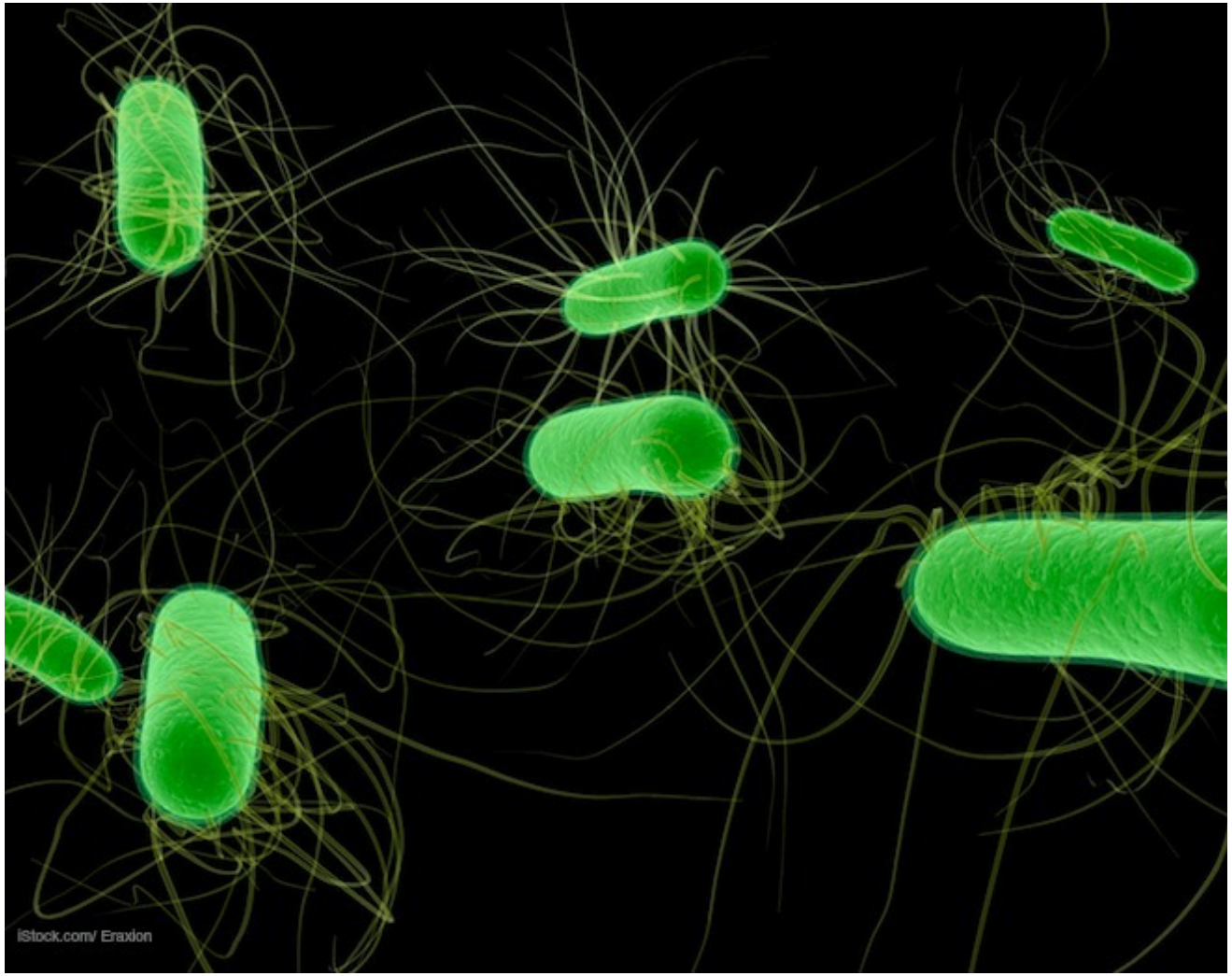
Escherichia coli



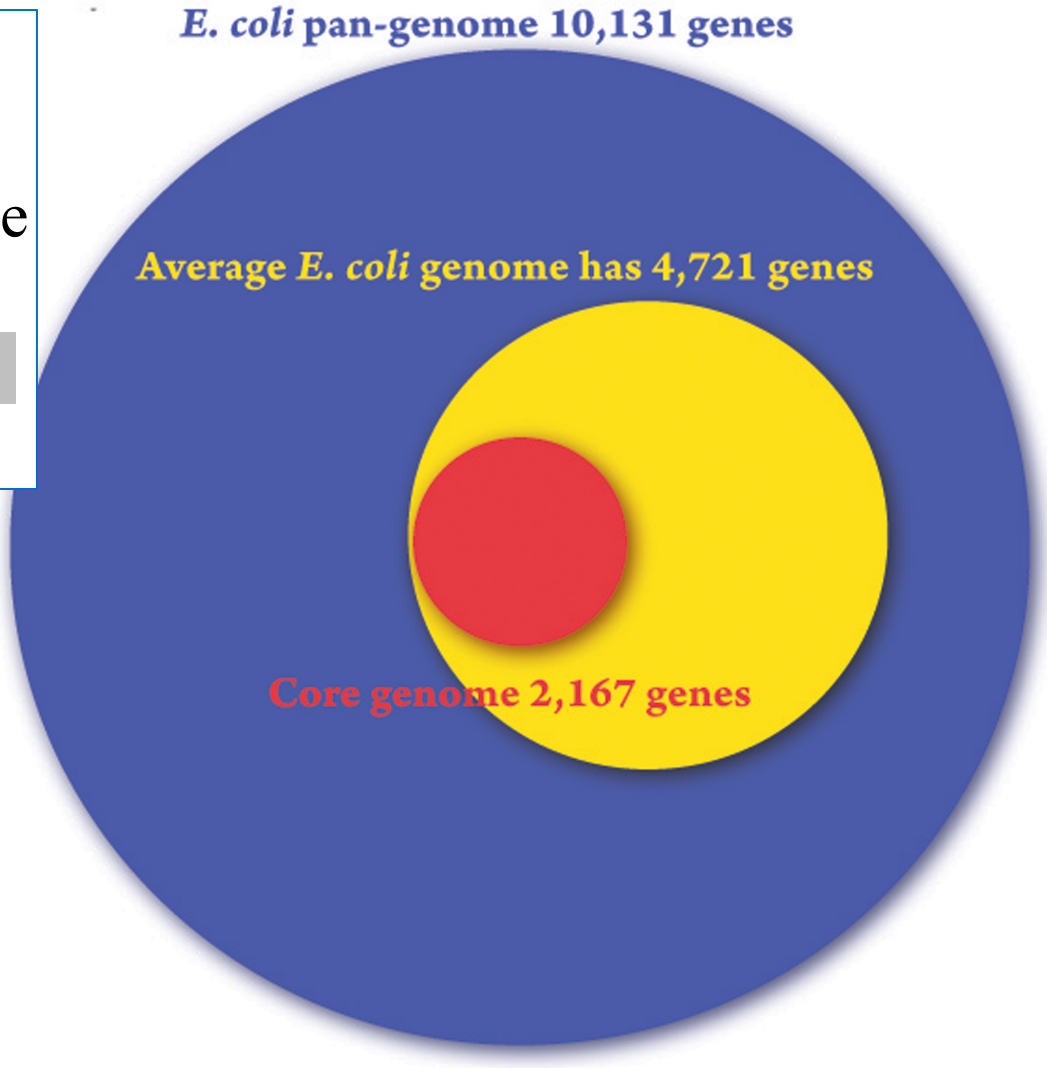
Gram negative bacillus (rod)

