Infectious & Toxin-Mediated Diarrhea

- Luis S. Marsano, MD
- Professor of Medicine
- Division of Gastroenterology, Hepatology and Nutrition
- University of Louisville and Louisville VAMC

- 2021

Scope of the Problem

47.8 million foodborne-related illnesses occur annually (one out of every six persons) in the United States.

Each year 31 major pathogens acquired in the United States caused 20% of the episodes:

- 9.4 million episodes of diarrheal illness,
- 55,961 hospitalizations, and
- 1,351 deaths.

Each year other unspecified agents resulted in 80% of the episodes:

- ~38.4 million episodes of domestically acquired foodborne illnesses.
- 71,878 hospitalizations and
- 1,686 deaths,

Scope of the Problem

Over 44 million US residents traveled abroad to non-Canadian and non-European destinations in 2014, resulting in:

- 4 to 17 million cases of traveler's diarrhea (TD) based on 10–40% attack rates

The cost of acute and chronic illness attributable to these infections is estimated to be upwards of US $145 billion to the US economy.

Helpful Questions to the Patient with Diarrhea

- **Food ingestion**:
  - **Poultry**: salmonella, campylobacter, shigella.
  - **Ground beef, unpasteurized juice**: Entero-Hemorrhagic E. coli.
  - **Pork**: tapeworm.
  - **Seafood/shellfish**: v. cholerae, v. vulnificus, v. parahemolyticus, salmonella, anisakis, tapeworm.
  - **Cheese, milk**: listeria.
  - **Eggs**: salmonella.
  - **Mayonnaise & cream pies**: S. aureus & clostridium.
  - **Fried rice**: B. cereus.
  - **Fresh berries**: cyclospora.
  - **Canned foods**: clostridium
  - **Spring or contaminated water**: v. cholerae, Norwalk agent, giardia, cryptosporidium.

Helpful Questions to the Patient with Diarrhea Exposure

Pet & livestock: salmonella, giardia, campylobacter, cryptosporidium.

Day-care center: shigella, campylobacter, cryptosporidium, giardia, c. difficile, virus.

Antibiotics, chemotherapy: c. difficile, K. oxytoca (amoxicillin +/- clavunate), c. perfringes (plasmid cpe).

Swimming pool: giardia, cryptosporidium.

Rectal intercourse: N. gonorrhea, N. meningitides, Chlamydia, syphilis, CMV, HSV

Anilingus: all enteric bacteria, virus, and parasites.

Infectious Doses of Enteric Pathogens

• Cryptosporidium parvum	$1\text{-}10^3$
• Entamoeba histolytica	$10\text{-}10^2$
• Giardia lamblia	$10\text{-}10^2$
• Shigella	$10\text{-}10^2$
• Campylobacter jejuni	$10^2\text{-}10^6$
• Salmonella	10^5
• Escherichia coli	10^8
• Vibrio cholerae	10^8

Types of Diarrhea

Non-Inflammatory

Mucosal Penetrating

Inflammatory

Non-Inflammatory Diarrhea

Site, Mechanism, Features, & Pathogens

Site:

- Proximal Small Bowel

Mechanism:

- Enterotoxin/adherence/ superficial invasion

Features:

- *Clinical: Watery diarrhea*
- Laboratory:
  - No fecal WBC
  - Minimal or no Lactoferrin

- **Pathogens**
  (Proximal Small Bowel)
- Salmonella (*)
- E. coli
- C. perfringes
- S. aureus
- Aeromonas hydrophila
- B. cereus
- V. cholerae
- Rotavirus
- Norwalk-like agents
- Cryptosporidium (*)
- Microsporidium (*)
- Giardia
- Cyclospora
- Isospora

(*) Dominant involvement: Proximal small bowel

Mucosal Penetrating Diarrhea

Site, Mechanism, Features, & Pathogens

- **Site:**
  - Distal small bowel
- **Mechanism:**
  - Mucosal penetration
- **Features:**
  - Clinical: Enteric fever
  - Laboratory Features:
    - Fecal mononuclear leukocytes

- **Pathogens**
  (Distal Small Bowel)
  - Salmonella typhi
  - Yersinia enterocolitica
  - Campylobacter fetus

Inflammatory Diarrhea

Site, Mechanism, Features, & Pathogens

- **Site:**
  - **Colon** (dominant involvement)
- **Mechanism:**
  - **Invasion and/or cytotoxin**
- **Features:**
  - **Clinical: dysenteria**
  - **Laboratory Features:**
    - **(+) fecal WBC**
    - **High Lactoferrin**

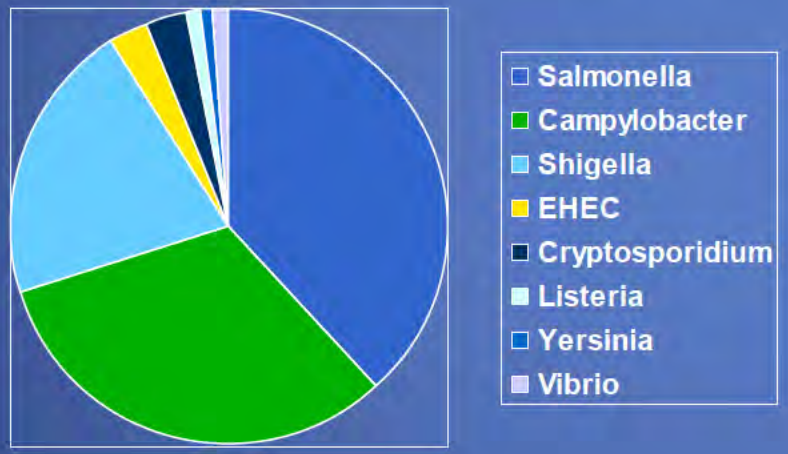
- **Pathogens (Colon)**
- **Campylobacter (*)**
- **Shigella**
- **C. difficile (WBC(+) in 30%)**
- **Yersinia**
- **V. parahemolyticus**
- **Enteroinvasive E. coli**
- **Plesiomonas shigelloides**
- **Klebsiella oxytoca**
- **CMV (*)**
- **Adenovirus**
- **HSV**
- **Entamoeba histolytica (WBC absent b/o destruction)**

* Dominant Colonic involvement

Common Infectious Etiologies

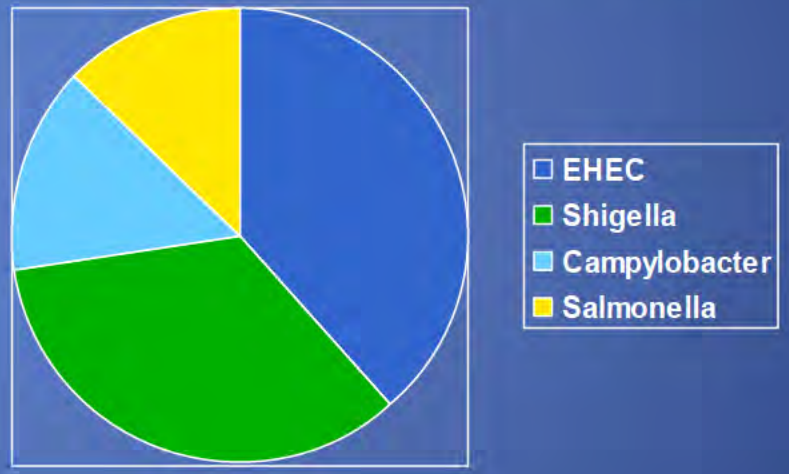
WATERY DIARRHEA

6% of Stool studies (+)



BLOODY DIARRHEA

20-30% Stool studies (+)



Complications & Extraintestinal Manifestations of Infectious Diarrhea

- **V. cholerae, E. coli**: volume depletion, shock & death
- **B. cereus**: Fulminant liver failure
- **V. vulnificus, V. parahemolyticus**: shock & death in: cirrhosis, Fe overload, or alcoholics.
- **C. difficile**: protein loosing enteropathy, toxic megacolon.
- **Enterohemorrhagic E. coli (EHEC)**: HUS & TTP
- **Salmonella**: sepsis, peritonitis, cholecystitis, pancreatitis, osteomyelitis, mycotic aneurism, intraabdominal abscess, Reiter S.
- **Campylobacter**: Guillian-Barre syndrome, Reiter S
- **Shigella**: seizures and encephalopathy, Reiter S.
- **Yersinia**: Thyroiditis, pericarditis, glomerulonephritis, myocarditis, HUS, Guillian-Barre, Reiter S.

ACG Guidelines for Acute Diarrheal Infections in Adults 2016

Stool Testing

- **Stool culture and culture-independent methods** if available **should be used** in:
  - individual patient **at high risk of spreading disease** to others, and
  - **known or suspected outbreaks**.
  - Level: (Strong recommendation, low level of evidence)
- **Stool diagnostic studies may be used** if available in:
  - cases of **dysentery,**
  - **moderate–severe disease, and**
  - **symptoms lasting > 7 days** to clarify the etiology.
  - Level: (Strong recommendation, very low level of evidence)

ACG Guidelines for Acute Diarrheal Infections in Adults 2016

Stool Testing

- **Sensitivity of Stool Test:**
  - Traditional methods of diagnosis (bacterial culture, microscopy with and without special stains and immunofluorescence, and antigen testing) fail to reveal the etiology of the majority (80%) of cases of acute diarrheal infection.
  - **FDA-approved culture-independent methods of diagnosis can be recommended at least as an adjunct** to traditional methods.
  - Level: (Strong recommendation, low level of evidence).

- **Antibiotic sensitivity** testing is **not recommended**.
  - (Strong recommendation, very low level of evidence)

Manufacturer	Test system	Platform	Pathogens detected		Detection time (h)
			Type	No.	
Biofire Diagnostics	**GI Panel**	FilmArray	B, V, P	22	1–2
Luminex	**GPP**	xTAG	B, V, P	15	<5
Nanosphere	EP	Verigene	B	6	2
Hologic/Gen-Probe	ProGastro SSCS	—	B	4	4
BD Diagnostics	EBP	BD MAX	B	4	3–4

FDA Approved Molecular Tests For Enteric Pathogens

- can detect microbes at non-pathogenic levels

FilmArray Gastrointestinal (GI) Panel

Reverse transcription PCR with detection of 22 pathogens in a freeze-dried format in 1 hour

- **Bacteria**
- Aeromonas
- Campylobacter
- Clostridium difficile (Toxin A/B)
- Plesiomonas shigelloides
- Salmonella
- Yersinia enterocolitica
- Diarrheagenic E. coli/Shigella
- Enteroaggregative E. coli (EAEC)
- Enteropathogenic E. coli (EPEC)
- Enterotoxigenic E. coli (ETEC) lt/st
- Shiga-like toxin-producing E. coli (STEC) stx1/stx2
- E. coli O157
- Shigella/Enteroinvasive E. coli (EIEC)
- **Vibrio**
- Vibrio cholerae
- **Virus**
- Adenovirus F 40/41
- Astrovirus
- Norovirus GI/GII
- Rotavirus A
- Sapovirus
- **Parasites**
- Cryptosporidium
- Cyclospora cayetanensis
- Entamoeba histolytica
- Giardia lamblia

Molecular Diagnostic Testing **xTAG GPP** (Luminex)

can detect microbes at non-pathogenic levels

- Bacteria & Toxins:
  - Campylobacter
  - C. difficile toxin A/B
  - E coli 0157
  - Enterotoxigenic E coli L/T S/T (ETEC)
  - Shiga-like toxin producing E coli (STEC) stx1/stx2
  - Salmonella
  - Shigella
- Parasites:
  - Giardia lamblia
  - Cryptosporidium
- Virus:
  - Norovirus GI/GII (Norwalk virus)
  - Rotavirus A

ACG Guidelines for Acute Diarrheal Infections in Adults 2016

Oral Hydration

- Most individuals with acute diarrhea or gastroenteritis can keep up with fluids and salt by consumption of water, juices, sports drinks, soups, and saltine crackers.
  - Level: (Strong recommendation, moderate level of evidence)
- B**alanced electrolyte rehydration (ORS) (Normalyte, Trioral) is preferred in:**
  - 1. **Elderly with severe diarrhea** or
  - **2. Traveler with cholera-like watery diarrhea**.

