Infections of the GI Tract

ACOI Board Review 2020

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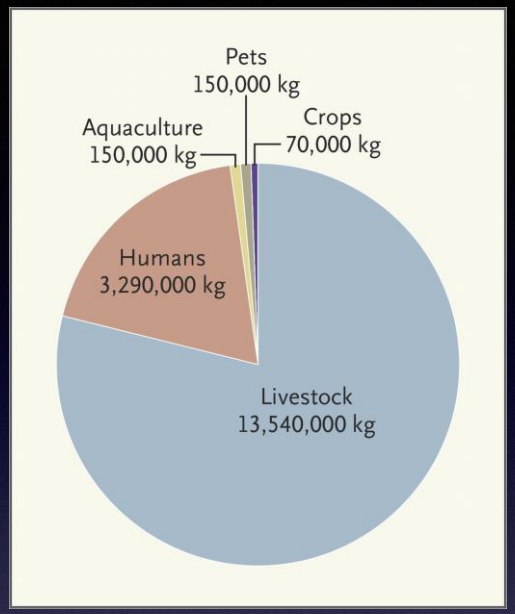
Foodborne illness

- At least:
  - 48 million cases/yr in U.S.
    - 128,000 hospitalizations
    - 3000 deaths
- No pathogens identified in most cases
- leafy green vegetables most common source, (including recent outbreaks of E. coli 0157:H7 in Canada and U.S.)
- Prevention: food irradiation

in the U.S. ….



Hollis A, Ahmed Z. N Engl J Med 2013; 369:2474-2476.

