Acute diarrheal Infections and Clostridium dificile

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Infectious Diseases

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Question 1.

Which of the following is the consistent with the definition of acute diarrhea? (More than one choice may be correct)

A. Three or more stools daily

B. Greater than 250 grams daily

C. Unformed (liquid) consistency

D. Less than 21 days ‘duration

Acute diarrhea $\leq 14\ days$

- Diarrhea- passage of loose or watery stools typically at least 3/24hr period.
  - Increased water content of stool
- Invasive diarrhea=dysentery- diarrhea with visible blood or mucus. Commonly associated with fever and abdominal pain

BRISTOL STOOL CHART

	Type 1	Separate hard lumps	**SEVERE CONSTIPATION**
	Type 2	Lumpy and sausage like	**MILD CONSTIPATION**
	Type 3	A sausage shape with cracks in the surface	**NORMAL**
	Type 4	Like a smooth, soft sausage or snake	**NORMAL**
	Type 5	Soft blobs with clear-cut edges	**LACKING FIBRE**
	Type 6	Mushy consistency with ragged edges	**MILD DIARRHEA**
	Type 7	Liquid consistency with no solid pieces	**SEVERE DIARRHEA**

Question 2.

A 36 year-old man is evaluated for a 10-day history of abdominal cramping, diarrhea, malaise, and nausea. Diarrhea is watery without mucus or blood. He returned 2 weeks ago from a 7-day trip to Lima, Peru.

On physical examination, temperature is 37.7 C (99.9 F), the remaining vital signs are normal. On abdominal examination, bowel sounds are present with diffuse tenderness to palpation. The abdomen is not distended; no guarding or rebound is noted.

Which of the following is the LEAST likely cause of his diarrhea?

A. Enterotoxigenic E. Coli
B. Norovirus
C. Shigella
D. Cryptosporidium

Differential Diagnosis: ***Acute Watery Diarrhea***

Causes of acute infectious diarrhea in adults in resource-rich settings

	Likely pathogens	Mean incubation period	Classic/common food sources	Other epidemiologic clues
Watery diarrhea	Norovirus	24 to 48 hours	Shellfish, prepared foods, vegetables, fruit	▪ Outbreaks in: • Restaurants • Health care facilities • Schools and childcare centers • Cruise ships • Military populations
	*Clostridium difficile**	N/A	N/A	▪ Antibiotic use ▪ Hospitalization ▪ Cancer chemotherapy ▪ Gastric acid suppression ▪ Inflammatory bowel disease
	Clostridium perfringens	8 to 16 hours	Meat, poultry, gravy, home-canned goods	
	Enterotoxigenic *Escherichia coli*	1 to 3 days	Fecally contaminated food or water	▪ Travel to resource-limited settings
	Other enteric viruses (rotavirus, enteric adenovirus, astrovirus, sapovirus)	10 to 72 hours	Fecally contaminated food or water	▪ Daycare centers ▪ Gastroenteritis in children ▪ Immunocompromised adults
	Giardia lamblia	7 to 14 days	Fecally contaminated food or water	▪ Daycare centers ▪ Swimming pools ▪ Travel, hiking, camping (particularly when there is contact with water in which beavers reside)
	Cryptosporidium parvum	2 to 28 days	Vegetables, fruit, unpasteurized milk	▪ Daycare centers ▪ Swimming pools and recreational water sources ▪ Animal exposure ▪ Chronic diarrhea in advanced HIV infection
	Listeria monocytogenes	1 day (gastroenteritis)	Processed/delicatessen meats, hot dogs, soft cheese, pâtés, and fruit	▪ Pregnancy ▪ Immunocompromising condition ▪ Extremes of age
	Cyclospora cayetanensis	1 to 11 days	Imported berries, herbs	▪ Chronic diarrhea in advanced HIV infection

Question 3.

A 27 year-old man presents to the ED for a 2-day history of bloody diarrhea with abdominal cramping.. Medical history is otherwise unremarkable, and he takes no medications.