ACG Guidelines for Acute Diarrheal Infections in Adults 2016

Symptomatic & Empiric Therapy

- **Probiotics or prebiotics** in adults are **not recommended**, except in cases of postantibiotic-associated illness.
  - Level: (Strong recommendation, moderate level of evidence)
- **Bismuth subsalicylates** to control rates of passage of stool in:
  - **travelers** during bouts of **mild-to-moderate illness**.
  - Level: (Strong recommendation, high level of evidence)
- If receiving **antibiotics for traveler's diarrhea**:
  - adjunctive **loperamide therapy** **should be administered** to decrease duration of diarrhea and increase chance for a cure.
  - Level: (Strong recommendation, moderate level of evidence)

ACG Guidelines for Acute Diarrheal Infections in Adults 2016

Empiric Antibiotic Therapy

Do not give empiric anti-microbial therapy for routine acute diarrheal infection, except in:

- cases of TD where the likelihood of bacterial pathogens is high enough to justify the potential side effects of antibiotics.
- Level: (Strong recommendation, high level of evidence)

Use of **antibiotics for community-acquired diarrhea should be discouraged** because:

- Most community-acquired diarrhea is viral in origin (norovirus, rotavirus, and adenovirus) and
- Diarrhea is not shortened by the use of antibiotics.
- Level: (Strong recommendation, very low-level evidence)

ACG Guidelines for Acute Diarrheal Infections in Adults 2016

Evaluation of Persistent Diarrhea

- **In patients with persistent symptoms (between 14 and 30 days):**
  - Recommended:
    - Stool culture and /or culture independent microbiologic studies (if not already done after 7 days of diarrhea)
  - Not recommended:
    - Serological and clinical lab testing.
    - Endoscopic evaluation for cases with negative stool work-up.
  - Level: (Strong recommendation, very low level of evidence)

ACG Guidelines for Acute Diarrheal Infections in Adults 2016

Prevention and Counseling

- **Community Acquired Diarrhea**
  - Patient level counseling on prevention of acute enteric infection is not routinely recommended.
    - May be considered in the individual or close contacts of the individual who is at high risk for complications.
  - Level: (Conditional, very low level of evidence)

ACG Guidelines for Acute Diarrheal Infections in Adults 2016

Prevention and Counseling

- **Travelers Diarrhea:**
  - Individuals should undergo **pre-travel counseling** regarding high-risk food/beverage avoidance to prevent traveler's diarrhea.
    - Level: (Conditional, very low level of evidence)
  - **Frequent and effective hand washing and alcohol-based hand sanitizers** are of limited value but may be useful where low-dose pathogens are expected, as during:
    - cruise ship outbreak of norovirus infection,
    - institutional outbreak, or
    - endemic diarrhea prevention.
    - Level: (Conditional recommendation, low level of evidence)

ACG Guidelines for Acute Diarrheal Infections in Adults 2016

Prevention and Counseling

- **Drugs for Prevention of Travelers Diarrhea:**
  - **Bismuth subsalicylates (**moderate effectiveness): for travelers without contraindications to its use and who can adhere to the frequent dosing. (Pepto-Bismol 2 tab QID; 50% protection)
    - Level: (Strong recommendation, high level of evidence)
  - **Antibiotic chemoprophylaxis** (moderate to good effectiveness): in high-risk groups for short-term use. (Rifaximin 200 mg TID x 14 days; 60% protection)
    - Level: (Strong recommendation, high level of evidence)
  - **Not Recommended: Probiotics, prebiotics, and symbiotic**.
    - Level: (Conditional recommendation, low level of evidence)

Antibiotic Therapy in Diarrhea

Risk of Empiric antibiotic therapy:

- Increases risk of HUS in EHEC (STEC, VTEC), and
- Prolongs shedding of salmonella,
- Do not give when you suspect:
  - C. difficile colitis (targeted therapy is OK), or
  - EHEC, or
  - Salmonella (except in special cases; see later)

Consider antibiotics for:

- Travelers diarrhea with > 4 BM/d, or with fever, blood, pus in stool,
- Diarrhea in immunocompromised
- Diarrhea longer than 7 d (after microbiology studies are sent),
- Diarrhea > 3 days + fever > 101 ^{0}F (after microbiology studies are sent)
- Dysentery (bloody diarrhea) with fever > 101 ^{0}F (after microbiology studies are sent)

Approach to empiric therapy and diagnostic-directed management of the adult patient with acute diarrhea (suspect infectious etiology)

- [a] Antibiotic regimens may be combined with loperamide, 4 mg first dose, and then 2 mg dose after each loose stool,
- not to exceed 16 mg in a 24-h period.
- [b] If symptoms are not resolved after 24 h, complete a 3-day course of antibiotics.
- [c] Use empirically as first line in Southeast Asia and India to cover fluoroquinolone-resistant *Campylobacter* or in other
- geographical areas if *Campylobacter* or resistant ETEC are suspected.
- [d] Preferred regimen for dysentery or febrile diarrhea.
- [e] Do not use if clinical suspicion for *Campylobacter*, *Salmonella*, *Shigella*, or other causes of invasive diarrhea.

Antibiotic[a]	Dose	Treatment duration
Levofloxacin	500 mg by mouth	Single dose[b] or 3-day course
Ciprofloxacin	750 mg by mouth or	Single dose[b]
	500 mg by mouth	3-day course
Ofloxacin	400 mg by mouth	Single dose[b] or 3-day course
Azithromycin[c,d]	**1,000 mg by mouth or**	**Single dose[b]**
	500 mg by mouth	**3-day course[d]**
Rifaximin[e]	200 mg by mouth three times daily	3-days

Antisecretory Drugs

- **Bismuth SS:** will reduce the stools passed by ~40%.
- **Crofelemer** (FULYZAQ):
  - cystic fibrosis transmembrane regulator chloride-channel blocker
  - Effective in some forms of diarrhea including TD and AIDS-associated diarrhea.
- **Zaldaride**:
  - calmodulin-inhibiting drug that has antisecretory properties related to intracellular concentrations of calcium.

Antisecretory Drugs

- **Racecadotril (Hidrasec):**
  - Specific enkephalinase inhibitor that prevents degradation of the endogenous antisecretory peptide neurotransmitter enkephalins that inhibit cyclic nucleotide secretory pathways
  - No effect on gut motility
  - Used successfully in pediatric diarrhea and in adults.

- **Loperamide** works through two mechanisms:
  - Primary effect: production of segmental contraction of the gut, which slows the intraluminal movement of fluids and allows greater absorption.
  - Secondary: inhibition of calmodulin leading to reduced mucosal secretion
  - 4 mg first dose, and then 2 mg dose after each loose stool, not to exceed 16 mg / 24-h period

Viral Foodborne Infections

Specific Causes of Foodborne Diarrhea – Viral

Norovirus / Norwalk Virus

- 40-60% of acute viral gastroenteritis epidemics in older children & adults
- **Pathology:** Villous shortening, crypt hyperplasia, PMN & MN cells in lamina propria.
- **Spread**: person-to-person, contaminated food or water.
- **Incubation**: 12-48 hours
- **Duration**: 12-48 hours
- **Symptoms:** nausea, vomiting, diarrhea, abdominal pain, muscle aches, headache, tiredness and low-grade fever.
- **Diagnosis**: Serology, stool PCR or E/M for stool virus
- **Immunity**: lasts only weeks to 4 months
- **Treatment**:
  - ORS, supportive.

Specific Causes of Foodborne Diarrhea – Viral

Rotavirus

- 60% of diarrhea in children < 2 years-old
- **Pathology:** Kills mature villous-tip cells
- **Spread**: fecal-oral
- **Season**: late-fall, winter, early-spring
- **Duration**: 3-10 days
- **Symptoms**:
  - Diarrhea, nausea, vomiting, cough, rhinitis, otitis.
  - Subclinical in adults.
- **Diagnosis**: Stool antigen (Rotazyme for type A), PCR
- **Treatment**:
  - ORS, supportive.

Specific Causes of Acute Diarrhea – Viral

Other Virus

HSV & CMV:

- May cause proctitis and diarrhea after anal sex.
- Colitis and diarrhea in immunocompromised patients.

Adenovirus, coronavirus, astrovirus, sapovirus.

Foodborne Bacterial Infections with diarrhea due to **Mucosal Invasion**

Specific Causes of Foodborne Diarrhea – Mucosal Invasion

Salmonella Gastroenteritis

- Causes 25-40% of food-borne infections in adults
- **Spread**: food-borne (food, flies, fingers, feces, fomites); meat, poultry, eggs, dairy products.
- **Incubation**: 8-48 hours
- **Duration**: usually 3-4 days (up to 3 weeks).
- **Symptoms**:
  - nausea, vomiting, abdominal cramps, low grade fever < 102 ^{0}F, watery diarrhea; sometimes severe dysenteria.

Specific Causes of Foodborne Diarrhea – Mucosal Invasion

Salmonella Gastroenteritis

- **Complications:**
  - osteomyelitis, septic or reactive arthritis, sepsis, peritonitis, cholecystitis, pancreatitis, mycotic aneurism, intraabdominal abscess, Reiter S.
- **Treatment**: ORS & support. Antibiotics prolong the disease.
  - **Treat with antibiotics only in: immunosupressed, age < 3 mo or > 50 y, hemolytic anemia, surgical prosthesis, valvular heart disease, severe atherosclerosis, cancer, uremia.**
  - TMP-SMX DS p.o. BID x 7 days; 14 days if immunosupressed.

Specific Causes of Foodborne Diarrhea – Mucosal Invasion

Campylobacter jejuni

- Most common cause of bacterial enteritis in many parts of the world.
- More frequent in young children, with secondary infections in household.
- **Spread**: fecal-oral, food-borne, water-borne.
- **Incubation**: 24-72 hours.
- **Duration**: usually 1 week

Specific Causes of Foodborne Diarrhea – Mucosal Invasion

Campylobacter jejuni

- **Symptoms**:
  - prodrome of malaise, coryza, headache, and fever;
  - then colicky periumbilical pain with profuse diarrhea, that improves and then worsens, with WBC's in stool.
- **Complications**:
  - Endocarditis, meningitis, Guillian-Barre, cholecystitis, pancreatitis, septic abortion, glomerulonephritis, reactive arthritis (HLA-B27), Reiter S.
- **Treatment**:
  - Erythromycin stearate 500 mg BID x 5 days

Specific Causes of Foodborne Diarrhea – Mucosal Invasion

Shigella

- **Spread**: person to person; most common in age 6 mo-10 y; adult infected from children. Well water contaminated with feces.
- **Incubation**: 36-72 hours.
- **Duration**: 1-30 days (1 week) without therapy
- **Symptoms**:
  - biphasic illness: fever in 30-40%;
  - cramps & voluminous watery diarrhea for 2-3 days, then dysenteria, with small bloody stool and tenesmus.
  - Cough & meningismus in 40% of small children.

Specific Causes of Foodborne Diarrhea – Mucosal Invasion

Shigella

- **Complications**:
  - Reiter syndrome, HUS, protein-loosing enteropathy, e. nodosum, keratoconjunctivitis, pneumonia, seizures, and encephalopathy.
- **Treatment**:
  - **Treat all patients.**
  - Ciprofloxacin 500 mg BID x 5 days, or TMP-SMX DS po BID x 5 days.

Specific Causes of Foodborne Diarrhea – Mucosal Invasion

Yersinia Enterocolitica

- **Spread**: food-borne (undercooked meats & oysters) & contact with infected pets.
- **Symptoms Children < 5y**:
  - fever, abdominal cramps, diarrhea for 1 or more weeks.
- **Symptoms Children > 5 y**:
  - mesenteric adenitis, or ileitis; sometimes ileal perforation.
- **Symptoms Adults**:
  - acute diarrhea,
  - followed 2-3 weeks later by arthritis, erythema nodosum, or erythema multiformis.
- **Post-infectious complications**:
  - Reiter S., thyroiditis, myocarditis, pericarditis, glomerulopathy, ankylosing spondylitis, IBD, e. nodosum, e. multiformis, & HUS.
- **Treatment**: ORS & support.
  - In septicemia: gentamicin 5 mg/kg iv; 50% mortality despite treatment.

Specific Causes of Foodborne Diarrhea – Mucosal Invasion

Plesiomona shigelloides

- **Source**: contaminated water or shellfish. Common in Japan.
- **Symptoms**:
  - Variable; from watery diarrhea, with abdominal pain, vomiting and fever, to dysenteria and sepsis.
  - Usually self-limited, but 30% have diarrhea > 3 weeks.
  - Sepsis in cirrhosis and immunocompromised.
- **Complications**:
  - Meningitis, osteomyelitis. Endophthalmitis.
- **Diagnosis**: Stool culture or PCR.
- **Treatment**:
  - Treat only in severe (> 8 BM/d) or prolonged disease (> 7 days);
  - Ciprofloxacin 500 mg BID

Foodborne Bacterial Infections with **Toxin Mediated Diarrhea**

Specific Causes of Foodborne Diarrhea – Toxin Mediated

Cholera

- Endemic in the Gulf Coast (Lousiana & Texas)
- Vibrio colonizes small bowel and produces cytotonic toxin, activating adenylate cyclase, causing secretory diarrhea.
- **Spread**: Water or food contaminated with stools.
- **Incubation**: 18-40 hours
- **Symptoms**:
  - vomiting and abdominal distension, followed by diarrhea of > 1 Liter/hour;
  - dehydration & shock.
- **Diagnosis**: Stool culture neutralized by antisera. Stool PCR.
- **Treatment**:
  - ORS; IV fluids only until ORS covers needs.
  - Tetracycline 500 mg QID x 5 days.

Specific Causes of Foodborne Diarrhea – Toxin Mediated

Staphylococcus aureus

- Second cause of food-borne diarrhea in USA (after salmonella).
- **Spread**:
  - Contaminated food with preformed cytotoxic, heat-stable, enterotoxin A.
  - Contamination most common in high salt & high sugar foods.
- **Incubation**: 1-6 hours
- **Duration**: 24-48 hours
- **Symptoms**:
  - Nausea, profuse vomiting, abdominal cramps followed by diarrhea.
  - No WBC in stool.
- **Treatment**:
  - Supportive.

Specific Causes of Foodborne Diarrhea – Toxin Mediated

Enterotoxigenic E. coli (ETEC)

- Major cause of Traveler's diarrhea, and of diarrhea in infants and toddlers in underdeveloped areas.
- Cytotonic toxins (3: one heat-labile, and two heat-stable), activate adenylate cyclase & guanilate cyclase.
- **Spread**: fecal-oral.
- **Symptoms**:
  - Profuse watery diarrhea, with abdominal cramps and nausea.
  - May have low-grade fever.
- **Duration**: 3-5 days
- **Diagnosis**: stool culture and serotype; Stool PCR.
- **Treatment**: ORS.
  - ***Mild***: Pepto-Bismol 2 tab QID, or Loperamide.
  - ***Severe/dysenteria***: Bactrim DS 1 BID x 3d; Ciprofloxacine 500 mg BID x 3 days.

Specific Causes of Foodborne Diarrhea – Toxin Mediated

Enterohemorrhagic E. coli (EHEC)

- **Serotypes:**
  - E. coli O157:H7 (sorbitol negative), & O26:H11,
- **Has shiga-like verocytotoxin I & II**; (STEC or VTEC)
  - cytotoxic to endothelial cells and enterocyte.
- **Sporadic and epidemic illness**.
- **Spread**:
  - Ingestion of contaminated ground beef, unpasteurized milk or apple cider. Lives in the intestine of ruminants.
  - Person-to-person.
- **Symptoms**:
  - watery diarrhea with abdominal cramps and tenderness,
  - followed by bloody stool with low-, or no fever.
- **Complications**:
  - HUS or TTP in 7%.
- **Treatment**: support.
  - Antibiotics increase risk of HUS or TTP

Specific Causes of Foodborne Diarrhea – Toxin Mediated

Clostridium perfringens

- **Source:**
  - Food poisoning due to meats cooked in bulk, with inadequate internal temperature to kill spores, and later inadequate cooling before reheating for consumption. [C. perfringes with **chromosomal** enterotoxin gene (cpe)]
  - C. perfringes can also cause antibiotic associated diarrhea without pseudomembranes (**plasmid** cpe gene).
  - Heat-labile cytotoxic enterotoxin.
- **Incubation**: 8-24 hours.
- **Duration**: 24 hours.
- **Symptoms**:
  - severe watery diarrhea, with intense abdominal cramps.
- **Diagnosis**: c. perfringens enterotoxin in stool, by Latex agglutination.
- **Treatment**:
  - a) Food poisoning: support,
  - b) Antibiotic associated colitis: Flagyl 500 mg po TID x 10 days

Specific Causes of Foodborne Diarrhea – Toxin Mediated

Bacillus cereus - Diarrhea

- **Source**: foods cooked slowly at low temperature, permitting bacterial proliferation.
  - B. cereus colonizes the small bowel and produces heat-labile cytotonic toxin.
- **Incubation**: 6-14 hours
- **Duration**: 20-36 hours
- **Symptoms**:
  - diarrhea and generalized abdominal cramps;
  - vomit is less frequent.
- **Diagnosis**: clinical features
- **Treatment**: ORS, support.

