Infectious Diarrhea

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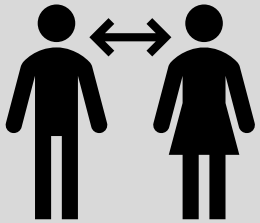
Objectives

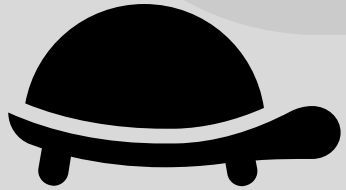
- Understand when to obtain stool studies
- Develop a framework for determining when treatment for infectious diarrhea is appropriate
- Understand benefits and drawbacks of fidaxomicin for treatment of *C difficile*

Overview

- Epidemiology
- Medical history
- Diagnostic testing
- Common pathogens and clinical presentation
- *Clostridium difficile*

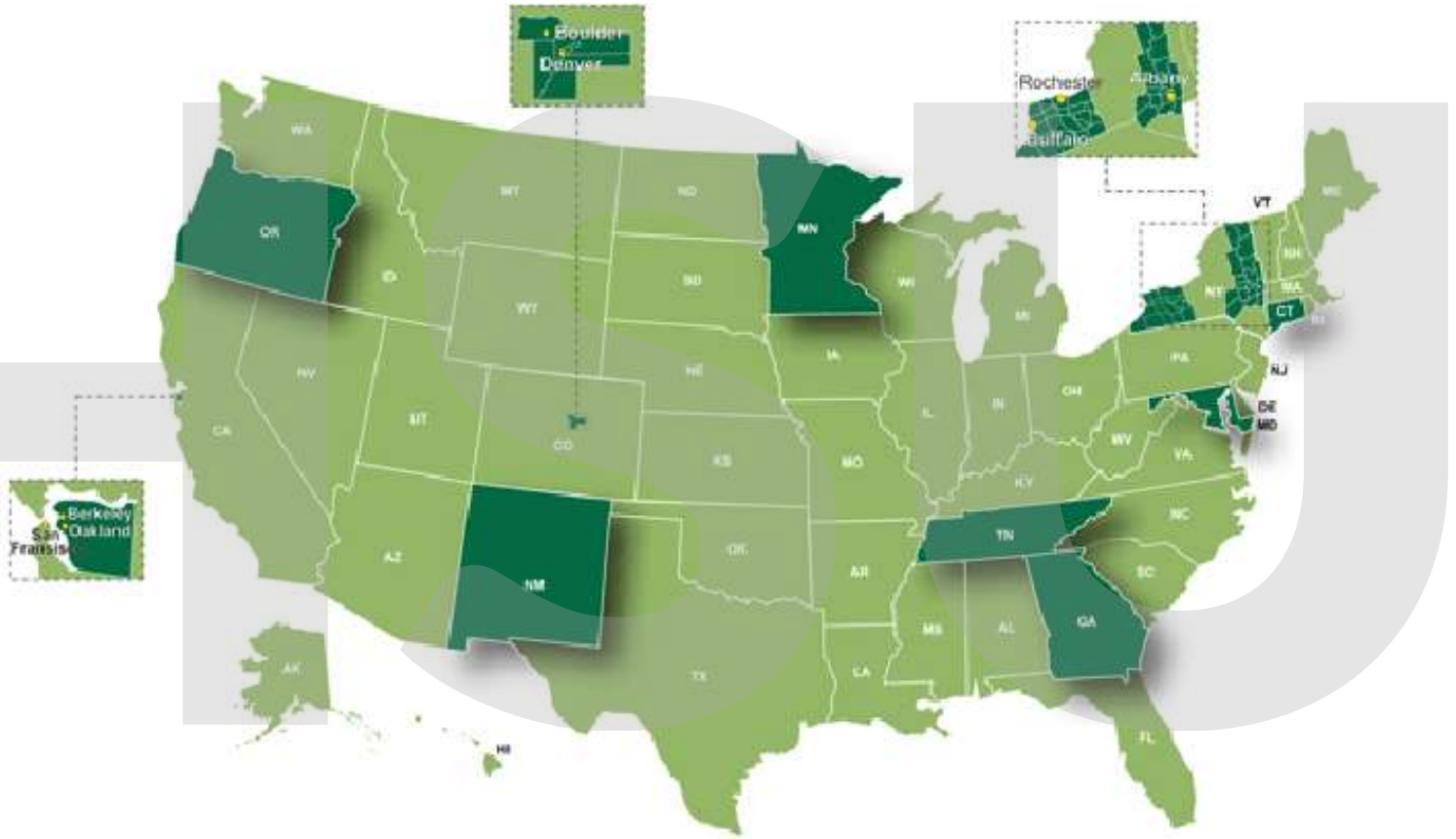
Routes of transmission





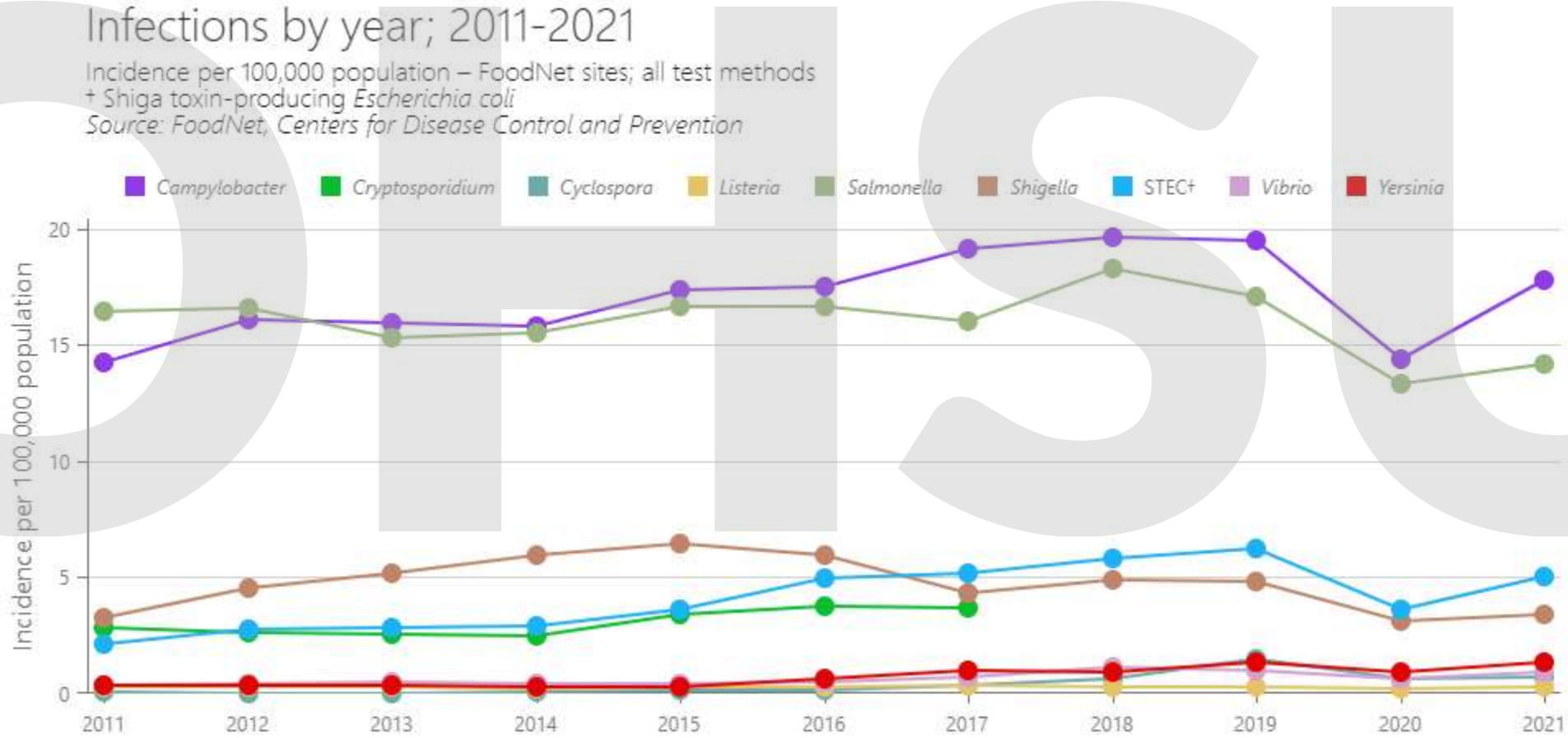
Setting

FoodNet surveillance 15% of U.S. population



CDC. Foodborne Diseases Active Surveillance Network (FoodNet). https://www.cdc.gov/foodnet/about/timeline.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Ffoodnet%2Fsurveillance-areas.html 2023.

