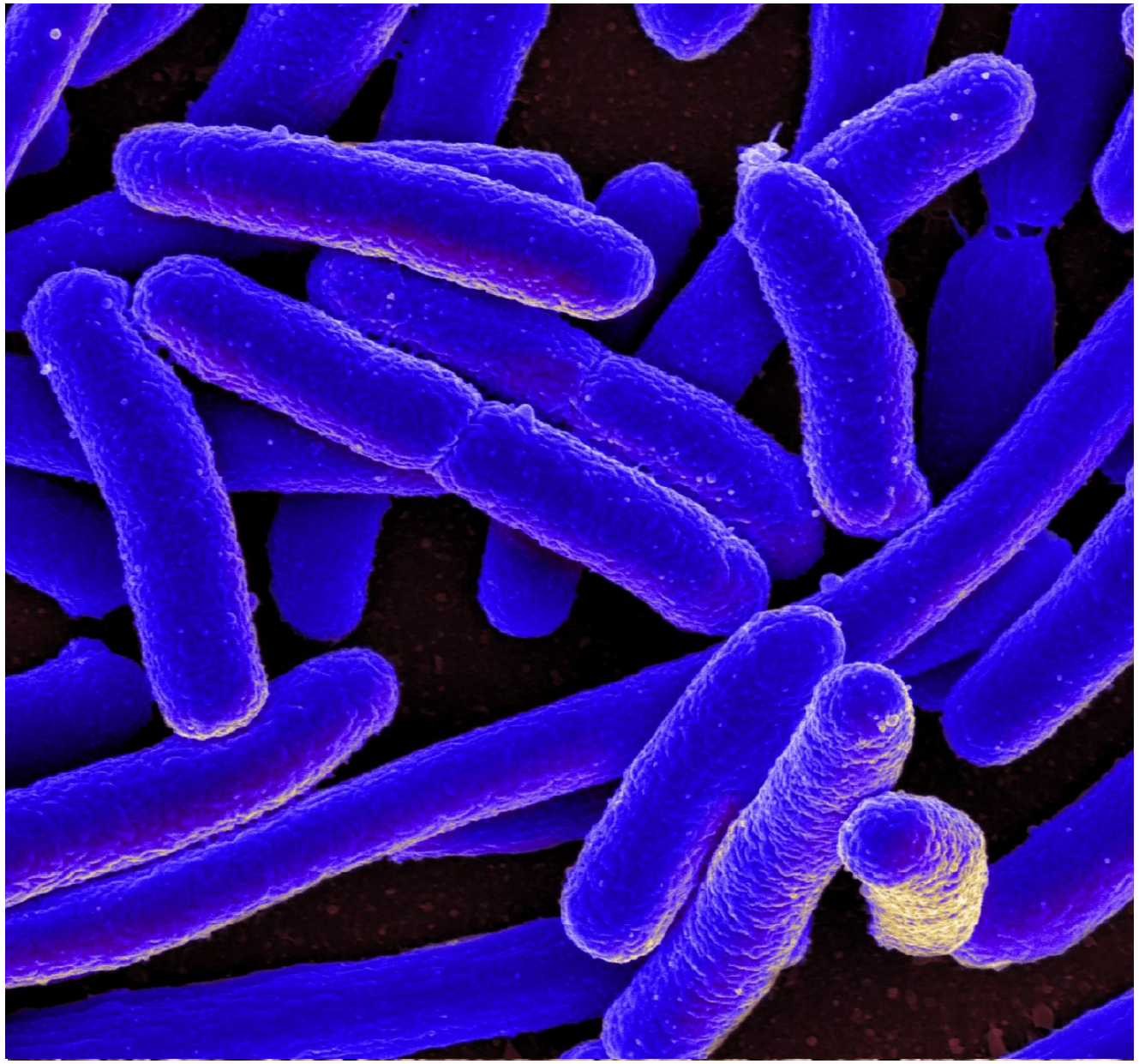


Escherichia coli

NM

05042021

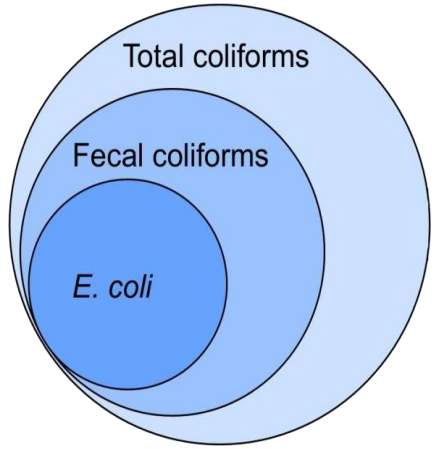
Revision (Lecture 1-2)

CONTENTS

- Characteristics
- Serotype
- Virotype
- Nomenclature
- *E. coli* (ETEC, EHEC, EPEC, EIEC, EAEC, DAEC)
- Pathogenesis
- Virulence factors
- *E. coli* outbreak
- Source of contamination
- Disease prevention

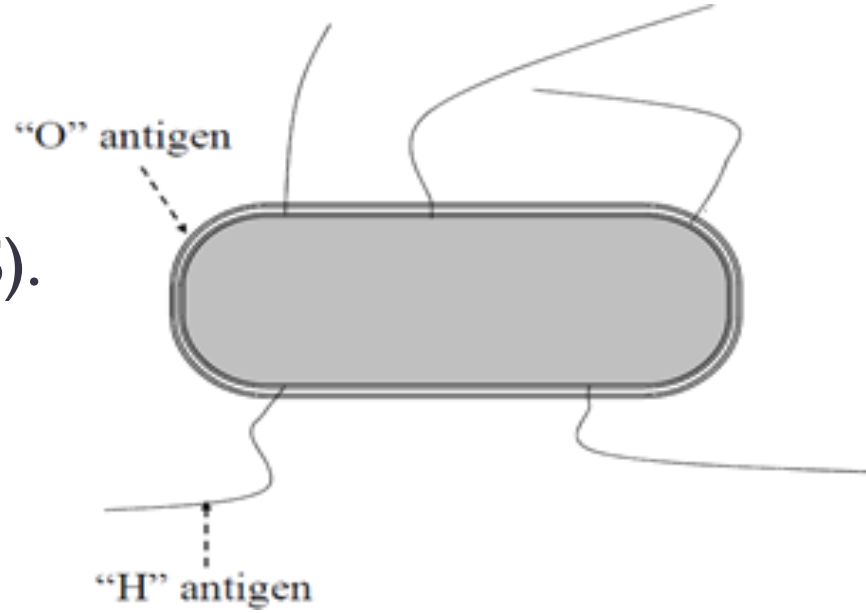
Escherichia coli

- *Enterobacteriaceae* family – large family of Gram negative bacteria, facultative anaerobic, non-spore forming rod, motile
- *Escherichia coli* is a symbiotic gut microbiota - 'coliform' in warm-blooded animal.
- Some *E. coli* provide many health benefits to the host: prevent colonization of the gut by harmful pathogens.
- The spread of coliforms (*E. coli*) from the gut is via faecal contamination.
- Only **some serotypes** of *E. coli* are **enterovirulent** / cause severe diarrheal diseases in humans.



SEROTYPE

- Based on the bacterial surface antigen
  - "O" ANTIGENT: heat stable lipopolysaccharide (LPS).
    - 170 known. Defines **serogroups**
  - "H" ANTIGENT:flagella
    - More than 50 known. Defines **serotypes**
  - "K" ANTIGENT:
    - More than 100 known. Defines **serotypes**



- Examples: *E. coli* O55:H6, *E. coli* O111:H8, *E. coli* O157:H7
- Serotyping – serological classification based on the reactivity of highly variable bacterial surface molecule (antibodies) with different antibodies

- **Serogroup 086** : human microbiota but rarely cause disease
- **Serogroup 055:** rarely found in human microbiota but always associated with diseases

- ***E. coli* 0157:H7** is associated with intestinal infection that can cause kidney failure in children (HUS)

VIROTYPE

- **Virotype** classification is based on the **presence** of certain **virulence factors** and their **interaction pattern** with the host cells such as **adhesion to/ invasion** of host cells and **toxin** production.
- The classification is more directly associated with the disease
- 6 groups of virulent *E. coli:*