Many flagella

Grows very fast 20-minute doubling time

E. coli are remarkably diverse

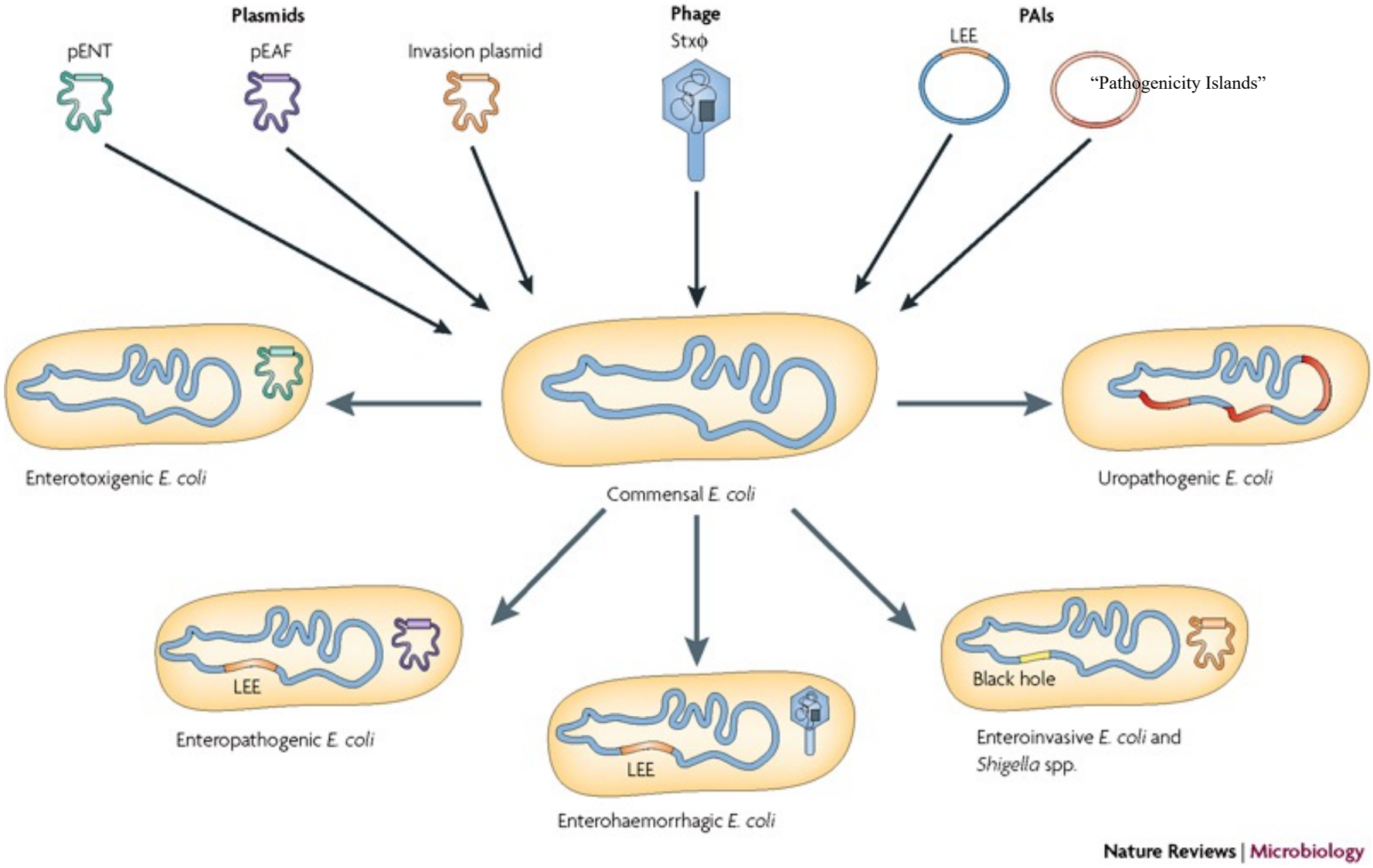
This Venn diagram shows that every E. coli strain MUST have Core 2,167 genes and on average each have 4,271 total genes but there are are 10,131 POSSIBLE genes that E. coli can carry.



Acquisition of mobile genetic elements can change *E. coli* from a commensal to a highly adapted and deadly pathogen!

Various strains of *E. coli* found in human populations have become highly pathogenic causing severe disease.