Specific Causes of Foodborne Illness – Toxin Mediated

Bacillus cereus - Vomiting

- **Source**: cooked food that stays unrefrigerated for long time, and has short "final cooking", like "fried rice".
  - Preformed heat-stable toxin
- **Incubation**: 2 hours
- **Duration**: few hours
- **Symptoms**:
  - Vomiting and abdominal cramps.
  - Diarrhea is infrequent.
- **Complications**:
  - Acute liver failure & lactic acidosis due to mitochondrial toxicity from cereulide.
- **Diagnosis**: clinical features
- **Treatment**: support.

Specific Causes of Foodborne Diarrhea – Toxin Mediated

Vibrio Parahaemolyticus

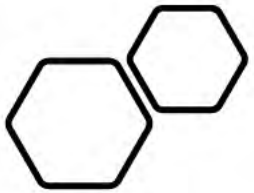
- **Source**: raw or poorly cooked fish or shellfish.
- **Pathogenesis**: variable; cytotonic and/or cytotoxic toxin, and/or mucosal invasion
- **Incubation**: 12-24 hours
- **Duration**: hours to 10 days
- **Symptoms**:
  - Explosive watery diarrhea, abdominal cramps, nausea, vomiting, headache; fever in 25%.
  - Infrequent dysenteria/ bloody stool
- **Diagnosis**: stool culture in TCBS agar medium.
- **Treatment**: support.
  - For prolonged illness: Tetracycline

Specific Causes of Foodborne Diarrhea – Toxin Mediated

Vibrio vulnificus & V. alginolyticus

- **Source**: contaminated seawater or seafood; oysters; Gulf of Mexico, East & West Coast
- **Incubation**: 3-7 days.
- **Symptoms**:
  - Diarrhea, otitis media, cellulitis with myonecrosis or fasciitis.
  - Cirrhotic, immunocompromised host, Fe overload patient, diabetic, & alcoholic: Sepsis, with skin necrosis or bullae in 50-75%; 55% mortality.
- **Diagnosis**: culture from blood or necrotic tissue.
- **Treatment**:
  - Doxycicline 100 mg IV BID + ceftazidime 2 g IV q 8 h, or
  - Ciprofloxacin 400 mg IV BID

Antibiotic Related Diarrhea



Antibiotic Related Diarrhea (ARD)

Enigmatic ARD

Cause: antibiotic drug associated;

- probably carbohydrate and/or bile salt malabsorption due to altered bowel flora.

Frequency: causes 80 % of ARD

Symptoms:

- Watery diarrhea.
- No pseudomembranes nor hemorrhage.

Treatment:

- Discontinue antibiotics,
- Zn supplementation,
- Probiotics (Culturelle – Lactobacillus GG); hydration,
- Loperamide up to 16 mg/d

Antibiotic Related Diarrhea (ARD)

Clostridioides difficile

- Overgrowth of C. difficile during or up to 6 weeks after antibiotics, or MTX, cyclophosphamide, 5-FU.
  - Causes 20% of ARD.
  - 500,000 cases/y with 30,000 deaths/y;
  - 5 billion excess cost/y.
  - Cytotoxic toxin A&B
- **Symptoms**:
  - watery diarrhea (sometimes bloody), abdominal pain, fever, leukocytosis;
  - may have hypoalbuminemia (protein loosing enteropathy).
- **Diagnosis**:
  - Toxin B(+) in stool (EIA, PCR, or cytotoxicity);
  - Flex. Sigm. with typical findings +/- Bx.;
  - WBC in stool may be (-); Stool lactoferrin (+) in 64-77%.

Healthcare vs Community Associated CDI
Site of Onset

Community Onset

Community Onset

Nursing Home Onset

Hospital Onset

Infection by Site of Exposure

Detection of C. difficile

Toxin Assays

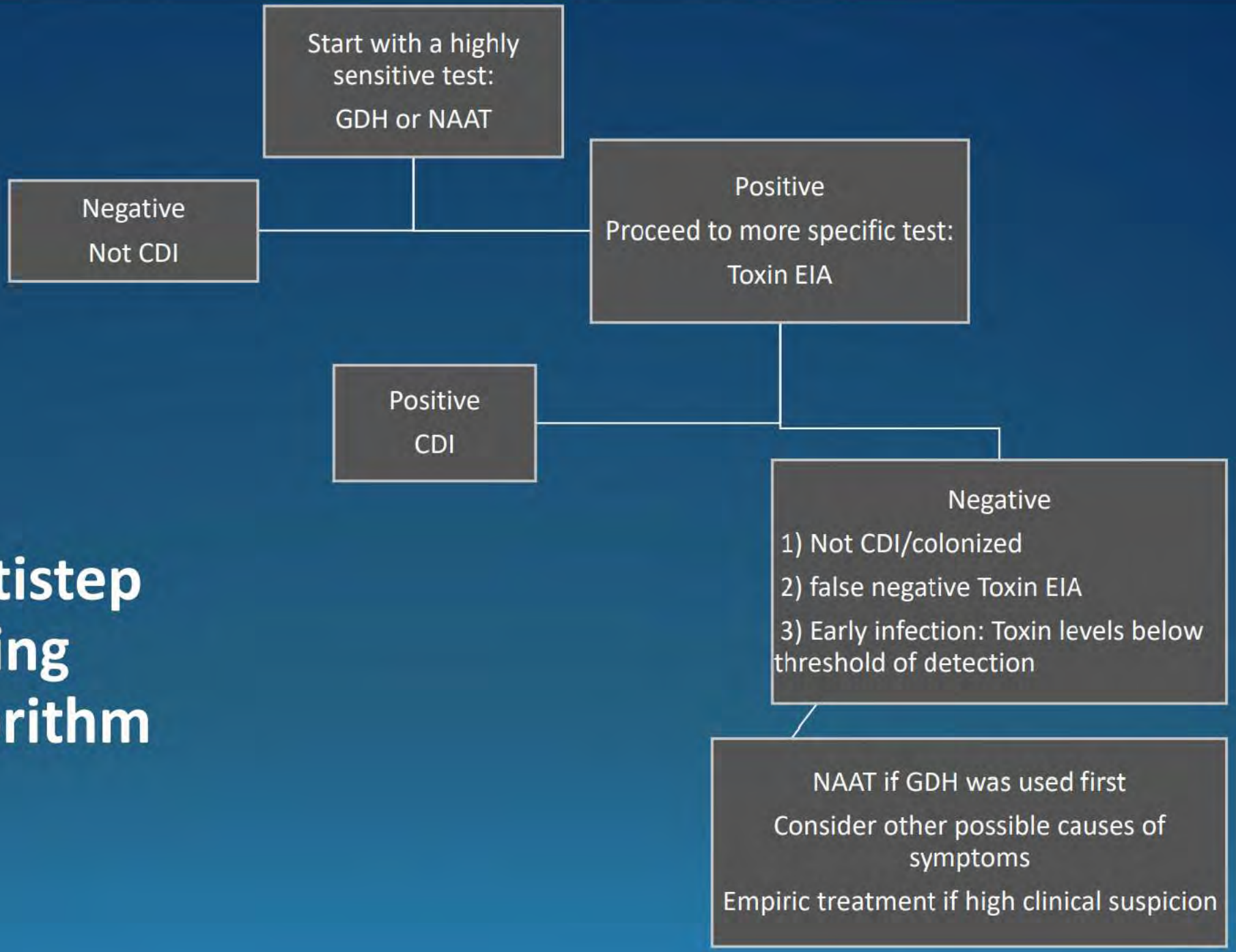
Test	Pro	Con
Cytotoxicity (Gold Standard; tests cytopathic effect)	Very sensitive (10 pg Toxin B) Very specific	Expensive Takes 2 days
EIA toxin A&B	Very specific (>95%) Cheap Takes < 24 h	Low sensitivity (60-90%) (100-1000 pg toxin B)
PCR (tests gene for toxin B)	Rapid (< 4h) Very sensitive Very specific (80-99%)	Expensive Does not differentiate colonization from infection

Bacteria Detection

Test	Pro	Con
GDH (common antigen testing for glutamate dehydrogenase)	High sensitivity Rapid Cheap	Intermediate specificity Does not differentiate colonization from infection
Stool culture (anaerobic stool culture)	Extremely sensitive	Turn over: 3 days Does not differentiate colonization from infection

Use stool toxin test as part of a **multistep algorithm** rather than NAAT alone:
- **Glutamate dehydrogenase [GDH]; if (+), get toxin (EIA);**
- GDH plus toxin (EIA), arbitrated by nucleic acid amplification test [NAAT];
- **NAAT; if (+), get toxin (EIA)**

Multistep Testing Algorithm



European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Guidelines

- No single commercial test can be used as a stand-alone

<u>Recommendations:</u>

- Two step approach (highly sensitive with reflex to highly specific test)
  - First: GDH or PCR testing.
  - Second: EIA for toxin A/B (high positive predictive value)

Antibiotic Related Diarrhea (ARD)

Clostridioides difficile

- **Complications**:
  - Protein-losing enteropathy, ascites,
  - toxic megacolon requiring colectomy;
  - risk high in > 64 y/o, immunosuppression & hospital acquisition.
- **Risk Factors for complicated nosocomial PMC**:
  - WBC > 15 K,
  - Creat > 2 mg/dL (> 1.5 times baseline)
  - (Risk: 0=10%; 1=28%; 2=60%)
- Mortality 16% over expected, due to due to "hypervirulent strain" PMC with "binary toxin" & "deletion in tcdC".
- Mortality due to "Fulminant" PMC: 53% (most within initial 48h)

The Scope of the Problem in IBD

- Prevalence is 2.5-8 fold higher then non-IBD patients
- 10% lifetime risk
- 4.5-fold higher risk of recurrence
- Patients with colitis are at the highest risk.

Sequela Of CDI in IBD

- Exacerbations of IBD
- Increased hospitalizations
- Increased LOS
- Escalation in IBD therapy
- Colectomy
- Higher mortality rates
- Failure of CDI medical therapy
- More CDI recurrences
- Increased health care costs.

Updated Infectious Diseases Society of America guidelines for the treatment of CDI (2018)

Clinical classification	Clinical features	Recommended treatment
Mild or moderate disease	-Diarrhea without evidence of Severe nor Complicated CDI	-Vancomycin 125 mg four times a day x 10 days -FDX 200 mg given twice daily for 10 days -Alternate if above agents are unavailable: metronidazole, 500 mg 3 times per day by mouth for 10 days
Severe disease or with IBD	-Creatinine > 1.5 mg/dL, or -Leukocytosis with a WBC count ≥15 × 10^9/l, or -Abdominal tenderness	-Vancomycin administered orally at a dose of 125 mg four times daily for 10-14 days -FDX 200 mg given twice daily for 10 days
Complicated disease	Any of the following attributable to CDI: -Admission to ICU for CDI -Hypotension +/- vasopressors -Fever ≥38.5 °C -Ileus or significant abdominal distention -Mental status changes -WBC ≥35,000 cells/mm^3 or <2,000 cells/mm^3 -Serum lactate levels >2.2 mmol/l -End organ failure (mechanical ventilation, renal failure, etc.)	-VAN, 500 mg 4 times per day by mouth or by nasogastric tube. -If ileus, consider adding rectal instillation of VAN (500 mg in 100 mL of 0.9% NaCl QID). -Intravenously administered metronidazole (500 mg every 8 hours) should be administered together with oral or rectal VAN (500 mg in 100 mL of 0.9% NaCl QID), particularly if ileus is present

Surgical Management for Severe CDI

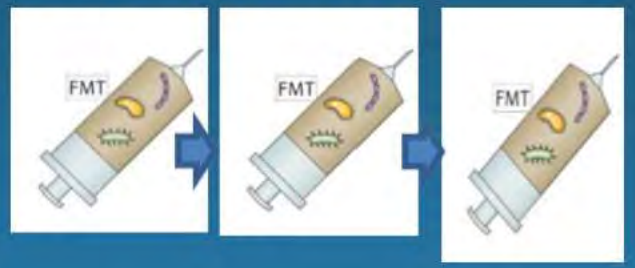
- If surgical management is necessary for severely ill patients:
  - Subtotal colectomy with preservation of the rectum (Strong recommendation, moderate quality of evidence).
  - Diverting loop ileostomy with colonic lavage followed by antegrade vancomycin flushes is an alternative approach that may lead to improved outcomes (Weak recommendation, low quality of evidence)