I. **entero**t**oxigenic *E. coli* (ETEC)**

II. **entero**p**athogenic *E. coli* (EPEC)**

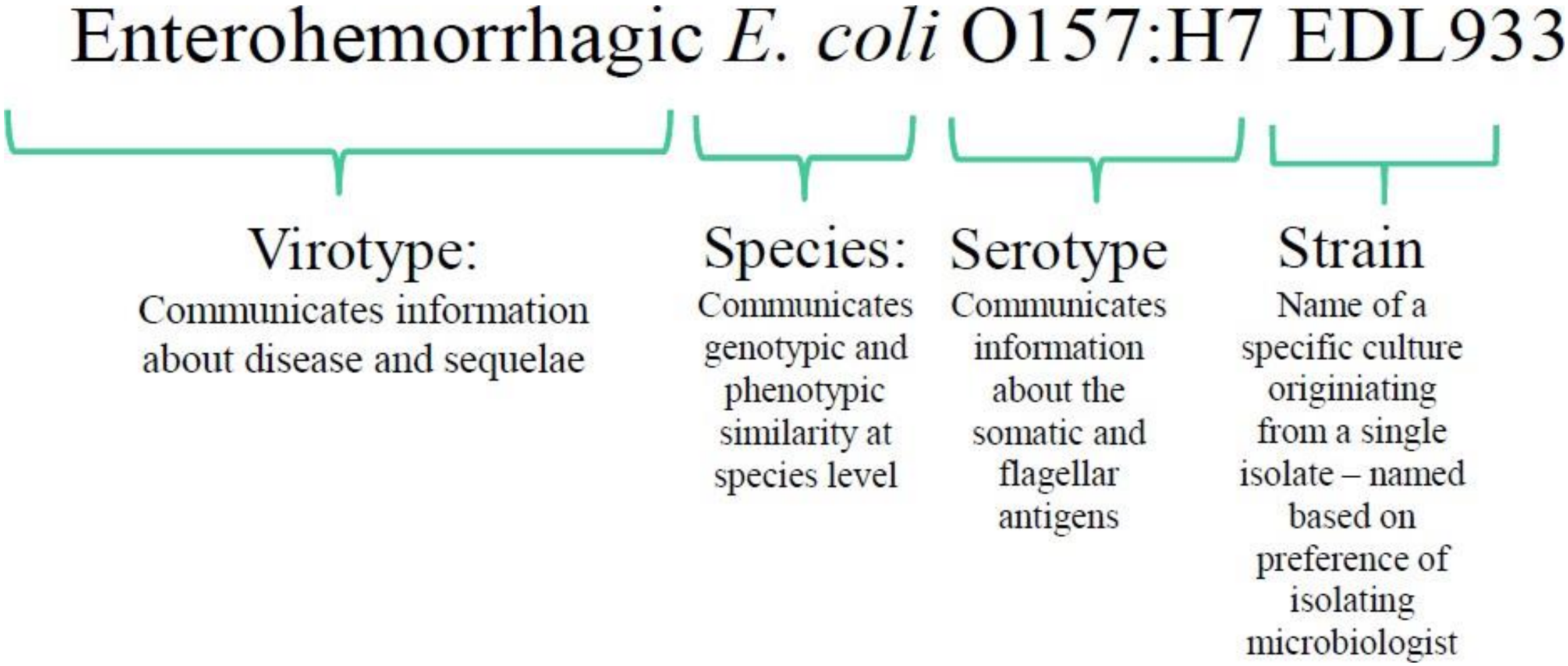
III. **entero**i**nvasive *E. coli* (EIEC)**

IV. **entero**h**emorrhagic *E. coli* (EHEC)**

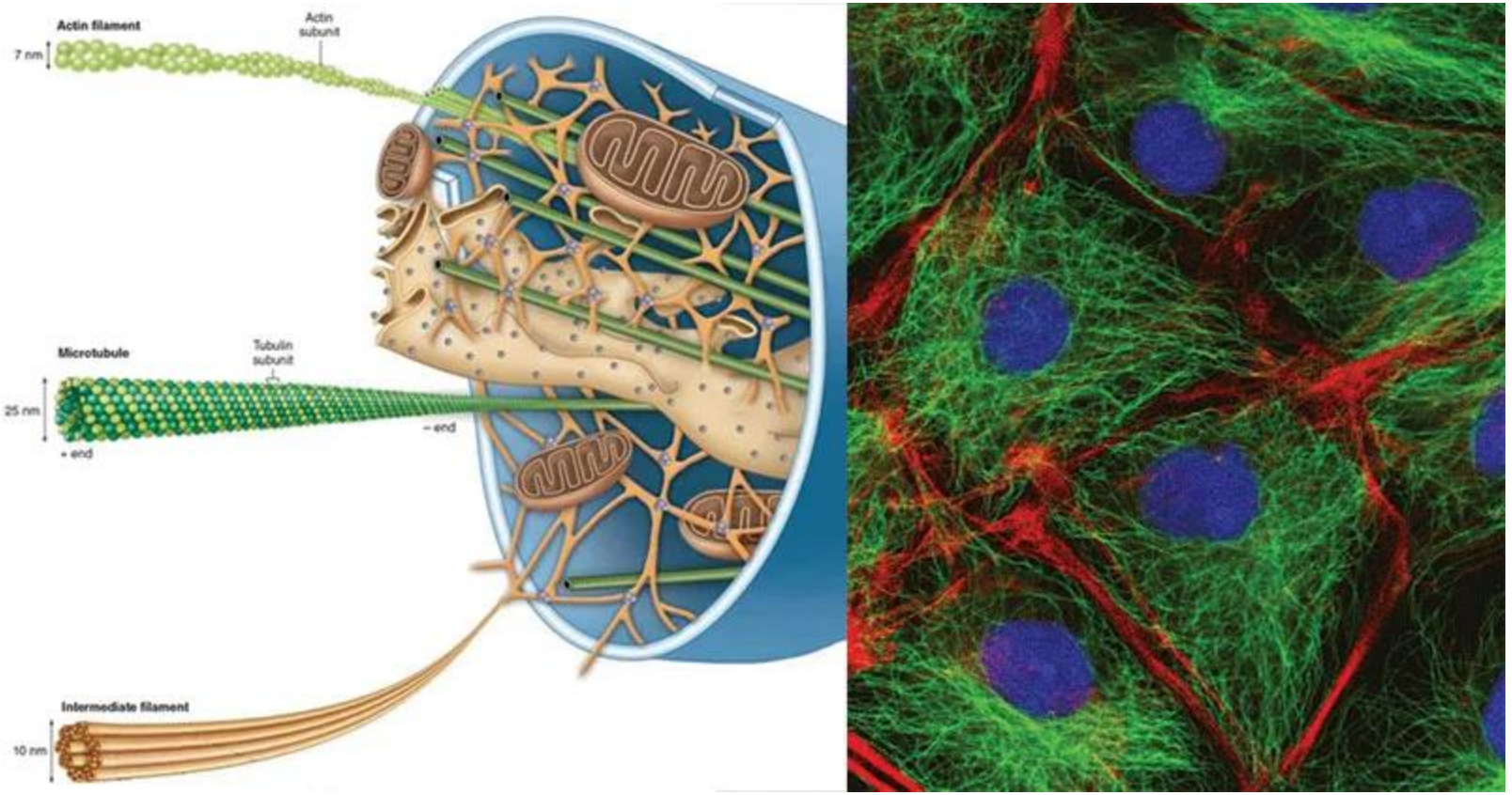
V. **entero**a**ggregative *E. coli*** (EAEC),