Campylobacter & Salmonella are the 2 most common foodborne pathogens



CDC. FoodNetFast. https://wwwn.cdc.gov/foodnetfast/ 2023.

Role of medical history

- Generate hypotheses about etiology
- Consider need for diagnostic testing and treatment
- Prevent spread, report outbreaks

What do you ask?

- **Symptoms**
  - Onset, duration
  - Characteristics – frequency, severity, quality (bloody?)
- **Exposures**
  - Food
  - Water sources
  - Travel and recreation
  - Healthcare, long-term care, daycare exposures
  - Occupation
  - Recent antibiotics, medications
  - Animal contacts
  - Sick contacts
  - Same illness in others?
- **Host factors** – immunocompromise, inflammatory bowel disease, pregnancy, cirrhosis

Case 1

45 y/o woman calls your clinic with 2-day history of non-bloody diarrhea, 4 stools/day. No fever, N/V, abdominal pain, or cramping. She just returned from a 2-week trip to Guatemala where she brushed her teeth with tap water and swam in Lake Atitlán. She has been able to stay hydrated and can run a few errands.

Which of the following stool studies should you order next?

(A) Stool culture

(B) Stool O&P

(C) Fecal leukocytes

(D) No diagnostic testing is indicated

Case 1

45 y/o woman calls your clinic with 2-day history of non-bloody diarrhea, 4 stools/day. No fever, N/V, abdominal pain, or cramping. She just returned from a 2-week trip to Guatemala where she brushed her teeth with tap water and swam in Lake Atitlán. She has been able to stay hydrated and can run a few errands.

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Travelers' diarrhea

- Affects 30-70% of travelers
- Usually self-limited
- Most common: enterotoxigenic *E.coli* (ETEC)
  - Bacteria 80-90% of travelers' diarrhea
  - Viruses 5-15%
  - Protozoa 10% (Giardia)

Travelers' diarrhea definitions and treatment

Definitions	Treatment
Mild – not distressing, doesn't interfere with planned activities	Antibiotic treatment not recommended
Moderate – distressing, interferes with planned activities	Antibiotics may be used
Severe – incapacitating, completely prevents planned activities (all dysentery* is severe)	Antibiotics should be used

*Bloody or mucoid

CDC. *CDC Yellow Book* 2022.

Are antibiotics for TD worth it?

- Remember: untreated bacterial diarrhea lasts ~3-7 days
- Antibiotics reduce duration by ~1 day

Stool cultures

- Typically identify *Salmonella, Shigella, Campylobacter*
- Obtain when:
  - Fever, bloody or mucoid stools, severe abdominal cramping, sepsis
  - High-risk host
  - Public health implications (food handlers, day-care staff, healthcare workers)

Case 2

35 y/o women presents to ED with abdominal pain and diarrhea. Diarrhea started 3 days ago as loose stools, but in the last day she noticed streaks of bright red blood. She also has abdominal cramping but no fever. Four days prior to illness onset, she attending a picnic where she ate potato salad and a hotdog. Two other attendees have also developed diarrhea.

What is the most likely cause of her illness?

(A) *Staphylococcus aureus*

(B) *Bacillus cereus*

(C) Shiga toxin-producing *E. coli*

(D) *Campylobacter jejuni*

Case 2

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What is the most likely cause of her illness?

(A) *Staphylococcus aureus*

(B) *Bacillus cereus*

(C) Shiga toxin-producing *E. coli* (STEC)

(D) *Campylobacter jejuni*

Shiga toxin-producing *E. coli* (STEC)

- O157:H7 strain associated with outbreaks in U.S. (packaged salads, baby spinach, Romaine lettuce)
- Diarrhea non-bloody -> bloody over 1-3 days, abdominal pain common, fever uncommon
- Most recover 5-7 days, 5-10% develop hemolytic uremic syndrome (HUS)

Shiga toxin-producing *E. coli* (STEC)

- If you suspect STEC, check with your lab to see if selective culture (Sorbitol-MacConkey agar) is needed
- Multiplex stool tests (culture-independent test)

Bacteria

- *Campylobacter (jejuni, coli, and upsaliensis)*
- *Clostridium difficile* (toxin A/B)
- *Plesiomonas shigelloides*
- *Salmonella*
- *Yersinia enterocolitica*
- *Vibrio (parahaemolyticus, vulnificus, and cholerae)*
- *Vibrio cholerae*

Diarrheagenic E.coli/Shigella

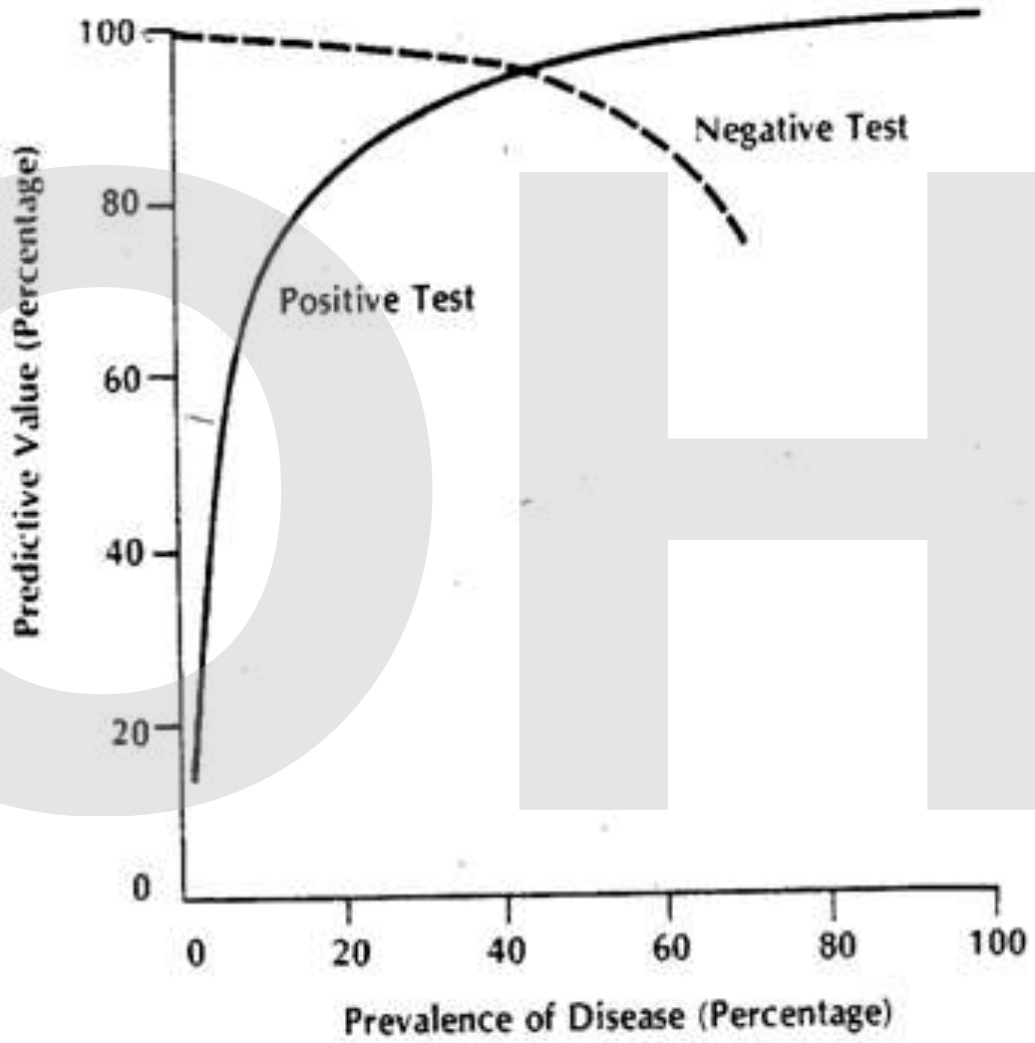
- *Enteroaggregative E. coli* (EAEC)
- *Enteropathogenic E. coli* (EPEC)
- *Enterotoxigenic E. coli* (ETEC) *lt/st*
- *Shiga-like toxin-producing E. coli* (STEC) *stx1/stx2*
    - *E. coli* O157
- *Shigella/Enteroinvasive E. coli* (EIEC)

