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Acute Gastrointestinal Infections

Inflammatory Diarrhea- *Campylobacter* & *Salmonella*

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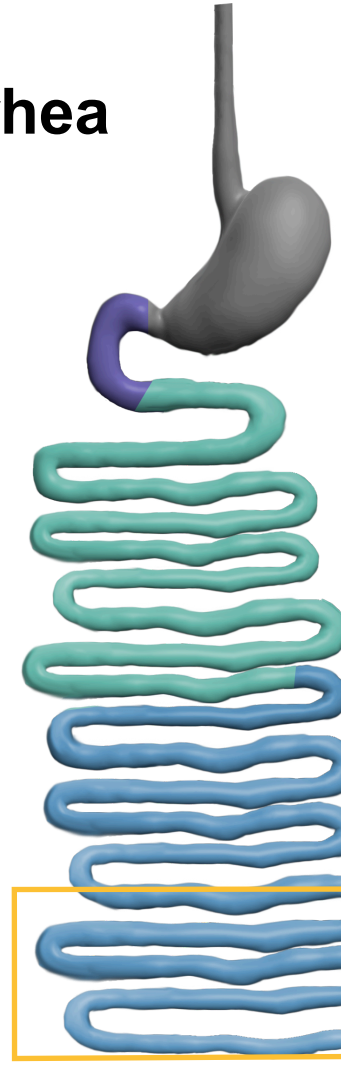
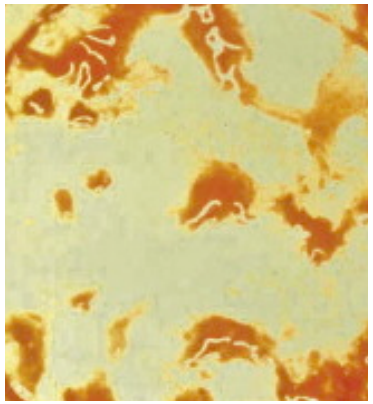
Learning Objectives

- Describe the epidemiology and pathogenesis of gastroenteritis due to *Campylobacter* and *Salmonella*
- Describe the concept of post-infectious autoimmune sequelae
- Distinguish between Non-typhoidal *Salmonella* and *Salmonella* Typhi

Inflammatory or Bloody Diarrhea

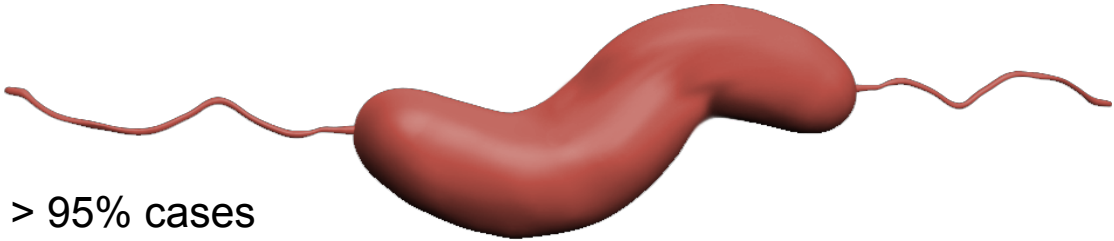
Clinical Features	Frequent small volume stools. May have streaks of blood, mucosy from pus. Pain on defecation (tenesmus), ileocolitis, colitis. Fever may be present.
Complications	Depend on etiology and host features- Hemolytic Uremic Syndrome, Bacteremia
Management	Consider stool cultures, antibiotics for some etiologies but may worsen others
Anatomical Location	Terminal ileum and colon
Pathogenesis	Damage to enterocytes with local inflammatory responses, direct invasion and cytotoxin damage- Locally invasive
Viruses	none in immunocompetent
Bacteria	*Shigella,* Shiga-toxigenic *E. coli (*EHEC, StEC*),* EIEC*,* ***Campylobacter jejuni,*** **non-Typhi-*Salmonella***
Protozoa	*Entamoeba histolytica*





Campylobacter

- Motile, spiral-shaped gram negative bacilli with single bi-polar flagella
- Not related to *E. coli*
  - epsilon-proteobacteria
- *Campylobacter jejuni* and *C. coli* cause > 95% cases
  - but more than 20 species are recognized as potential pathgens
- Grow best in microaerophilic environment
- Many are thermophiles
  - Grow best at 42°C
- Commensals in birds and mammals including chickens, domestic pets, pigs, and cattle.