On physical examination, temperature is 37.1 C (98.8 F), blood pressure is 120/76 mm Hg, pulse rate is 100/min, and respiration rate is 16/min. On abdominal examination, bowel sounds are present with diffuse tenderness to palpation but no guarding or rebound.

Laboratory studies:
Hematocrit 39%
Leukocyte count 18,000/uL
Platelet count 190,000/uL
Creatinine 1.3 mg/dL

Which of the following is the LEAST likely cause of his diarrhea?

A. Non-typhoidal salmonella
B. Listeria monocytogenes
C. Enterohemorrhagic E. coli
D. Campylobacter

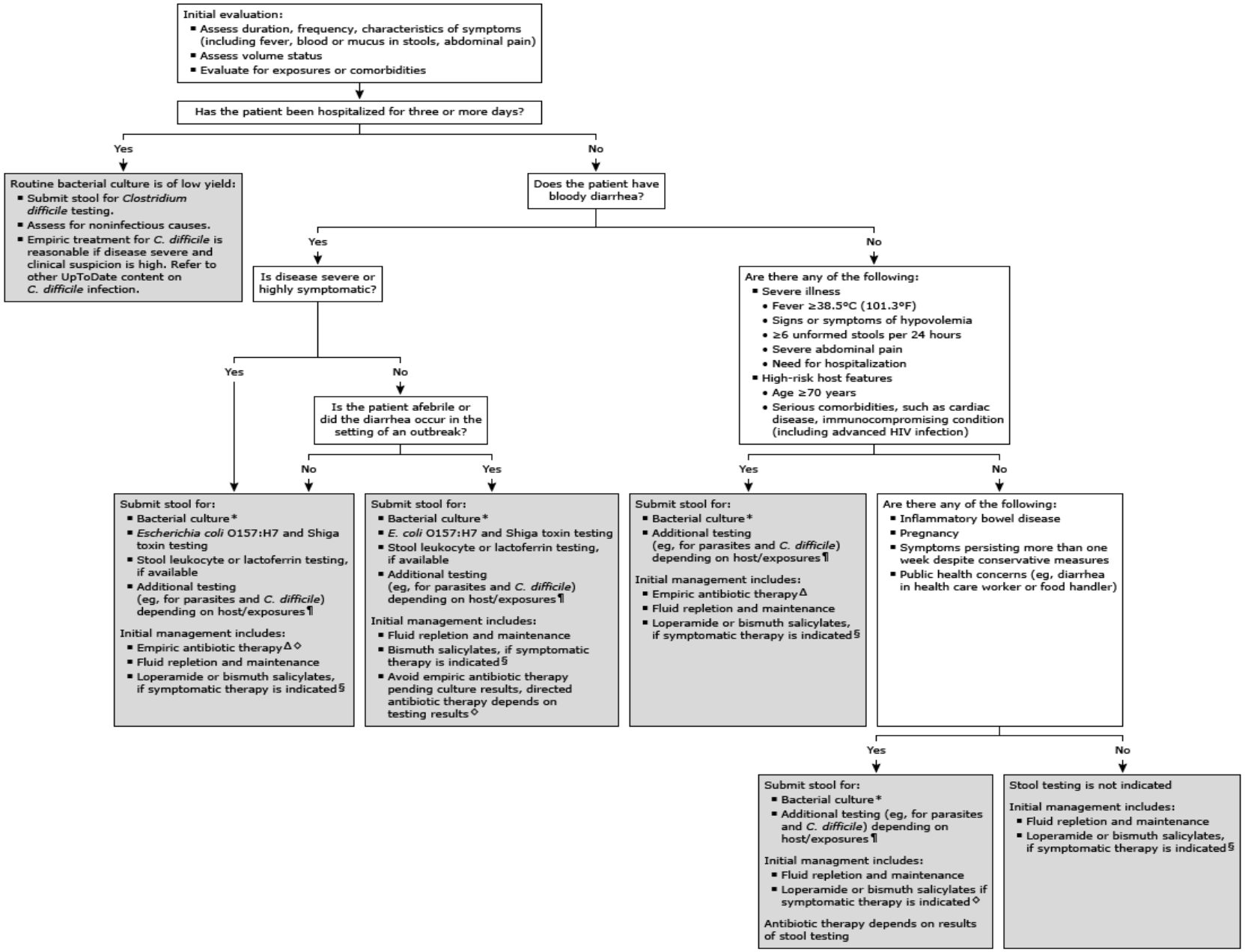
Differential Diagnosis for Acute Bloody Diarrhea/ Dysentery