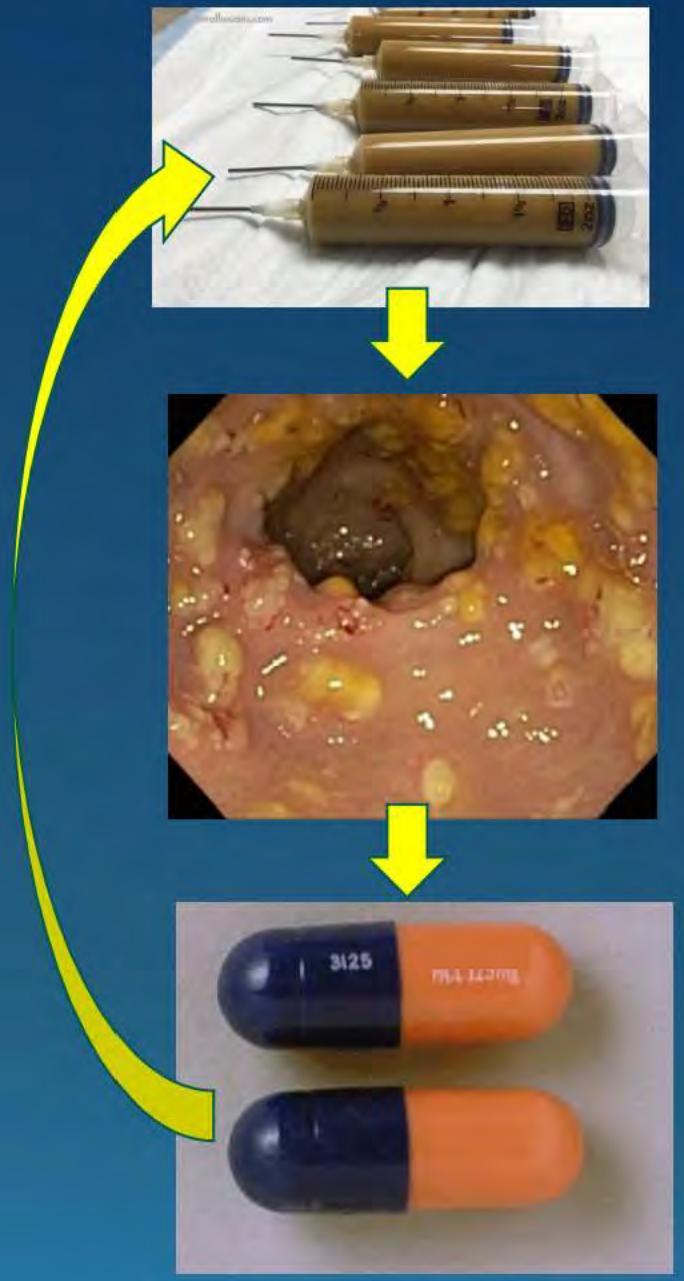
FMT for Acute/Severe and Fulminant CDI

- Consider for patients with severe and fulminant CDI refractory to antibiotics, particularly poor surgical candidates
  - *Strong recommendation, low quality of evidence*

- FMT plus selected use of vancomycin in severe and fulminant CDI inpatients (including 7 toxic megacolon)
  - 91% (52/57) cure at one month
  - No serious adverse events
  - 30 day survival 95%

- Multiple FMTs more effective than single FMT
  - FMT-S 75% cured (21/28)
  - FMT-M 100% cured (28/28)
  - On average # 3 FMTs given





Fischer M. Aliment Pharm Thera 2015; Ianiro Aliment Pharmacol Thera 2018

Special Populations

- *Pregnant, Peripartum, Breastfeeding*: Recommend the use of vancomycin as first-line therapy for treatment of CDI.
- *Immunocompromised*: Recommend the use of vancomycin or fidaxomicin as first-line therapy for treatment of CDI.

Treatment of Recurrent CDI

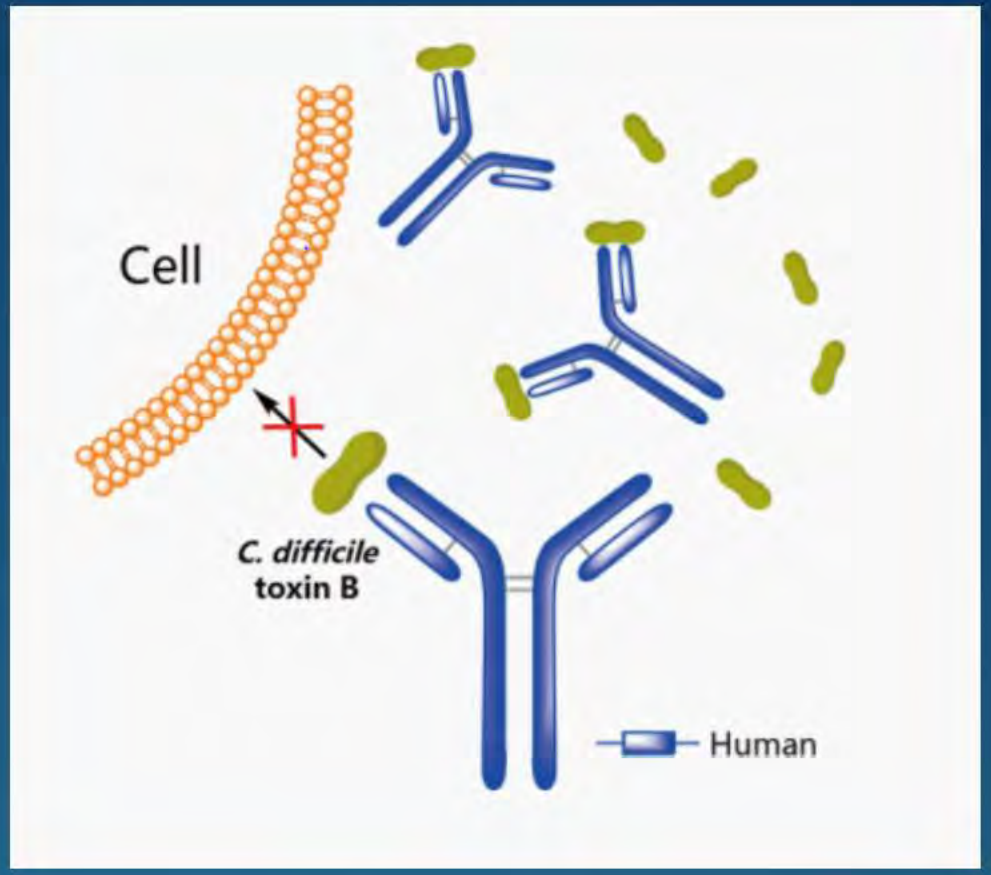
Recurrence Number	Regimen
First Recurrence	-VAN 125 mg given 4 times daily for 10 days, if metronidazole was used for the initial episode. -Use a prolonged tapered and pulsed VAN regimen if a standard regimen was used for the initial episode (eg, 125 mg 4 times per day for 10–14 days, 2 times per day for a week, once per day for a week, and then every 2 or 3 days for 2–8 weeks), OR -FDX 200 mg given twice daily for 10 days, if VAN was used for the initial episode
Second, or Subsequent Recurrence	-VAN in a tapered and pulsed regimen, OR -VAN, 125 mg 4 times per day by mouth for 10 days followed by rifaximin 400 mg 3 times daily for 20 days, OR -FDX 200 mg given twice daily for 10 days, OR -Fecal microbiota transplantation

Suppressive and Prophylactic Vancomycin

- Long-term suppressive oral vancomycin may be used to prevent further recurrences in patients who are not candidates for FMT or fail FMT.
  - *Conditional recommendation, very low quality of evidence*
  - Suggested Dose: 125 mg PO QD (may be increased to BID or TID if needed)
- Oral vancomycin prophylaxis (OVP) may be considered during subsequent systemic antibiotic use in patients with a history of CDI who are at high risk of recurrence to prevent further recurrence
  - *Conditional recommendation, low quality of evidence*
  - Age > 65 or immunocompromised and hospitalized with CDI in past 3 months

Immunotherapy: Bezlotoxumab

- IgG monoclonal antibody to toxin B
  - Single dose infusion ($4000)
  - MODIFY I/II: Recurrence: 16-17% vs 26-28% with placebo (NNT=10)
- Consider for prevention of CDI recurrence in patients who are at high risk of recurrence.
  - *Conditional recommendation, moderate quality of evidence*
- Recommended Patient Population: ≥ 65 years with at least one of these additional risk factors:
  - 2nd episode of CDI within the past 6 months
  - Immunocompromised
  - Severe CDI



Caution in patients with a history of heart failure or severe underlying cardiovascular comorbidities

Wilcox MC NEJM 2017

Treating CDI in patients with IBD

- Individuals with IBD have nearly 5X risk of developing CDI
  - More likely to have community onset, be younger and suffer recurrences.
  - More likely to need escalation of therapy or hospitalization
  - IBD patients hospitalized with CDI have 4X higher mortality than IBD alone
- Recommend CDI testing in IBD patients with an acute flare associated with diarrhea.
  - *Strong recommendation, low quality of evidence*
- Suggest vancomycin 125 mg PO QID for a minimum of 14d in patients with IBD and CDI.
  - *Strong recommendation, very low quality of evidence*
- Consider FMT for recurrent CDI patients with IBD.
  - *Strong recommendation, very low quality of evidence*
- IBD therapy should not be held during anti-CDI therapy in the setting of disease flare, and escalation of therapy may be considered if there is no symptomatic improvement with treatment of CDI
  - Optimize IBD therapy while treating the CDI

Hashash JG. Curr Gastroenterol Rep 2014
Horton HA. Antimicrob Agents Chemother 2014

Bezlotoxumab To Prevent CDI Recurrence in IBD

- A fully humanized monoclonal antibody that binds to C.difficile toxin B
- Indicated to prevent recurrence of CDI
- To be used after a course of antibiotics

- Found to decrease recurrence rates by 10% overall, but 25% in patients with IBD.
  - A single infusion of bezlotoxumab provided a 27.2% absolute reduction (95% CI −57.9, 9.6) in the incidence of rCDI in participants with IBD (50% relative reduction).
  - (26.7% vs 53.8%)

Wilcox et al. NEJM 2017, Kelly et al. Gastro 2018.

How Effective is FMT for recurrent CDI in IBD patients?

Study	N	Inclusion	Delivery	CDI Cure Rate	IBD Flare Rate*
Khalili et al.	35 (22 UC, 13CD)	≥ 2 Episodes	Capsule (77%) Colo (23%)	97%	54%
Newman et al.	56 (28 UC, 28 CD)	Failure after one extended course of antibiotics	colonoscopy	85.7%	25%
Fischer et al.	67 (32 UC, 35 CD)	≥3 Episodes	colonoscopy	79%	17.9%

* Or treatment escalation

IBD Outcomes

- CD cohort:
  - 73.3% (11/15) had IBD improvement
  - 26.6% (4) had no change in clinical scores.
- UC cohort
  - 62% (22/34) had IBD improvement
  - 29.4% (11/34)had no change in clinical scores.
  - 4% (1/34) experienced a *de novo* flare.

Prospective study of 50 patients with IBD + Recurrent CDI (>/= 2) Treated with FMT;
-Evaluation of CDI recurrence Response 8-weeks post-FMT: **8% had Recurrence**
-Evaluation of IBD evolution for 12 weeks after FMT: **see data above**

Allegretti et al. IBDJ 2020

Should PPIs be discontinued?

- Associations between PPI use and CDI (heterogeneity, unknown confounders, lack of dose:response relationships)
  - Hospitalized patients not on antibiotics NNH (range, 202-367)
  - Hospitalized patients on antibiotics NNH (range, 28-50)
- Large RCT of 17,000 patients randomized to pantoprazole or placebo
  - 9 CDI in PPI group, 4 in control group (NS)
- Recommend against discontinuation if there is a valid indication for use.
  - *Strong recommendation, very low quality of evidence*

Moayyedi P Gastroenterol 2019

Fecal Flora Reconstitution (FFR)

Rohlke, F., Surawicz, C. M. & Stollman, N. Fecal flora reconstitution for recurrent *Clostridium difficile* infection: results and methodology. *J. Clin. Gastroenterol.* **44**, 567–570 (2010)

- **Preparation of recipient:**
  - Informed consent
  - The patients' prior treatment regimens (generally vancomycin) is stopped 1 to 3 days before the FFR procedure.
  - Patient is prepped for the FFR with a standard 4.0 liter polyethelyne glycol purge taken the evening before their procedure

Commercial Fecal Microbiota

- Vendor: OpenBiome
- Cost: $ 250/each
- Recommend purchase: 5 doses to decrease shipping cost
- Shipping: 5 days
- Storage: stored in a -20° C (-4° F) freezer, and should only be thawed immediately before treatment
- http://www.openbiome.org/work-with-us/

Antibiotic Related Diarrhea (ARD)

Clostridium perfringes Type A

- Proliferation of C. perfringes type A with **plasmid cpe gene**, after antibiotics
- Causes 5-15% of cases of pseudomembranous colitis.
- **Symptoms**:
  - Watery diarrhea after antibiotics, abdominal pain.
  - May give fever & leukocytosis.
- **Dx**: culture of c. perfringes in stool (plasmid cpe (+)); have to order specifically.
- **Treatment**:
  - discontinue antibiotics.

Antibiotic Related Diarrhea (ARD)

Klebsiella Oxytoca

- Proliferation of K. oxytoca in the colon (downstream from cecum) after antibiotics (usually penicillin derivate +/- clavulanate); toxin mediated.
- **Symptoms**:
  - sudden onset of hemorrhagic diarrhea 3 to 7 days after antibiotics;
  - abdominal cramps, leukocytosis and high CRP.
- **Diagnosis**:
  - Culture of K. oxytoca (have to order specifically)
  - Suggested in colonoscopy by: segmental hemorrhagic colitis (edema + petechiae +/- erosions or linear ulcers; no pseudomembranes), more severe in right side of colon, with rectal sparing.
- **Treatment**:
  - discontinue antibiotics and NSAIDs;
  - resolution in 4 days.