Campylobacter transmission

- Most common source
  - improperly cooked chicken carcasses
  - raw chicken fluids cross contaminate uncooked food.
- Campylobacter can be cultured from 60% to 100% of chickens purchased in supermarkets

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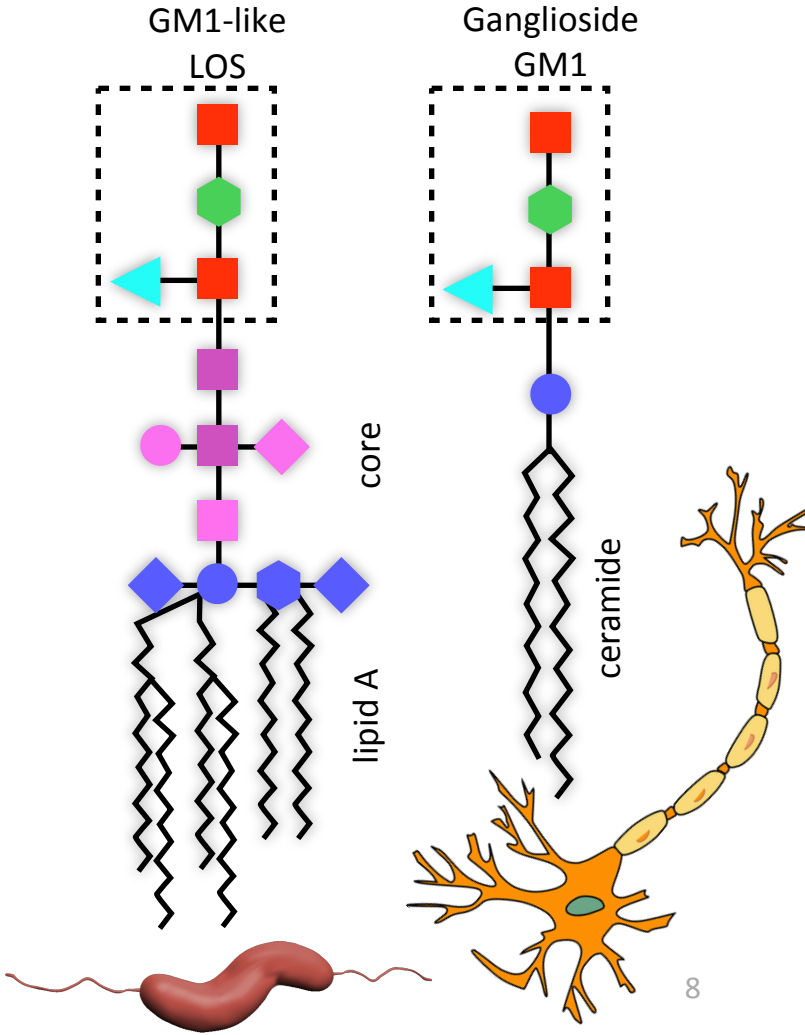
Campylobacter

- Most common cause of bacterial diarrhea in the U.S.
- More than 1% of the population are infected annually (mostly in children under 5). 20% are hospitalized
- Incubation 1 day to 1 week.
- Fever, headache, myalgia, malaise, watery and inflammatory diarrhea with abdominal pain.
- Post Infectious sequelae
  - reactive arthritis
  - irritable bowel syndrome
  - Guillain-Barré syndrome