VI. **d**iffusely **a**dherent ***E. coli*** (DAEC).

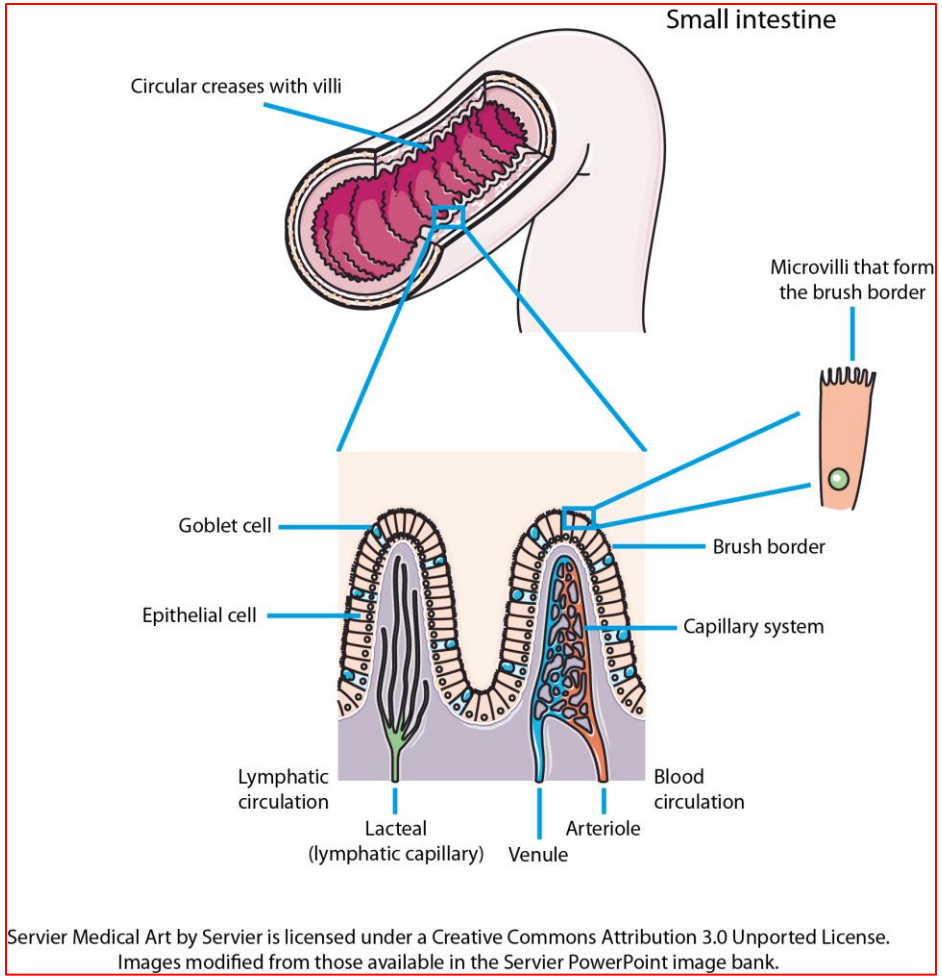
CLASSIFICATION AND NOMENCLATURE



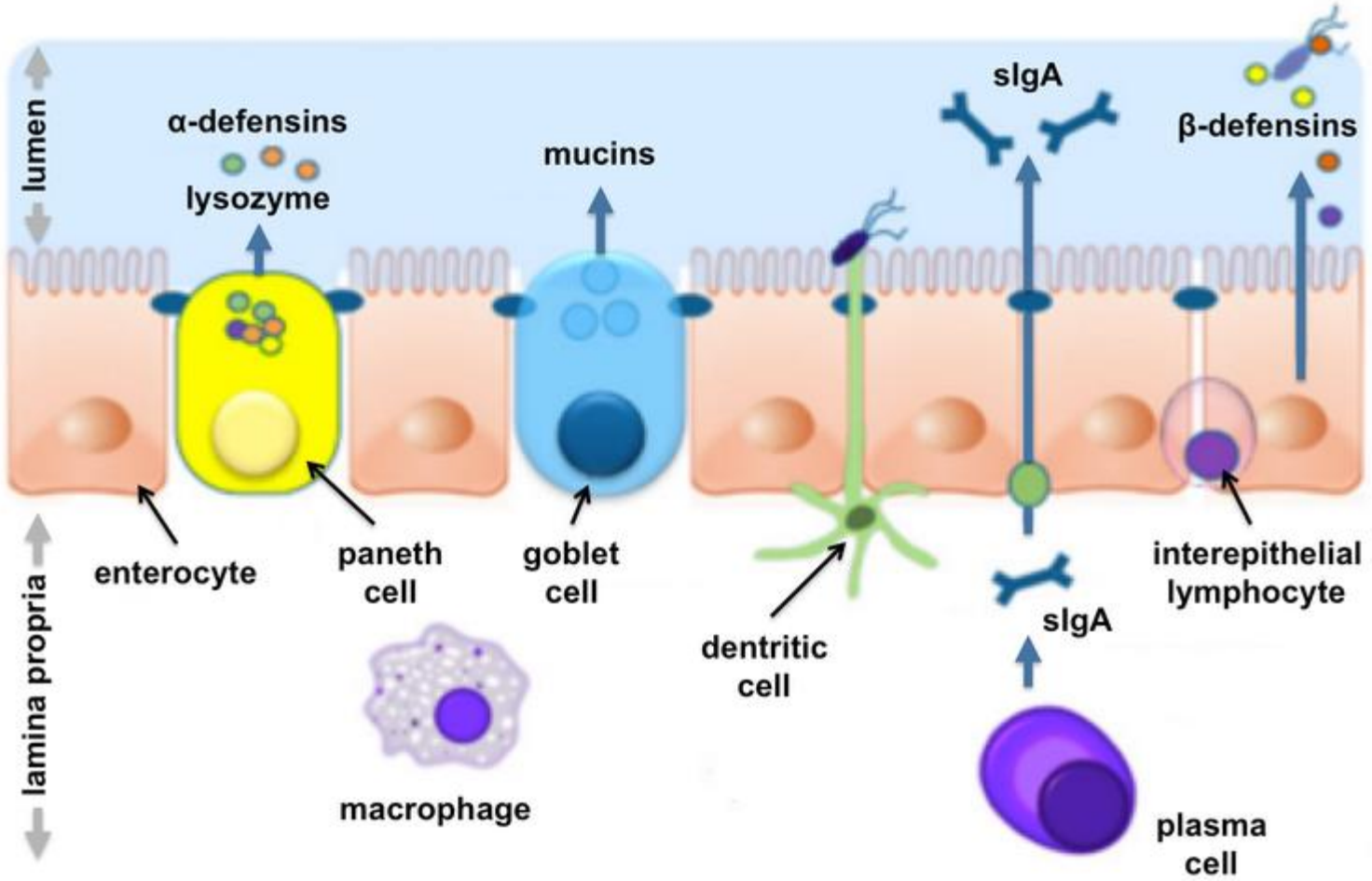
Cell structure : cytoskeleton



Small intestine



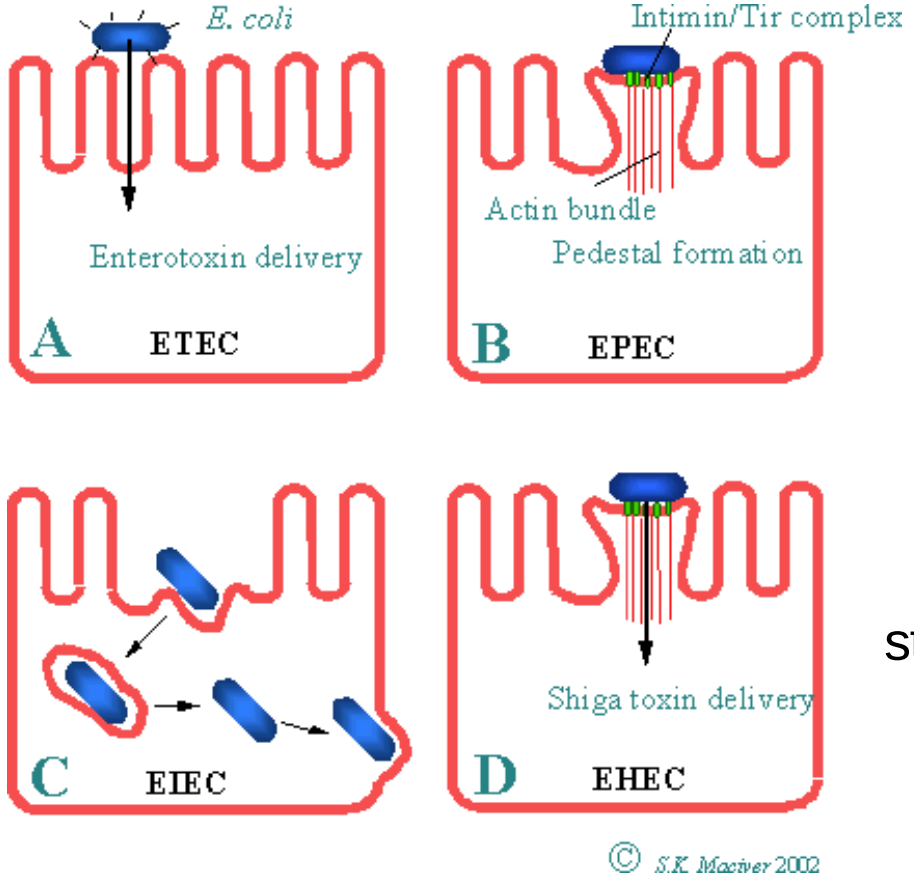
Intestinal mucosal barrier



http://bugs-in-your-guts.com/?p=91

ETEC adhere (bind loosely) to mucosal epithelial cells via fimbriae, secrete **toxins** into the gut and gain entry into the cell **without disruption of cytoskeleton**.

EIEC invade epithelial cells, escape from immune system by **digesting** the phagolyosome, can **grow** and divide in the cell cytoplasm & gain **entry** to neighboring cells by bursting through and digesting membranes.



EPEC adhere & bind strongly to mucosal epithelial cells and produce **attachment /effacement** lesion to **destroys** the brush border microvilli, and becomes firmly attached through the **actin pedestal** consisting of actin and actin binding proteins.

EHEC (STEC group), operates **like EPEC**, bind strongly to epithelial cells, produce **attachment/effacement** lesion and toxins (**Shiga toxins).** The toxins travel & destroy ribosomes & stop protein synthesis. This results in the death of the cell.

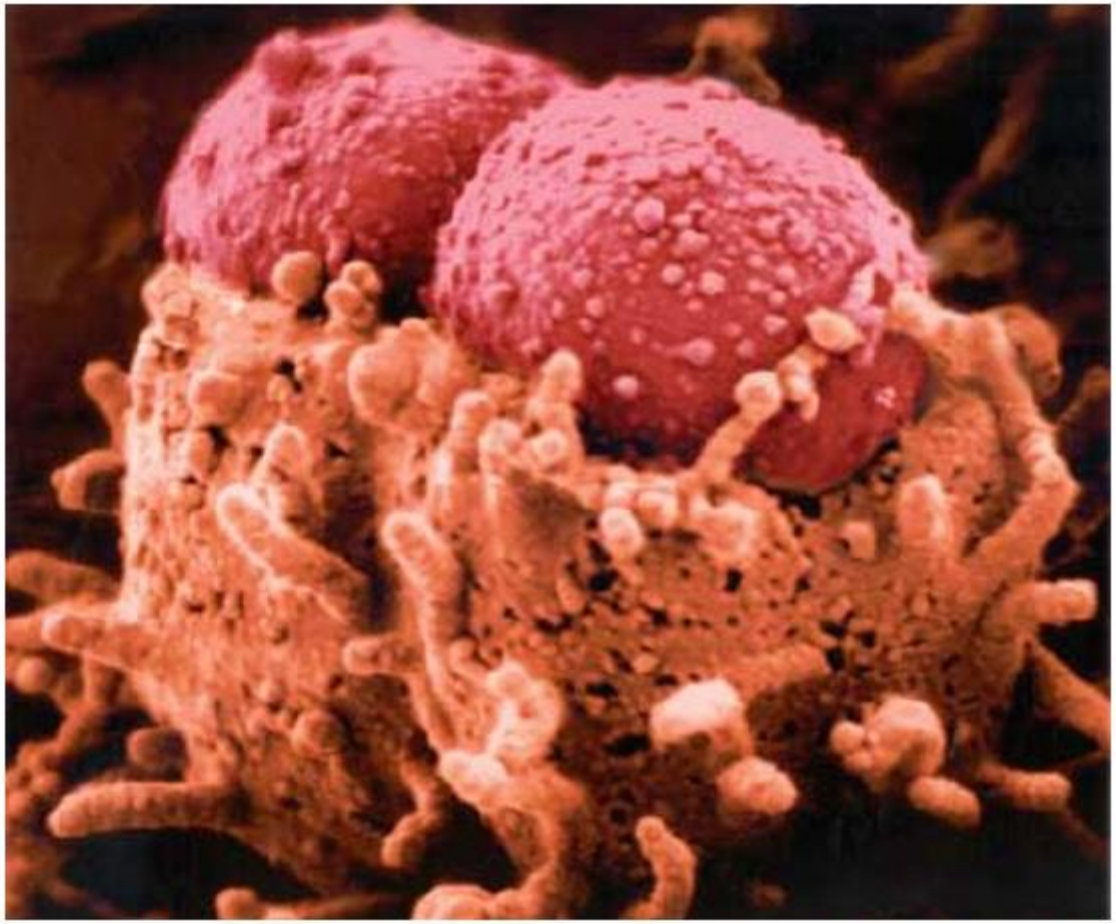


Figure 3 | **Attaching and effacing histopathology caused by EPEC and EHEC.** The attaching and effacing histopathology results in pedestal-like structures, which rise up from the epithelial cell on which the bacteria perch. Image courtesy of J. Girón.