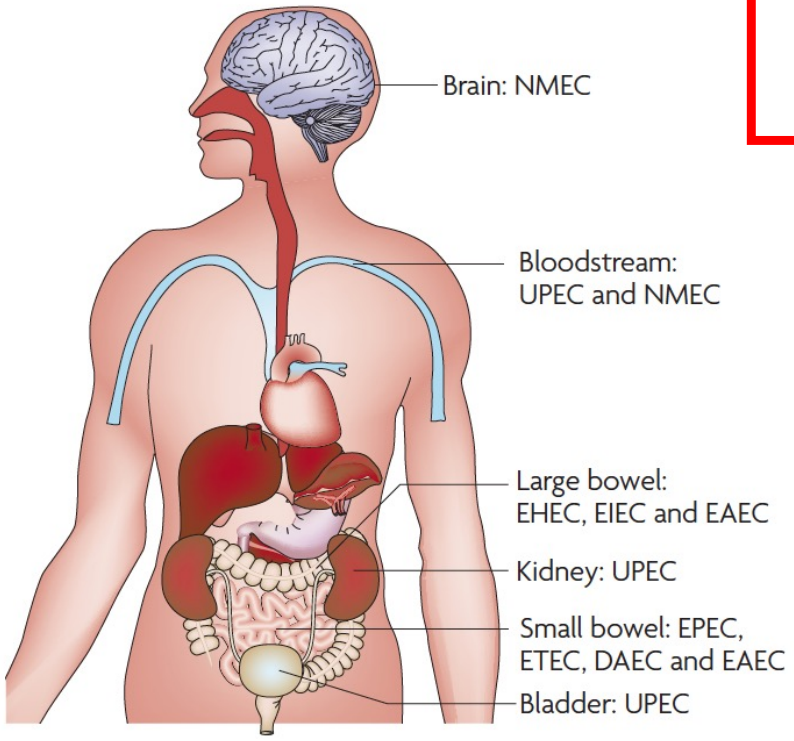
Turning a commensal into a pathogen



"selfish" DNA elements can turn "good" bacteria into pathogens

8 “pathovars” of pathogenic E. coli

~400 Million Infections annually worldwide
(WHO Estimates)



Enterohaemorrhagic E. coli (EHEC)

Enteropathogenic E. coli (EPEC)

Enterotoxigenic E. coli (ETEC)

Uropathogenic E. coli (UPEC)

Diffusely adherent E. coli (DAEC)

Enteroinvasive E. coli (EIEC)

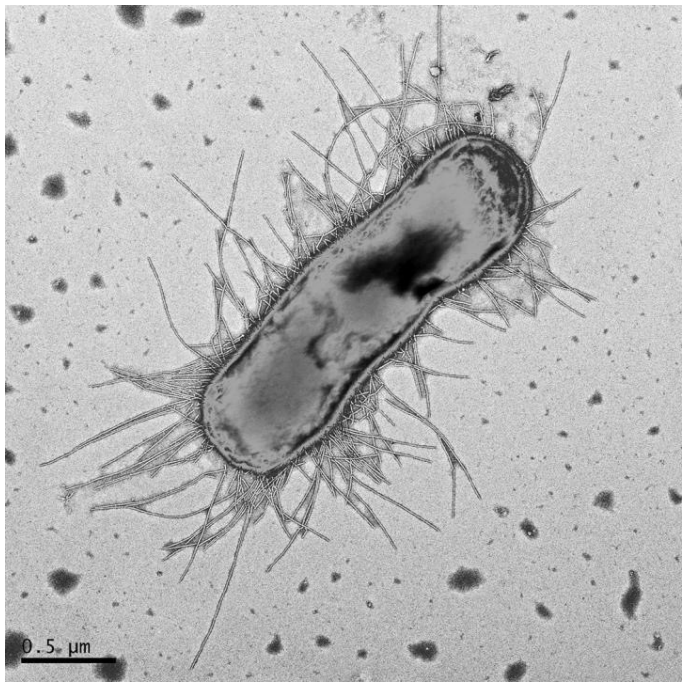
Enteroaggegrative E. coli (EAEC)

Neonatalmeningitis E. coli (NMEC)

EPEC versus EHEC/STEC

EPEC

- Causes childhood diarrhea
- Transmits human to human
- **No Shiga toxin**

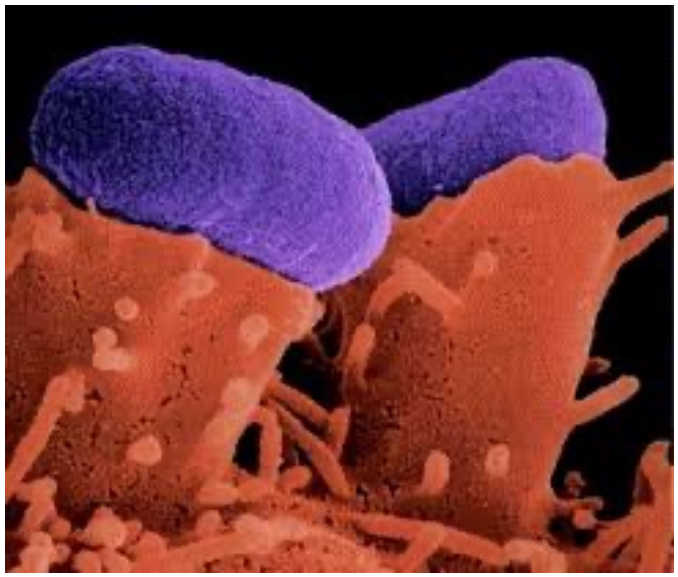


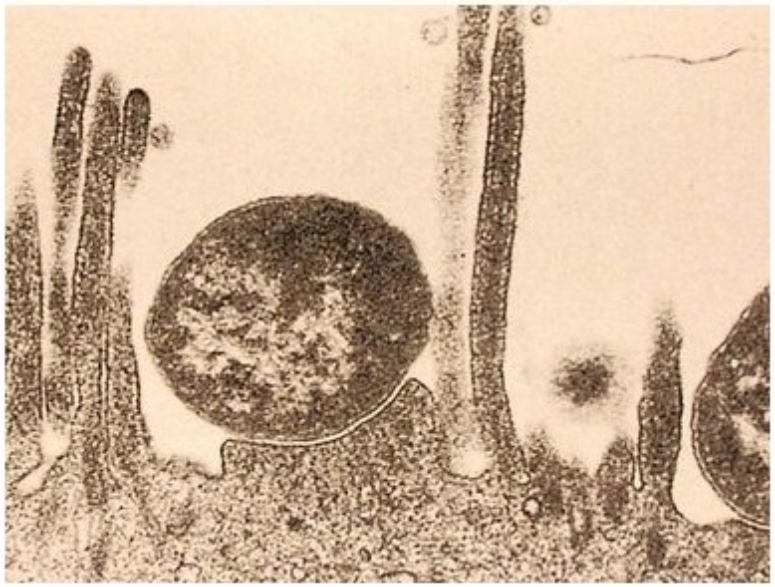
EHEC/STEC

- Food/water-borne pathogen in industrialized countries
- **Zoonotic from cattle or other animals**
- Secreted **Shiga toxin-** can lead to **Hemolytic Uremic Syndrome (HUS):** lysed cells can clog kidneys and lead to kidney failure
- Shiga toxin-producing Escherichia coli (STEC) are estimated to cause 265,000 illnesses each year in the US with more than 3,600 hospitalizations and 30 deaths.