Guillain-Barré syndrome

- Autoimmune ascending paralysis
- Campylobacteriosis is most commonly identified antecedent in Guillain-Barré syndrome
  - 30:100,000 cases of campylobacter gastroenteritis.
- 10 days to 4 weeks after GI infection
- Molecular Mimicry:
  - Antibodies to lipooligosaccharide antigens cross react with human gangliosides (GM1 GD1a) in peripheral nerve sheaths



Treatment

- Self limited gastroenteritis
- Can treat with antibiotics to shorten symptoms or in severe cases
  - Base treatment on culture results and sensitivities
- Antibiotic resistance increasing because of use of antibiotics in poultry rearing
  - Fluoroquinolones used to be the main therapy but now some countries have up to 80% resistance (26% in U.S.)
  - increase in resistance matches fluoroquinolone release for use in animals in 1990s.

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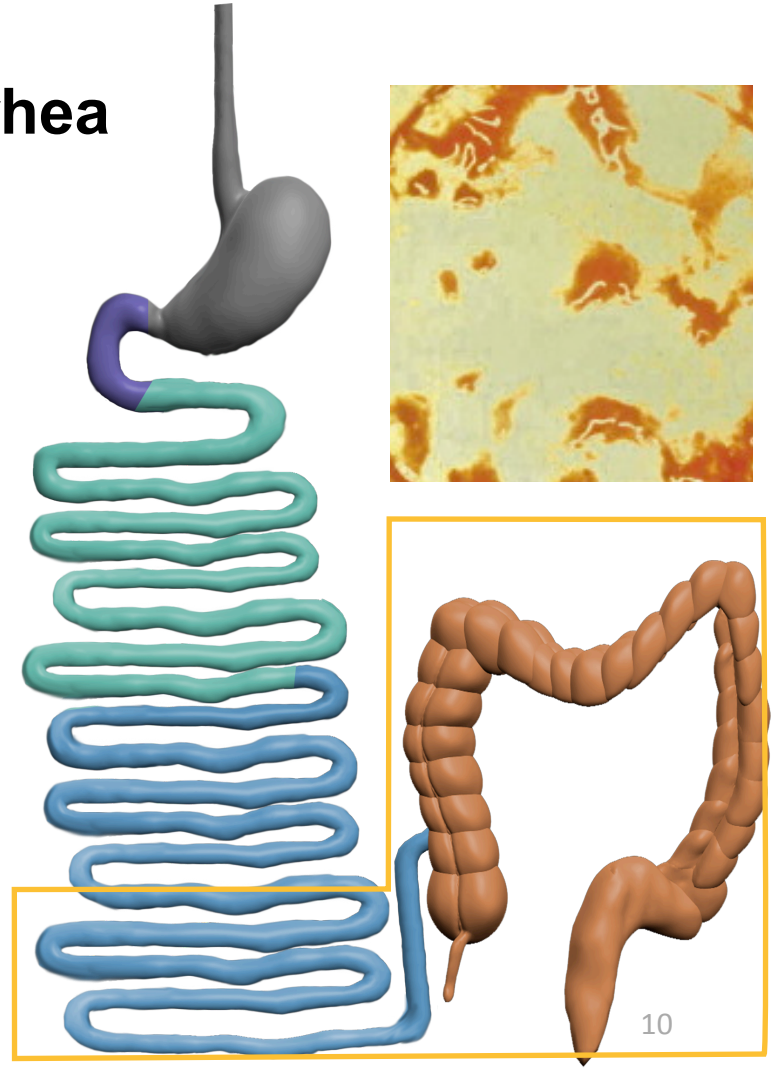
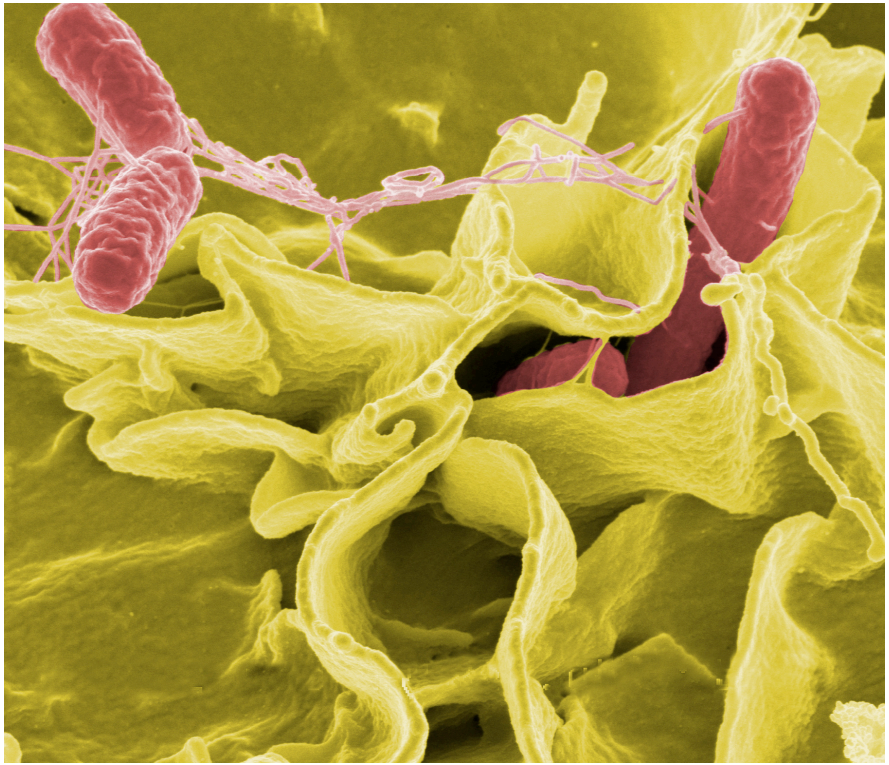