Inflammatory diarrhea (fever, mucoid or bloody stools)¶	Nontyphoidal *Salmonella*	1 to 3 days	Poultry, eggs, and egg products, fresh produce, meat, fish, unpasteurized milk or juice, nut butters, spices	▪ Animal contact (petting zoos, reptiles, live poultry, other pets) ▪ Travel to resource-limited settings
	Campylobacter spp	1 to 3 days	Poultry, meat, unpasteurized milk	▪ Travel to resource-limited settings ▪ Animal contact (young puppies or kittens, occupational contact)
	Shigella spp	1 to 3 days	Raw vegetables	▪ Daycare centers ▪ Crowded living conditions ▪ Men who have sex with men ▪ Travel to resource-limited settings
	Enterohemorrhagic *E. coli*	1 to 8 days	Ground beef and other meat, fresh produce, unpasteurized milk and juice	▪ Daycare centers ▪ Nursing homes ▪ Extremes of age
	Yersinia spp	4 to 6 days	Pork or pork products, untreated water	▪ Abnormalities of iron-metabolism (eg, cirrhosis, hemochromatosis, thalassemia) ▪ Blood transfusion
	Vibrio parahemolyticus	1 to 3 days	Raw seafood and shellfish	▪ Cirrhosis
	Entamoeba histolytica	1 to 3 weeks	Fecally contaminated food or water	▪ Travel to resource-limited settings ▪ Men who have sex with men

* *Clostridium difficile* can also present with inflammatory diarrhea.

acute diarrhea: diagnosis

- Diagnosis
  - History
  - History
  - History
  - Ok send a stool culture/molecular


Initial evaluation:
Assess duration, frequency, characteristics of symptoms (including fever, blood or mucus in stools, abdominal pain)
Assess volume status
Evaluate for exposures or comorbidities
Has the patient been hospitalized for three or more days?
Yes
No
Routine bacterial culture is of low yield:
Submit stool for Clostridium difficile testing.
Assess for noninfectious causes.
Empiric treatment for C. difficile is reasonable if disease severe and clinical suspicion is high. Refer to other UpToDate content on C. difficile infection.
Does the patient have bloody diarrhea?
Yes
No
Is disease severe or highly symptomatic?
Are there any of the following:
Severe illness
Fever ≥38.5°C (101.3°F)
Signs or symptoms of hypovolemia
≥6 unformed stools per 24 hours
Severe abdominal pain
Need for hospitalization
High-risk host features
Age ≥70 years
Serious comorbidities, such as cardiac disease, immunocompromising condition (including advanced HIV infection)
Yes
No
Is the patient afebrile or did the diarrhea occur in the setting of an outbreak?
No
Yes
Yes
No
Submit stool for:
Bacterial culture*
Escherichia coli O157:H7 and Shiga toxin testing
Stool leukocyte or lactoferrin testing, if available
Additional testing (eg, for parasites and C. difficile) depending on host/exposures¶
Initial management includes:
Empiric antibiotic therapyΔ◇
Fluid repletion and maintenance
Loperamide or bismuth salicylates, if symptomatic therapy is indicated§
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Bismuth salicylates, if symptomatic therapy is indicated§
Avoid empiric antibiotic therapy pending culture results, directed antibiotic therapy depends on testing results◇
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Bacterial culture*
Additional testing (eg, for parasites and C. difficile) depending on host/exposures¶
Initial management includes:
Empiric antibiotic therapyΔ
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Are there any of the following:
Inflammatory bowel disease
Pregnancy
Symptoms persisting more than one week despite conservative measures
Public health concerns (eg, diarrhea in health care worker or food handler)
Yes
No
Submit stool for:
Bacterial culture*
Additional testing (eg, for parasites and C. difficile) depending on host/exposures¶
Initial managment includes:
Fluid repletion and maintenance
Loperamide or bismuth salicylates if symptomatic therapy is indicated◇
Antibiotic therapy depends on results of stool testing
Stool testing is not indicated
Initial management includes:
Fluid repletion and maintenance
Loperamide or bismuth salicylates, if symptomatic therapy is indicated§