Parasites

- *Cryptosporidium*
- *Cyclospora cayetanensis*
- *Entamoeba histolytica*
- *Giardia lamblia*

Viruses

- Adenovirus F40/41
- Astrovirus
- Norovirus GI/GII
- Rotavirus A
- Sapovirus (I, II, IV, and V)



Remember

PPV depends on prevalence in the community

Pennsylvania State University 2022

Shiga toxin-producing *E. coli* (STEC)

- Management is supportive (fluids)
- Avoid antibiotics (associated with higher risk hemolytic uremic syndrome [HUS], don't reduce symptoms)
- Also avoid: antimotility agents (higher risk HUS), NSAIDs

Phillip and Freedman. *Curr Opin Gatroenterol* 2022; 38:30.

Case 3

35 y/o man presents to clinic with 3 months of abdominal cramping, flatulence, foul-smelling stools. No history of inflammatory bowel disease or lactose intolerance. No anorectal discharge or pain, no weight loss. He denies any travel outside of Oregon. No pets or recent camping. Drinks municipal water. Has had 3 male sexual partners in the last 6 months. HIV screen 1 month ago negative.

What diagnostic test(s) would you order?

(A) Stool culture

(B) Stool O&P

(C) Fecal leukocytes

(D) No diagnostic testing is indicated

(E) Other

Case 3

35 y/o man presents to clinic with 3 months of abdominal cramping, flatulence, foul-smelling stools. No history of inflammatory bowel disease or lactose intolerance. No anorectal discharge or pain, no weight loss. He denies any travel outside of Oregon. No pets or recent camping. Drinks municipal water. Has had 3 male sexual partners in the last 6 months. HIV screen 1 month ago negative.

What diagnostic test(s) would you order?

(A) Stool culture

(B) Stool O&P

(C) Fecal leukocytes

(D) No diagnostic testing is indicated

(E) Other

- Common parasitic pathogens in persistent diarrhea:
  - *Giardia*
  - *Cryptosporidium*
  - *Entamoeba histolytica*
- Stool O&P
  - Generally not useful in acute diarrhea
  - Fresh stool, up to 3 specimens on separate days to improve yield
  - Sensitivity low
- Antigen testing: *Giardia, Cryptosporidium, Entamoeba*

Case 4

33 y/o woman with no PMH presents to urgent care with 2 days of mucoid, non-bloody diarrhea. She reports low-grade fever but no nausea or vomiting. She works at a daycare where three children have recently had diarrheal illness. She is advised to stay hydrated and is not prescribed antibiotics. Two days later, a stool culture is reported to be growing *Shigella sonnei*. When contacted, she reports her diarrhea has resolved and would like to return to work.

What is the most appropriate treatment at this time?

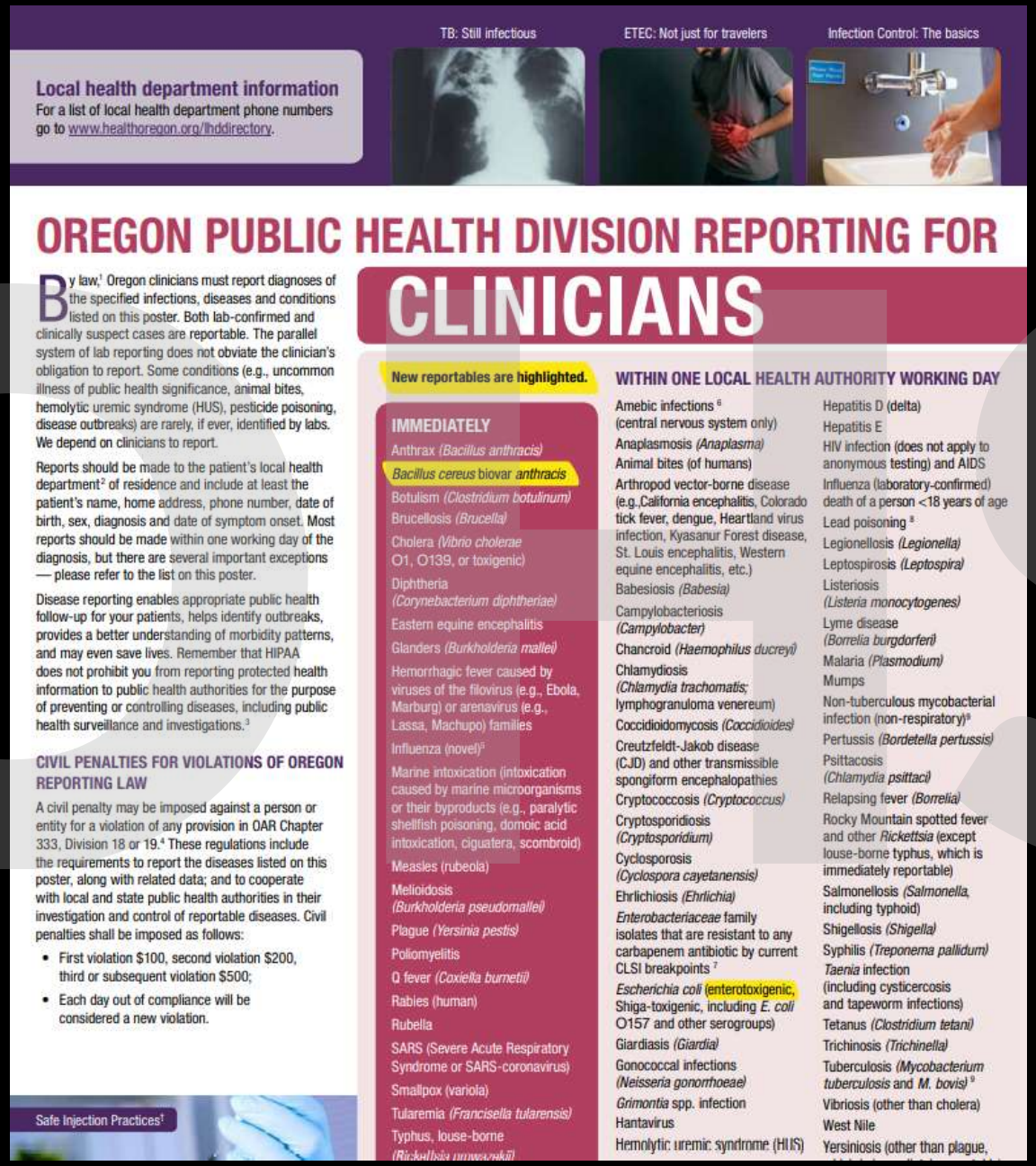
(A) No treatment

(B) Ciprofloxacin

(C) Azithromycin

Shigellosis

- Typically self-limited illness, lasts 5-7 days
- Treatment in immunocompetent persons with non-severe illness usually not recommended unless there are concerns about spread (food handlers, daycare workers)
- Groups at risk: young children, travelers, MSM, immunocompromised
- Increasing antibiotic resistance even in U.S.
- Follow-up stool cultures are <u>not</u> recommended in most recovered persons except in specific situations recommended by local public health authorities



TB: Still infectious

ETEC: Not just for travelers

Infection Control: The basics

Local health department information
For a list of local health department phone numbers go to www.healthoregon.org/lhddirectory.