Salmonella gastroenteritis

- *Salmonella* are close relatives of *E. coli* and *Shigella*
- More than 2000 serovars have been identified
  - i.e. *Salmonella enterica* serovar Typhi
- Range of diseases include asymptomatic carriage, mild gastroenteritis, enteric fever.
- For clinical purposes divided into
  - typhoidal vs non-typhoidal
  - non-typhoidal strains cause mostly AGE
  - typhoidal cause enteric fever



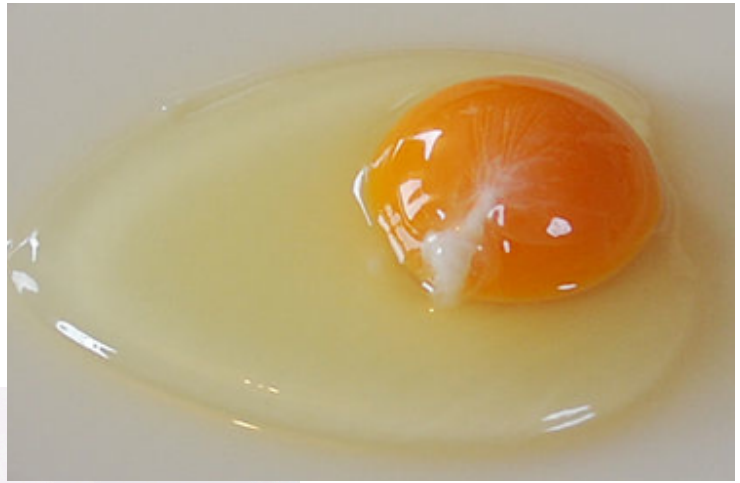
Lots of *Salmonellas*

Serotype	Host	Disease
Typhi	Humans	Typhoid fever
Paratyphi	Humans	Typhoid fever
Gallinarum	Poultry	Fowl typhoid
Pullorum	Poultry	Pullorum disease
Enteriditis	Rodents	Murine typhoid
Typhimurium	Rodents	Murine typhoid
Typhimurium	Cattle	Bacteremia
Dublin	Cattle	Bacteremia
Cholerasuis	Swine	Bacteremia