ENTEROTOXIGENIC *E.coli* (ETEC)

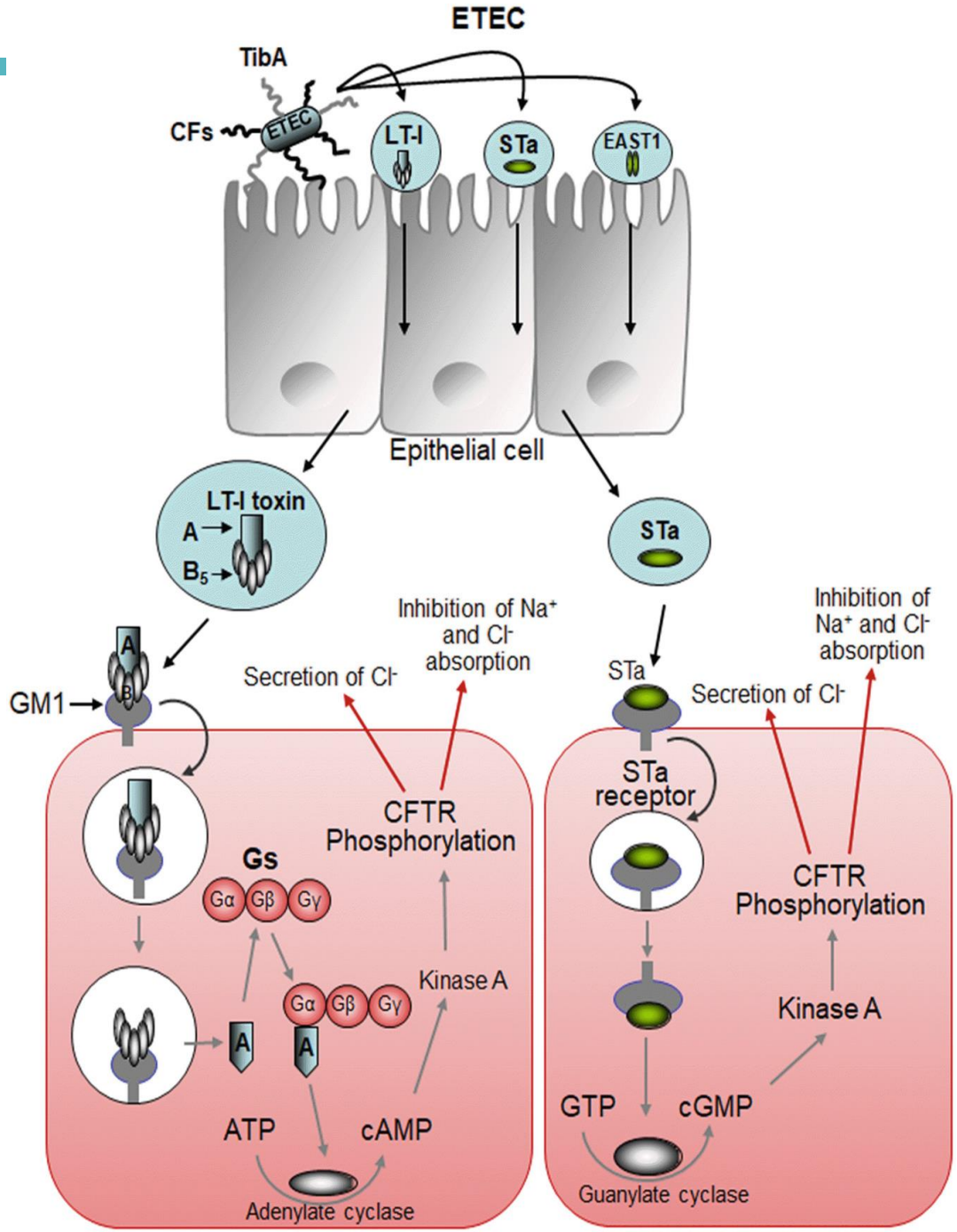
- First reported to cause cholera-like illness in adult and children in India.
- Cause **travelers' diarrhea**, diarrhea in infants, and in less-developed countries due to poor sanitary conditions.
- Native people may be resistant due to frequent exposure.
- Infection leads to watery diarrhea which may last up to a week.
- Symptoms include watery diarrhea, vomiting, massive dehydration, abdominal cramps, sometimes nausea and headache.
- Mortality: 380,000 deaths (worldwide)/year, mostly among children
- Infective dose: **10^6 – 10^9** ETEC cells (adult), less in children
- Onset: 8 – 44 h (Usually 26 h)
- Mortality rate < 1%

Virulence factors

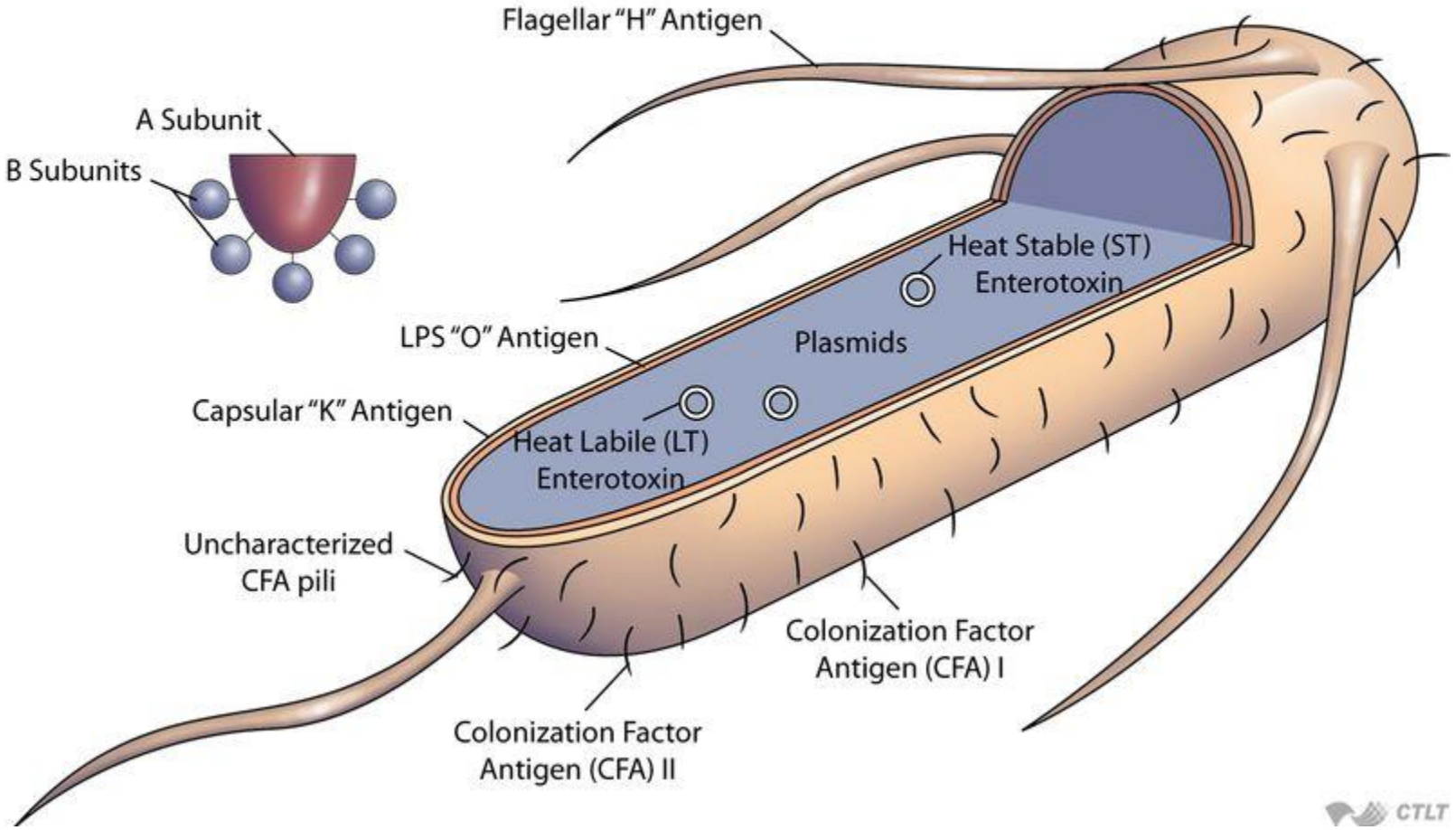
- **Adhesion factors**→ allow bacteria to attach to intestinal mucosa
  - Fimbrial colonization factors / colonization factor antigen (CFA)
  - TibA (afimbrial adhesion factor) – aid in bacterial aggregation on epithelial cells and promote biofilm formation
  - **Toxins**
    - Heat-stable (ST) toxins – stable after incubation at 100°C for 30 minutes.
    - Heat-labile (LT) toxin – toxin activity is lost in 30 min under these conditions .A-B type toxins which resembles cholera toxin & produce symptoms similar to *Vibrio cholerae*
- *E.coli* establishes itself by adhering to the epithelium of the small intestine via adhesion factor antigens followed by expression of ST or LT enterotoxins.