Case.

A 57 year-old man is hospitalized for a 2-day history of diarrhea. He has five liquid bowel movements per day. One week ago, he completed a course of levofloxacin for treatment of community acquired pneumonia. He works at a long-term care facility as a janitor. He has a history of peptic ulcer disease and is on a PPI daily.

On physical examination, temperature is 38.1 C (100.5 F), blood pressure is 116/70 mm Hg, pulse is 98/min, and respiration rate is 19/min. The abdomen is nondistended with normal bowel sounds. Moderate abdominal tenderness is present without guarding or rebound. Mental status is normal.

Leukocyte count: 18,000/ul (78% PMN, 3% band, 19% lymph)
Albumin: 2.8 g/dL
Creatinine: 1.6 mg/dL
Lactate: normal

How many risk factors do you identify to be a link to his diagnosis of C. diff colitis?

A. One
B. Three
C. Four
D. Five

Epidemiology and Risk Factors

- Who are carriers?
  - Patients are carriers and the source in the presence of absence of active infection
  - Healthy 3%; hospitalized and LTC facilities 20-50%
- How is infection acquired?
  - Fecal oral transmission

- Antibiotics
  - Disruption of barrier function of normal colonic flora
  - C diff antibiotic resistance to clindamycin and quinolone seem to play a role in increase virulence
- Age
- Gastric suppression
  - Both PPI and H2 blockers