Antibiotic Related Diarrhea (ARD)

Others

Staphyloccocus aureus:

- *(Need to give specific order to culture for S. aureus).*
- *treat with Vancomycin 500 mg po QID x 10 days.*

Salmonella species:

- treat with cipro 500 mg po QID x 5-7 days

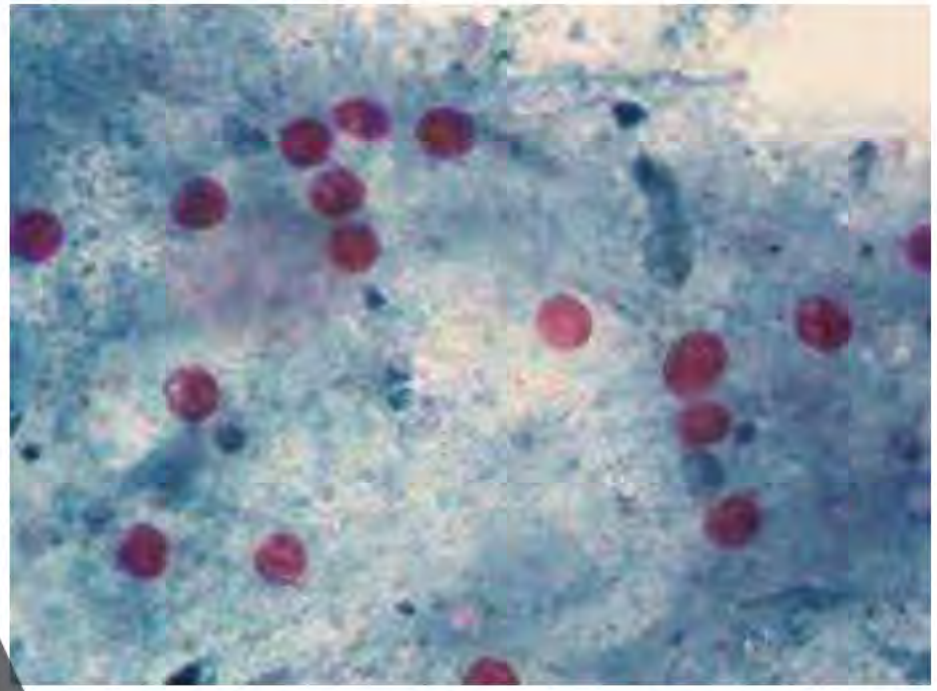
Diarrhea due to Protozoa

Giardia lamblia

- **Prevalence:**
  - healthy adults < 2%; homosexuals 4-18%.
- **Symptoms:**
  - Intermittent bloating and abdominal cramps, with watery and low grade steatorrhea; “sulfuric belching”.
  - Rare fever.
- **Diagnosis:**
  - Giardia Ag in stool; stool PCR
  - Duodenal aspirate, string-test, or Bx.
- **Treatment:**
  - Metronidazole 250 mg po TID x 5-7 days; Quinacrine 100 mg TID x 5 days; Nitazoxanide (Alinia) 500 mg TID x 3 days.
  - Patients with IgA or IgM deficiency need 6-8 weeks of therapy.

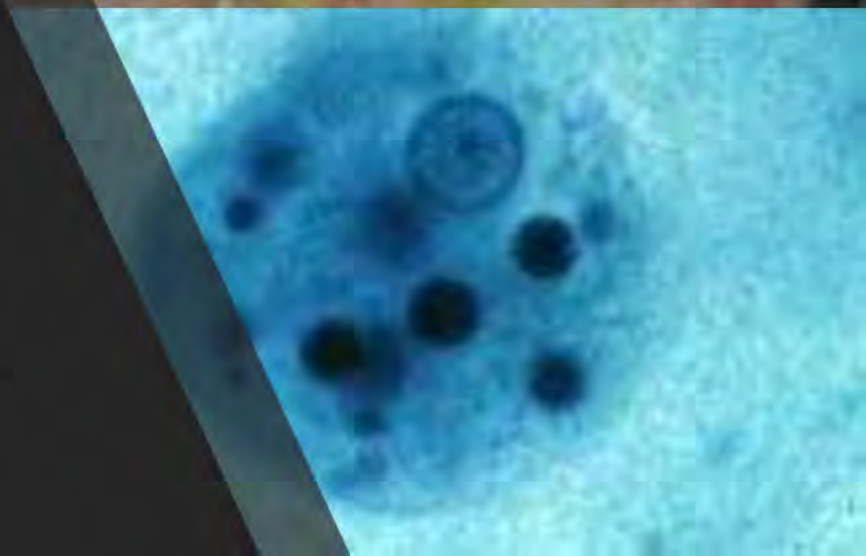
Cryptosporidium parvum

- **Transmission**:
  - usually person-to-person; domestic animal reservoir.
  - causes 4% of acute diarrhea in small children;
  - frequent in AIDS.
- **Symptoms**:
  - a) **Immunocompetent host**: explosive, profuse watery diarrhea, with abdominal cramps; lasts 5-11 days.
  - b) **Immunocompromised host**: extremely severe diarrhea (up to 17 L/day), which may persist for months. Fever in 30%.
- **Diagnosis**:
  - AFB stain or fluorescent Ab in stool; Stool PCR
  - Small bowel Bx.
- **Treatment**:
  - a) Immunocompetent: Nitazoxanide (Alinia) 500 mg TID x 3 days
  - b) Immunosuppressed: Paramomycin 500 mg with food, TID x 2-4 weeks + HAART



Amebiasis
Entamoeba histolytica

- **Prevalence**:
  - 1-5% of US population;
  - 20-30% in male homosexuals.
  - Only Zymodemes II & XI are invasive.
- **Symptoms**:
  - Usually asymptomatic.
  - Bloody diarrhea, fever, abdominal cramps, malaise, and tenesmus.
  - Cecal involvement more common than rectal disease.
  - Infrequent toxic megacolon or perforation.
- **Diagnosis**:
  - Stool Ag. - O&P x 4-6 samples. - Stool PCR.
  - Colonoscopy or Flex. Sigm with Bx (non-specific colitis).
  - Serology (+) in 88% of colitis (99% in liver abscess).
  - Stool WBC usually (-) due to destruction.
- **Treatment**:
  - Metronidazole 750 mg TID x 5-10 d, or Tinidazole 2 gm/d x 3 d, **PLUS**
  - Diloxanide 500 mg TID x 10 d, or Iodoquinol 650 mg TID x 20 d or Paramomycin 25-35 mg/k per day, divided TID, x 7 days



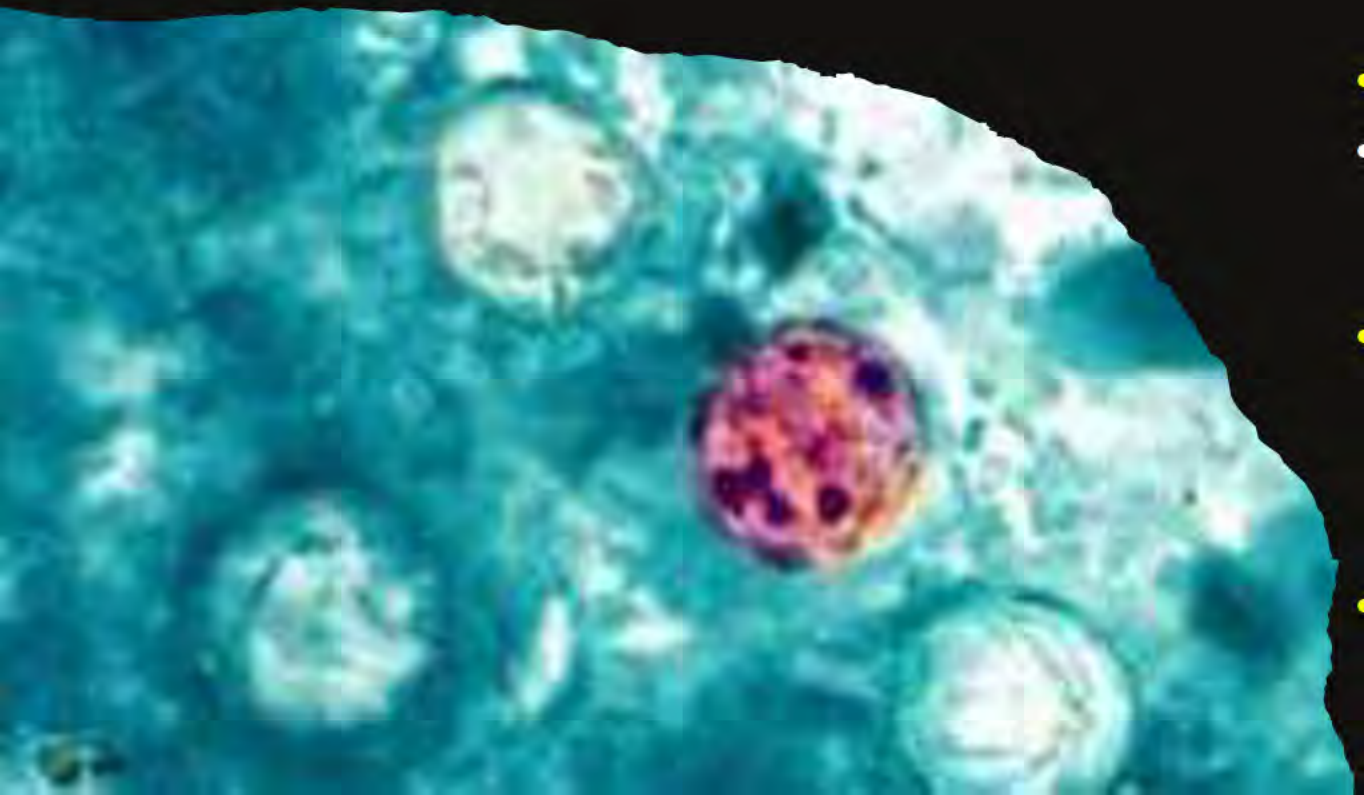
Balantidium coli

- **Source**:
  - ingestion of contaminated short stalk vegetables
- **Symptoms**:
  - frequently asymptomatic;
  - mild to moderate, acute or chronic recurrent diarrhea.
- **Treatment**:
  - Tetracycline 500 mg QID x 10 days

Isospora belli

- **Transmission:**
  - fecal-oral
  - more common in children and male homosexuals.
- **Symptoms:**
  - fever, headache, abdominal cramps, diarrhea with mild malabsorption.
  - In normal host lasts a few weeks;
  - lasts months to years in immunocompromised host.
- **Diagnosis:**
  - duodenal aspirate & Bx.
  - Stool incubated at room temperature x 2 days; then Zn sulfate flotation & AFB stain.
- **Treatment:**
  - Bactrim

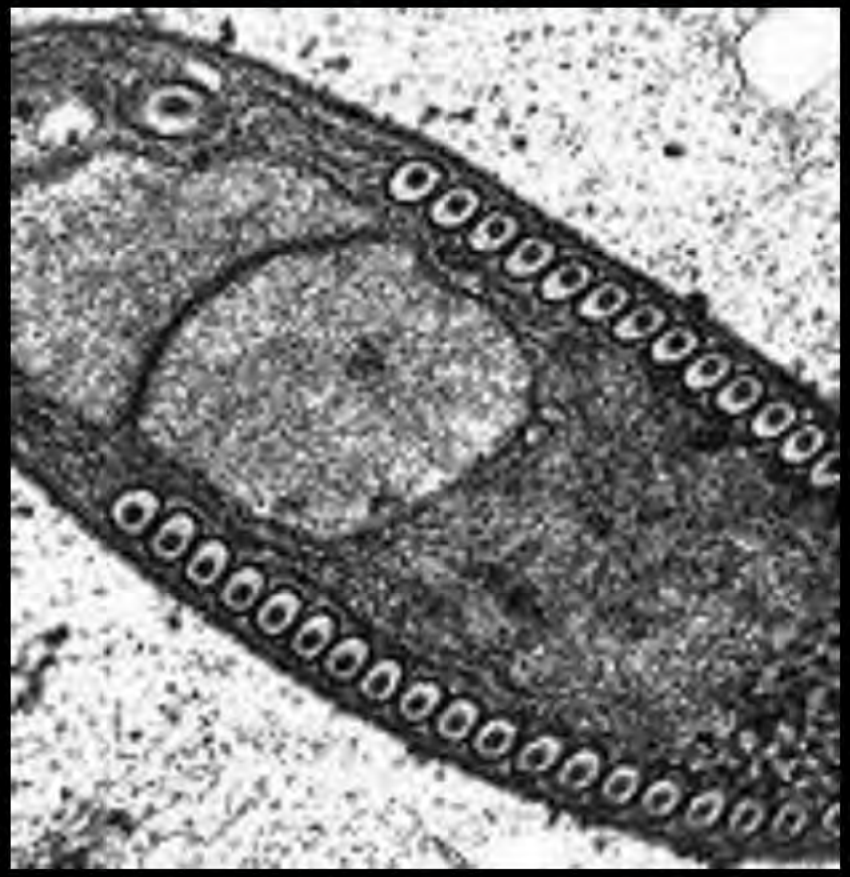
Cyclospora cayetanensis



- **Source:**
  - contaminated fresh berries or water
- **Symptoms:**
  - Abrupt onset of watery diarrhea; fever in 30%.
  - Diarrhea improves in 3-4 days, and then relapses.
  - Anorexia, fatigue, nausea, malabsorption with 5-10% weight loss.
- **Duration:** 2-12 weeks, with abrupt end.
- **Pathology**: Acute & chronic inflammation in distal duodenum, with villous atrophy, and/or crypt hyperplasia.
- **Diagnosis:**
  - spherical 9-10 micron with red stain in AFB. - Stool PCR.
  - Duodenal aspirate (+) in 25%
- **Treatment:**
  - Bactrim DS BID x 7-10 days.

Microsporidiosis
Enterocytozoan bienusi & Encephalitozoon intestinalis

- **Symptoms**:
  - self limited diarrhea in immunocompetent.
  - In immunocompromised gives chronic diarrhea for months.
- **Treatment**:
  - Enterocytozoan bienusi:
    - fumagillin 60 mg/d x 14 days.
  - Encephalitozoon intestinalis:
    - albendazole 400 mg BID x 3-4 weeks.



Foodborne Diarrhea due to Fish & Shellfish associated Toxins

Specific Causes of Foodborne Diarrhea – Toxin Mediated

Ciguatera

- **Cause:** heat-stable Ciguatoxin accumulated in large-fish muscles after eating smaller fish.
- **Geography:** Common in fish from Hawaii & Florida
- **Associated fish**:
  - Barracuda, red-snapper, amberjack, grouper, and goatfish.
- **Onset**: minutes to 30 hours
- **Duration**: 1-9 days; sensory disturbance for months.
- **Symptoms**:
  - nausea, vomiting, cramps, diarrhea, malaise, myalgia, arthralgia, blurred vision, pain in teeth, reversal of hot-cold sensation, sharp pain in extremities, bradycardia; respiratory paralysis in severe cases.
- **Treatment**:
  - Mannitol 20% solution; 1 g/kg IV over 45 min.
  - Gastric lavage and cathartics.
  - Atropine for bradycardia. May need respiratory support.
  - Amitryptiline, gabapentin for chronic neuropathy.
  - Amitryptiline or Fluoxetine for depression and fatigue.
  - Symptoms may recur after eating fish, nuts, caffeine or alcohol.

