ENTERIC PATHOGENS AND FOOD POISONING

Epidemiology

- Foodborne diseases each year in US:
  - affects 1 in 4 Americans
  - 76 million illnesses
  - 325,000 hospitalizations
  - 5,000 deaths
    - 1,500 of those deaths caused by *Salmonella*, *Listeria*

Epidemiology

- Many unrecognized or unreported
  - mild disease undetected
  - same pathogens in water and person to person
  - emerging pathogens unidentifiable
- Greatest risk
  - elderly
  - children
  - immunocompromised

Gastroenteritis

- *E. coli*
- Shigella spp.
- Salmonella spp.
- Yersinia spp.
- Campylobacter spp.
- Vibrio spp.
- viruses
- protozoa

Food poisoning

- *Staphylococcus aureus*
- *Bacillus cereus*
- *Clostridium pefringens*
- *Clostridium botulinum*
- *Vibrio parahaemolyticus*
- *Listeria monocytogenes*

Source of enteric infections

human fecal contamination of food and water (direct, water, soil)

naturally infected animal foods - meats and dairy products (non-typhoid *Salmonella, Campylobacter*, *Vibrio vulnificus*)

contamination of food (usually fruits and vegetables) with soil - environmental (*Clostridium perfringens*).

some enteric pathogens are human only (*Salmonella enterica* serovar Typhi, Shigella)

Pathogenesis

Entry: all oral (ingestion of the bacteria or ingestion of preformed toxin

Spread - three possibilities:
1. do not spread past the intestinal mucosa
2. invade laterally within the intestines
3. invade deeper to the draining lymph nodes, lymphatics, blood, and all through the body

Multiply
1. lots of food, but little or no oxygen in large intestine
2. chemical barriers to growth and multiplication - acid, bile
3. competition from normal flora
4. intracellular pathogens have difficult hurdles

Damage 1. toxins
2. invasion of epithelium
3. attaching-effacing adherence
4. inflammation

Symptoms

vomiting
- rapid onset
- usually toxin

watery diarrhea
- large volume, usually without blood or pus
- usually small intestinal effects (secretory bowel)
- usually from toxin

bloody diarrhea (does not equal dysentery)
(bloody, mucoid diarrhea)
- smaller volume, pus (white cells), can be bloody, fever, abdominal pain
- usually from large intestine (inflammatory bowel)
- usually invasive organisms

Prevention

food handling (personnel)

food preparation

public health considerations

In the Home

- drink pasteurized milk and juices
- wash hands carefully and frequently
  - after using the bathroom
  - changing infant's diapers
  - cleaning up animal feces
- wash hands before preparing food

In the Home

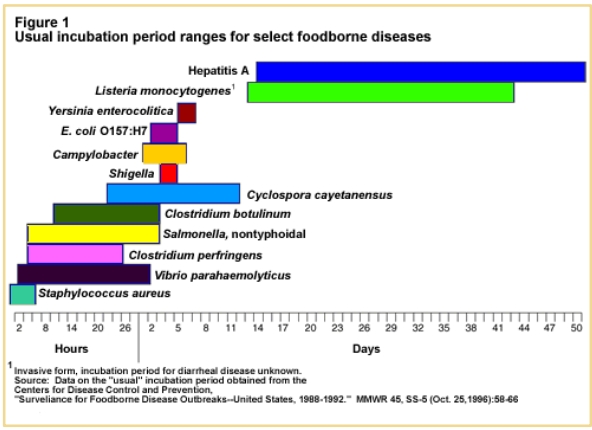
- wash raw fruits and vegetables before eating
- after contact with raw meat or poultry
  - wash hands, utensils and kitchen surfaces
  - hot soapy water
- defrost meats in the refrigerator

In the Home

- cook beef/beef products thoroughly
  - internal temperature of min. 71 °C
- cook poultry and eggs thoroughly
  - Internal temperature of min. 77-83 °C
- eat cooked food promptly
- refrigerate leftovers within 2 hours after cooking
- store in shallow containers