Pathogenesis of ETEC

- Heat-labile toxin (LT) consist of 2 subunit (A-B).
- B-subunit bind to host cell antigen (GM1)
- A-subunit is internalized & bind to Gs protein (protein that control cAMP (cyclic adenosine monophosphate: a messenger in biological process. E.g. regulation of ion channel)
- Gs is inactivated and cause increase in cAMP production
- Rise of cAMP con. And this will activate CFTR (chloride ion channel) – secretion of chloride ion is increased and uptake is inhibited
- The toxins increase secretion of chloride ions and water from intestinal cell
- The ion imbalance causes intestinal cells to loose the control of water flow resulting in diarrhea
- LT also stimulate production of cytokines and cause mild inflammation of mucosa cells



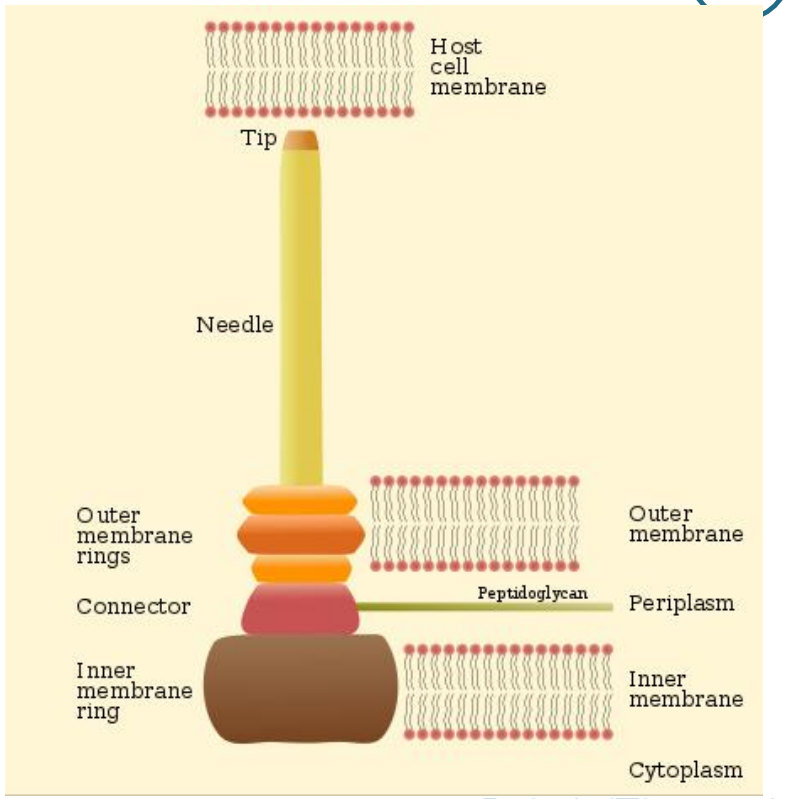
Virulence Factors of Enterotoxigenic *E. Coli*

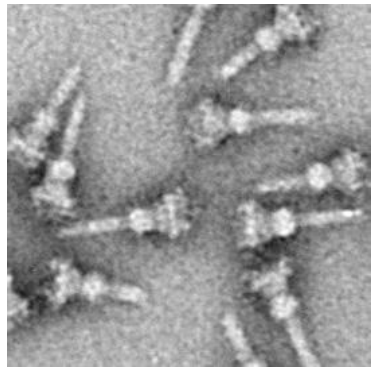


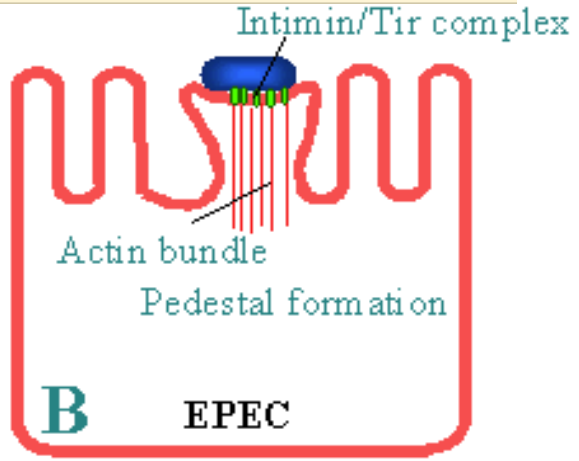
"Virulence factors of entertoxigenic E. coli" from Epidemiology of Infectious Diseases. Available at: http://ocw.jhsph.edu. Copyright © Johns Hopkins Bloomberg School of Public Health. Creative Commons BY-NC-SA.

ENTEROPATHOGENIC *E. coli* (EPEC)

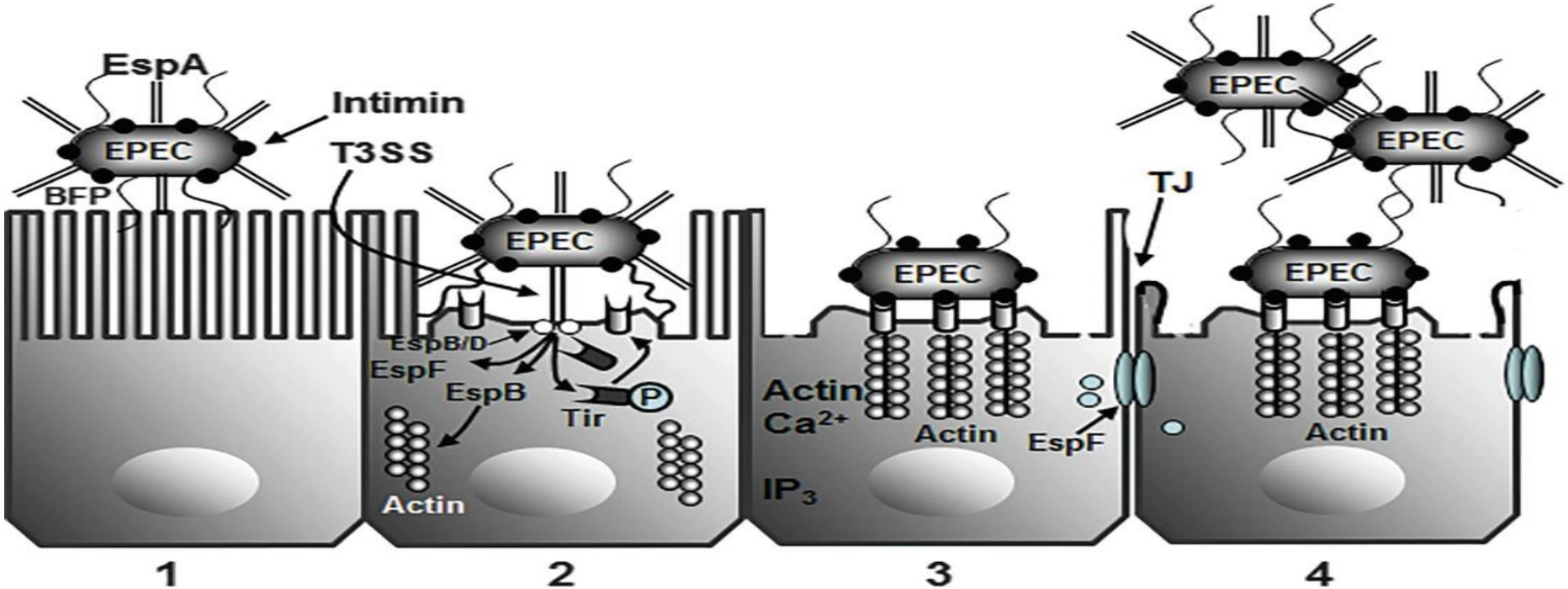
- **Highly invasive** and cause **inflammatory response** and potential **fatal diarrhea** in children – but **no toxin** production
- **Bloody diarrhea** is associated with attachment and an acute tissue- destructive process
- Pathogenesis & virulent factors
  - Expression of **adhesion factors** – adhesion fimbriae called Bundle Forming Pili (BFP), Intimin, EspA, Type III secretion system (T3SS)
  - **T3SS** injects the Translocated Intimin Receptor (**TIR**) and several **effector molecules** directly into the host cell
  - **TIR** facilitate binding with bacterial intimin
  - The **effector protein activate signalling pathway** allowing **actin polymerization** and **depolymerization** to **alter cytoskeletal structure**







- Cytoskeletal rearrangement and pedestal formation
  - cause a dramatic change in the ultra structure of epithelial cells
  - characterized by the formation of a ‘cup-like’ or ‘pedestal’ structures due to the cellular actin rearrangement.
  - Formation of ‘**attaching and effacing**’ (A/E) lesion due to extensive re-arrangement of actin
  - microvilli structures gradually disappear - **lesion**
  - A **pedestal structure** is formed due to the massive host cell cytoskeletal rearrangement



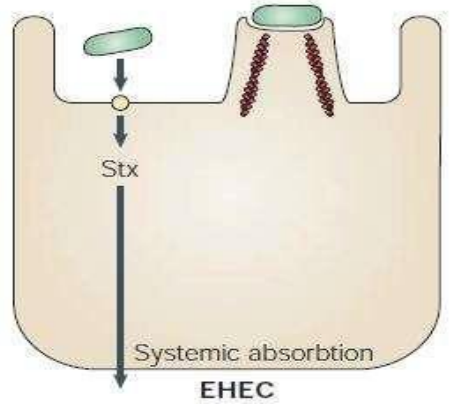
ENTEROHAEMORRHAGIC *E. coli* (EHEC)

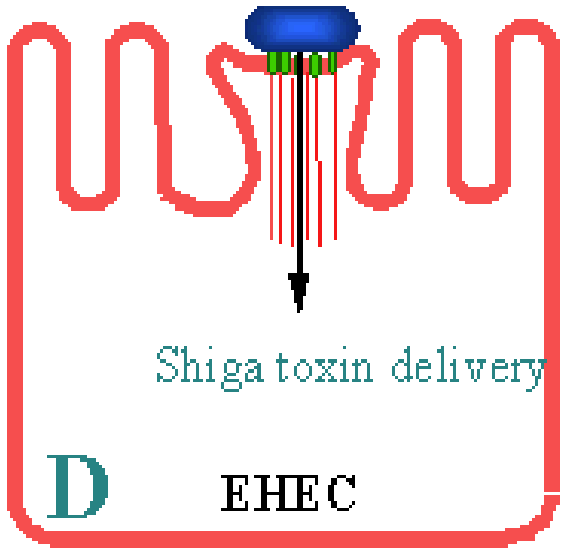
- E.g. *Escherichia coli* O157:H7. Similar to other *E. coli* but:
  - Does not ferment sorbitol in 48 hr at 35 to 37°C
  - Grow rapidly at 30 – 42°C, grow poorly at 44 – 45°C, does not grow < 10°C but can survive at -20°C
  - Some strains resistant to pH < 4.5 (survival in the intestine)
  - Destroyed by pasteurization (temp: 64.3°C time: 9.6s)
  - Produce Shiga-like toxins (Stx)→ EHEC is also refer to STEC (Shiga-toxin producing *E. coli*)
  - Receptor for Stx are found on kidney and intestinal cells.
- *E. coli* O157:H7 acquired its pathological character when a bacteriophage transmitted toxin genetic code from *Shigella* to a formerly benign species of *E. coli*.
- **Infectious dose** of *E. coli* O157's is incredibly low:just **10 to 10^2**