Case continued…

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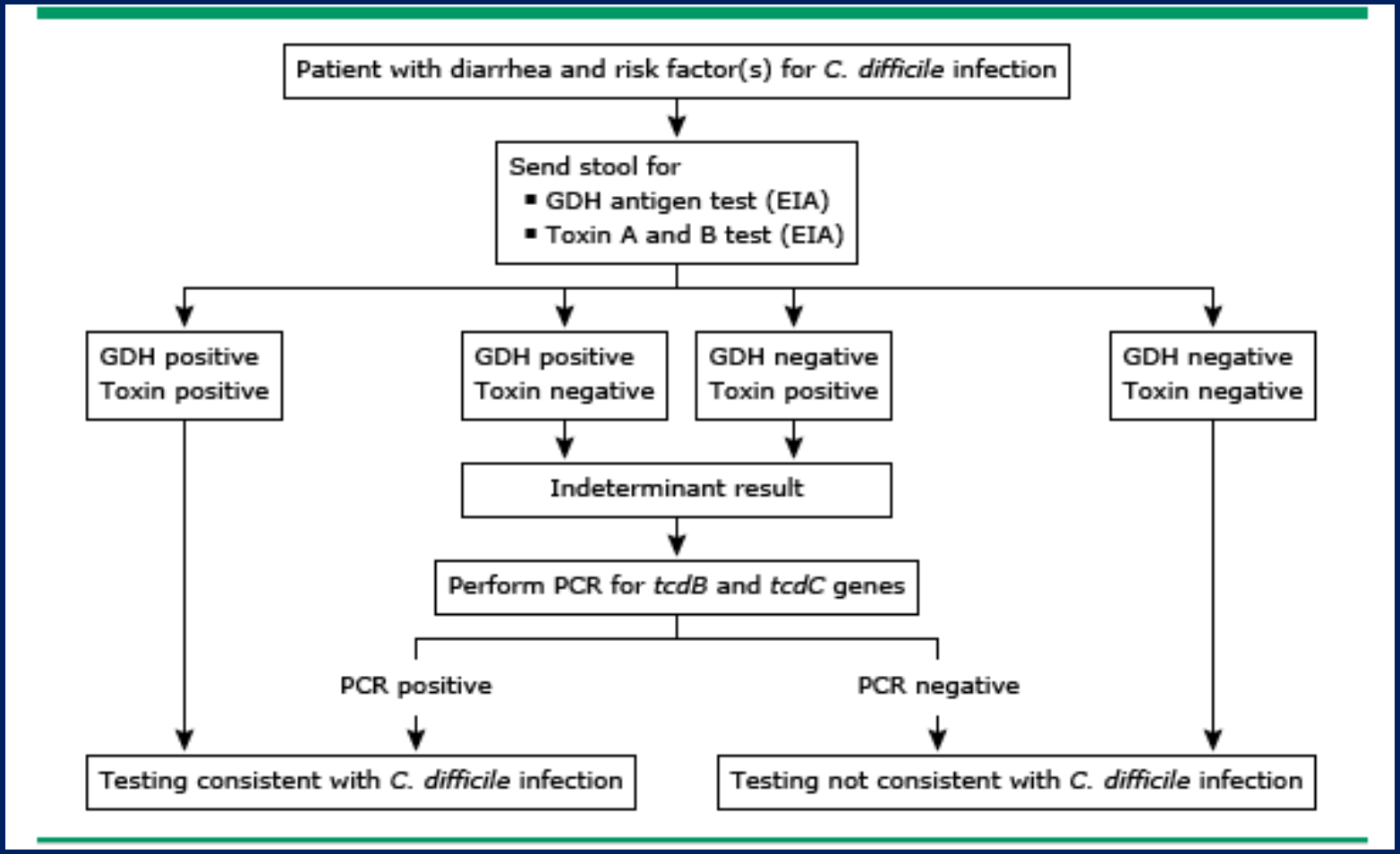
The C. diff stool GDH EIA test is positive but the toxin EIA is negative.

Which of the following is the interpretation of this test?

A. The patient is colonized with C. diff but does not have acute infection
B. The patient may have C. diff; further testing is needed
C. The patient does not have C. diff; other diagnoses must be considered

Approach to diagnosis of CDI



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Leukocyte count: 18,000/ul (78% PMN, 3% band, 19% lymph)

Albumin: 2.8 g/dL

Creatinine: 1.6 mg/dL

Lactate: normal

The C. diff stool PCR returns positive.

Which of the following is the appropriate classification of this patient's severity and why?

A. Mild
B. Moderate
C. Severe

Classification of disease

For the purposes of the treatment decisions in the following discussion, determination of disease severity is left to clinician judgment and may include any or all of the above criteria.

Classification	Presentation
Nonsevere	WBC≤15,000 cells/mL and sCr<1.5 mg/dL
Severe	WBC>15,000 cells/mL and SCr ≥1.5 mg/dL
Fulminant (severe complicated)	Hypotension or shock, ileus, or megacolon

Initial clinical manifestations

- Watery diarrhea
  - Mild 3-5
  - Moderate 6-9
  - Severe >10
- Abdominal pain
- Cramping
- Fever

- Leukocytosis
  On average >15K

- Endoscopy: shallow ulceration as this progresses get leakage of serum proteins, mucus, and inflammatory cells which congeal on the mucosal surface making pseudomembranes