Specific Causes of Foodborne Diarrhea – Toxin Mediated

Scombroid

- **Cause:** histamine & saurine in flesh of fish by action of marine bacteria
  - Fish tastes sharp and peppery.
- **Geography:** Fish from Hawaii & California.
- **Associated fish**: tuna, mackerel, albacore, bonito, skip jack, mahi-mahi.
- **Onset**: minutes to 2 hours
- **Duration**: 4-10 hours.
- **Symptoms**:
  - flushing, headache, dizziness, burning in mouth, abdominal cramps, nausea, vomiting, diarrhea & bronchospasm.
- **Treatment**:
  - anti-histamines + H-2 blockers, bronchodilators & epinephrine for bronchospasm;
  - cathartics & gastric lavage.

Specific Causes of Foodborne Diarrhea – Toxin Mediated

Paralytic Shellfish Poisoning

- **Cause:** heat-stable saxitoxins, from dinoflagellates, concentrated in
  - bivalved mollusks,
    - worse in "red tide".
    - outbreaks in summer.
- **Geography:** New England, West Coast, Alaska.
- **Onset**: 30 minutes - 3 hours; may be fatal in hours.
- **Duration**: hours to few days.
- **Symptoms**:
  - nausea, vomiting, diarrhea,
  - paresthesia in lips, mouth, face and extremities;
  - dysphonia, dysphagia, weakness, paralysis and respiratory insufficiency.
- **Treatment**:
  - respiratory support;
  - gastric lavage and cathartics.

Specific Causes of Foodborne Diarrhea – Toxin Mediated

Neurotoxic Shellfish Poisoning

- **Cause:** heat-stable brevotoxin, from dinoflagellates, concentrated in
  - Mollusks.
    - Associated to "red tide".
- **Geography:** Gulf Coast, North Carolina, and Florida
- **Onset**: few hours
- **Duration**: hours to days.
- **Symptoms**:
  - Nausea, vomiting, diarrhea,
  - Paresthesias, reversal of hot-cold sensation, ataxia.
  - Respiratory symptoms after aerolization.
- **Treatment**:
  - Symptomatic; IV fluids, cathartics, bronchodilators.

Specific Causes of Foodborne Diarrhea – Toxin Mediated

Diarrheic Shellfish Poisoning

- **Cause:** okadaic acid or dinophysistoxin-1 in
  - mussels, scallops, or clams.
- **Geography:** Described in Japan & Europe;
  - the organism has been found in U.S. coast.
- **Onset**: few hours
- **Duration**: hours to days.
- **Symptoms**:
  - nausea, vomiting, abdominal pain & diarrhea.
- **Treatment**:
  - symptomatic

Specific Causes of Foodborne Diarrhea – Toxin Mediated

Amnestic Shellfish Poisoning

- **Cause:** domoic acid concentrated in
  - shellfish (Razor clams, Dungeness crabs), and
  - anchovies.
- **Geography:**
  - described in Canada;
  - toxin-producing blooms found in Maine & Texas
- **Onset**: few hours
- **Duration**: hours to days.
- **Symptoms**:
  - nausea, vomiting, abdominal cramps, headache, diarrhea, and loss of short-term memory.
  - Anterograde memory deficits may persist for months; neuronal necrosis in hippocampus and amygdala.
- **Treatment**:
  - Symptomatic; cathartics; benzodiazepines for seizures.

Gastro-Intestinal Disease due to Helminths Nematodes, Cestodes, Trematodes

Gastro-Intestinal Nematodes

Ascaris Lumbricoides

- **Organism:** Is a nematode. **Male 15-30 cm**; **female 20-35 cm**.
  - Each female produces 200000 eggs/d that mature in 2-3 wks.
  - Life expectancy 1 y.
- **Magnitude:** 1.3 Billion infected worldwide; 60000 deaths/y.
- **Acquisition & Life Cycle:**
  - Ingestion of eggs in contaminated food;
  - the larva hatch in the duodenum, penetrate intestine wall into blood and lymphatic vessels, then go through the liver, then the heart cavities, then into lung circulation.
  - they then penetrate into alveoli and migrate inside bronchial tree for 20 d;
  - finally enter esophagus and migrate to SB.
  - They mature in 2-3 months an produce new eggs. Infestation can be up to 1000 worms/person.

Ascaris Lumbricoides

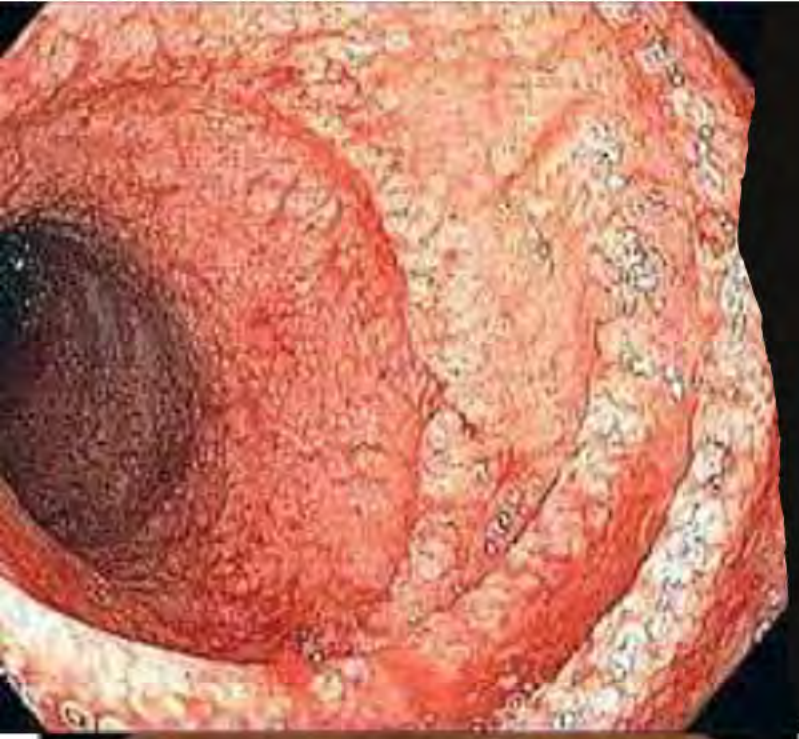
- **Clinical Manifestations:**
  - Initial infection with large number of larva may cause pneumonitis with asthma attacks (Loffler syndrome), and severe eosinophilia.
  - Chronic infestation with large number of worms may cause intestinal obstruction.
  - Intestinal parasitosis causes mild or no eosinophilia.
  - Penetration into appendix may cause appendicitis.
  - Penetration into biliary tree is more common in children and young adults. May cause severe biliary cholic with fever, nausea, and vomiting.
    - Jaundice occurs in 10-20%.
    - Exquisitely tender hepatomegaly develops in 50%.
    - Ascaris can cause rupture of bile duct with bile peritonitis.
    - Rarely they penetrate portal or hepatic veins.
    - Worm embolism to pulmonary artery may occur.
  - Pancreatitis may occur when the pancreatic duct is penetrated.

Ascaris Lumbricoides

- **Diagnosis:**
  - Stool or duodenal aspirate O&P.
  - Contrast X-Ray may show the parasite with contrast inside its own intestine. U/S may show bile duct worm.
  - ERCP may show the parasite in the bile duct. Endoscopy may show adult worms.
- **Treatment:**
  - Mechanical removal of biliary or hepatic worms + Albendazole 400 mg PO x 1
  - In intestinal obstruction, patient are first decompressed with NGT suction, and then one dose of Piperazine 150 mg/kg (max 3.5 gm) is given, followed by doses of 65 mg/kg given then q 12h x 6 doses.
  - Pulmonary disease with Glucocorticoids + Albendazole 400 mg PO and repeat 1 month later.

Strongyloides stercoralis

- **Organism:** Is a nematode that can be free living in the soil (male & female), or a female hermaphrodite in the human duodenum/jejunum; adult is **2-3 mm long**.
- **Magnitude of the Problem:** 35 million infected worldwide.
- **Acquisition & Life Cycle:**
  - Free living adults copulate and produce rhabditiform larvae;
  - they mature to filariform larvae that can penetrate the skin of feet or hands of humans ("ground itch" or "larva currens", advancing 5-10 cm/h), and
  - then enter lymphatics and veins and are carried to the Rt hearth and then to the lungs.
  - then they migrate through the bronchial tree to the trachea and are finally swallowed.
  - Finally, they colonize the duodenum and jejunum.
  - In the SB the female turns hermaphrodite and produces 40 eggs/d.
  - In the bowel the eggs mature to rhabditiform larvae that are excreted, and
  - **sometimes the rhabditiform larvae matures in the bowel into filariform larvae and causes autoinfection, with persistent infection for many decades.**
  - Infestation may persist for 75 years after leaving endemic area.



Strongyloides stercoralis

- **Clinical Presentation:**
  - Most patients are asymptomatic. Some have abdominal pain, weight loss, diarrhea, and even malabsorption. May develop serpiginois urticarial rash in the buttocks from stool filariform larvae re-infecting through the skin (larva currens).
  - HYPERINFECTION: Immunocompromised patients may develop massive hyper-infection syndrome that can be lethal.
  - They have fever, abdominal pain, diarrhea, hematochezia, vomiting, cough, dyspnea, wheezing, hemoptysis, and shock.
  - They may have bacteremia and meningitis.
  - Patients may have mild jaundice, altered mental status, abdominal tenderness, peritoneal signs, and hepatomegaly but no splenomegaly.
  - Sigmoid colon may show hemorrhagic colitis.
- **Laboratory:**
  - Eosinophilia is common but may not be present.
  - Hypoalbuminemia with protein-losing enteropathy, mild elevation of bili, variable elevation of AST, ALT and alk phosph.
  - Blood cultures frequently (+) for gram(-) bacteria.

Strongyloides stercoralis

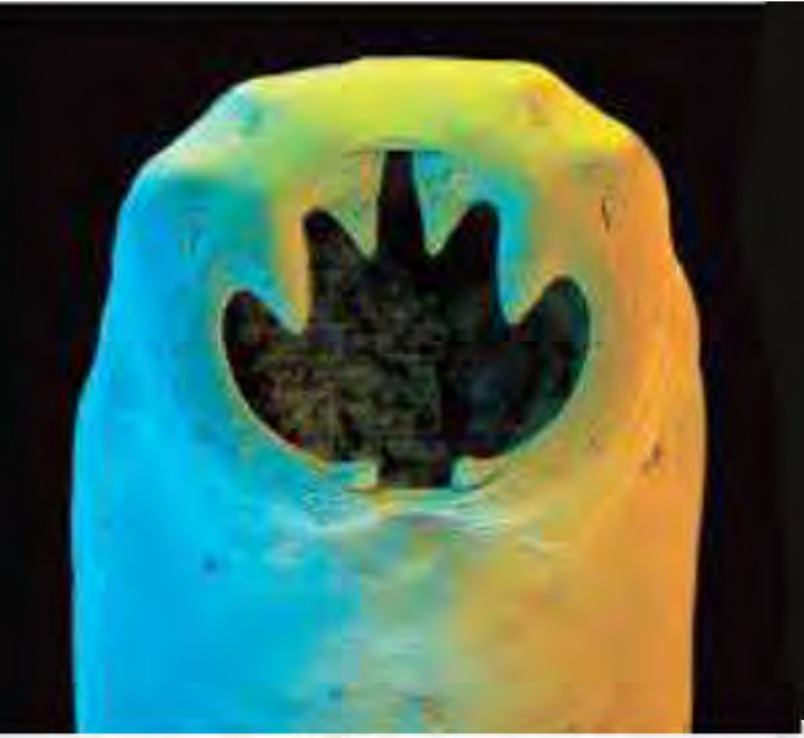
- **Diagnosis:**
  - duodenal aspirate is superior to stool study.
  - May show the parasite, larvae, or less commonly eggs.
  - Larvae may be found in sputum, ascites, urine, or lymph nodes.
  - Serologic tests using crude larval antigens, such as the enzyme-linked immunoassay offered by the Centers for Disease Control and Prevention, have 95% sensitivity but poor specificity to rule out *Strongyloides* infection when microscopic examinations are negative or not performed.
  - PCR in stool, or serum luciferase immunoprecipitation systems to detect IgG antibodies to a recombinant *Strongyloides* antigen (NIE) and *S. stercoralis* immunoreactive antigen (SsIR) has sensitivity and specificity of 100%
- **Treatment:**
  - Uncomplicated disease: Ivermectin 0.2 mg/kg PO, then repeat in 2 weeks.
  - If immunocompromised, give Ivermectin for 2 consecutive days, and repeat 2 weeks later for 2 consecutive days
  - Hyperinfection: Systemic antibiotics plus Ivermectin 0.2 mg/kg PO x >/= 14 days (until stool larva is negative)

Capillaria (Paracapillaria) philippinensis

- **Organism:** very small nematode, **male 3.9 mm**, and **female 5.3 mm**. Endemic to the Philippines and Thailand. Reported in Egypt, Japan, Taiwan, and Iran.
- **Acquisition:** By eating raw fish infested with the parasite. Parasite replicates in the bowel with ever-increasing number of intestinal worms (up to 30000 in 5 months).
- **Life Cycle:** The hosts are birds; in the bird small intestine, the larvae mature into adults. Adult worms mate and female produces eggs or larvae. The bird stool contaminates ponds and rivers and fish eat the worms. Human eats raw fish.
- **Clinical Presentation:**
  - Vague abdominal pain and borborygmi.
  - Patients begin to have diarrhea 2 to 3 weeks after infection.
  - Diarrhea becomes persistent and increasingly voluminous.
  - Patients rapidly waste from escalating steatorrhea and protein-losing enteropathy. Eventually they manifest emaciation, anasarca, and hypotension; diarrhea produces severe hypokalemia.
  - Patients die from cardiac failure or secondary bacterial sepsis usually 2 months after onset of symptoms.

Capillaria (Paracapillaria) philippinensis

- Diagnosis: finding eggs and larvae in stool specimens bur stool examination is not sensitive. Push or balloon endoscopy shows jejunal mucosal scalloping and biopsies of involved mucosa can demonstrate the helminths.
- Treatment: albendazole 200 mg orally twice daily for 10 days or mebendazole 200 mg orally twice daily for 20 days to prevent recurrence. Albendazole is better tolerated.