- Shiga-toxin form **attaching and effacing (A/E) lesions** on epithelial cells (causes inflammation of the intestinal wall).
- Pathogenesis & virulent factors

1. Attachment and effacement

- **Fimbriae** mediated the adhesion of bacteria to the microvilli
- Unlike EPEC, EHEC does not express bundle-forming pili (BFP)
- **Type III secretion system** (T3SS) injects translocated intimin receptor (**TIR)** and delivers virulence effector **proteins** directly to the host cell
- **Intimin** (a protein on bacterial surface) **bind to TIR** receptor leading to disruption of actin cytoskeleton, actin polymerization, cytoskeletal re-arrangement, and effacement of microvilli
- **Pedestal** is formed beneath the adherent bacteria
- A/E pathogenesis cause cell inflammation, and diarrhea.
- **Shiga toxin** is released and **bind to GB3/GB4 receptor** on host cells – **stop protein synthesis, enter blood circulation**





2. **Shiga-like toxins**

- 2 types
  - **Stx1** - The sequence is highly conserved and has high similarity to Stx produced by *Shigella dysenteriae* type 1.
  - **Stx2** –Les related to Stx1. **Highly toxic** (1000 x higher than Stx1) and has the greatest risk of developing **hemolytic uremic syndrome (HUS)**
- The Stx has been shown to posses:
  - Nephrotoxic – massive damage to kidney tubules, bloody urine, and HUS.
  - Neurotoxic – causing neurological disorder called thrombotic thrombocytopenic purpura (TTP) which is characterized by hemolysis, thrombocytopenia, renal failure, and fever.
  - Enterotoxic – causing fluid accumulation and diarrhea
  - Cytotoxic – inhibition of cellular protein synthesis and leads to cell death

Hemorrhagic colitis (bloody diarrhea)

- Estimates
  - 73,000 cases annually & 2,100 people are hospitalized
  - 61 people die as a direct result of *E. coli* infections and complications (mortality rate: ~ 3%).
  - Infection via fecal-oral route
- Develops in 3-4 days (Incubation period)
- Symptoms of **Hemorrhagic colitis**
  - Severe cramping
  - Diarrhea: range from mild (watery) to severe **bloody** diarrhea
  - Vomiting, occasionally
  - Fever: rare
  - In most cases, symptoms last ~ a week and disease subsides
  - Antibiotics do not improve the illness; may increase risk of complications (HUS)

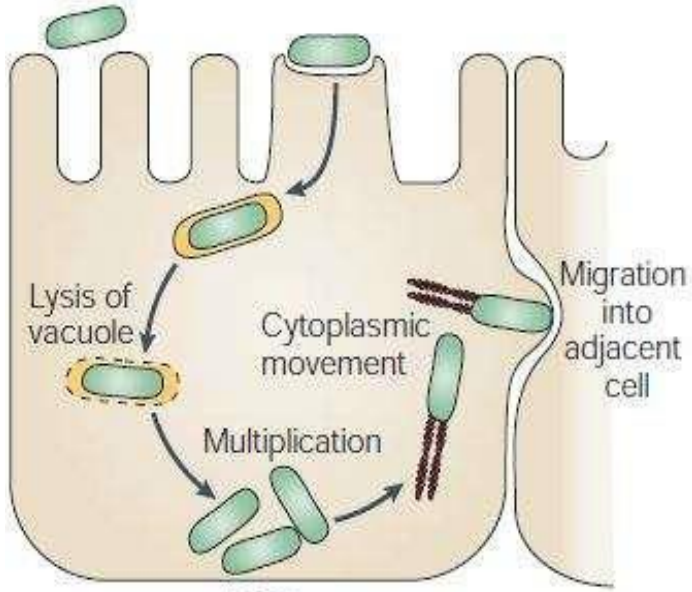
Hemolytic Uremic Syndrome (HUS)

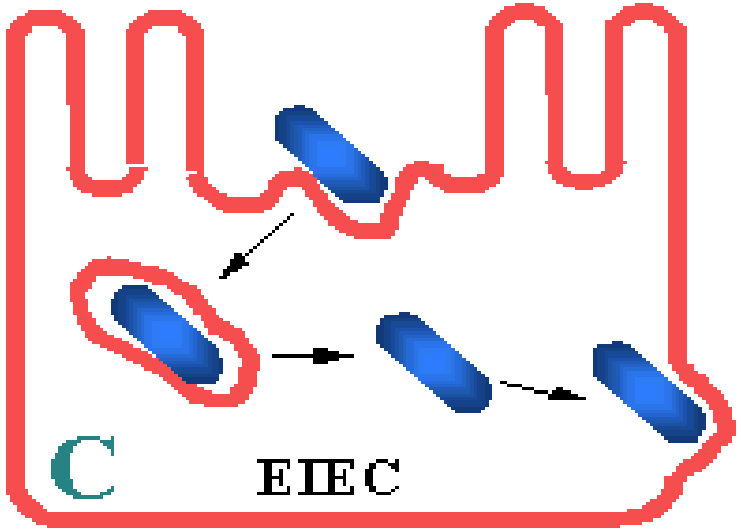
- Although most people recover from an *E. coli* O157:H7 infection,about 5-10% of infected individuals develop HUS, a fatal disease.
- HUS develops when the toxin (Stx2) enters the circulation by binding to special receptors (**Gb3/Gb4**).
- These receptors, appear to concentrate in kidneys,especially in children, but also other organs (e.g., pancreas,and brain).
- As the inflammatory reaction process accelerates, red blood cells are destroyed and cellular debris aggregates. The result is formation of microthrombi within particularly susceptible organs such as the kidneys and brain.

https://youtu.be/w-zbjM8wruk

ENTEROINVASIVE *E. coli* (EIEC)

- Transmitted through faecal-oral route and actively invade colonic cells – MID 10^6
- Illness is characterized by presence of **blood and mucus in stools** of infected individuals.
- Pathogenesis & virulence factors:
  - Following ingestion, organisms invade epithelial cells of the intestine resulting in a mild form of dysentery (a type of gastroenteritis that results in diarrhea with blood)
  - Has the ability to induce entry into epithelial cells by **digesting the phagolyosome.**
  - Can grow and divide in the cell cytoplasm & gain entry to neighboring cells by bursting through and digesting membranes.



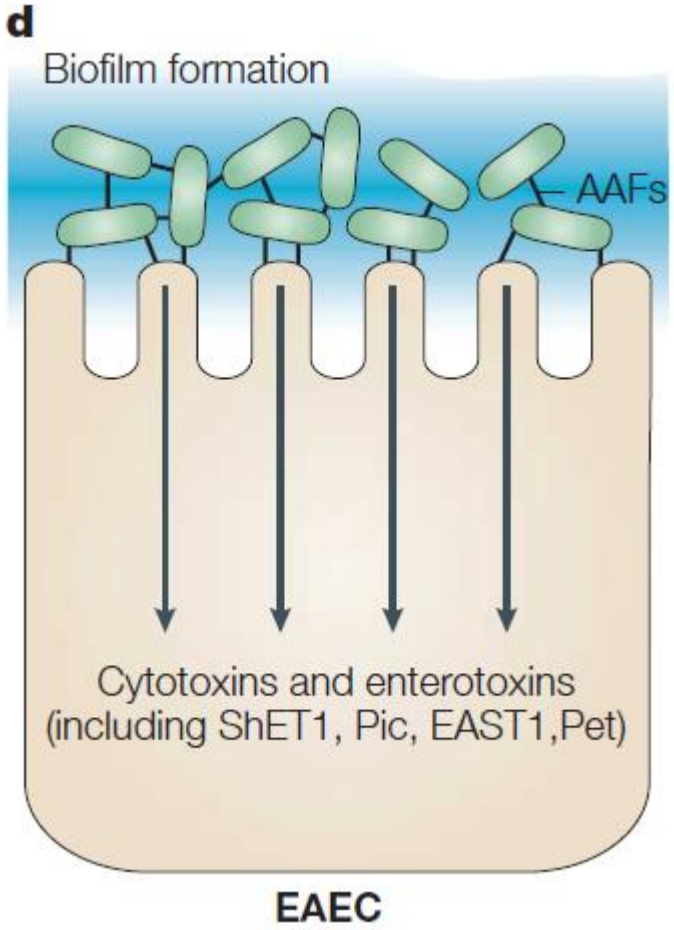


Pathogenicity and characteristics of foodborne illness caused by pathogenic *E. coli*

E. coli group	E. coli/host interaction	Time to onset of illness	Duration of illness	Symptoms
ETEC enterotoxigenic	ETEC adhere to small intestinal mucosa and produce toxins that act on the mucosal cells	8 – 44 h Average 26 h	6 hrs – 3 days Average 24 h	**Watery diarrhea**, low-grade fever, abdominal cramp, abdominal cramp, nausea. Extreme diarrhea with rice-water like stool when severe – leading to dehydration.
EPEC enteropathogenic	EPEC attach to/invade the intestinal mucosal cells causing cell structure alterations	17 – 72 h Average 36 h	6 hrs – 3 days Average 24 h	- Infant: Severe diarrhea (>14 days), fever, vomiting, abdominal pain, - Adult: **Watery diarrhea** with prominent amount of **mucus** (without blood), nausea, vomiting, abdominal cramp, headache, fever
EIEC enteroinvasive	EIEC invade cells in the **colon** and spread laterally cell to cell	8 – 24 h Average 11 h	Days to weeks	blood and mucus in stool, diarrhea, fever, headache, abdominal cramp
EHEC enterohaemorrhagic	EHEC attach to and efface mucosal cells and produce toxin	3 – 9 days Average 4 weeks	2 – 9 days, Average 4 days	- **Haemorrhagic colitis:** sudden onset of severe crampy abdominal pain, grossly **bloody diarrhea**, vomiting, no fever - **Haemolytic uraemic syndrome (HUS)**: **bloody diarrhea,** acute **renal failure** in children, acute nephropathy, **seizures, coma, death**

