C) is present in about 50% of the patients.
- The spectrum of disease ranges from a few loose stools to a severe dysentery-like syndrome
- Occasionally patients may require hospitalization due to severe dehydration ( IV fluids and fever reduction), which is more common among infants and the elderly

# Salmonella

## Prevention of salmonellosis

To help protect yourself and others from salmonellosis: Thoroughly cook food derived from animal products - especially poultry, pork, eggs and meat dishes.

- Don't use dirty or cracked eggs.
- Keep your kitchen clean. Raw foods can contaminate surfaces.
- Store raw and cooked foods `separately.
- Wash hands thoroughly with soap and hot running water for 20 seconds before handling food.
- Store high risk foods at or below 5°C or at or above 60°C to prevent growth of bacteria.
- Do not handle cooked foods with the same utensils used for raw foods, unless they have been thoroughly washed between use.
- To prevent the spread of infection: Keep children home from school, child care or kindergarten until symptoms have stopped.
- Food handlers, childcare workers and healthcare workers must not work until symptoms have stopped.
- Clean bathrooms and other surfaces regularly.

*Thank you*