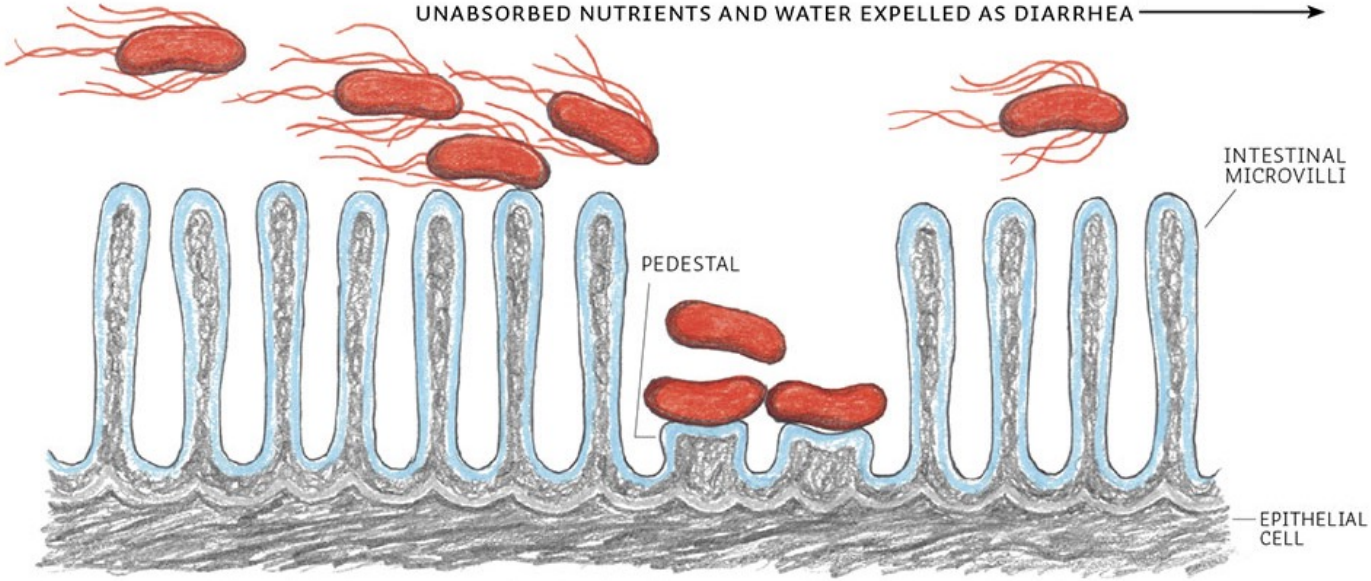
EPEC and EHEC Similarities: Share many virulence determinants
Same distinctive mechanism of intestinal colonization

EPEC and EHEC attach via pedestals

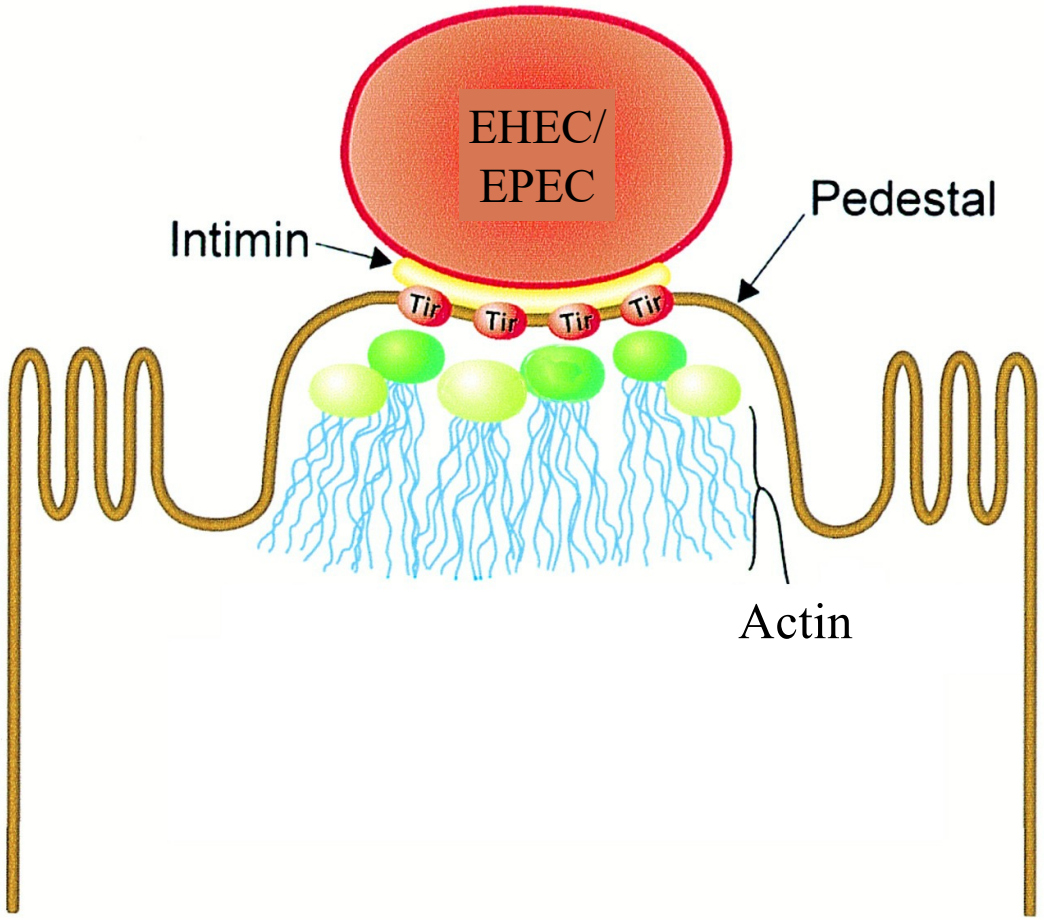




How do bacteria stay attached in intestine and keep from being washed out?