OREGON PUBLIC HEALTH DIVISION REPORTING FOR CLINICIANS

By law,[1] Oregon clinicians must report diagnoses of the specified infections, diseases and conditions listed on this poster. Both lab-confirmed and clinically suspect cases are reportable. The parallel system of lab reporting does not obviate the clinician's obligation to report. Some conditions (e.g., uncommon illness of public health significance, animal bites, hemolytic uremic syndrome (HUS), pesticide poisoning, disease outbreaks) are rarely, if ever, identified by labs. We depend on clinicians to report.

Reports should be made to the patient's local health department[2] of residence and include at least the patient's name, home address, phone number, date of birth, sex, diagnosis and date of symptom onset. Most reports should be made within one working day of the diagnosis, but there are several important exceptions — please refer to the list on this poster.

Disease reporting enables appropriate public health follow-up for your patients, helps identify outbreaks, provides a better understanding of morbidity patterns, and may even save lives. Remember that HIPAA does not prohibit you from reporting protected health information to public health authorities for the purpose of preventing or controlling diseases, including public health surveillance and investigations.[3]

CIVIL PENALTIES FOR VIOLATIONS OF OREGON REPORTING LAW

A civil penalty may be imposed against a person or entity for a violation of any provision in OAR Chapter 333, Division 18 or 19.[4] These regulations include the requirements to report the diseases listed on this poster, along with related data; and to cooperate with local and state public health authorities in their investigation and control of reportable diseases. Civil penalties shall be imposed as follows:

- First violation $100, second violation $200, third or subsequent violation $500;
- Each day out of compliance will be considered a new violation.

Safe Injection Practices[1]

New reportables are highlighted.

IMMEDIATELY

- Anthrax *(Bacillus anthracis)*
- *Bacillus cereus* biovar *anthracis*
- Botulism *(Clostridium botulinum)*
- Brucellosis *(Brucella)*
- Cholera *(Vibrio cholerae* O1, O139, or toxigenic)
- Diphtheria *(Corynebacterium diphtheriae)*
- Eastern equine encephalitis
- Glanders *(Burkholderia mallei)*
- Hemorrhagic fever caused by viruses of the filovirus (e.g., Ebola, Marburg) or arenavirus (e.g., Lassa, Machupo) families
- Influenza (novel)[5]
- Marine intoxication (intoxication caused by marine microorganisms or their byproducts (e.g., paralytic shellfish poisoning, domoic acid intoxication, ciguatera, scombroid)
- Measles (rubeola)
- Melioidosis *(Burkholderia pseudomallei)*
- Plague *(Yersinia pestis)*
- Poliomyelitis
- Q fever *(Coxiella burnetii)*
- Rabies (human)
- Rubella
- SARS (Severe Acute Respiratory Syndrome or SARS-coronavirus)
- Smallpox (variola)
- Tularemia *(Francisella tularensis)*
- Typhus, louse-borne *(Rickettsia prowazekii)*

WITHIN ONE LOCAL HEALTH AUTHORITY WORKING DAY

- Amebic infections[6] (central nervous system only)
- Anaplasmosis *(Anaplasma)*
- Animal bites (of humans)
- Arthropod vector-borne disease (e.g.,California encephalitis, Colorado tick fever, dengue, Heartland virus infection, Kyasanur Forest disease, St. Louis encephalitis, Western equine encephalitis, etc.)
- Babesiosis *(Babesia)*
- Campylobacteriosis *(Campylobacter)*
- Chancroid *(Haemophilus ducreyi)*
- Chlamydiosis *(Chlamydia trachomatis;* lymphogranuloma venereum)
- Coccidioidomycosis *(Coccidioides)*
- Creutzfeldt-Jakob disease (CJD) and other transmissible spongiform encephalopathies
- Cryptococcosis *(Cryptococcus)*
- Cryptosporidiosis *(Cryptosporidium)*
- Cyclosporosis *(Cyclospora cayetanensis)*
- Ehrlichiosis *(Ehrlichia)*
- *Enterobacteriaceae* family isolates that are resistant to any carbapenem antibiotic by current CLSI breakpoints[7]
- *Escherichia coli* (enterotoxigenic, Shiga-toxigenic, including *E. coli* O157 and other serogroups)
- Giardiasis *(Giardia)*
- Gonococcal infections *(Neisseria gonorrhoeae)*
- *Grimontia* spp. infection
- Hantavirus
- Hemolytic uremic syndrome (HUS)
- Hepatitis D (delta)
- Hepatitis E
- HIV infection (does not apply to anonymous testing) and AIDS
- Influenza (laboratory-confirmed) death of a person <18 years of age
- Lead poisoning[8]
- Legionellosis *(Legionella)*
- Leptospirosis *(Leptospira)*
- Listeriosis *(Listeria monocytogenes)*
- Lyme disease *(Borrelia burgdorferi)*
- Malaria *(Plasmodium)*
- Mumps
- Non-tuberculous mycobacterial infection (non-respiratory)[9]
- Pertussis *(Bordetella pertussis)*
- Psittacosis *(Chlamydia psittaci)*
- Relapsing fever *(Borrelia)*
- Rocky Mountain spotted fever and other *Rickettsia* (except louse-borne typhus, which is immediately reportable)
- Salmonellosis *(Salmonella,* including typhoid)
- Shigellosis *(Shigella)*
- Syphilis *(Treponema pallidum)*
- *Taenia* infection (including cysticercosis and tapeworm infections)
- Tetanus *(Clostridium tetani)*
- Trichinosis *(Trichinella)*
- Tuberculosis *(Mycobacterium tuberculosis* and *M. bovis)*[9]
- Vibriosis (other than cholera)
- West Nile
- Yersiniosis (other than plague,

https://www.oregon.gov/oha/PH/DISEASESCONDITIONS/COMMUNICABLEDISEASE/REPORTINGCOMMUNICABLEDISEASE/Documents/ReportingPosters/poster-clinicians.pdf

Oregon Health Authority regulations

- "Restrictions on cases with shigellosis or Shiga-toxigenic Escherichia coli infection shall not be lifted until results of licensed laboratory tests of two consecutive approved fecal specimens collected not less than 24 hours apart show no identifiable pathogens."
- "If sufficient measures have been taken to prevent transmission, or the disease is no longer communicable, worksite, child-care and school restrictions can be removed at the discretion of the local public health authority."

https://www.oregon.gov/oha/PH/DISEASESCONDITIONS/DISEASESAZ/Pages/shigellosis.aspx

Case 4

33 y/o woman with no PMH presents to urgent care with 2 days of mucoid, non-bloody diarrhea. She reports low-grade fever but no nausea or vomiting. She works at a daycare where three children have recently had diarrheal illness. She is advised to stay hydrated and is not prescribed antibiotics. Two days later, a stool culture is reported to be growing *Shigella sonnei*. When contacted, she reports her diarrhea has resolved and would like to return to work.

What is the most appropriate treatment at this time?