Salmonella gastroenteritis

- In the U.S. *Salmonella enterica* serovar Enteritidis is the most common cause of Salmonella infection
- Infection is commonly associated with contaminated eggs and chickens
- Infection is inside the eggs not just on the surface

Salmonella gastroenteritis



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Salmonella in reptiles and amphibians

- *Salmonella* colonize the intestines of humans, mammals, birds, reptiles, amphibians and insects.
- In the U.S. 74,000 annual cases of salmonellosis are due to infected pet reptiles and amphibians
- The sale or distribution of turtles with a carapace length of less than 4 inches has been banned in the US since 1975 (Title 21 CFR 1240.62).
- 4 inches was chosen with the thought that most young children wouldn't try to put a turtle larger than this in their mouth
- The Centers for Disease Control (CDC) estimates that the ban prevents 100,000 cases of reptile-associated *Salmonella* a year

A few *Salmonella* Foodborne outbreaks

2007
Veggie Booty
Salmonella Wandsworth

2007
Pot Pies
Salmonella 14

2014
Nut Butter
Salmonella Braenderup

2007
Peanut butter
Salmonella Tennessee

2010
Eggs
Salmonella Enteritidis

2012
Dog Food
Salmonella Infantis

2011
alfalfa sprouts
Salmonella Enteritidis

Salmonella gastroenteritis pathogenesis

- Reduced gastric acid in neonates or people on anti-acid medication can also reduce infectious dose
- Host normal microbiota is protective against colonization by pathogens (**colonization resistance**)
    - Salmonella must compete for colonization
        - People on antibiotics prior to an outbreak are more susceptible

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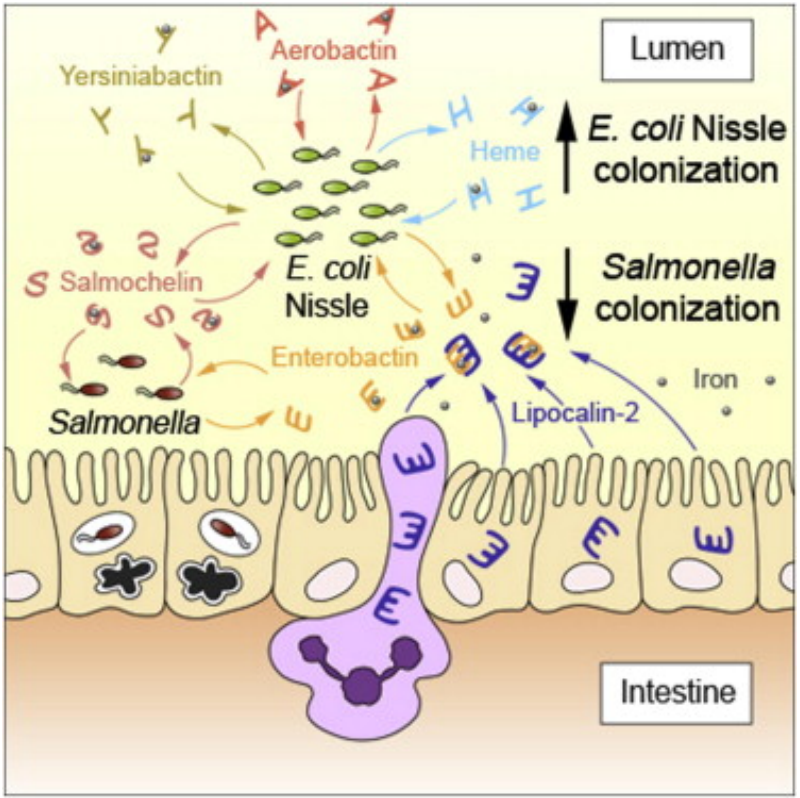
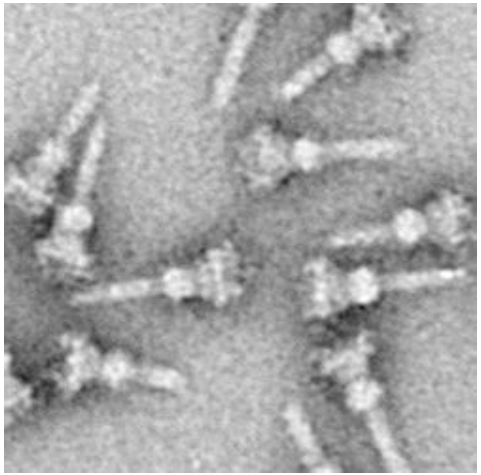
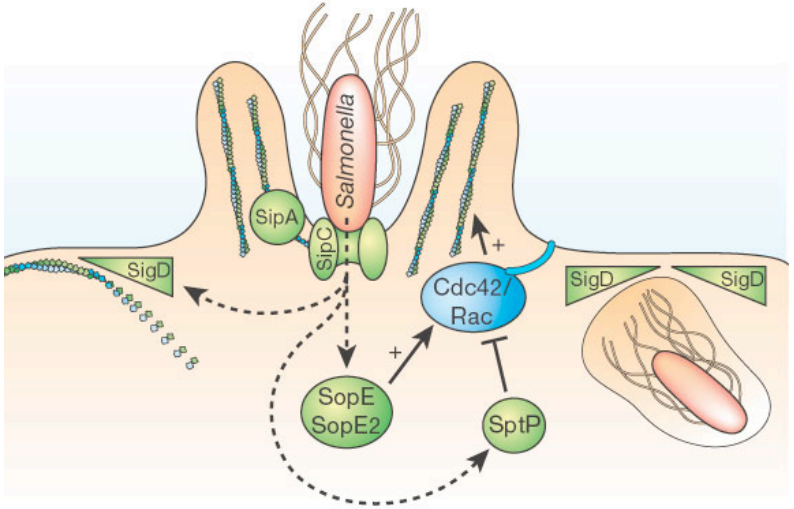