The enteric pathogenes (summary)

	Small intestine	Large intestine	Invasive	Toxic
Shigella spp.	-	+	+	-
Salmonella enterica	+	-	+/-	-
ETEC	+	-	-	+
EIEC	-	+	+	-
EPEC	+	-	-	-
EHEC	-	+	-	+
Campylobacter spp.	-	+	+	-
Yersinia spp.	+	-	+	-
Vibrio cholerae	+	-	-	+



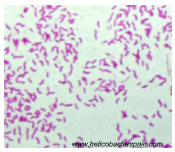
Invasive enteric pathogenes

Campylobacter jejuni

- vibrio-shaped (gull-shaped)

- leading cause of bacterial diarrhea, can be as severe as dysentery

- culture: 42ºC, Campy agar, microaerophilic



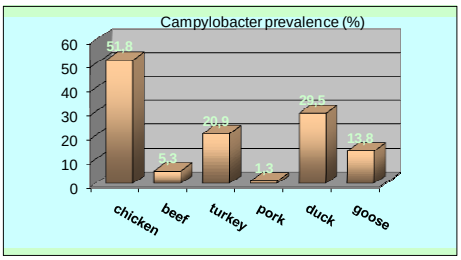
Epidemiology

- 2.4 million people each year (US)
  - children under 5 years old
  - young adults (ages 15-29)
- very few deaths
- can lead to Guillain-Barré Syndrome
  - leading cause of acute paralysis
  - develops 2-4 weeks after *Campylobacter* infection (after diarrheal signs disappear)

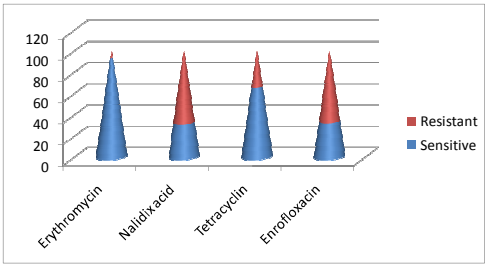
Campylobacteriosis

- Sources
  - raw or undercooked poultry
  - non-chlorinated water
  - raw milk
  - infected animal or human feces
    - poultry, cattle, puppies, kittens, pet birds
- Clinical signs
  - diarrhea, abdominal cramps, fever, nausea
  - duration: 2-5 days

Campylobacter prevalence in Hungary



Sensitivity pattern of Campylobacter spp. in Hungary



Salmonella spp.

- nomenclature: one species (*Salmonella enterica*) with thousands of serovars (Typhi, Typhimurium, Enteritidis, etc.). Most of us take a shortcut and use the genus and serovar names

- three forms of disease: typhoid fever (enteric fever), gastroenteritis, septicemia
- carrier state also possible

typhoid (enteric) fever - *S. typhi, S. paratyphi*

symptoms: few intestinal symptoms, mainly systemic - fever, shock, headache, myalgia, lethargy, splenomegaly, hepatomegaly

reservoir: only humans!
- invade gut-associated lymphoid tissue of small intestine
- infect lymph nodes, blood, spleen, liver, bone marrow, other focal organs (e.g., gall bladder)

- resistance to phagocytes (intracellular) and serum/ complement
- cell-mediated immunity more important
- *S. typhi* and *S. paratyphi* C - Vi capsular antigen also involved in virulence

endotoxin + inflammation

vaccine: for *S. typhi*
- killed cells administered i.m. - not good
- new vaccines - attenuated strains fed orally to stimulate mucosal immunity

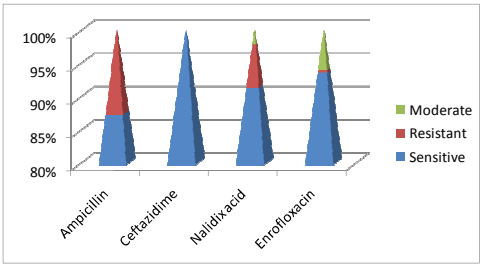
Salmonellosis gastroenteritica

- many serotypes can cause disease
- *S. enteritidis* and *typhimurium*
  - 41% of all human cases
  - most common serovars in U.S.
- 1.4 million cases annually (US)
  - 580 deaths