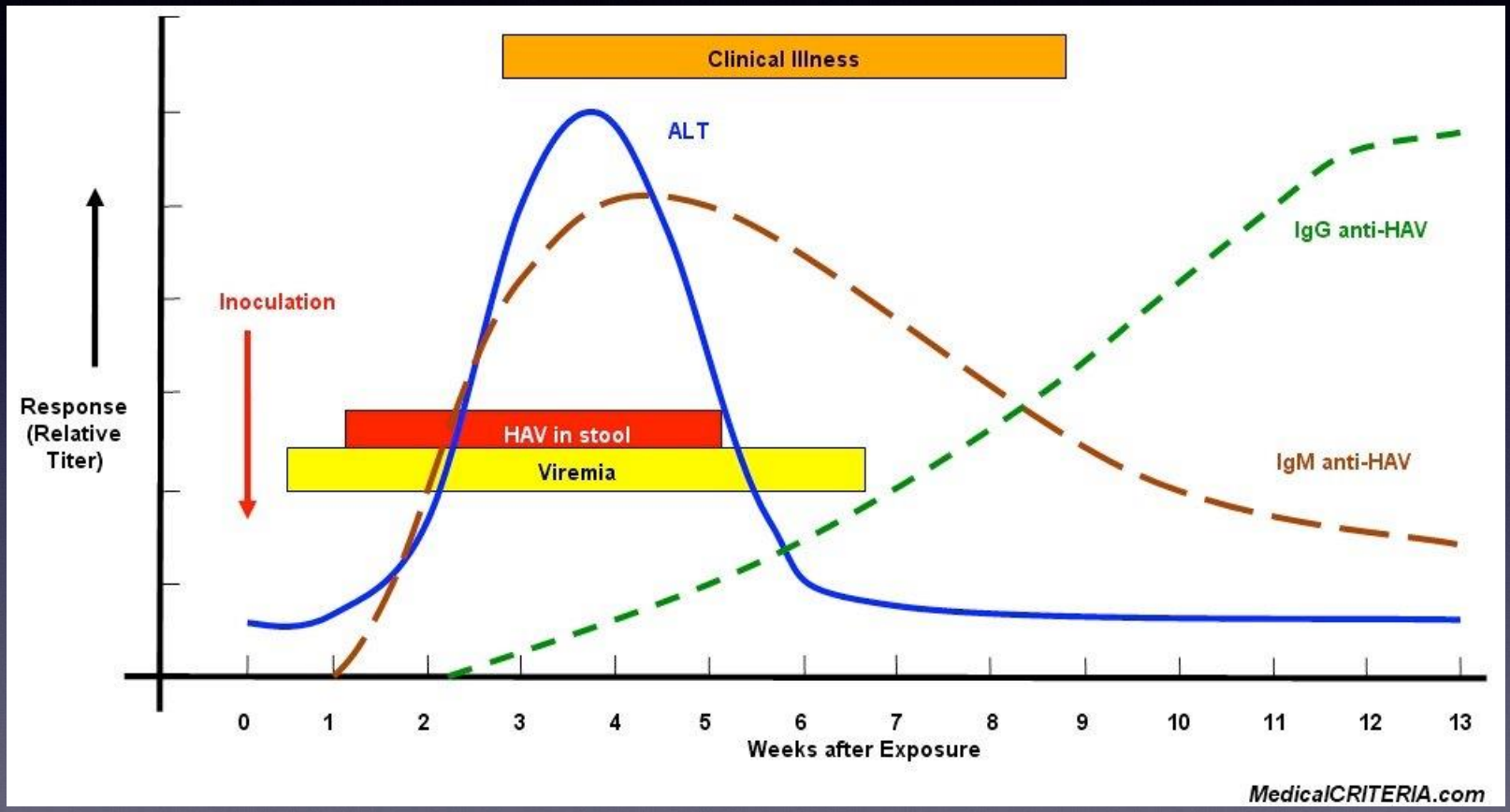
Hepatitis A

- RNA virus spread by fecal/oral transmission (e.g., food handlers), including contaminated food/water
- Tradtionally, greatest risk for U.S. citizens: international travel (1/2 of cases)
- Incubation period: ~30days (range 15 - 49 days)
- Dx: IgM anti-HAV ab
- Contagiousness: from incubation period until 1 week after jaundice appears
- Tx: supportive, including hydration

Hepatitis A

- **New** - recent and ongoing outbreak prevalent in:
  - MSM
  - homeless
  - drug abusers (not necessarily intravenous)
- “point-source” [fomites; person-to-person (hygiene?)]
- more severe illness than usually described
- higher mortality than usually described
- Prevention: vaccine
  - Passive immunization w/ immune globulin w/in 2 weeks of exposure, though efficacy unclear

Hepatitis A


Clinical Illness
ALT
IgG anti-HAV
Inoculation
Response
(Relative
Titer)
HAV in stool
Viremia
IgM anti-HAV
0
1
2
3
4
5
6
7
8
9
10
11
12
13
Weeks after Exposure
MedicalCRITERIA.com

Hepatitis E

- Most common cause of acute hepatitis/ jaundice in the world
- 20,000,000 infections annually
  - 3.4 million cases of acute hepatitis; 70,000 deaths
  - 21% of adults in U.S. are seropositive
- 4 genotypes; 2 very different epidemiologic patterns of disease
- best known for association w/ fulminant hepatitis / death in pregnancy

Clostridium difficile

- Both nosocomial and “community-associated” diarrhea
- 3 toxins:
  - A (presence of anti-toxin A ab in pt may be protective)
  - B - essential for virulence. Anti-toxin B abs protect against recurrence [Dx: Cytopathic effect of toxin B (“Gold standard”); multiple other tests now available, including PCR]
  - Binary - unclear significance
- Colonization may protect against infection due to either immunity or non-toxin producing strains
- NAP1/027 strain may cause more severe dx due to deletion of gene controlling toxin production

Loo et al NEJM Nov. 3, 2011

C. difficile

- Acquisition of C. diff spores
  - Prior or current hospitalization
  - Exposure to infant carriers or infected adults
  - HCW use of alcohol-based agents rather than soap and water
- Older age
- Antibiotics (particularly quinolones, clindamycin, 3rd and 4th generation cephalosporins)
- Feeding tubes, GI surgery, kidney disease
- Chemotherapy, organ transplant
- PPI's, NSAIDs
- Inability to generate antibodies to toxins
- trehalose (a sugar used as a food additive)? - believed to support the growth of C. diff

- Dx: (challenging) if PCR alone - high false + rate
- Tx:
  - p.o. metronidazole only for mild illness and no longer "preferred" for first line rx
  - p.o. vancomycin for more severe disease (may also be better than metronidazole for mild dx)
  - Fidaxomicin (Dificid®) $$$$ (decreases relapse rate in non-NAP1/027 strains)
- Life threatening:
  - I.V. metronidazole + p.o. vancomycin at higher dose
  - Vancomycin via cecostomy tube or retention enema
  - Colectomy