Salmonella invades



- Reaches the terminal ileum and colon.
- Actively invades intracellularly using a effectors it injects through a T3SS
  - M-cells in the Peyer's patches
  - dentritic cells
  - Perhaps enterocytes directly
- Can replicate within macrophages and dendritic cells and then invade epithelial cells through the basolateral side

Salmonella invades



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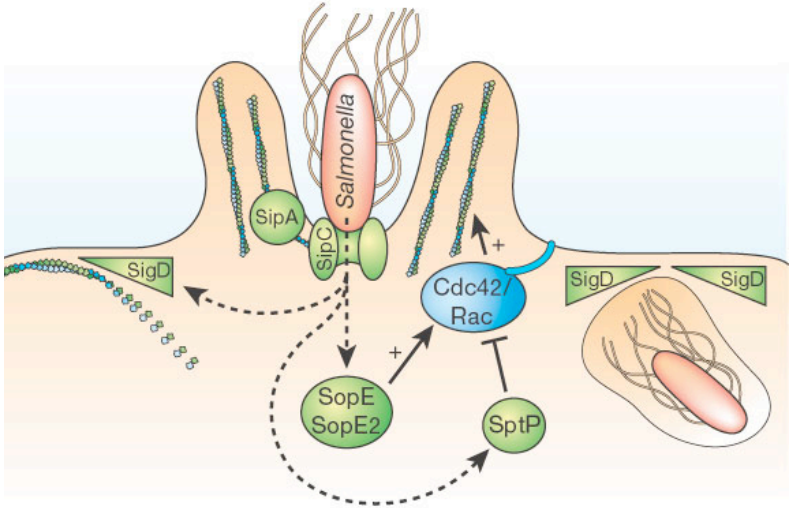