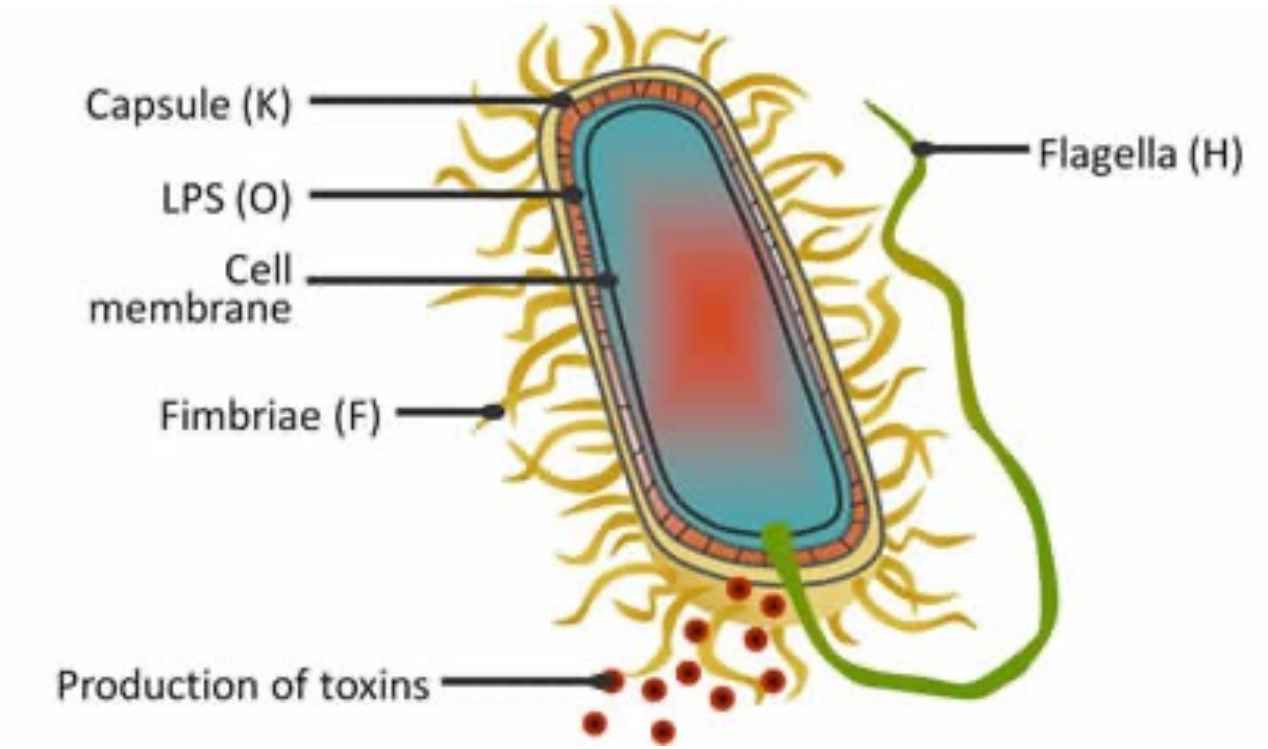
EHEC/EPEC induce pedestal formation to stay attached



EHEC/EPEC inject an *E. coli* receptor protein into the epithelial cells.
The *E. coli* protein in epithelial cells binds to the bacteria enabling attachment.
By attaching to cell "pedestal" the *E. coli* prevent being washed away.

Serotyping by E. coli antigens

Surface antigens include polysaccharide side chains (O antigen), capsular antigen (K) and flagellar protein (H). **200 O antigens, 80 K antigens, and 56 H antigens**



Let's focus on EHEC aka STEC

EHEC is also know as Shiga toxin producing E. coli (STEC)

E. coli O157:H7 found on contaminated beef

Several serotypes in EHEC are frequently associated with human diseases such as O26:H11, O91:H21, O111:H8, and O157:H7. ***E. coli* O157:H7** is the most frequently isolated serotype of EHEC from ill persons in the US, Japan, and UK.

EHEC/STEC Shiga toxin

- Shiga toxin (Stx) genes are found in pathogenic *E. coli* (such as O157/H7) and *Shigella dysenteriae*.

- Shiga toxin forms a pentamer of B subunits that bind and enter host cells and allows a single A subunit to enter the cell.
- The A subunit of the toxin injures the **eukaryotic ribosome** and **inhibits protein synthesis** in target cells and can kill cells.
- Shiga toxin can attack epithelial cells, endothelial cells and immune cells

- Shiga toxin can attack cells in **intestine** (colitis/diarrhea), attack **kidney cells and endothelial cells** in kidney (HUS).
- Antibodies to Stx are protective against severe disease.

EHEC outbreak- Jack in the Box 1992

- Over 600 people sickened in 6 states – mostly children

4 deaths, 50 case of kidney failure from hemolytic uremic syndrome (HUS)

- Cause - knowingly undercooking burgers!
- Two class action and hundreds of individual suits.

Shareholders started litigation, congressional investigation

- USDA began testing all ground beef

for *E. coli* O157/H7 in 1994.

Jack in the box

Other famous EHEC outbreaks in US

1996 Odwalla Unpasteurized Apple Juice
66 cases, 1 death (16-month-old girl)

2002 ConAgra Beef Co. 19 million pounds of meat recalled.
35 cases, 1 death. Contaminated meat was shipped to at least 21 states

2006 Natural Selection Foods Company Prepackaged Spinach
199 cases in 26 states. 3 deaths, 31 develop Hemolytic Uremic Syndrome (HUS)