- Relapse: optimal approach not clear (Note: 20 - 35% risk of 1 relapse; if this occurs, ~60% risk of additional relapses)
  - Fidaxomicin (Dificid®) $$$$ (for NAP1-negative strains)
  - Repeat original rx?; longer courses?; tapering doses?
  - Saccharomyces boulardii lyo (Floristor ®)? or other probiotics (Note: DO NOT use this or other probiotics if pt is on chemotx)
  - Rifaximin (Xifaxan ®); Nitazoxanide (Alinia ®)
  - IVIG
  - Fecal transplant - optimal route?
  - Monoclonal antitoxin ab, e.g. Bezlotoxumab, when added to conventional tx, may decrease relapse rate somewhat (Wilcox et al. NEJM 2017)
  - Tigecycline (Tygacil ®)

Noroviruses

"Winter Vomiting Disease"

- 2/3 of all food-borne illnesses; water sources as well. Often affect **cruise ships**, ECFs
- Majority of (presumptive) viral gastroenteritis outbreaks in adults; extremely high attack rate, w/ secondary transmission as high as 90%
- 10^6 - $5x10^9$ viral particles/gm of stool
- Infectious dose: 18 - 1000 particles
- Person to person spread; contaminated food, water, environmental surfaces, vomitus
- Viral shedding may precede illness and continues after recovery
- 1/3 of infected persons may be asymptomatic

Noroviruses

- Virus persists on environmental surfaces; alcohol-based sanitizers may be sub-optimal
- Acute onset N/V, non-bloody diarrhea, lasting 12-72 hrs
- Fever (50%), myalgia, headache
- 12 - 48 hr incubation
- Dx: clinical, PCR
- Multiple strains - no cross protection; new pandemic strains every 2 - 4 years
- No long term immunity, though some individuals may be genetically resistant to at least some strains

Glass et; NEJM Oct. 29, 2009

S. aureus (Preformed Toxin)

- Severe vomiting w/in 4 - 6 hrs; minimal diarrhea
- Fever uncommon
- Egg products, cream, mayonnaise (potato salad)
- Foods w/ high salt/protein content, including pork, particularly ham
- (Preformed) toxin is heat stable; cooking does not prevent illness
- Tx: supportive

Bacillus cereus (PreformedToxin)

- Short and long incubation syndromes
- Short incubation (1 - 6 hrs); ~ S. aureus:
  - ingestion of preformed toxin (heat stable)
  - profuse vomiting; minimal diarrhea
  - fever uncommon
  - commonly from fried rice
- Tx: supportive

Traveler's Diarrhea

- Usually enterotoxigenic E. coli
- Contaminated food or water
- 12 hr to several days incubation
- diarrhea predominates
- Prophylaxis:
  - Pepto-bismol ®
  - rifaximin
- Tx: rifaximin or.....
  - quinolones (Mexico); macrolides (Asia)

Vibrio cholerae

- Contaminated water/poor sanitation
- Following an earthquake, huge outbreak in Haiti, imported by U.N. relief workers. Catastrophic outbreak, contributing to huge, ongoing humanitarian crisis in Yemen
- Massive amounts of painless, odorless diarrhea - “rice-water” stools
- Toxin mediated
- No fever
- Tx: hydration/electrolytes; doxycycline, azithromycin, quinolones; phage therapy

Listeria monocytogenes

- Gram + rod
- 24 hr incubation w/ fever, headache, abdominal pain and diarrhea
- For Boards, -> meningoencephalitis in immunocompromised patients, including extremes of age, cell-mediated immunodeficiencies, pregnancy, HIV
- Unpasteurized/contaminated dairy products; raw milk
- Hot dogs, deli meats, Mexican - style cheeses, cantaloupes, avocados
- Grows well at low temperatures - “leftovers”
- Tx: supportive for GI illness, though some give abs to prevent CNS dx in high risk pts

E. coli 0157:H7 (Shiga toxin)

(and other, toxin-producing similar strains)