Necator americanus and *Ancylostoma duodenale*

- **Organism and Scope of the Problem:** Worldwide, an estimated 440 million people are infested with hookworm, usually by N. americanus, A. duodenale, or a mixture of both.
  - Adult male worm measures **7 to 9 by 0.4-0.5 mm**, while the **female is 9 to 11 mm long by 0.4-0.5 mm** wide
  - *N. americanus* predominates in the Americas, South Pacific, Indonesia, southern India, and central Africa.
  - *A. duodenale* is more common in North Africa, the Middle East, Europe, Pakistan, and northern India.
- **Life Cycle:**
  - Infective third-stage hookworm larvae penetrate intact skin, typically between the toes, when walking barefoot on contaminated ground. Larvae migrate through the dermis to reach blood vessels, a migration that can cause a pruritic, serpiginous rash, cutaneous larva migrans.
  - Larvae of *N. americanus* and *A. duodenale* then larvae migrate with venous flow through the right side of the heart to the lungs. *A. duodenale* larvae can arrest their migration and become dormant for many months before proceeding to the lungs.
  - Once in the lungs, larvae penetrate the alveoli and enter the air spaces, after which they migrate up the pulmonary tree, are swallowed with saliva, and pass into the small intestine, where they mature.
  - Mature worms mate and lay eggs. Each female N. americanus lays about 10,000 eggs a day, and each female A. duodenale lays about 20,000 eggs a day.
  - Eggs are deposited with feces in moist, shady soil, where they hatch to release larvae. The larvae molt twice after which they move to the soil surface and await a suitable host.

Necator americanus and Ancylostoma duodenale

- Clinical Manifestations:
  - Light infestations with N. americanus and A. duodenale cause no symptoms.
  - Moderate and heavy hookworm infestation: iron deficiency. Adult worms feed on intestinal epithelial cells and blood.
  - Intestinal blood loss is 0.01 to 0.04 mL/day per adult N. americanus and 0.05 to 0.3 mL/day per adult A. duodenale.
  - With a moderate number of worms, this blood loss becomes appreciable.
  - The average North American diet is high in iron (more than 20 mg/day) so anemia might not develop, even with a burden of up to 800 adult hookworms.
- Diagnosis: Stool exam for eggs in fixed specimen of 3 separate stool samples. Adult may be seen in VCE or Enteroscopy.
- Treatment: Albendazole 400 mg single dose or Mebendazole 100 mg BID x 3 days.

Ancylostoma ceylanicum

- A. ceylanicum have been reported in West New Guinea, Philippines, Taiwan, Thailand, India, Laos, and Malaysia. Has multiple hosts (humans + pets like dogs and cats). Adult worm is **8-10 mm**.
- Clinical manifestations: Light infections with A. ceylanicum can be asymptomatic but heavy infections can cause anemia.
- Diagnosis: Stool parasite eggs x 3 samples. VCE and Enteroscopy may find the parasite.
- Treatment: single dose Albendazole 400 mg PO

Ancylostoma Caninum

- Worldwide distribution. Is the hookworm of dogs and cats.
- *A. caninum* does not fully mature in the human host; eggs are not produced. **Females are 14-16 mm; males 10-12 mm**
- Clinical Presentation:
  - Cutaneous larva migrans, a distinctive serpiginous rash caused by an abortive migration of the parasite in an unsupportive host.
  - Eosinophilic enteritis , although not all eosinophilic enteritis is caused by this parasite. Patients have colicky mid-abdominal pain and peripheral eosinophilia. On endoscopy of the terminal ileum, patients may have scattered small superficial aphthous ulcers and mucosal hemorrhage with mucosal eosinophils; no eosinophils in gastric biopsy.
  - A. caninum also may be a cause of abdominal pain without eosinophilia or eosinophilic enteritis
- Treatment: Empirical Albendazole 400 mg x 1 dose.

Trichuris trichiura (Whipworm)

- Worldwide distribution. An estimated 800 million people harbor T. trichiura . It occurs in temperate and tropical countries and remains prevalent in areas with suboptimal sanitation.
- Organism: The adult is about **4 cm long**. The male has a curled posterior end. Looks like a whip, with the head in the thin end and the reproductive organs in the wide section.
- Life Cycle:
  - Eggs, passed in the feces, contain a zygote and are not infective until embryonation, which takes place in the soil over 2–4 weeks, producing the L1 larva inside the egg.
  - Following human ingestion, the larva is released in the stomach and passes into the intestine. It penetrates the epithelium in the mucosal crypts of the cecum.
  - The larva develops by molting, and the adult develops from the L4 stage, migrating with the epithelial cells up the sides of the crypts in the cecum.
  - Each female produces 3000–20 000 eggs per day; the life expectancy of a worm within the host has been estimated at 1–3 years

Trichuris trichiura (Whipworm)

- Clinical Presentation:
  - Most infections are asymptomatic.
  - In heavy infections, stools become loose and frequent and there is tenesmus.
  - Frequency can exceed 12 stools per 24 hours and nocturnal stooling is especially characteristic.
  - Stools consist largely of mucus but may also be watery. There is a characteristic acrid smell. Frank blood is common.
  - Trichuriasis is frequently identified causes of recurrent rectal prolapse and the worms may be seen on the prolapsed mucosa. Children may have severe anemia and growth-retardation.
- Diagnosis: Stool for parasite eggs x 3 (Kato-Katz technique). Proctoscopy showing worms on the rectal mucosa is more reliable evidence of Trichuris colitis.
- Treatment: mebendazole 200 mg/day on 3 successive days is recommended, or albendazole 400 mg/day for 3 days. Heavily infested patients might require 7 days of treatment.

Enterobius vermicularis (Pinworm)

- Worldwide distribution. Small nematode with **female measuring 9–12 mm** in length and 0.5 mm in width and **male 2.5 mm**. The eggs that are deposited on the perianal skin are immediately infective.
- Life Cycle:
  - Adult worms inhabit the lumen of the cecum and appendix.
  - The life span of the adult female is 4–10 weeks; the adult male, only about 2 weeks.
  - Following fertilization, the gravid adult female migrates from the large intestine onto the perianal skin, where she deposits up to 11 000 eggs by uterine contraction and rupture.
  - The sticky eggs adhere to the anal skin and embryonate rapidly over about 6 hours to reach the infective L3 larval stage, still inside the eggshell.
  - The intense pruritus induced by the adult female and the eggs facilitates fecal–oral transfer of eggs.
  - The minimum interval between egg ingestion and the next egg deposition is between 3 and 4 weeks.

Enterobius vermicularis

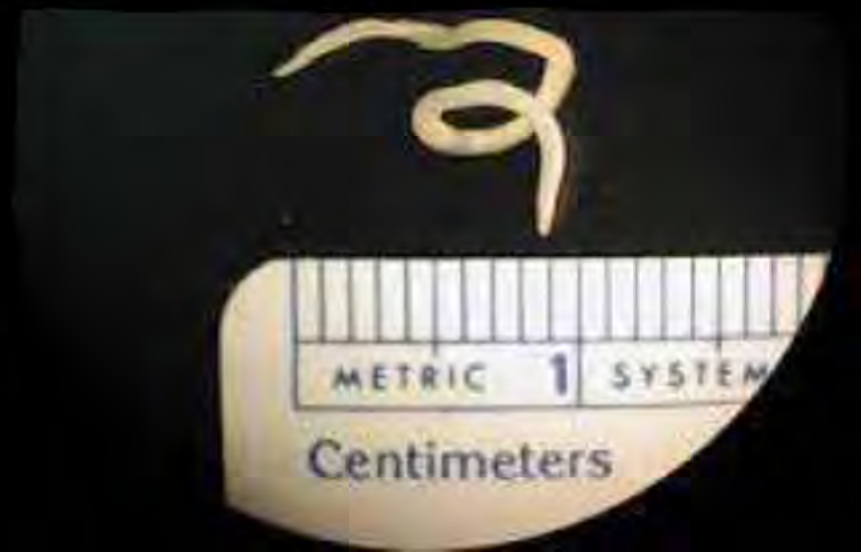
- Clinical Manifestations:
  - The most common is pruritus ani. When very heavy infection is present, an eczematous reaction with bacterial superinfection may occur.
  - Other manifestations include teeth grinding, enuresis, insomnia, nausea, vomiting, abdominal pain, conjunctivitis, and less likely appendicitis.
  - Infection of the female genital tract: vulvar and cervical granulomas, salpingitis, oophoritis, tuboovarian abscess, and peritonitis.
  - Eosinophilic colitis has also been reported and appears to occur early in infection, since only larvae rather than eggs have been identified in such cases.
- Treatment:
  - single 100-mg oral dose of mebendazole or 400-mg oral dose of albendazole.
  - Re-infestation is common, and patients should receive a second treatment after 15 days.
  - All members of the family should be treated and clothes and bed linens should be washed.

Trichostrongyliasis

- The Organism: **Female is 3-10 mm** long, and **males 2-8 mm**. Normal host are herbivorous.
- Distribution: worldwide, but prevalences are highest in the Middle East, the former southern Soviet republics, India, North Africa, Southeast Asia, Japan, Siberia, Central Africa, and central and southern China. Reported sporadic cases are in Australia, Hawaii, the United States, France, and South America.
- The parasite lives embedded in the intestinal mucosa of herbivorous animals worldwide.
  - Trichostrongylus produce eggs that, after passage in feces reach the soil, mature rapidly and hatch into larvae that become infective.
  - Infection is acquired by the ingestion of larvae with soil or more commonly with infected vegetation (grass)
- Clinical Manifestations: Male and female worms live embedded in the small intestinal mucosa where, if in sufficient numbers, they are capable of producing trauma, desquamation of the mucosa, and hemorrhages. Eosinophilia can be very elevated
- Treatment: Pyrantel pamoate is recommended. Alternative agents include mebendazole and albendazole.

Anisakis and *Pseudoterranova* (Anisakiasis and Pseudoterranoviasis)

- Organism: Anisakiasis ("herring worm disease") and pseudoterranoviasis ("cod worm disease"). Adults are **2-3 cm long**.
- Acquisition: by eating raw marine fish in food such as sushi, sashimi, oka, poisson cru, and ceviche.
- Mechanism of Injury:
  - Anisakiasis is mostly a GI tract infection, with rare ectopic locations in the peritoneal cavity, other abdominal organs, and once in the lungs.
  - Usually one larva, uncommonly two and rarely several.
  - The parasite burrows the cephalic end into the GI mucosa. Because humans are abnormal hosts, the parasite dies, producing an abscess characterized by marked inflammation and tissue eosinophilia.
  - This abscess occurs anywhere in the GI tract, often of sufficient size to allow clinical palpation or radiographic imaging. Sometimes the larva reaches the peritoneal cavity, producing an abscess in the omentum, occasionally on the surface of other viscera.

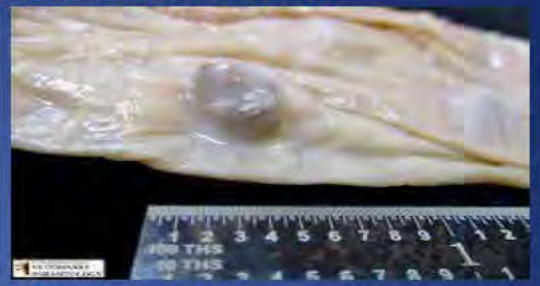


Anisakis and *Pseudoterranova*

(Anisakiasis and Pseudoterranoviasis)

- Clinical Presentation:
  - The main symptoms are abdominal, with epigastric pain accompanied by nausea and vomiting, sometimes with expulsion of the worm.
  - Clinical and radiographic signs and symptoms of intestinal obstruction may be evident, accompanied by diarrhea, followed by normal stools or constipation, and blood and mucus in the stools.
  - Palpation may demonstrate a discrete mass, which in contrast radiographs appears as an intestinal wall defect. The mass and symptoms resolve spontaneously in some instances.
  - Mild fever, leukocytosis, and eosinophilia are usually present, as is a certain amount of peritoneal fluid, which is rich in leukocytes and eosinophils.
  - Endoscopic examination of the stomach and duodenum may reveal a red, bleeding, often-ulcerated lesion, sometimes with the worm at the center attached by its cephalic end to the mucosa, the rest of the body extending into the lumen.
- Treatment: Extracting the worm cures the condition.

Oesophagostomum bifurcum, O. Stephanostomum (Nodule Worm)



- Organism: small nematode; adult measures **1.5-3 cm**.
  - Prevalent in Togo and northern Ghana were 250,000 people infected and at least 1 million at risk.
  - Also found in Uganda, Kenya, Côte d'Ivoire, Ethiopia, Sudan, Guinea, Nigeria, Brunei, Malaysia, Indonesia, and Brazil.
- Infection Cycle:
  - Adult worms live attached to the mucosa of the colon, mate, and produce 5000 eggs per day.
  - Eggs passed in feces mature in soil and produce larvae that enter a new host orally and reach the wall of the large intestine to develop in abscess-like cavity or **nodule of 1-2 cm diameter**.
  - The larvae will mature into adulthood in the nodule and then leave the abscess and attach to the colonic mucosa and produce eggs.
  - The nodules may affect peritoneal surface, omentum, kidneys, spleen, other viscera, and sometimes lesions push into the abdominal wall, where they can be seen and felt as well-demarcated painful tumors.
  - Lesions encountered in the periumbilical area are known as "Dapaong tumor".

Oesophagostomum bifurcum, O. Stephanostomum

Clinical manifestations:

- Abdominal mass, sometimes large or painful;
- Acute intestinal symptoms, often of obstruction, due mostly to peritoneal adhesions.
- Asymptomatic persons, mostly children, may present because of a painless or disfiguring abdominal mass.

Diagnosis:

- Eggs are identical to hookworm eggs.
- A PCR assay has detected O. bifurcum in human feces, and multiplex real-time PCR studies of fecal samples differentiate Ancylostoma , Necator , and Oesophagostomum infections.