2006 Taco Bell
67 cases in five states

2007 Topp's Ground Beef Patties
40 cases, 2 developed HUS. Recalled 21.7 million pounds of ground beef.

2010 Bravo Farms Cheese
38 infected from cheese sold at Costco, 1 case of HUS

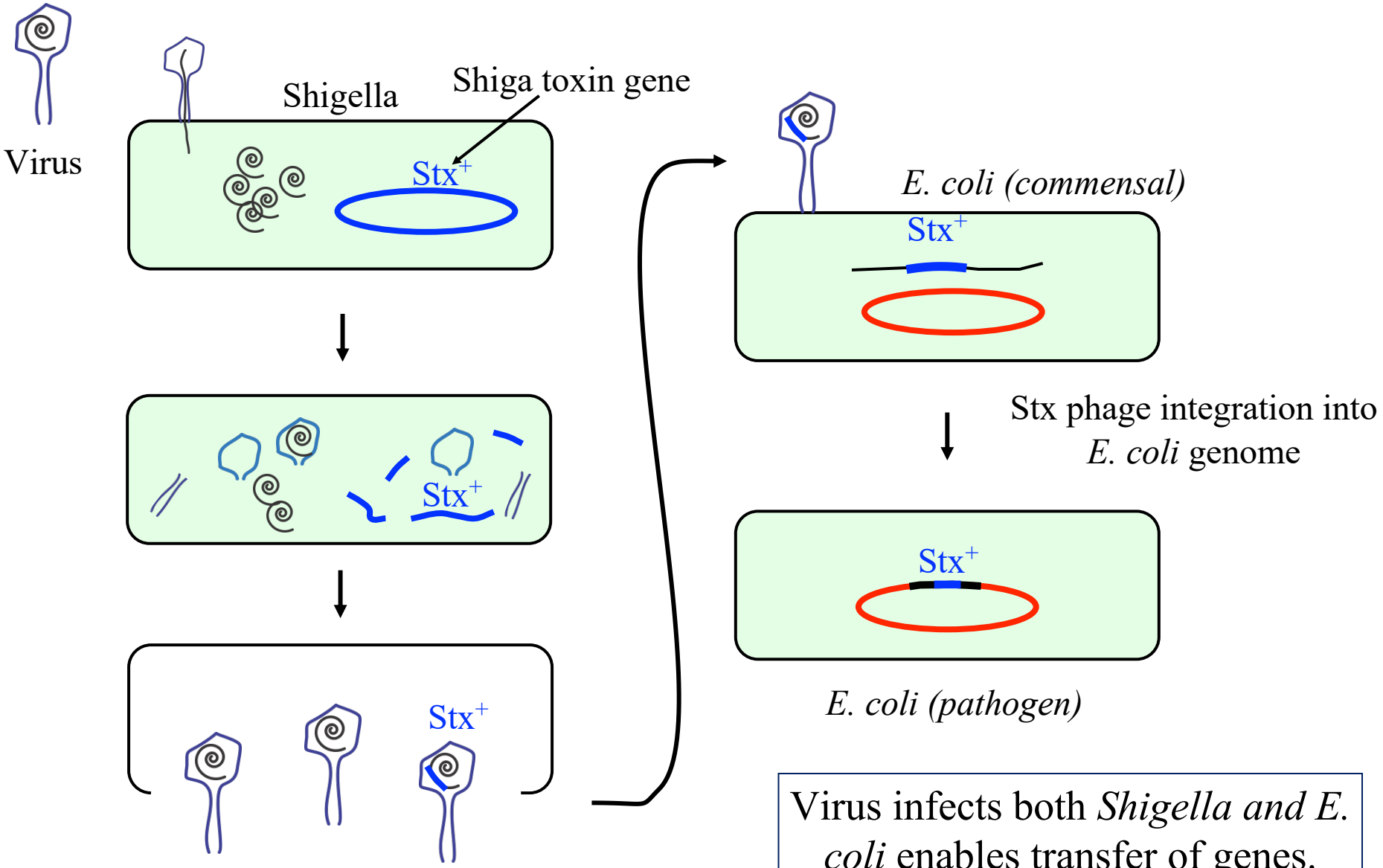
2015 Chipotle
53 infected in 9 states. Chipotle closes 43 restaurants in Oregon and Washington

2017 I.M. Healthy Brand SoyNut Butter
32 cases in a nine-state outbreak

2018 CA Romaine Lettuce
65 cases and 2 developed HUS

CDC: ~100,000 EHEC infections occur each year in the US alone.

How did EHEC acquire Shiga toxin?

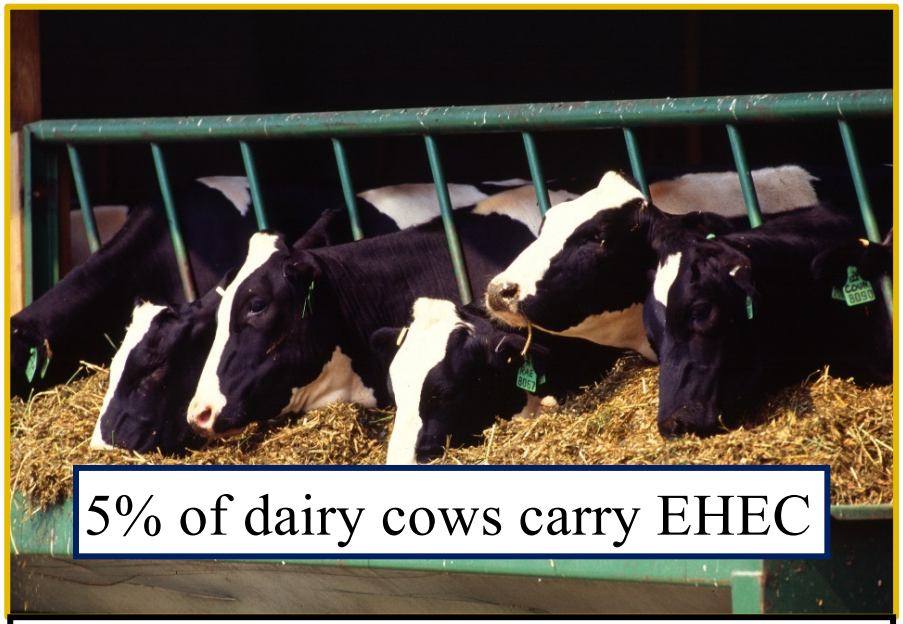


Recombination of shiga toxin gene into phage

Virus infects both *Shigella and E. coli* enables transfer of genes.

EHEC - Transmission in animals

Healthy cattle are the major reservoirs of E. coli O157:H7 (no symptoms). Contaminated bovine products and crops are predominant sources for human infections.