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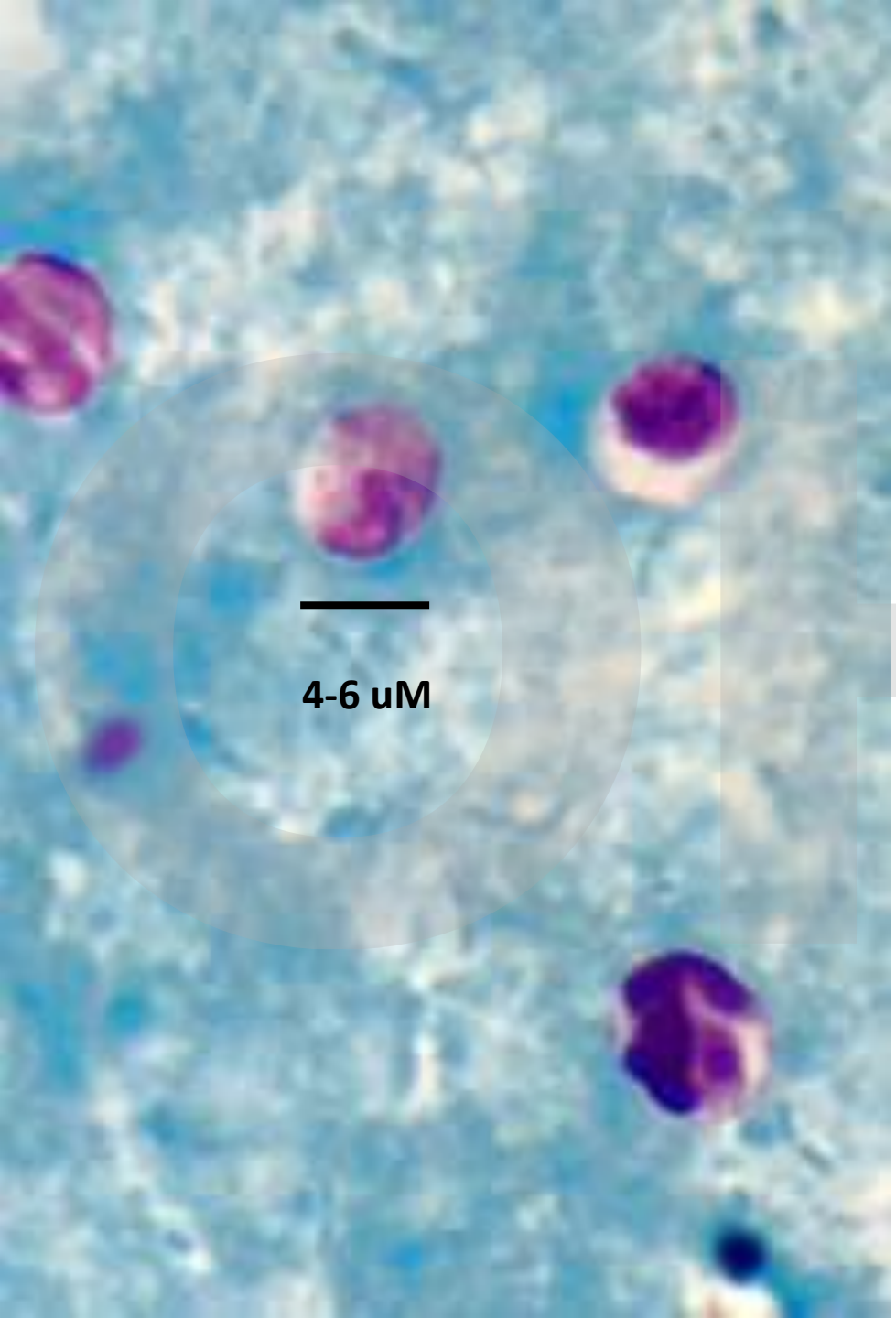


Case 5

7 y/o healthy boy living in Minneapolis developed watery diarrhea 1 week after swimming in a local pool in July. Diarrhea has persisted for 10 days and is accompanied by low grade fever and malaise. ~2-3 stools/day, able to stay hydrated.

Seen by PCP who performs an initial diagnostic evaluation (shown on left). Assistance with treatment is requested.

What do you recommend?

A. Nothing, illness expected to be self-limited and resolve over next few days.

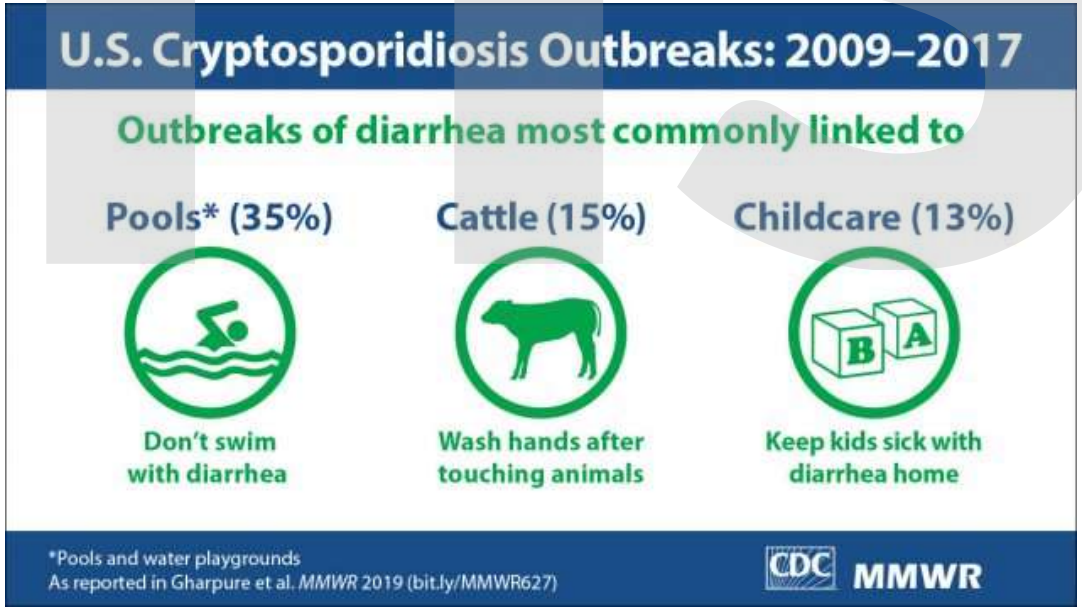
B. Nitazoxanide x3 days

C. Paromomycin x7 days

CDC. DPDx. 2019.

Cryptosporidiosis - epidemiology

- Leading cause of outbreaks of diarrhea linked to water (summer seasonal peak)
- Third leading cause of diarrhea associated with animal contact
- *C parvum* and *C hominis* most common species that affect humans



Cryptosporidiosis - clinical

- Incubation ~7-10 days
- Immunocompetent
  - Typically self-limited, resolving in 10-14 days
  - Range of presentations: asymptomatic -> severe dehydration
  - Supportive care vs nitazoxanide x3 days
- Immunocompromised
  - Can cause prolonged debilitating diarrhea, weight loss, malabsorption
  - HIV/AIDS particularly CD4 <100
  - Effective ART most important
  - Nitazoxanide x14 days (evidence of benefit less certain)

Cryptosporidiosis – public health

- Infected swimmers can excrete 10^7–10^8 oocysts/episode diarrhea (human infectious dose ≤10 oocysts)
- Oocysts can be chlorine tolerant
- Avoid swimming in public pools for **2 weeks** after diarrhea has resolved