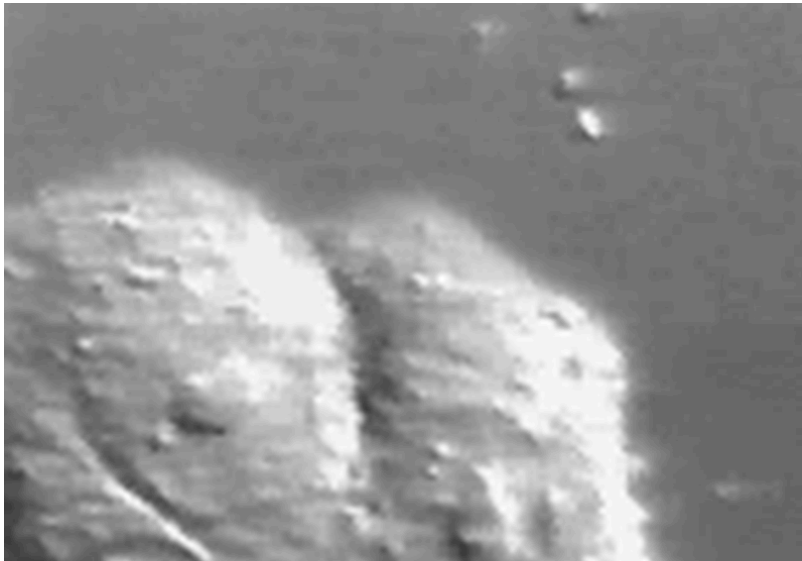

Salmonella intracellular life

- *Salmonella* (unlike *Shigella)* remain in the vacuole and actively remodel the vacuole to obtain nutrients and avoid clearance
- PAMP recognition of LPS, flagellin, etc
  - Cytokine production and cell death
  - Neutrophilic inflammatory colitis
- The inflammation it causes is beneficial to *Salmonella* because it kills many of the resident bacteria in the lumen

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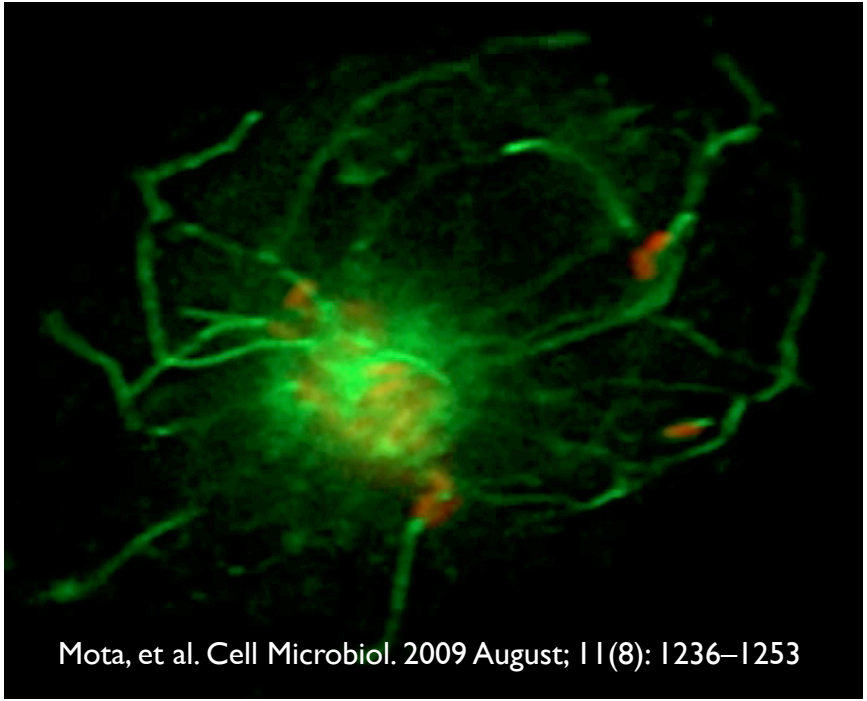