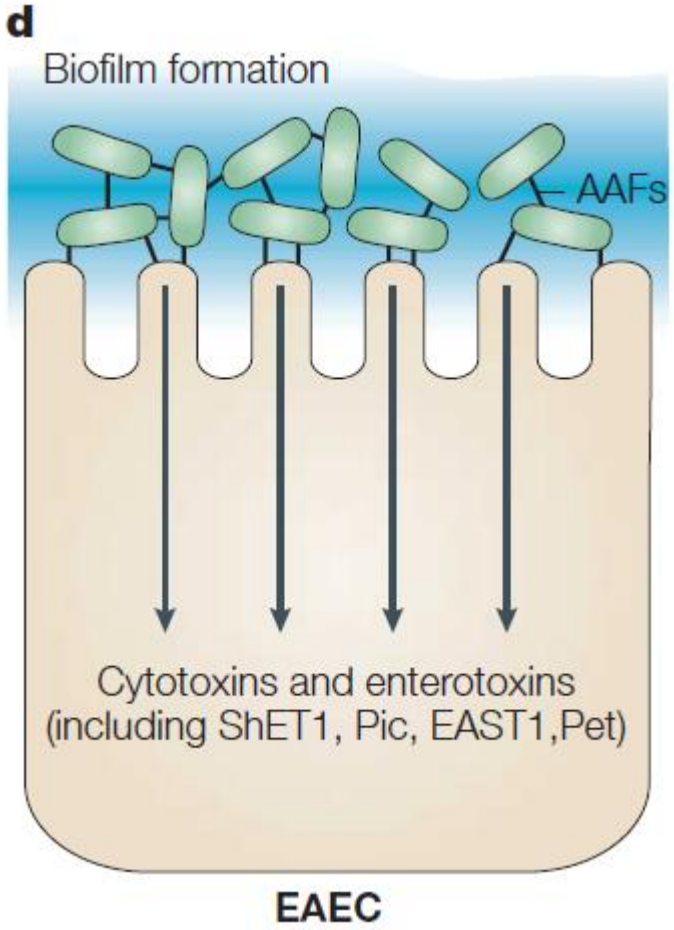
ENTEROAGGREGATIVE *E. coli* (EAEC)

- EAEC causes persistent diarrhea, lasting for more tha 14 days
- Diarrhea in children is similar to ETEC but cause mucosal damage
- Virulence factors
  - Adhesion factors – aggregative adherence fimbriae (AAF) on the outer membrane
    - Responsible for 'clumping' of cells, or adherence to each other
  - Toxins
    - enterotoxins
    - cytotoxins



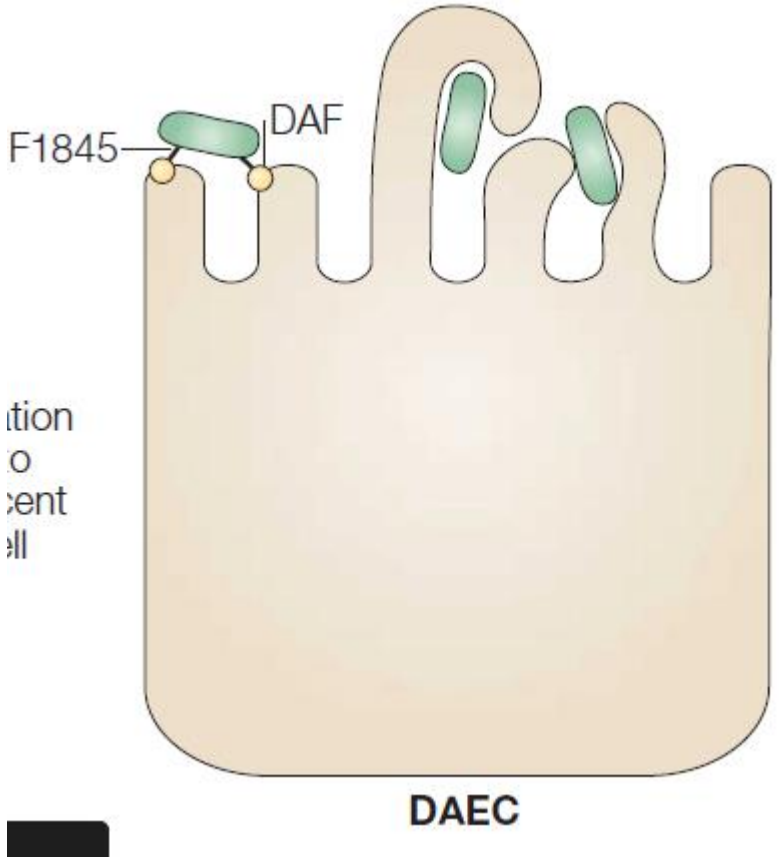
Pathogenesis

- EAEC adhere to the intestinal cell, forming aggregates – “stach-brick’ adherence
- Enhance mucus secretion from the goblet cells and trap themselves in mucus forming biofilms
- It does not invade epithelial cells, but produce cytotoxins that responsible for histopathological effect
  - Shirtening of vili
  - Inflammation
- Infection results in mucoid stool and persistent diarrhea



DIFFUSELY ADHERING *E. coli* (DAEC)

- Cause watery diarrhea in children without blood
- Characterized by the growth of finger-like cellular projection, which wrap around bacteria



CASES OF *E. coli*

Mother files complaint against McDonald's after daughter diagnosed with 'hamburger disease' in South Korea

PHOTO: McDonald's

by **JO HE-RIM**
THE KOREA HERALD/ASIA NEWS NETWORK
| Jul 06, 2017

A mother on Wednesday filed a complaint against McDonalds Korea, claiming her daughter was diagnosed with the "hamburger disease" after eating a burger with an undercooked patty in one of its outlets.

Discarded cucumbers piled up near Bucharest, Germany as Europe searched for a *E. coli* Outbreak.

June 2011

https://www.nytimes.com/2011/06/07/science/earth/07ecoli.html

what is bacteriophage - Google S | Reports of Selected E. coli Outbre | Close

cdc.gov/ecoli/outbreaks.html

Apps | ScienceDirect | Remote UI: Portal:... | Sci-Hub: removing... | New Tab | InCites jcr | USM Campusonline... | OER@USM | Physic... | Campylobacter jeju...

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

A-Z Index

Search

E. coli (Escherichia coli)

CDC > E.coli Homepage

- *E.coli* Homepage
- Questions & Answers
- Symptoms
- Prevention
- Outbreaks
  - Timeline for Reporting Cases of *E. coli* O157 Infection

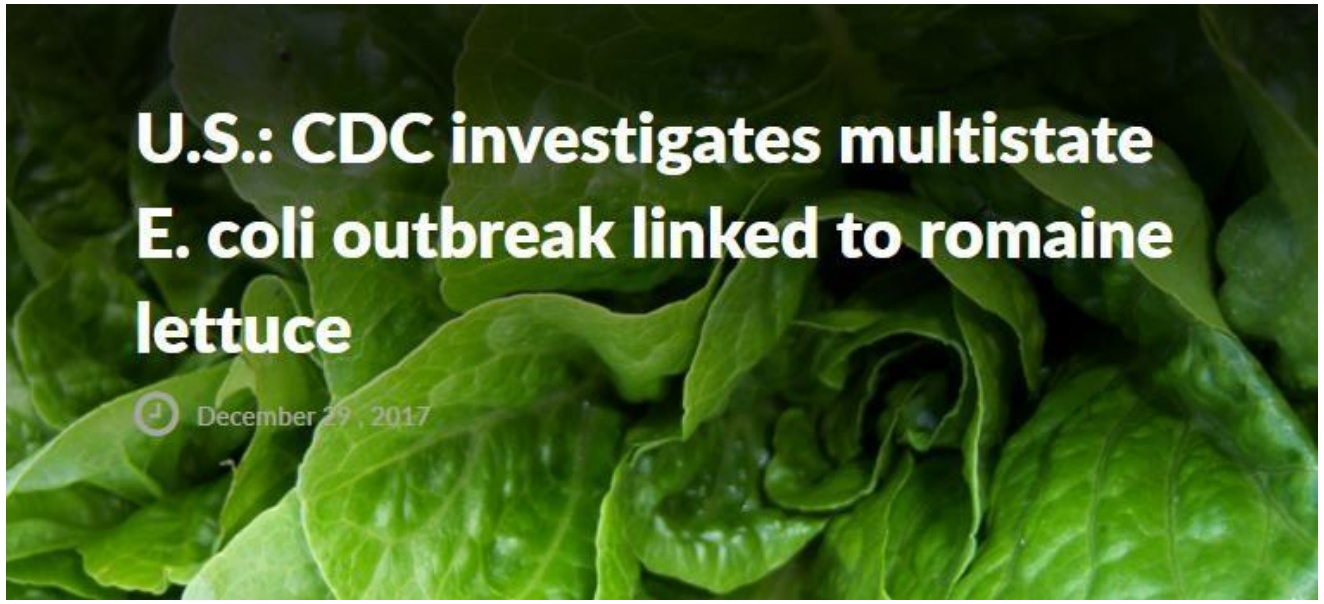
Reports of Selected *E. coli* Outbreak Investigations