Treatment:

- In acute cases, treatment is often surgical, and diagnosis is confirmed by gross and microscopic examination of the removed specimen.
- Albendazole 400 mg po once, is effective against hookworms and Oesophagostomum.
- Pyrantel pamoate is effective against Oesophagostomum , but not against hookworms

Intestinal Cestodes

Diphyllobothrium Species

- The Organism: Fish tapeworm (Diphyllobothrium species) is the largest parasite of humans, reaching lengths of up to 40 feet (**12 m**).
- Prevalence: Trout, salmon, pike, perch, and whitefish all can harbor D. latum .
  - About 20 million people worldwide are infected with Diphyllobothrium species and prevalence seems to be increasing in Russia, South Korea, Japan, and Brazil.
  - Endemic in northern Europe, Russia, and Alaska, but fish tapeworm has been reported in Africa, Japan, Taiwan, Australia, South America, North America, and Canada.
- Life Cycle: Has 2 intermediate hosts.
  - Parasite eggs that reach water embryonate and then release free-swimming larvae called coracidia.
  - Coracidia are ingested by water fleas (Cyclops and Diaptomus) and develop into procercoid larvae.
  - Fish eat these procercoid larvae, and the parasite changes into the infective plerocercoid form.
  - The plerocercoid larva migrates to and embeds in fish muscle and various organs, growing to 2 cm in length.
  - If an infected fish is consumed by another fish, the plerocercoid larva simply migrates into the flesh of the second fish.
  - People acquire the parasite by eating raw or undercooked freshwater fish.

Diphyllobothrium Species

- **Clinical manifestations:**
  - Fish tapeworm is not invasive and usually causes no direct symptoms. The worm obtains nutrients such as vitamin B12 by absorbing luminal contents through its surface. D. latum also produces a substance that splits B 12 from intrinsic factor in the intestine, thereby further preventing host absorption of the vitamin. Rarely, B 12 deficiency is severe enough to result in megaloblastic anemia and neurologic symptoms.
  - Some patients complain of vague abdominal pain and others describe the sensation that "something is moving inside."
  - Others describe bloating, sore tongue, sore gums, allergic symptoms, headache, hunger pains, loss of appetite, or increased appetite.
  - Rarely, mechanical intestinal obstruction may occur as a result of several worms becoming entangled. Diarrhea may also occur.
- **Diagnosis:**
  - Identification of D. latum eggs in stool specimens.
  - Occasionally, diagnosis is made because the patient passes proglottids and brings them in for identification or
  - Worm is seen on endoscopy.
- **Treatment:**
  - Praziquantel is effective in a single oral dose of 10 mg/kg. Patients should be warned that they might pass a rather long worm 2 to 5 hours after taking the medication.
  - Albendazole 400 mg each day for 3 days also kills the tapeworms.

Taenia saginata, Taenia asiatica, and Taenia solium

- **Organism:** Taenia solium is **2-8 m** with 1000 proglotides, T. saginata and T. asiatica are **4-10 m** with 1-2000 proglotides. T. solium and T. asiatica parasite from pork, and T. saginata beef.
- Global distribution with > 50 million infected. Human is the definitive host.
- **Acquisition:**
  - Via ingestion of poorly cooked pork or beef that carries metacestodes (cysticerci);
  - from there the scolex evaginates and attaches to the upper jejunum by its well-developed holdfast organs.
  - After 12 weeks of maturation the scolex neck generates Proglottids that mature and fill with eggs and are replaced by new proglottids.
  - Mature proglotides are eliminated in the stool.

Taenia saginata, Taenia asiatica, and Taenia solium

- **Clinical intestinal manifestations:**
  - Most are asymptomatic. T. saginata, carriers eliminate motile proglottids through migration to the perianal area and appear in their underwear. T. solium proglottids are not motile, and fewer are passed in the stool.
  - Symptomatic patients complain of mild abdominal discomfort, cramps, colicky pain, nausea, vomiting, fatigue, anorexia, and weight loss.
  - Intestinal perforation, intestinal obstruction, pancreatitis, cholangitis, and cholecystitis as a result of aberrant proglottid migration have rarely been reported.
- **T. solium can cause cysticercosis.**
  - Human cysticercosis follows ingestion of eggs from a human tapeworm carrier (fecal-oral route).
  - Eggs hatch in the upper intestines, releasing oncospheres (invasive larvae) that penetrate the intestinal mucosa using their hooklets and excretory proteases, enter the bloodstream, and migrate to the tissues, where they mature into cysticerci.
  - Cysticerci may lodge in skeletal and cardiac muscle, subcutaneous tissue, and even lung tissue, but, in most of these locations, cysticerci cause few symptoms and spontaneously degenerate, which may lead to formation of calcified granulomas.
  - Neurocysticercosis results from the minority of parasites that invade the central nervous system (CNS), including the brain, cerebral ventricles, or eye.

Taenia saginata, Taenia asiatica, and Taenia solium

- **Diagnosis:**
  - Microscopic exam of proglottids and eggs.
  - Stool CoAg enzyme-linked immunosorbent assay (ELISA) for worm somatic or excretory-secretory products is at least twofold more sensitive at identifying human carriers compared with traditional stool examination.
  - Copro-PCR, can make species-specific diagnoses before treatment, using a single fecal sample to detect a T. solium oncosphere-specific protein (100% sensitive and specific).
- **Treatment:**
  - All three forms of human taeniasis can be eliminated (85%–98% efficacy) with a single oral dose of **Niclosamide** (2 g PO) as preferred agent, or praziquantel (5–10 mg/kg PO) x 1 code.
  - Praziquantel presents a small risk that asymptomatic viable brain cysts of T. solium will be activated during treatment, resulting in neurologic sequelae of seizures and headache.

Hymenolepis nana and Hymenolepis diminuta

- They are cosmopolitan in distribution. H. nana is common in warmer climates whereas H. diminuta only occasionally infects humans.
- Organism: H. nana is approximately **5 mm long** and H. diminuta is **3-5 mm**.
- Life Cycle:
  - H. nana is spread from hand to mouth.
  - H. nana eggs are passed in the feces and ingested by a new human or the same host (autoinfection).
  - The embryo hatches in the small intestine and penetrates a villus, where it becomes a cysticercoid larva.
  - Upon maturation, in 3 or 4 days, it emerges from the tissue and attaches to the intestinal mucosa by its scolex.
  - In 2 or 3 weeks, the new worm is producing eggs.
  - Hyperinfection can occur when eggs liberated in the small intestine hatch and immediately penetrate a villus to undergo a new cycle. As a result of hyperinfection, children may harbor many hundreds or even thousands of adult worms.
  - The entire life history from ingestion of the egg to adulthood requires approximately 10–14 days. Eggs are first seen in the stools in approximately 25–30 days.

Hymenolepis nana and Hymenolepis diminuta

- Clinical Manifestations:
  - Most cases are asymptomatic. Young children may develop symptoms when many worms are present.
  - Patients may have loose bowel movements or occasionally frank diarrhea with mucus but no blood. Diffuse, persistent abdominal pain is the most common complaint.
  - Pruritus ani and nasi are occasionally encountered.
  - Many children have sleep and behavioral disturbances that resolve after successful therapy.
  - Serious neurologic disturbances such as seizures have been reported.
  - Many patients with hymenolepiasis have a moderate eosinophilia of 5–10% and skin eruptions.
- Diagnosis: by finding ova in stool.
- Treatment:
  - Praziquantel is the drug of choice and is highly effective in a single dose of 25 mg/kg. It not only eliminates adult worms but also, unlike other anthelminthics, is efficiently absorbed and kills the larval stages (cysticercoids) in the submucosa.
  - Stools of the entire family must be checked before therapy is initiated because other members of a household are commonly infected, and they must also be treated for therapy to be successful.
  - Post-treatment stool examinations should be done after 5 weeks and again after 3 months.

Dipylidium Caninum

- Dipylidium caninum , is a frequent parasite of cats and wild carnivores worldwide. It is an occasional parasite of the small intestine of humans.
- The adult worm is approximately **15–20 cm long** and usually has approximately 60–175 proglottids each with 15-25 eggs.
- Life cycle:
  - The infected cat or human eliminates proglottis in stool.
  - In the soil the eggs are ingested by flea larva.
  - In the adult flea they develop as cysticercoid larva.
  - Human or other carnivore ingests the flea.
  - Cysticercoid larva scolex develops and attach to small bowel.
  - Scolex grows proglottids with eggs.
  - Proglottids are eliminated in the stool.

Dipylidium Caninum

Clinical Manifestations:

- Most common symptom is noting proglottids in stool, which are similar in size and color to grains of rice.
- Some children have intestinal disturbances, including abdominal pain and diarrhea.
- Allergic manifestations such as urticaria and pruritus ani have been reported;
- Intestinal obstruction has been a rare complication.

Treatment:

- Praziquantel 5–10 mg/kg once for both adults and children.
- An alternative therapy is 2 g of niclosamide once for adults and 25 mg/kg once for children.
- Periodic treatment of pets for tapeworm infection and periodic use of insecticides to kill ectoparasites will control the spread of this infection.

Intestinal Trematodes

Fasciolopsis buski

- Largest intestinal trematode that colonizes humans. Adults measure **7.5 cm long and 2 cm wide**.
- Endemic in southeast Asia and Indonesia.
- Life Cycle:
  - Human ingests freshwater plant with encysted metacercaria.
  - Metacercariae excyst in the **duodenum** and attach to the small intestinal mucosa.
  - Within 3 months, they mature to adult flatworms and begin to lay eggs. Lives for 1 year.
  - The eggs pass with feces and, if they are deposited into fresh water, they embryonate.
  - Each egg releases a ciliated miracidium that seeks a suitable snail to infect.
  - The miracidium enters the snail and develops into a sporocyst that asexually multiplies, releasing numerous cercariae.
  - The cercariae swim to freshwater plants, and each encysts to form a metacercaria on the plant's surface, awaiting ingestion by a mammal.
- Clinical manifestations: Usually asymptomatic. Massive infestation can cause diarrhea, abdominal pain and anasarca.
- Diagnosis: eggs in stool.
- Treatment: praziquantel 25 mg/kg given orally once or for 3 doses in 1 day (total 75 mg/kg)

Heterophyes Species

- 10 human species of intestinal fluke in the family Heterophyidae,
  - the three most prevalent are Heterophyes heterophyes , H. nocens , and Metagonimus yokogawai.
  - They measure **1–2 mm in length**, are oval to pear-shaped, and have spiny integuments.
  - Most common in Egypt, Iran, and Sudan, Korea, China, Taiwan, Indonesia, Russia, Japan, Vietnam and the Philippines.
- Life Cycle:
  - Infection acquired by eating raw or incompletely cooked freshwater or brackish water fish infested with cysts.
  - In the small intestine they excyst and complete their development to adult flukes within 1–2 weeks.
  - Infected adult eliminates operculate eggs in the stool that are difficult to speciate.
  - The eggs are embryonated when passed and are ingested by a snail intermediate host.
  - Cercariae from the snail enter freshwater fish, encyst as metacercariae.
  - Fish is eaten eaten raw and continues cycle. Adult lives up to 1 year.

Heterophyes Species

Clinical Manifestations:

- Symptoms begin 9 days following ingestion of the metacercaria, with dyspepsia, and colicky abdominal pain, diarrhea, and eosinophilia. A mild focal inflammatory reaction and superficial erosions are produced at the site of attachment.
- The fluke may penetrate the mucosa, and eggs may embolize from these intramucosal sites via lymphatics to the systemic vascular system.
- Eggs have been found in capillaries of brain, heart, lungs, spleen, and liver, where space-occupying granulomatous lesions induce clinical pathology.
- Myocarditis can follow the occlusion of myocardial vessels by eggs and the resultant granulomatous and fibrotic host reaction. Thickened mitral valves containing ova has been reported

Treatment: Praziquantel 25 mg/kg TID x 1 day

Echinostoma Species

- Are primarily parasites of birds and mammals but are common among certain populations of Asia.
  - Fifteen species have been reported in humans.
  - Measure **5–15 × 1–2 mm**.
  - Most common in Philippines and Thailand and less commonly in Southeast Asia, eastern and South Asia, Egypt and Central and South America. Usually fro eating undercooked snails, clams, tadpoles, frogs, and fish.
- Life Cycle:
  - Infected mammal or bird eliminates eggs in the stool.
  - The eggs embryonate in freshwater in 14 days, and the miracidia enter the snail host.
  - Cercariae emerge from the snail and encyst as metacercaria in the same snail from which they emerged or in other snails, clams, fish, or tadpoles, which serve as second intermediate hosts.
  - Any of these, if eaten uncooked, the matacercaria infect the human final host
  - Metacercaria attaches to small intestine wall and matures into a fluke and produces eggs.

Echinostoma Species

Clinical manifestations:

- Flukes attach to small intestinal mucosa, producing inflammatory lesions and shallow ulcers at the sites of attachment.
- Symptoms are rare in any but the heaviest infections (approximately 500 flukes), which are uncommon.
- The presentation may include colicky abdominal pain and loose bowel movements and at times diarrhea and eosinophilia.

Diagnosis:

- Diagnosis is by finding eggs in the stool or adults on endoscopy.
- Echinostoma eggs resemble those of F. buski but are smaller.

Treatment: Treatment is one 25 mg/kg dose of praziquantel given orally once, or 3 times (75 mg/kg).

Gastrodiscoidiasis

- G. hominis inhabits the cecum and ascending colon.
  - Adult of G. hominis are large flukes **(8–14 × 5.5–7.5 mm).**
  - Seen in Southeast Asia and sporadically in Guyana, Zambia, Nigeria and the Volga Delta in Russia.
- Gastrodiscoidiasis is a foodborne disease associated with the consumption of water plants or even animal products such as snails.
- Life Cycle:
  - Unembryonated eggs are laid, and in a freshwater environment, the miracidium hatchs and infects the first intermediate host Helicorbis coenosus.
  - After the development of mother and daughter rediae, the cercariae actively emerge from the snail to encyst in aquatic plants, snails, tadpoles, frogs or crayfish.
  - Definitive host becomes infected after swallowing metacercariae with contaminated vegetables or raw or undercooked crustaceans, molluscs or amphibians

Gastrodiscoidiasis

Clinical Manifestations: Headache and epigastric pain are possible reactions to metabolites released by the parasite.

Diagnosis: eggs in the stool or parasite seen in endoscopy.

Treatment: Praziquantel x 25 mg/kg/day x 3 doses, or soapsuds enemas.

Thank you for your attention