Salmonellosis

- Sources
  - raw poultry and eggs
  - raw milk
  - raw beef
  - unwashed fruit
  - reptile pets: snakes, turtles, lizards
- Signs
  - onset: 12-72 hours
  - diarrhea, fever, cramps
  - duration: 4-7 days

Sensitivity pattern of Salmonellae in Hungary



Salmonellae (summary)

	strictly human adapted	broad host range	primarily animal adapted
	S. typhi *S. paratyphi* A, B, C	many strains, e.g. *S. typhimurium* *S. enteritidis*	certain strains, e.g. *S. choleraesuis*
disease	enteric fever	enterocolitis septicemia in immuno-compromised.	bacteremia, septicemia
infectious dose	moderate	high	probably high
infectious source	infected humans	human & zoonotic	zoonotic
transmission	food (enrichment) direct contact	food (enrichment)	food (enrichment)
prevention by proper food handling	+	+	+
vaccine	+	-	-

Shigella spp.

S. dysenteriae, S. flexnerii, S. boydii, S. sonnei (*Shigella* and EIEC are essentially identical organisms)

reservoir: - humans only

spread: laterally in intestines

Shigella dysenteriae (only) - potent cytotoxin (Shiga toxin) - Shiga toxin is an A-B toxin

- inactivates ribosomes (deglycosylates rRNA) halting protein synthesis and killing the host cell

Pathogenesis

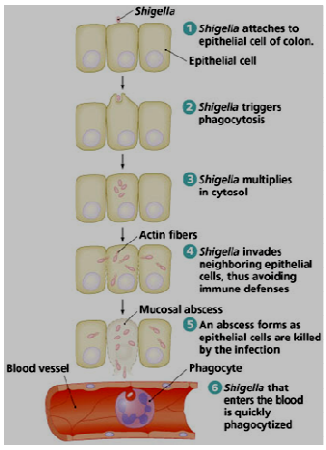
-plasmid-encoded cellular invasion of epithelial cells of the colon (type III secretion system for injection of proteins into host)

- lyse vacuole and replicate in cytoplasm

-use host actin polymerization to move directly from cell to cell cause cell death (cytotoxicity) and ulceration, inflammation

-resistant to phagocytes (intracellular)

-resistant to complement (LPS)



Shigellosis

- Bacillary dysentery
  - most cases *Shigella sonnei*
  - 90,000 cases every year in U.S.
- Sources:
  - human fecal contamination of food, beverages, vegetables, water
- Signs:
  - bloody, mucoid diarrhea, tenesmus, cramps, fever
  - onset: 2 days
  - duration: 5-7 days

Yersinia spp.

Y. enterocolitica

- intestinal infection mostly with zoonotic source (although human to human feco-oral transmission also occurs)
- *enterocolitis* – diarrhea, abdominal pain inflammation, exulceration, fecal leukocytes,
- *mesenteric lymphadenitis* (pseudoappendicitis)

Y. pseudotuberculosis

- intestinal infection from zoonotic source
- *mesenteric lymphadenitis, septicemia*

Intestinal *E. coli* infections

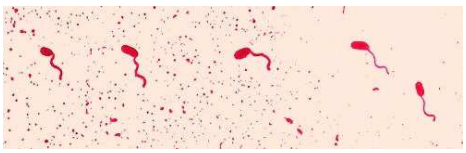
are due to virulence factors mediating
enhaced attachment to or invasion into the intestinal mucosa