Animal transmission through fecal contamination of food or water

There are cow "Super-shedders"

- Animals colonized at terminal rectum
- Remain infected for long periods
- May shed more than 95% of E. coli in a herd

EHEC Sources of Human Transmission

Undercooked or unpasteurized animal products
- Ground beef
- Other meats
- Milk, cheese

Foods contaminated with animal feces
- Fruits
- Vegetables

Contaminated water
- Private wells
- Swimming (lakes, streams)

Contaminated soil
- Campgrounds
- Sites grazed by livestock

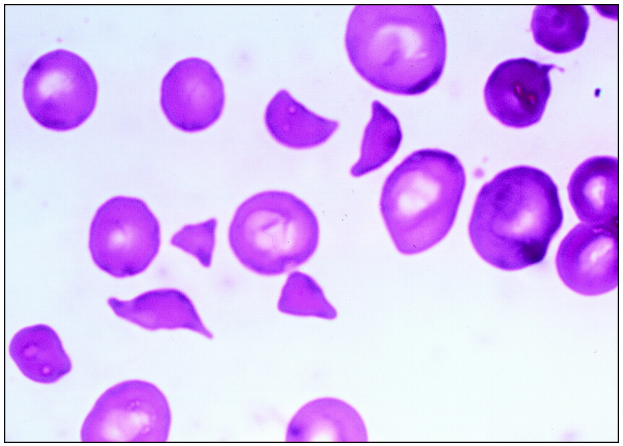
EHEC/STEC Disease in Humans

Hemorrhagic colitis

- Bloody diarrhea
- Severe abdominal cramps
- +/- fever, nausea/vomiting
- Many cases self-limiting, resolve in ~1 week

Hemolytic uremic syndrome (HUS)

- Children, elderly, immunocompromised
- Kidney failure, hemolytic anemia, thrombocytopenia (tiny blood clots clog capillaries)

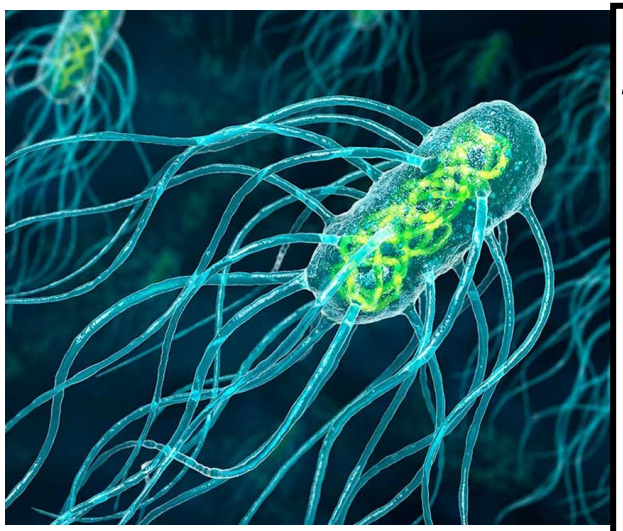


Treatment for EHEC/STEC

- Mainly supportive
- Antibiotics are usually avoided as they may not reduce symptoms nor prevent complications or reduce shedding of bacteria.
- Antibiotics may increase risk of HUS

Salmonella

Salmonella enterica

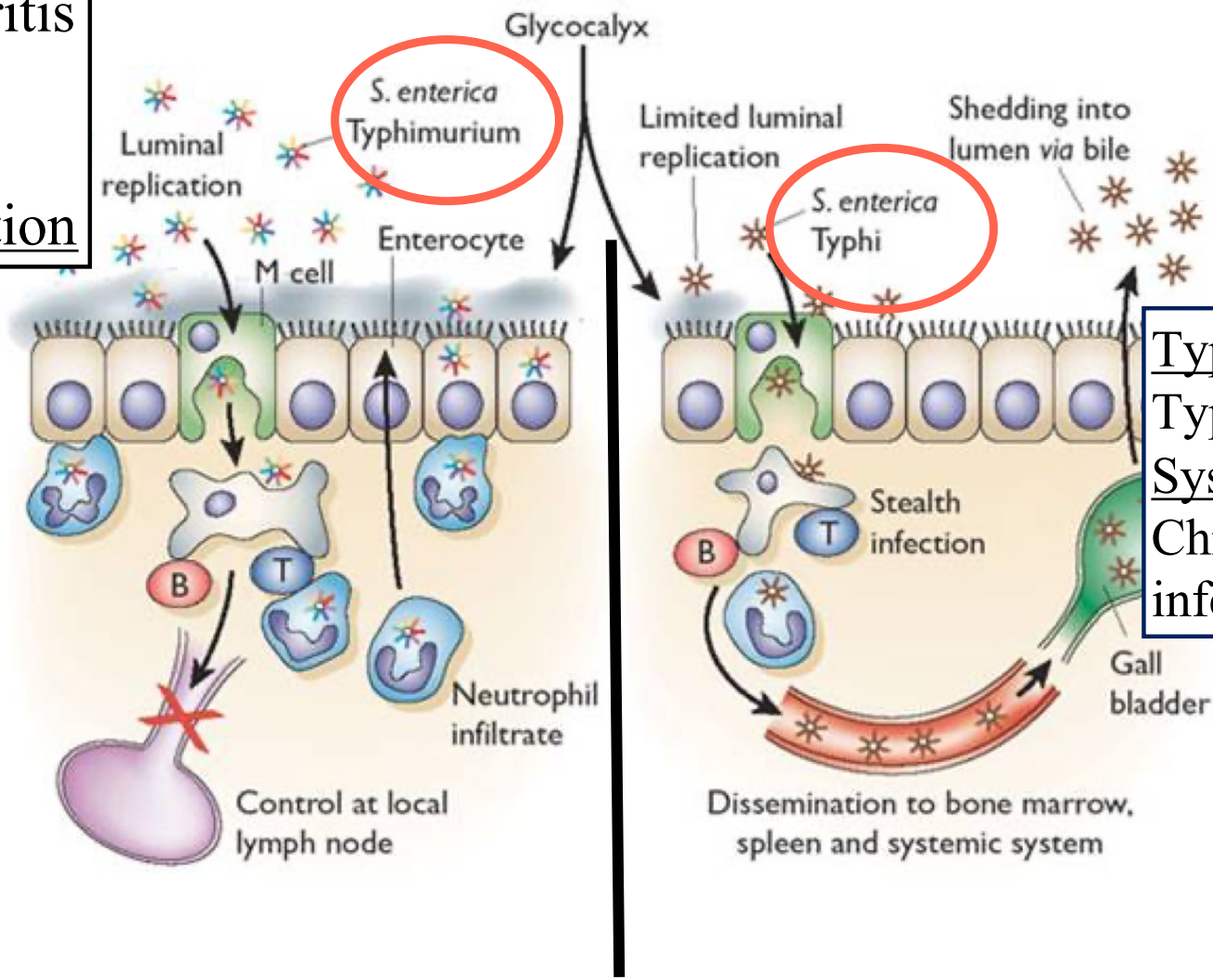


Salmonella enterica comprises a number of subspecies, all of which are common sources of food poisoning. Two main "serovars" of *Salmonella enterica*:

	S. Typhimurium	S. Typhi
Disease:	Gastroenteritis	Typhoid fever Makes typhoid toxin
Duration:	Short-term infections of GI tract	Life-threatening systemic infection 3-5% are carriers that shed high levels
Host range:	Broad range humans/animals	Human-specific
Global burden:	78 M infections/59 K deaths	11.8 M infections/128 K deaths

Salmonella enterica

Typhimurium
Gastroenteritis
-diarrhea
Localized
acute infection



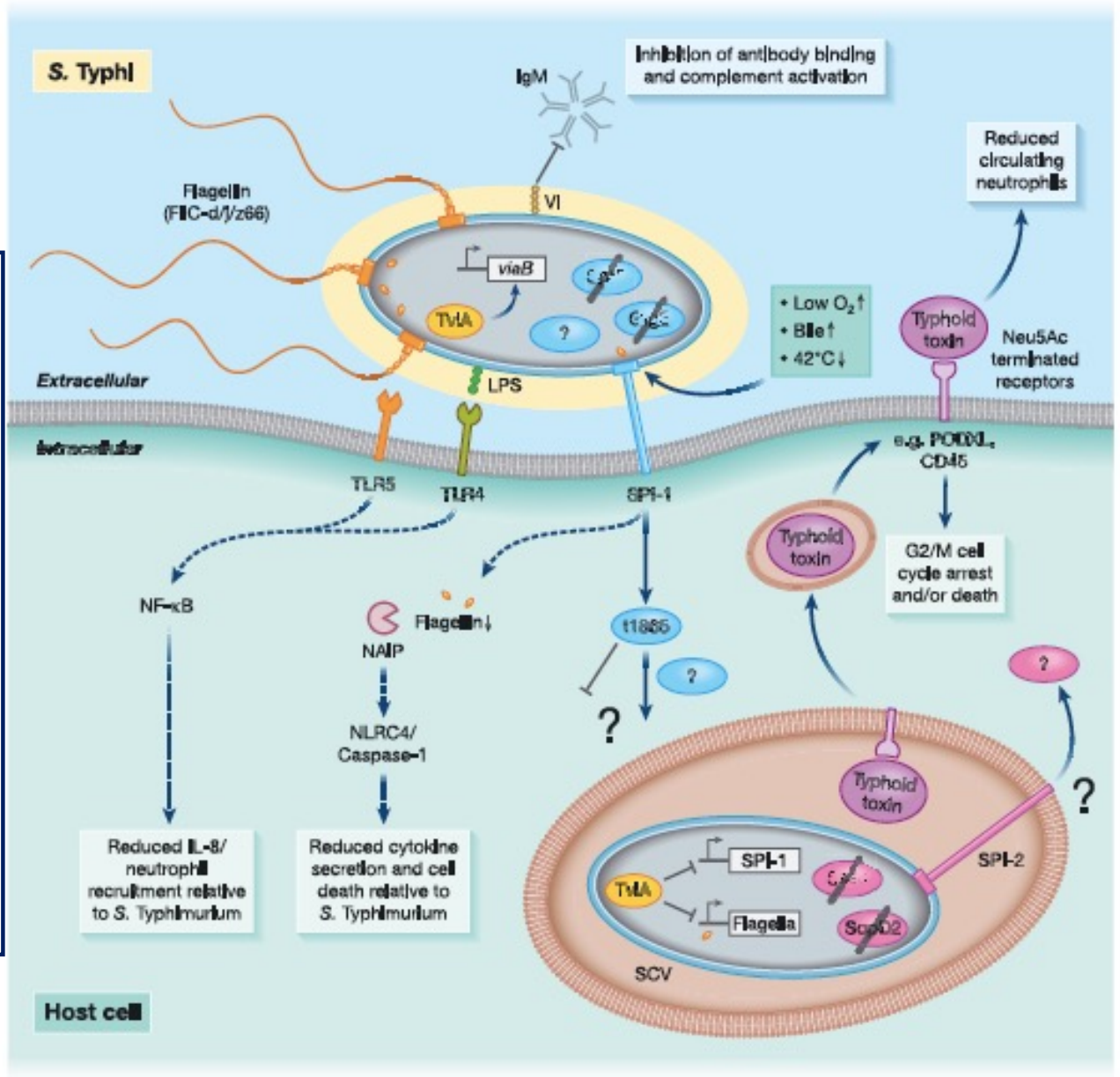
Typhi
Typhoid disease
Systemic infection
Chronic/recurrent
infections

Both types of infections/diseases are treatable with antibiotics, but drug resistance is spreading.

Chronic S. Typhi

Bacterial evasion

1. Inhibit antibody binding and complement.
2. Block LPS and flagellin (PAMPs) binding to TLRs.
3. Toxin kills cells and inhibits neutrophils.



S. Typhi has virulence factors including typhoid toxin and can infect and replicate intracellularly.

Mary Mallon - aka Typhoid Mary

Mallon was a cook in the New York City area for multiple families

1900 - first job, residents developed typhoid fever 2 weeks after she started

1901 - moved to new family, they also developed typhoid and 1 death

Moved again, 7/8 people in family became ill.

1906 - another family, 10/11 hospitalized with typhoid

1906 - new family for summer, 6/11 developed typhoid

Many more, estimated that she caused 50 fatalities

She vehemently denied that she was the source, but admitted to not following proper hygiene.

After her death (stroke/pneumonia), autopsy revealed live S. Typhi in her gallbladder.

Chronic carriage in 1-5% of cases

Large number of bacteria can be shed