Treatment of First Episode of C. difficile Based on Severity

Clinical definition	Treatment*
Nonsevere disease Supportive clinical data: White blood cell count ≤15,000 cells/mL and serum creatinine <1.5 mg/dL	
Initial episode	▪ Vancomycin 125 mg orally four times daily for 10 days, **OR** ▪ Fidaxomicin 200 mg orally twice daily for 10 days ▪ If above agents are unavailable: Metronidazole 500 mg orally three times daily for 10 days¶
Severe disease◇ Supportive clinical data: White blood cell count >15,000 cells/mL and/or serum creatinine ≥1.5 mg/dL	▪ Vancomycin 125 mg orally four times daily for 10 days, **OR** ▪ Fidaxomicin 200 mg orally twice daily for 10 days
Fulminant disease (previously referred to as severe, complicated *C. difficile* infection)◇ Supportive clinical data: Hypotension or shock, ileus, megacolon	▪ Enteric vancomycin plus parenteral metronidazole: • Vancomycin 500 mg orally or via nasogastric tube four times daily, **AND** • Metronidazole 500 mg intravenously every 8 hours ▪ If ileus is present, rectal vancomycin may be administered as a retention enema (500 mg in 100 mL normal saline per rectum; retained for as long as possible and readministered every 6 hours)§

Case continued…

The patient is started on appropriate medical therapy. On day 3 of therapy, he develops worsening abdominal pain and distention.

On physical exam, he appears in mild distress due to pain. Temperature is 39 C (102.2 F), BP 130/90, HR 115, RR 22, 02 sat 95% on RA. His abdomen is distended and quiet, with diffuse tenderness to mild palpation. There is some voluntary guarding but no rebound. He has stopped producing stool for the last 8 hours.

A stat CT scan reveals a dilated, edematous colon diffusely with a diameter of 7 cm in the transverse colon.

Which of the following is the most appropriate therapy for the patient at this time?

A. Fecal microbiota transplant

B. Oral vancomycin

C. Oral vancomycin and intravenous metronidazole

D. Rectal vancomycin

Complications

- Fulminant colitis
- Toxic megacolon and perforation
- Post infectious irritable bowel syndrome

Relapse vs Reinfection

- Occurs in 10-25% of cases
- Recurrence may present in days to weeks
- Clinical presentation similar to or more severe than initial.
- Usually recurrence (~88%)
- May be related to variability in host immune response.

Relapse Medical Management

First recurrence	▪ If vancomycin was used for the initial episode: • Vancomycin pulsed-tapered regimen: ○ 125 mg orally four times daily for 10 to 14 days, then ○ 125 mg orally twice daily for 7 days, then ○ 125 mg orally once daily for 7 days, then ○ 125 mg orally every 2 or 3 days for 2 to 8 weeks, **OR** • Fidaxomicin 200 mg orally twice daily for 10 days ▪ If fidaxomicin or metronidazole was used for the initial episode: Vancomycin 125 mg orally four times daily for 10 days
Second or subsequent recurrence	▪ Vancomycin pulsed-tapered regimen (outlined above), **OR** ▪ Fidaxomicin 200 mg orally twice daily for 10 days, **OR** ▪ Vancomycin followed by rifaximin: • Vancomycin 125 mg orally four times per day for 10 days, then • Rifaximin 400 mg three times daily for 20 days, **OR** ▪ Fecal microbiota transplantation[Δ]

C diff and Inflammatory bowel Disease

- High level of carriage in patient with IBD (8%vs1%)
- Diagnosis can be difficult as symptoms and presentation of both diseases very similar
- Can often be underlying cause for a flare
- Treatment with oral vancomycin clears infection/symptoms

- Testing is part of the algorithm

Adjunctive therapies

- Probiotics:
  - Prevention: for patient felt to be at increased risk
  - Patient with recurrent disease that is not severe and no sig. comorbidities.
  - *Saccharomyces boulardii* and *Lacobacillus rhamnosus GG*
- Monoclonal antibodies against Toxins A and B
  - Now clinically available
- Fecal microbiota transplantation
  - Upper or lower (enema vs colonoscope)
  - There is now a pill for that
  - >92-95% cure rates
  - Did well even in immunocompromised settings

Recurrence

- Persistent spores
- Change in colonic microenvironment
- Immunity
- NOT antibiotic resistance

Treatment for recurrent CDI

- I highly recommend “The Nekahi Taper”