- Undercooked hamburger; apple cider, raw milk, sprouts, Romaine lettuce, visitors to dairy or "petting" farms (New: flour!)
- 3 - 4 day incubation period
- Bloody diarrhea (> 90% of cases) w/ severe abdominal pain
- Usually no fever
- TTP in adults; T.T.P.-H.U.S. in 10% of infected children < 10 y.o.
- Tx: controversial whether abs make things worse; therefore, supportive - NO ABS - especially QUINOLONES, NO anti-motility agents

Shigella

- Fecal - oral transmission
- Often acquired outside the U.S., e.g. cruise ships
- High attack rate w/ secondary person-to-person spread common [due to low # organisms (<200) necessary to cause dx]
- Bloody, mucousy stools; fever, cramps, tenesmus
- If bacteremic -> think HIV

Shigella

- Usually self limited - no need to treat
- Current recommendations are to treat only immunocompromized or those ill enough to require hospitalization (CDC.gov/shigella)
- Tx: ceftriaxone or azithro if kids; azithro or quinolones if adults (historically - ampicillin, not amoxicillin)

Typhoid Fever - Salmonella typhi

- Following international travel, particularly India, Southeast Asia, sub-Saharan Africa
- ~220,000 deaths in 2014
- High fever, hepatosplenomegaly
- Relative bradycardia/leukopenia
- Fecal leukocytes sometimes emphasized as mononuclear
- Constipation common, though diarrhea also seen; bowel perforation w/ high mortality

Salmonella typhi

- "Rose spots"
  - macular rash from which S. typhi can be isolated
- Tx:
  - azithromycin
  - quinolones
  - 3rd gen. cephalosporins
- Prevention: avoiding fecal contamination of food/water supply, vaccine (note: humans are the only reservoir for this organism)

A British Concentration Camp in South Africa; 1902

Salmonella non-typhi

- 94,000,000 cases/yr (80,000,000 foodborne)
- 155,000 deaths
- Highest incidence in east/Southeast Asia
- 70% of food-borne outbreaks; S. typhimurium, S. enteritidis most common in U.S.
- 8-12 hr to 2 day incubation period common
- Headache/nausea/muscle pain
- Diarrhea, chills/fever, abdominal pain

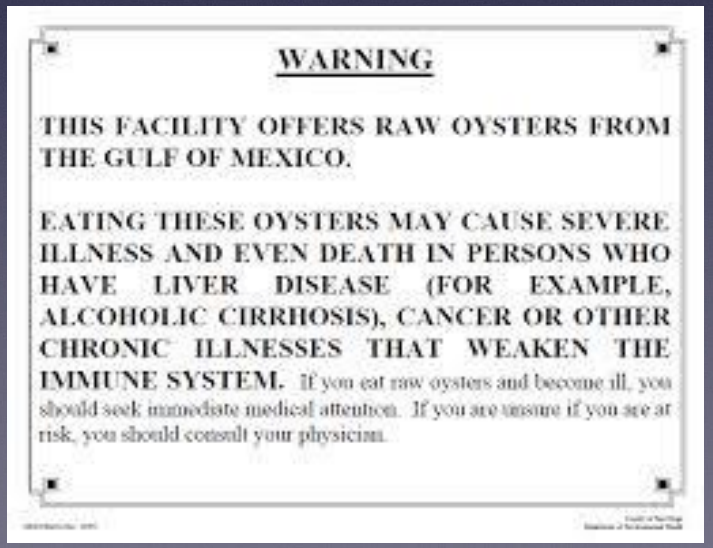
Salmonella non-typhi

- (Pooled) eggs, poultry (including baby chicks at Easter), peanut butter; numerous other foods
- Reptiles, including turtles and iguanas
- No blood (sometimes) distinguishes from shigella
- Usually treat only if bacteremic (if young, consider HIV) or….high risk of becoming so, w/ prosthetic valve or aortic aneurysm
- If multiple blood cultures + for S. choleraesuis or S. typhimurium, think endovascular infection (e.g. infected aneurysm), especially in the elderly
- Tx: quinolones; 3rd gen. cephalosporins; azithromycin

- reported in 35 states as of 3/17/18
- (outbreak investigation ended 5/18)

Vibrio vulnificus

- Ingestion of **raw oysters,** other filter-feeding mollusks, during warmer months, w/in past 7 days by pts w/ cirrhosis, other immunocompromised conditions
- GI illness w/ bacteremia, overwhelming sepsis
- Distinctive bullous skin lesions



Falcon LM, Pham L. N Engl J Med 2005;353:1604-1604.