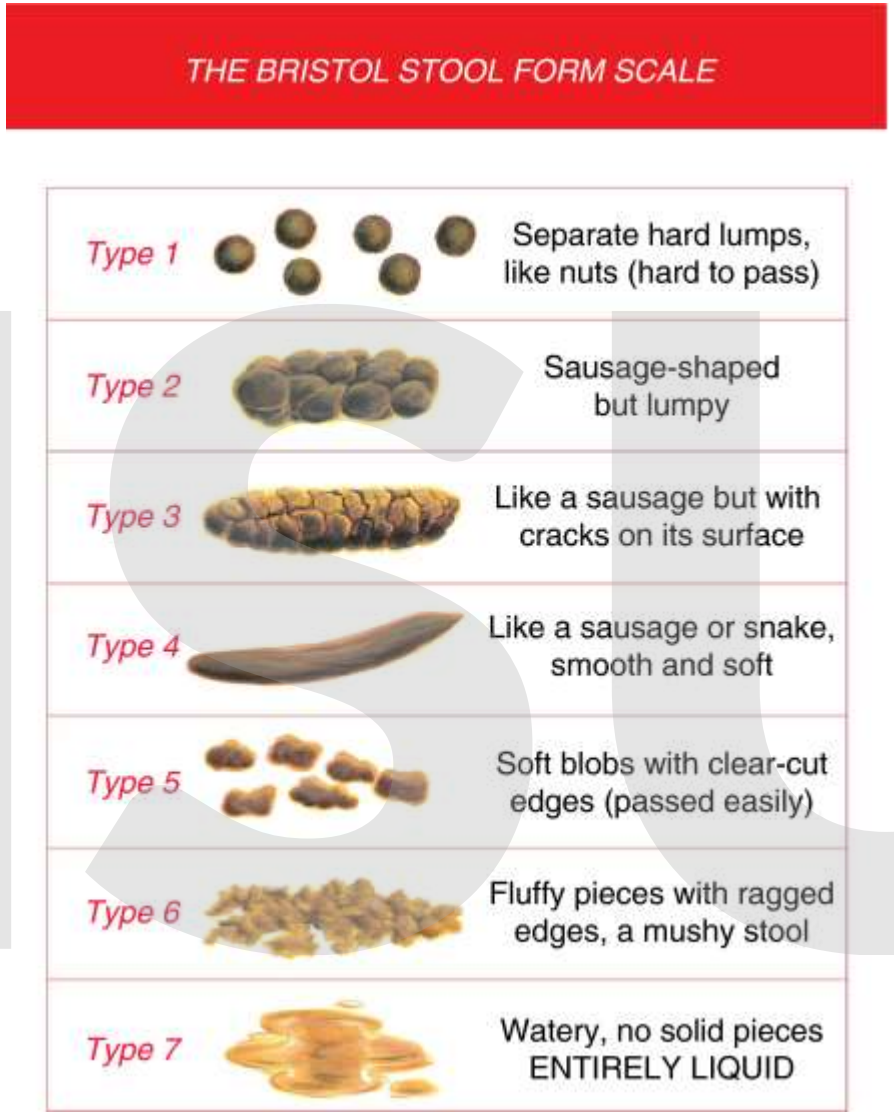
C. difficile testing

Indications

- Recent antibiotic use
- Healthcare-associated diarrhea
- Persistent diarrhea and no etiology established

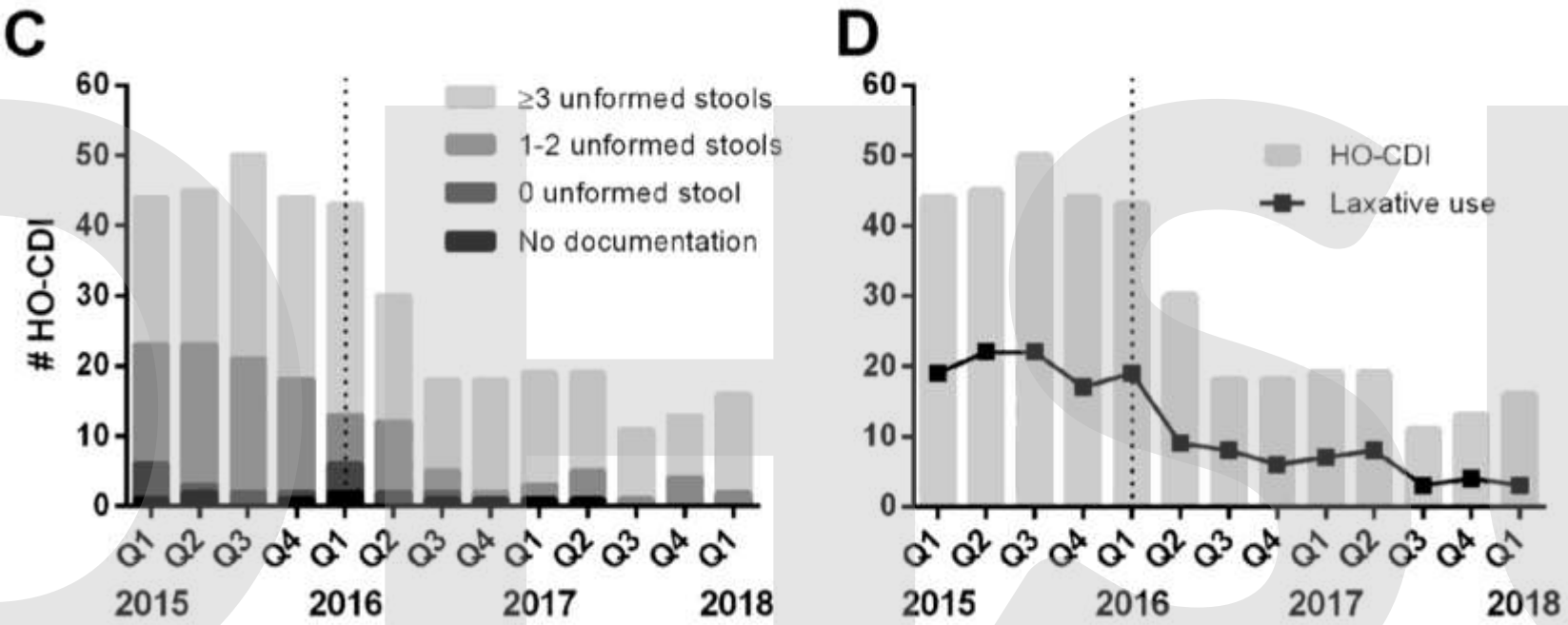
Remember

- ≥3 unformed stools in 24 hours
- No recent laxatives



Blake et al. *Aliment Pharmacol Ther* 2016;44:693-703.

Preanalytical Screening is the Key to Reducing CDI



- Patients without clinically significant diarrhea or with prior laxative use accounted for ~70% reported HO-CDI events
- 95% patients with inappropriate testing received treatment

Chow et al. *J Clin Microbiol* 2019; 57:e01553-18.

What testing algorithm do you use?

(1) Nucleic acid amplification test (NAAT) alone
(2) 2-step glutamate dehydrogenase (GDH) and toxin A/B EIA → NAAT
(3) 2-step NAAT → toxin A/B EIA
(4) Other 2-step algorithm
(5) Don't know

Table 1. Diagnostic Tests for Toxigenic *Clostridium difficile*[a]

Tests by Type and Method	Target(s)	Characteristics
Gold standards		
Toxigenic culture	Toxigenic *C difficile*	Reference standard Difficult to perform Time consuming (24-48 h)
Cell cytotoxicity assay	Toxins A or B[b]	Reference standard Highly sensitive for toxin compared with EIA Difficult to perform Time consuming (24-48 h)
Rapid diagnostic tests		
EIA	GDH	GDH alone insufficient for diagnosis (must be paired with a test for toxin) Rapid Variable sensitivity and specificity
EIA	Toxins A or B[b]	Rapid Variable sensitivity and specificity
NAAT		Rapid but more expensive than EIA Highly sensitive and specific for presence of toxigenic *C difficile* May increase detection of colonization and not true CDI

GDH more sensitive than toxin assays and a useful screening tool but expressed by both toxigenic and nontoxigenic strains

~15-20% of population is asymptomatically colonized

Bagdasarian et al. *JAMA* 2015; 313:398-408.
Fang et al. *J Clin Microbiol* 2017; 55:670-80.

- Per IDSA, multistep algorithms generally preferred
  - GDH + toxin
  - GDH + toxin arbitrated by NAAT
  - NAAT + toxin
- If your facility uses NAAT alone, remember that appropriate specimen submission is critical

Case 6

72 y/o man with diabetes, PVD, and CKD presents to ED diarrhea following antibiotic treatment for a skin and soft tissue infection. Reports 4-5 loose stools per day over the last two days. Also reports a prior history of CDI 6 months ago treated with 10-day course vancomycin. VSS, WBC 8, Cr 1.3 (baseline). Toxin A/B EIA and *C. difficile* NAAT (+).

Which of the following treatments would you initiate?