E. coli	**disease**	**virulence factor**
EPEC	infanthood diarrhea (enteritis)	pili (EAF, BFP), intimin attaching-effacing
ETEC	travellers' diarrhea, *cholera like*, watery diarrhea (enteritis)	CFA, toxins (LT, ST)
EIEC	*dysentery like* diarrhea (colitis, purulent, bloody stool)	invasion plasmid shared with shigellae
EHEC	hemorrhagic colitis (haemolytic-uraemic syndr.)	verotoxins (Shiga-like toxins)
EAEC	acute and chronic diarrhea (enteritis)	aggregative adhesion fimbriae (AAF)

Toxin producer enteric pathogenes

Vibrio cholerae

- Gram-negative, comma shaped bacterium
- Classification:
- O antigen O1 (Inaba, Ogawa Hikojima serotpyes)
-Biotypes: El Tor and Classic



Pathogenesis

A-B type toxins encoded by phage (lysogenic conversion)
B portion binds to GM1 gangliosides of host cells
A portion ADP-ribosylates stimulatory G protein of adenylate cyclase locking it in „on" form, increases intracellular cAMP
secretion of water and salts into lumen of intestine
absorptive functions intact; no cellular damage

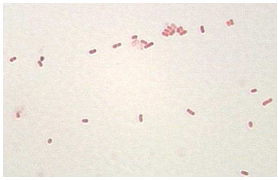
severe - rice water stool, death by dehydration; many cases are asymptomatic-mild

Treatment and control

Treatment
oral or i.v. fluid and electrolyte replacement + antibiotics (tetracycline)

Vaccines
killed cells injected intramuscularly (50 % effectivity),
live, attenuated (not available in US)

Enterotoxinogenic *Escherichia coli* (ETEC) – traveler's diarrhea



- mild to severe self-limiting diarrhea
- contaminated water, vegetables
- adherence factors – pili
- localized to epithelial surface

heat labile enterotoxins (LT) – similar to cholera toxin (antigenically related to cholera toxin) and heat stable (ST) enterotoxin

heat stable enterotoxin (ST) of *E. coli*
is very small protein - single chain peptide
binds quanylin receptor – acts like hormone
increases cyclic GMP
stimulates water and salt secretion

ST, LT of *E. coli* are plasmid encoded

E. coli O157:H7

- Enterohemorrhagic *Escherichia coli* (EHEC)
  - surface proteins; toxin
- Sources
  - undercooked or raw hamburger; salami
- Signs
  - watery or bloody diarrhea, nausea, cramps
  - onset: 2-5 days
  - duration: 5-10 days
- Complication
  - Hemolytic Uremic Syndrome (HUS)
    - acute kidney failure in children
    - life threatening

Pathogenesis

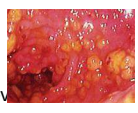
although bloody diarrhea appears like invasive dysentery (e.g., *Shigella*), the bacteria do not invade the epithelium, therefore little fever or pus in stool

secrete a Shiga-like toxin (SLT/Stx) (see Shiga toxin)

SLT may be transported into the blood where damage occurs to endothelial cells of the vasculature or kidneys

C. difficile

- Gram-positive, anaerobic, spore forming rod
- antibiotic-associated pseudomembranous colitis
- enterotoxin and cytotoxin (A/B)
- incubation period: days to weeks after antibiotic therapy
- abrupt onset of bloody diarrhea and fev
- lab.diagnosis: demostration of toxin in the stool, and culture
- treatment: metronidazole, vancomycin

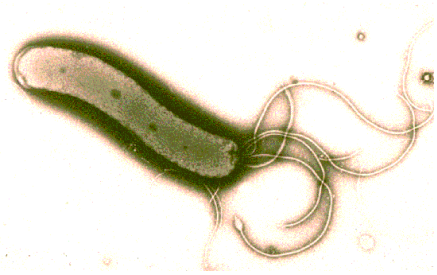


Other enteric pathogenes

Enteropathogenic *E. coli* (EPEC) - diarrhea in infants and children

EPEC adhere through intimate association (attaching-effacing lesion leading to destruction of microvilli)
- plasmid-encoded pili
- injection of bacterial proteins into host epithelial cells (type III secretion)
- one protein acts as receptor for EA factor
- stimulates secretion of ATP - diarrhea