Vibrio vulnificus

- With liver disease/hemachromatosis:
  - 80 x more likely to become ill
  - 200 x more likely to die
  - 60% mortality
- 1% of seafood-related illnesses, 80-90% of seafood-related deaths (~50 deaths/yr in U.S.)
- Found in salt water, in warmer months, where water temps > 22 C
- Tx: doxycycline/gentamicin/3rd generation cephalosporins; surgery

Campylobacter jejuni

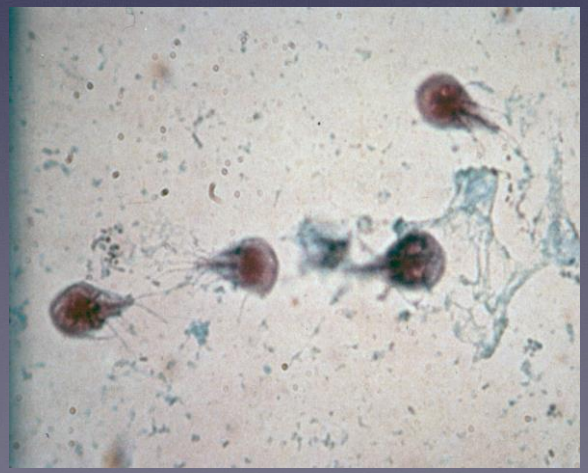
- Poultry, international travel [the latest: puppies]
- Pseudoappendicitis; colitis, fever, bloody diarrhea; these pts may appear quite ill
- If bacteremic, think HIV
- Corkscrew or spiral shaped organisms on gm stain of stool
- Often precedes Gullain-Barre' syndrome
- Recently linked to immunoproliferative small bowel disease (alpha chain disease), a small intestinal MALT (lymphoma)
- Tx: macrolides

Yersinia enterocolitica

- From pork, including chitterlings
- Grows well at low temperatures - “leftovers”
- Mesenteric adenitis, pseudoappendicitis
- Protracted courses of diarrhea
- Also assoc. w/ sepsis from blood transfusion
  - Explosive diarrhea
  - > 50% mortality following rapid onset septic shock
  - Rx: TMX-SMP/doxycycline/quinolones
- Reactive arthritis if HLA-B27
- Tx of diarrhea: supportive

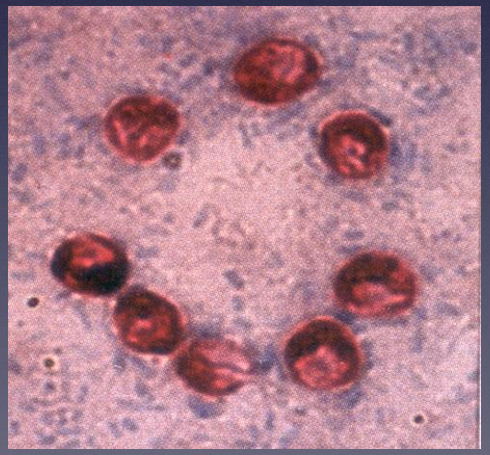
Giardiasis

- Travel to Russia; camping in the Rockies (drinking from fresh water streams)
- Chronic, watery diarrhea, malabsorption, bloating, flatulence
- No fever, no eosinophilia, no fecal leukocytes
- Common source outbreaks from day care centers (human-human spread)
- Prolonged disease w/ IgA deficiency
- Dx: antigen detection
- Tx:
  - metronidazole
  - quinacrine; nitrazoxanide (Alinia®)



Cryptosporidium

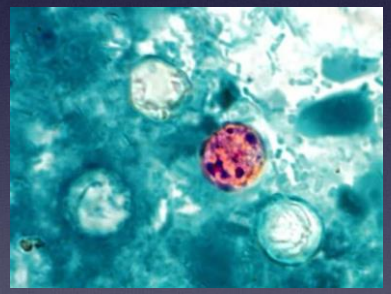
- Travel to Russia, day care centers, swimming pools; animal contact, esp. if animal has diarrhea
- Continuous/prolonged watery diarrhea w/ cramping in HIV+ patients w/ low CD4. Prolonged cases of diarrhea in immunocompetent hosts as well
- 3 - 6 microns in diameter
- No established effective treatment in HIV (other than treating the HIV itself)
- In immunocompetent: nitrazoxanide ®)