(A) Vancomycin

(B) Fidaxomicin

(C) Metronidazole

(D) Other

Case 6

72 y/o man with diabetes, PVD, and CKD presents to ED diarrhea following antibiotic treatment for a skin and soft tissue infection. Reports 4-5 loose stools per day over the last two days. Also reports a prior history of CDI 6 months ago treated with 10-day course vancomycin. VSS, WBC 8, Cr 1.3 (baseline). Toxin A/B EIA and *C. difficile* NAAT (+).

Which of the following treatments would you initiate?

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(C) Metronidazole

(D) Other

Clinical Infectious Diseases

IDSA GUIDELINES

Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of *Clostridioides difficile* Infection in Adults

Stuart Johnson,[1,2] Valéry Lavergne,[3,4] Andrew M. Skinner,[1,2] Anne J. Gonzales-Luna,[5] Kevin W. Garey,[5] Ciaran P. Kelly,[6] and Mark H. Wilcox[7]

[1]Department of Research and Medicine, Edward Hines Jr Veterans Administration Hospital, Hines, Illinois, USA; [2]Loyola University Medical Center, Maywood, Illinois, USA; [3]Department of Medical Microbiology and Infection Control, Vancouver General Hospital, Vancouver, British Columbia, Canada; [4]Research Center, University of Montreal, Montreal, Quebec, Canada; [5]Department of Pharmacy Practice and Translational Research, University of Houston College of Pharmacy, Houston, Texas, USA; [6]Department of Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts, USA; and [7]Department of Microbiology, Leeds Teaching Hospitals NHS Trust, and Leeds Institute of Medical Research, University of Leeds, Leeds, United Kingdom

CME

ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of *Clostridioides difficile* Infections

Colleen R. Kelly, MD, AGAF, FACG[1], Monika Fischer, MD, MSc, AGAF, FACG[2], Jessica R. Allegretti, MD, MPH, FACG[3], Kerry LaPlante, PharmD, FCCP, FIDSA[4], David B. Stewart, MD, FACS, FASCRS[5], Berkeley N. Limketkai, MD, PhD, FACG (GRADE Methodologist)[6] and Neil H. Stollman, MD, FACG[7]

Clostridioides difficile **infection occurs when the bacterium produces toxin that causes diarrhea and inflammation of the colon. These guidelines indicate the preferred approach to the management of adults with *C. difficile* infection and represent the official practice recommendations of the American College of Gastroenterology. The scientific evidence for these guidelines was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation process. In instances where the evidence was not appropriate for Grading of Recommendations Assessment, Development, and Evaluation but there was consensus of significant clinical merit, key concept statements were developed using expert consensus. These guidelines are meant to be broadly applicable and should be viewed as the preferred, but not the only, approach to clinical scenarios.**

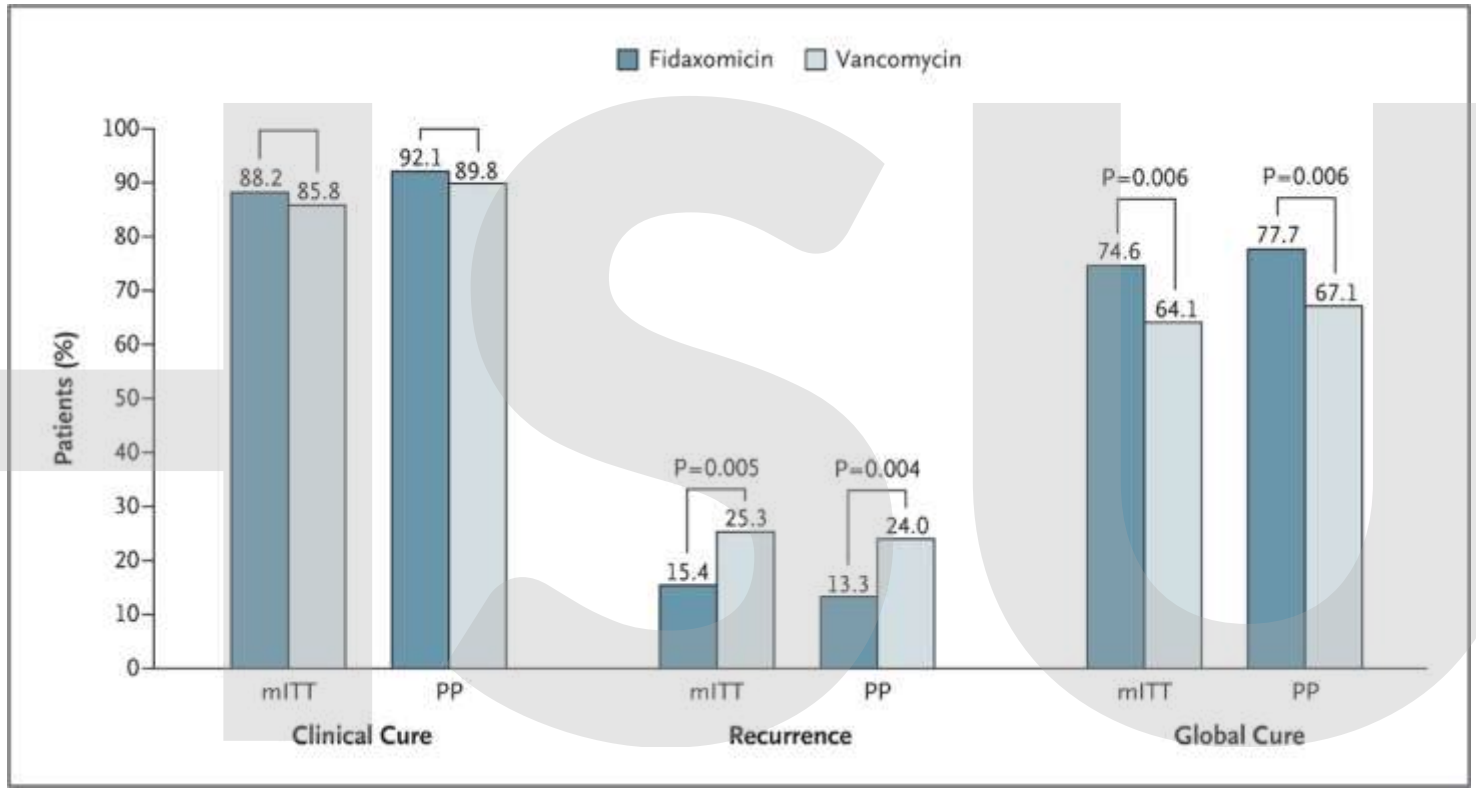
Am J Gastroenterol 2021;116:1124–1147. https://doi.org/10.14309/ajg.0000000000001278; published online May 18, 2021

2021 IDSA/SHEA treatment guidelines

Clinical Presentation	Recommended Treatment	Alternative Treatment(s)
Initial episode	Fidaxomicin 200 mg PO BID x10 days	Acceptable alternative: vancomycin 125 mg PO 4x/day x10 days
First recurrence	Fidaxomicin 200 mg PO BID x10 days *or* BID x5 days → QOD x20 days	Tapered/pulsed vancomycin 125 mg PO 4x/day x10-14 days → BID x7 days → daily x7 days → q2-3 days x2-8 weeks OR vancomycin 125 mg 4x/day x10 days