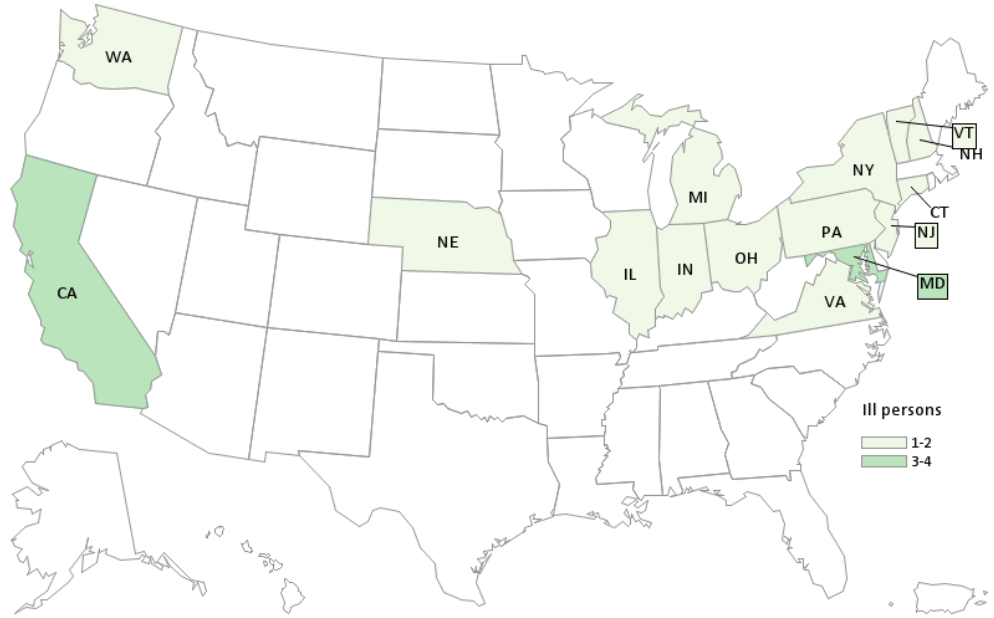
When two or more people get the same illness from the same contaminated food or drink, the event is called a foodborne disease outbreak. The list on this page primarily represents multistate foodborne outbreak investigations involving *E. coli* since 2006 where CDC was the lead public health agency. For a complete listing of reported outbreaks please use the Foodborne Outbreak Online Database (FOOD) tool.

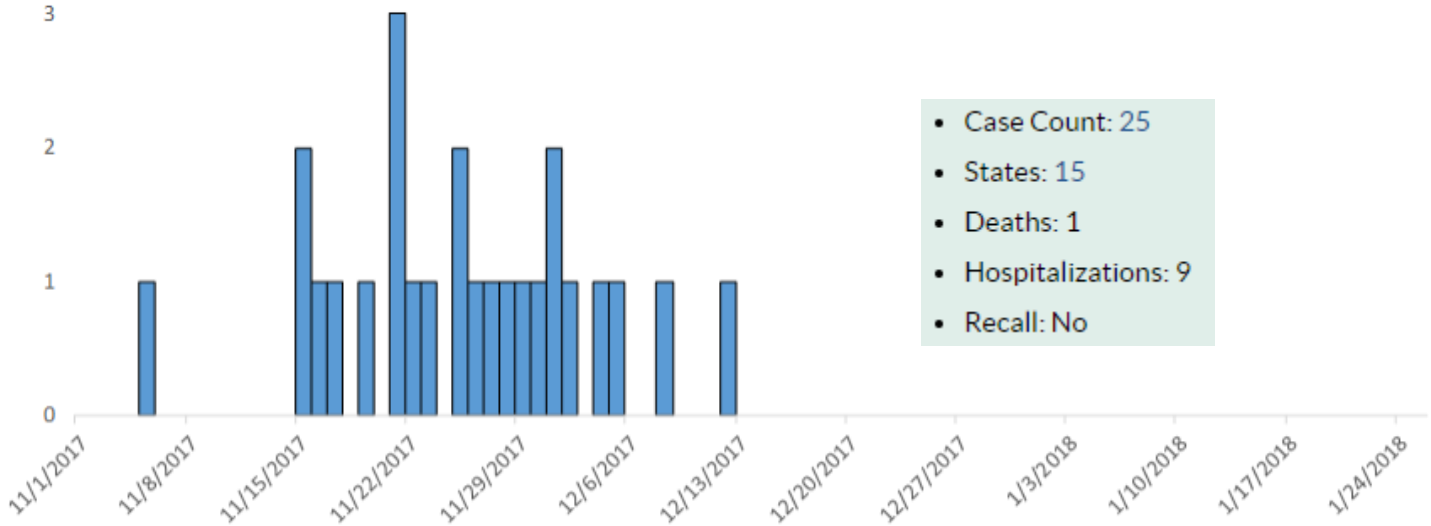
E. coli Factsheet

Type here to search | ENG | 12:35 PM 27/2/2020

https://www.cdc.gov/ecoli/outbreaks.html







- The most recent illness started on December 12, 2017.
- The source of the romaine lettuce linked to the Canadian outbreak.
- Source no longer available after a month.

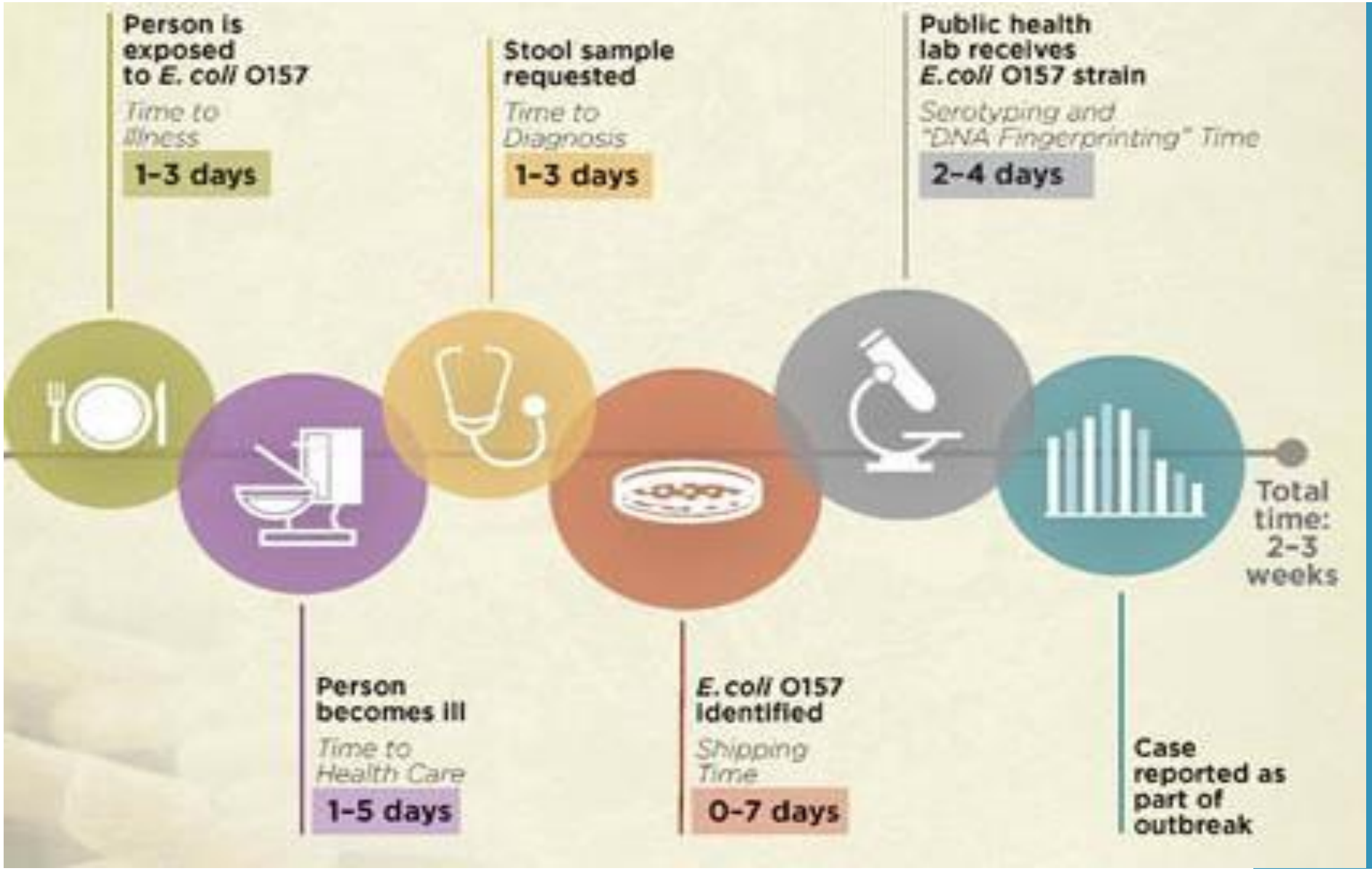
https://www.cdc.gov/ecoli/2017/o157h7-12-17/index.html

CASES OF *E. coli* IN THE US

1993	2006	2006	2015
Jack in the Box hamburgers	Dole baby spinach	Taco Bell fast food	Chipotle Mexican Grill fast food
			
100 ill 4 deaths	**205 ill 3 deaths**	**71 ill 0 deaths**	**55 ill 0 deaths**

https://www.healthline.com/health/worst-foodborne-illness-outbreaks#emsalmonellaem

TIMELINE FOR REPORTING CASES OF *E. coli* O157 INFECTION



SOURCES AND CARRIER FOODS

- Cattle:
  - Raw and undercooked ground beef.
  - Raw and improperly pasteurized milk
- Other sources (Any relevance to cattle?):
  - Unpasteurized apple cider and juice: 1996 outbreaks
  - Lettuce, alfalfa sprouts
  - Drinking water: Walkerton, Ontario outbreak 2000, 7 death, 2300's ill (worst public health disaster in Canadian history)

DISEASE PREVENTION

- Cook ground beef and hamburger thoroughly, to >71°C (internal).
- Keep raw meat separate from ready-to-eat foods.
- Never place cooked hamburgers on the unwashed plate that held raw patties.
- Drink only pasteurized milk, juice, or cider.
- Wash fruits and vegetables thoroughly, especially those that will not be cooked.
- Susceptible individuals should avoid eating alfalfa sprouts.
- Drink water that has been treated with chlorine or other effective disinfectants, or bottled water that has be sterilized with ozone or reverse osmosis.

E. coli O157:H7

Part 1: Transmission of bacteria
https://youtu.be/qTIGCAgaqVk

Part 2: Pathogenesis & complications
https://youtu.be/w-zbjM8wruk

THANK YOU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