Helicobacter pylori



Gastric and duodenal ulcer - *Helicobacter pylori*
- similar in morphology to *Campylobacter*

- human to human spread

- survives in stomach tissues - urease production neutralizes acid

- apoptosis of T cells, antigenic mimicry - LPS/Lewis antigens

inflammation

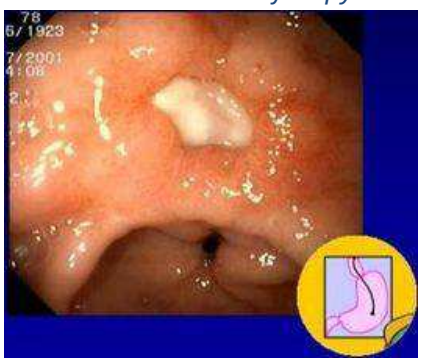
vacuolating cytotoxin

epidemiological association with gastric adenocarcinoma

Diagnosis – biopsy and urease staining, urease breath test, culture

Treatment - multiple antibiotics (metronidazole and amoxicillin) + proton pump inhibitors (omeprasol, lansoprasol)

Gastric ulcer caused by *H. pylori*



Food poisoning

Staphylococcus aureus

- Gram-positive cocci (grape like clusters)

- contamination from infected food handler (human reservoir)

- enterotoxins released into food
  a. heat stable
  b. superantigens

- rapid onset, profuse vomiting, possibly diarrhea, no fever

Clostridium perfringens

- Gram-positive, anaerobic spore forming rod
- lecithinase, capsule, enterotoxin
- rewarmed meat dishes, huged numbers ingested
- incubation period: 8-16 hours
- abrupt onset of profuse diarrhea, vomiting occasionally
- recovery usual without treatment in 1-4 days

Botulism

- *Clostridium botulinum*
  - Gram positive anaerobic spore forming rod
  - neurotoxin leads to flaccid paralysis
  - infants at greatest risk
  - annually: 10-30 outbreaks; ~110 cases (US)
- Sources: home-canned foods, honey (infants)
  - onset: 18-36 hours

Pathogenesis, treatment

botulinum toxin

a. neurotoxin - causes flaccid paralysis by inhibiting release of acetylcholine (no stimulatory signal)
b. A-B type; heat labile
c. encoded on lysogenic bacteriophage

Symptoms
ocular -> pharyngeal -> respiratory paralysis -> death

double vision, drooping eyelids, difficulty speaking and swallowing

Treatment - supportive therapy (respiratory), anti-toxin

other diseases: - infant botulism and wound botulism

Bacillus cereus

- rice-associated diarrhea and vomiting
- Gram-positive rod, aerobic spore forming

- environmental - naturally contaminated rice

- improperly cooked and held at warm temperature enables bacteria to grow

- enterotoxins secreted into food

Can also be produced in intestines after ingestion of vegetative cells during sporulation.

Listeria monocytogenes

- Gram-positive rod, (4 ºC)
- zoonotic
- transmission: unpasteurized milk, cheese, undercooked meet , raw vegetables
- mild, self-limiting gastroenteritis (watery diarrhea, fever, headache, abdominal cramps, little vomiting
- meningitis, sepsis (newborn, immunsuppressed adults)

Vibrio parahemolyticus

- halophilic vibrio
- difficult to grow

- improperly cooked seafood (environmental)
- oyster epidemic summer 1999

cramping, pain, vomiting, diarrhea, self-limiting
virulence factor - hemolysin (Kanagawa factor)
possibly also invasion of epithelium

Vibrio vulnificus

- a Florida and gulf coast specialty
- sepsis and wound infection in susceptible people (e.g., hemochromatosis, liver disease)

- eating raw oysters (environmental) and wound infection

- orally or in wound infection
- highly invasive through tissues and blood

- replicates very rapidly in tissues

Vibrio vulnificus bullous lesions