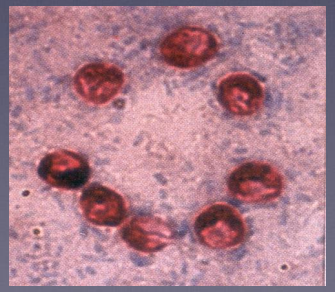


as seen on acid-fast stain

Cyclospora cayatanensis

- Imported raspberries (Guatemala), other fresh produce (basil, mesclun lettuce) grown in tropical/sub-tropical climates
- Stagnant water; travel to Nepal, Peru, Caribbean; increased during the rainy seasons
- ~7 day incubation
- Acid-fast ("big cryptosporidium"); 7.5 - 10 microns in diameter
- Tx: trimethoprim-sulfa





Amebiasis
Entamoeba histolytica (vs. E. dispar)

- Isoenzymes ("zymodemes") determine invasiveness
- Colitis, tenesmus, bloody diarrhea in patient from tropical Africa, Asia, Latin America
- "flask shaped" colonic ulcers
- Liver abscess: "anchovy paste"
  solitary right lobe
- Tx:
  - of abscess component - metronidazole
  - of intestinal component - paromomycin, diloxanide

Ciguatera Poisoning

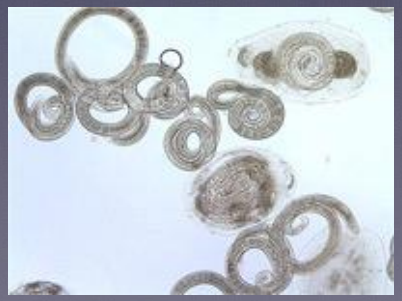
- Tropical fish: barracuda, snapper, amberjack, grouper
- Onset: 1 to 12 hrs
- Pruritis; circumoral and extremity paresthesias
- Sensation of loose or painful teeth
- Painful intercourse
- Sensation of temperature reversal; “shock-like” sensation when touching metal
- Rx: mannitol, amitriptyline (Elavil ®)

Botulism

- N/V, diarrhea, dry mouth, followed by **descending paralysis** w/in 18-36 hrs
- Bilateral cranial nerve palsies w/ early ptosis and/or double vision
- dysphagia
- home canned foods, fermented fish; skin popping “black tar” heroin
- GI complaints 6-24 hrs after ingestion, followed by acute liver and renal failure

Trichinosis

- T. spiralis
- Diarrhea followed by myalgia, periorbital edema
- Eosinophilia
- Undercooked pork, wild game
- Rx: Albendazole + prednisone



	Onset (hrs)	Preformed toxin?	Fever?	? Vomiting predominant
S. aureus	1 - 6	yes	no	yes
C. perfringens	8 - 16	no	no	no
E. coli	12	no	+/-	no
V. cholerae	12	no	dehydration	no
B. cereus				
a.	1 - 6	yes	no	yes
b.	8 - 24	no	no	no

	Fever	Bloody?	Bacteremia?	Ab's effective?
Shigella	yes	yes	yes	yes
Salmonella (non-typhi)	yes	no	no	no
V. parahemolyticus	yes	yes	no	maybe
E. coli	yes	no	no	no
E. coli 0157:H7	usually not	yes	no	Contraindicated ??
Campylobacter	yes	yes	+/-	yes
Yersinia	yes	yes	yes	no

Blackburn’s Rule # 2

Blackburn's Rule # 2

There has never been an outbreak of food poisoning from beer and french fries!!

Added References:

- Gupta SB et al. Antibodies to Toxin B Are Protective against *Clostridium difficile* Infection Recurrence. CID 2016; 63:730-734
- McDonald LC et al. Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). CID 2018;xx:1-48
- Shane AL et al. 2017 Infectious Diseases Society of America Clinical Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea. CID 2017;65:1963-1973