Non-inferior clinical cure rates

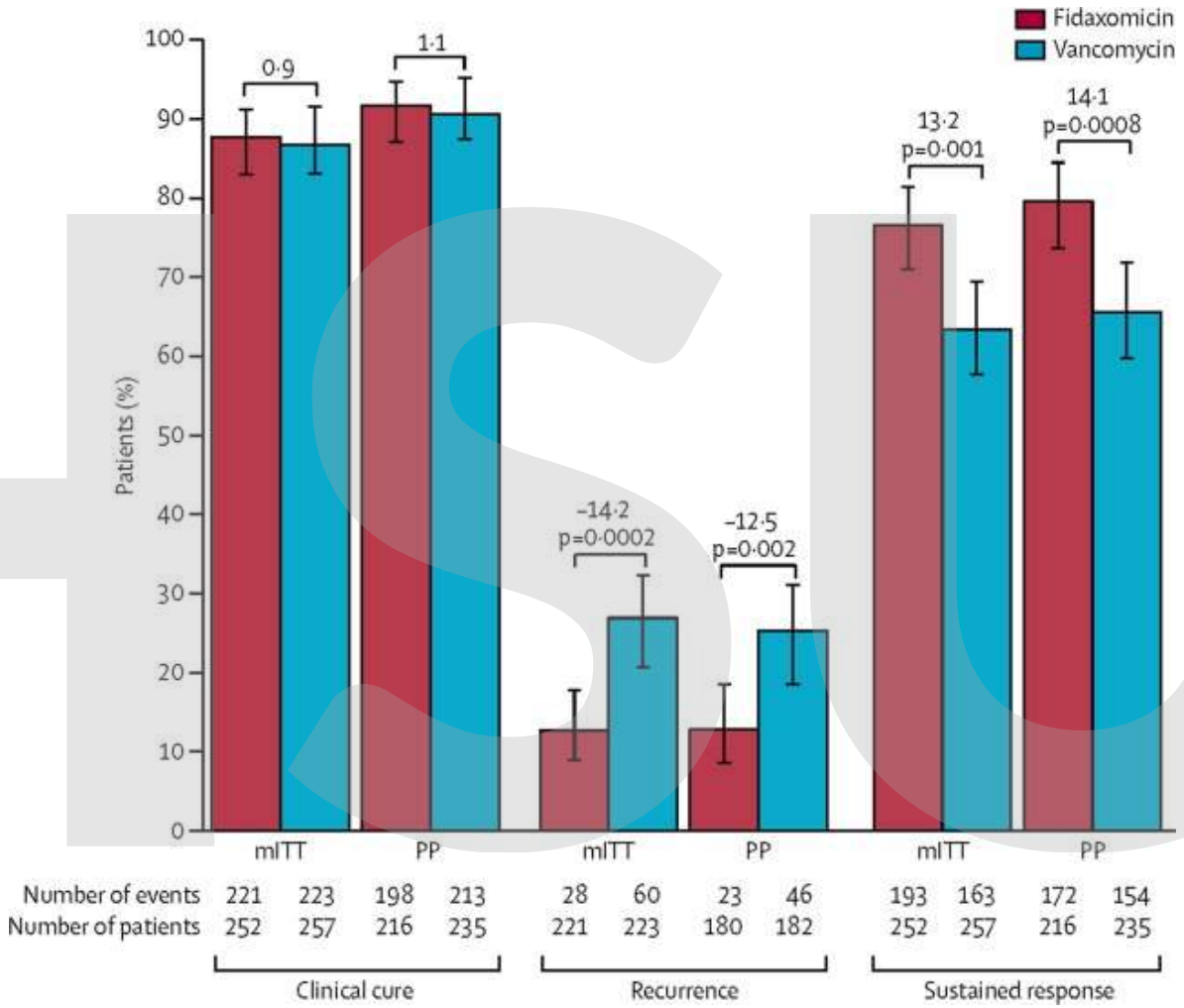
Less recurrence in fidaxomicin arm



Louie et al. *NEJM* 2011; 364:422-431.

Non-inferior clinical cure rates

Less recurrence in fidaxomicin arm



Cornely et al. *Lancet Infect Dis* 2012; 12:281-9.

- Up to 25% patients experience recurrent CDI within 30 days of vancomycin or metronidazole treatment
- Risk factors for recurrence: advanced age ≥65 years, immunocompromised host, severe presentation
- Sustained response of CDI 4-weeks after end of therapy, fidaxomicin vs vancomycin:
  - Initial episode: RR 1.16 (95% CI 1.09-1.24), RD 101 per 1000 (57-151)
  - Recurrent episode: 1.27 (95% CI 1.05-1.54), RD 151 per 1000 (34-269)
- Non-sustained response of CDI fidaxomicin vs vancomycin:
  - Initial episode: RR 0.723
  - Recurrent episode: RR 0.657

Kelly CP. *Clin Microbiol Infect*. 2012;18(Suppl 6):21-7.
Johnson SJ et al. Focused Update Guidelines on Management of *Clostridioides difficile* Infection in Adults. 2021.

2021 IDSA/SHEA treatment guidelines

Clinical Presentation	Recommended Treatment
Second or subsequent recurrence	Fidaxomicin 200 mg PO BID x10 days *or* BID x5 days → QOD x20 days --- Tapered/pulsed vancomycin --- Vancomycin 125 mg PO 4x/day → rifaximin 400 mg PO TID x20 days --- Fecal microbiota transplantation (after treatment for 3 episodes) --- Adjunctive treatment: bezlotoxumab 10 mg/kg IV x1

2021 ACG guidelines

TREATMENT OF CDI

Non-severe CDI

Recommendations

4. We recommend that oral vancomycin 125 mg 4 times daily for 10 days be used to treat an initial episode of nonsevere CDI (strong recommendation, low quality of evidence).
5. We recommend that oral fidaxomicin 200 mg twice daily for 10 days be used for an initial episode of nonsevere CDI (strong recommendation, moderate quality of evidence).
6. Oral metronidazole 500 mg 3 times daily for 10 days may be considered for treatment of an initial nonsevere CDI in low-risk patients (strong recommendation/moderate quality of evidence).

Severe CDI

Recommendations

7. As initial therapy for severe CDI, we recommend vancomycin 125 mg 4 times a day for 10 days (strong recommendation, low quality of evidence).
8. As initial therapy for severe CDI, we recommend fidaxomicin 200 mg twice daily or 10 days (conditional recommendation, very low quality of evidence).

2021 ACG guidelines

Treatment of Recurrent CDI

Recommendations

12. We suggest tapering/pulsed-dose vancomycin for patients experiencing a first recurrence after an initial course of fidaxomicin, vancomycin, or metronidazole (strong recommendation, very low quality of evidence).
13. We recommend fidaxomicin for patients experiencing a first recurrence after an initial course of vancomycin or metronidazole (strong recommendation, moderate quality of evidence).

- Major limitation of fidaxomicin is cost
- Estimated 462,000 *C. difficile* cases in the U.S. in 2017
- Total estimated CDI-attributable cost per year in U.S. $6.3 billion

Guh et al. *NEJM* 2020; 382:1320-30.
Zhang et al. *BMC Infect Dis* 2016; 16:447.

Summary

- Obtain stool cultures in:
  - Patients with fever, bloody/mucoid stools
  - Immunocompromise or high-risk
  - Public health concerns
- Not all acute diarrhea should be treated with antibiotics (e.g., mild travelers' diarrhea, STEC)
- Fidaxomicin treatment for CDI is associated with a lower risk of recurrence compared with vancomycin

Resources

1. Centers for Disease Control and Prevention. Travelers' Diarrhea. *CDC Yellow Book* Travelers' Diarrhea - Chapter 2 - 2020 Yellow Book | Travelers' Health | CDC. Accessed 28 May 2022.
2. Oregon Health Authority. Communicable Disease Rules and Reporting. https://www.oregon.gov/oha/PH/DISEASESCONDITIONS/COMMUNICABLEDISEASE/REPORTINGCOMMUNICABLEDISEASE/Pages/index.aspx. Accessed 28 May 2022.
3. Shane AL, Mody RK, Crump JA, et al. 2017 Infectious Disease Society of America Clinical Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea. *Clin Infect Dis* 2017;65(12):e45-80.
4. Bagdasarian N, Rao K, and Malani PN. Diagnosis and treatment of *Clostridium difficile* in adults. *JAMA* 2015; 313:398-408.
5. Johnson SJ, Lavergne V, Skinner AM, et al. Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of *Clostridioides difficile* Infection in Adults. *Clin Infect Dis* 2021;73(5):e1029-1044.
6. Kelly CR, Fischer M, Allegretti JR, et al. ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of *Clostridioides difficile* Infections. *Am J Gastroenterol* 2021;116:1124-1147.