Mota, et al. Cell Microbiol. 2009 August; 11(8): 1236–1253

Salmonella gastroenteritis diagnosis and treatment

- Non-typhoidal Salmonella can be detected in stool cultures after differentiation from normal gram negative flora
  - Important for distinguishing between *Salmonella*, *Campylobacter*, *Shigella* and StEC
  - Antibiotic susceptibility can be obtained from cultures
- In immunocompetent adults and children over 1 year with mild symptoms no antimicrobials are needed
  - Supportive care with fluid management
  - If severe symptoms may benefit from antibiotics but antibiotics prolong carriage and may prompt relapse

Salmonella gastroenteritis complications

- Immunocompromised hosts can develop more invasive systemic disease from *Salmonella* gastroenteritis
  - HIV patients
  - Neonates
  - Patients on immunosuppressive medications like steroids
  - cancer
  - Organ transplants
  - Sickle cell anemia
- Complications include
  - bacteremia
  - meningitis
  - Focal infections i.e. osteomyelitis, septic arthritis, endocarditis

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Credits: Inflammatory Diarrhea- Campylobacter & Salmonella

Slide 4: Dysenteric stool. Figure 18.6 Typical dysenteric stool is a small-volume mix of blood and pus. Such stools may be passed 30 or more times per day, often with increased pain (tenesmus). From: Shigellosis. Tropical Infectious Diseases: Principles, Pathogens and Practice. Keusch, Gerald T.; Salam, Mohammed A.; Kopecko, Dennis J. January 1, 2011. Pages 137-144. © 2011.
https://www.clinicalkey.com

Slide 6: Cutting board with chicken.
http://www.consumerreports.org/cro/magazine-archive/2010/january/food/chicken-safety/dirty-birds/chicken-safety-dirty-birds.htm

Slide 7: Scanning electron microscope image shows the characteristic spiral, or corkscrew, shape of C. jejuni. Photo by De Wood; digital colorization by Chris Pooley. Agricultural Research Service (ARS) is the U.S. Department of Agriculture's chief scientific research agency
http://commons.wikimedia.org/wiki/File:ARS_Campylobacter_jejuni.jpg

Slide 14: Johns Hopkins Magazine. June 2009. Cover..
http://pages.jh.edu/~jhumag/0609web/

Slide 11: Salmonella invading a cell.
http://commons.wikimedia.org/wiki/File:SalmonellaNIAID.jpg

Slide 11: Eggs.
http://commons.wikimedia.org/wiki/File:Chicken_egg_2009-06-04.jpg

Slide 14: Boy with turtles. Proceedings PulseNet Outbreaks
http://www.aphl.org/conferences/proceedings/Documents/2012/2012-PulseNet-OutbreakNet/024-Simmons.pdf

Credits: Inflammatory Diarrhea- Campylobacter & Salmonella

Slide 16: Graphic Abstract. Probiotic Bacteria Reduce Salmonella Typhimurium Intestinal Colonization by Competing for Iron. Deriu et al. Cell Host & Microbe 14, 26–37, July 17, 2013 a2013 Elsevier Inc
https://www.clinicalkey.com

Slide 17: Salmonella invasion diagram. From Microbial pathogenesis and cytoskeletal function. Gruenheid and Finlay Nature 422, 775-781(17 April 2003)

Slide 18: Salmonella intracellular vacuole. Mota et al. SCAMP3 is a component of the Salmonella-induced tubular network and reveals an interaction between bacterial effectors and post-Golgi trafficking. Cell Microbiol. 2009 August; 11(8): 1236–1253.

Slide 19: Xylose lysine deoxycholate agar (XLD agar) is a selective growth medium used in the isolation of Salmonella and Shigella species from clinical samples and from food
http://commons.wikimedia.org/wiki/File:Salmonella_growing_on_XLD_agar.JPG

Slide 20: Salmonella osteomyelitis. From: Rayan et al. Distal tibia osteomyelitis duei to Salmonella in a patient with Thallasemia. J Orthopaed Traumatol (2009) 10:31–33