11 – Helicobacter and Clostridium Difficile

Speaker: David Aronoff, MD

IDBR INFECTIOUS DISEASE BOARD REVIEW AUGUST 17-21, 2024

Helicobacter* and *Clostridioides difficile

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IDBR INFECTIOUS DISEASE BOARD REVIEW AUGUST 17-21, 2024

- **Disclosures of Financial Relationships with Relevant Commercial Interests**

  - None

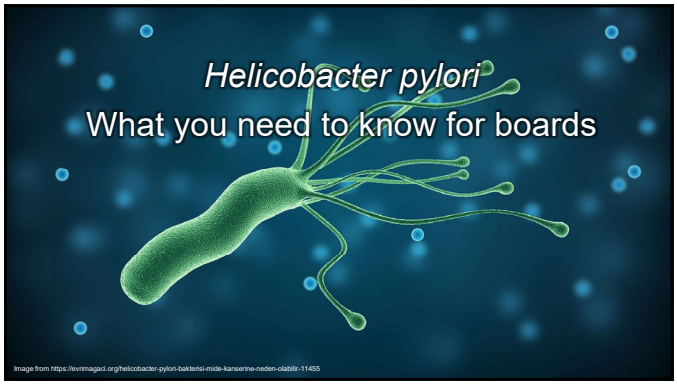

Image from https://evrimagaci.org/helicobacter-pylori-bakterisi-mide-kanserine-neden-olabilir-11455

Helicobacter pylori Microbiology

- Spiral-shaped, Gram-negative rod
- Flagellated
- Non-invasive
- Catalase +, oxidase +
- Grows best at pH 6-8

Urease + → **Survival, Colonization, Diagnosis**

Urea → CO_2 + NH_3 → ↑**pH**

Image from https://www.news-medical.net/life-sciences/Helicobacter-pylori-Life-Cycle.aspx

Helicobacter pylori: Take Home Points

- Hp causes peptic ulcer disease (PUD), chronic gastritis, gastric adenocarcinoma, & gastric mucosa associated lymphoid tissue (MALT) lymphoma
- Hp does **not** cause reflux/GERD
- Test for Hp if h/o MALT lymphoma, active PUD, early gastric cancer
- Consider testing: Pts <60 years of age with dyspepsia & w/o alarm features, chronic NSAID use, unexplained iron deficiency, immune thrombocytopenia

Helicobacter pylori: Take Home Points

- Test after stopping PPI (2 wks) & antibiotics (4 wks)
  - Urea breath test, stool antigen, or biopsy can diagnos Hp
  - NEVER TEST WITH SEROLOGY
- Endoscopy for diagnosis if alarm symptoms

ALARM SYMPTOMS
- **Unexplained iron-def anemia**
- **GI bleeding**
- **Unintentional weight Loss**
- **Palpable mass**
- **Severe abdominal pain**
- **Persistent vomiting**
- **Progressive dysphagia / odynophagia**

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Helicobacter pylori: Take Home Points

- All patients with active infection should be offered treatment
- Initial antibiotic regimen guided by the presence of risk factors for macrolide resistance & presence of a penicillin allergy
  - In the **USA** macrolide resistance is generally >15% so **avoid macrolides**
  - **Bismuth quadruple therapy** = bismuth/metronidazole/tetracycline/PPI (double dose PPI)
  - Treat for **14 days**

Helicobacter pylori: Take Home Points

- **Test of cure** to confirm eradication must be performed in all patients treated for Hp at least 4 weeks after treatment
  - PPI therapy should be withheld for 1-2 weeks before testing because of bacteriostatic effects of PPI on Hp

Saniee P, *et al. Helicobacter.* 2016 Apr;21(2):143-52. doi: 10.1111/hel.12246

Question #1

A young woman undergoes upper endoscopy for unexplained nausea & vomiting. The stomach appears normal. Surveillance biopsies are taken & the gastric biopsy urease test is positive. The biopsies are most likely to show:

A. Hp organisms, but no gastric or esophageal inflammation.
B. Hp organisms plus gastric inflammation (gastritis).
C. Hp organisms plus esophagitis.
D. Neither Hp organisms, nor inflammation because the urease test is often false positive with a normal endoscopy.

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Question #2

What is the most likely source for humans to acquire *H. pylori* infection?

A. Perinatally from mother
B. Ingestion of raw vegetables
C. Ingestion of undercooked meat
D. Ingested tap water from a municipal source
E. Contact with infected secretions from another human

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Helicobacter pylori

- Humans are the only natural Hp host
- Infects > 50% of the world's population
  - US ~20-40%*
- A leading chronic infection in humans
- Majority are asymptomatic but **all have chronic active gastritis**
- Severity of gastritis varies depending on the Hp strain & the host

*At greater risk: indigenous Americans, Black/AA, Hispanic, & immigrants from high-cancer-risk countries like Japan, Korea, Taiwan & China

Lee Y, *et al. Annu Rev Med* (2022)
Crowe SE, *NEJM* (2019)

Helicobacter pylori & Cancer

Hp is a carcinogen that causes an inflammation-driven cancer

- 1-3% of infected individuals will develop cancer
- Hp causes 15% of the total cancer burden globally
- Up to 89% of all gastric cancer is attributable to Hp

Chronic active gastritis
↓
Atrophic gastritis
↓
Epithelial metaplasia
↓
Intraepithelial neoplasia
↓
Invasive carcinoma

Lee Y, *et al. Annu Rev Med* (2022)
Shah SC, *et al Gastroenterology* (2021)

Transmission of *H. pylori*

- Transmission likely **fecal-oral** or **oral-oral**
- Intrafamilial spread very common
  - Person-to-person, esp. mother-to-child but not during pregnancy
- Low socioeconomic status, poor sanitation, crowding associated with ↑transmission

JAMA 282:2240, 1999 & *Crowe SE, UpToDate* (2018)
Zhou XZ, *et al. Gut.* (2023) May;72(5):855-869. doi: 10.1136/gutjnl-2022-328965. PMID: 36690433

Disease Paths for *Helicobacter pylori* Infection

Asymptomatic gastritis	85-90%
Peptic ulcer (DU, GU)	1-17%
Gastric cancer	0.1-3%
MALT lymphoma	<0.01%

DU, duodenal ulcer
GU, gastric ulcer
MALT, mucosal-associated lymphoid tissue

Lee Y, *et al. Annu Rev Med* (2022)
NEJM 347: 1175, 2002
Gut 66:6, 2017

H. pylori: Disease Associations

- #1 cause of chronic gastritis
- PUD: 90% of DU, 80% of GU
- MALT lymphomas (72 – 98%)
- Gastric Cancer (60 – 90%)

Hp causal

H. pylori is a World Health Organization-designated carcinogen & the strongest known risk factor for non-cardia gastric adenocarcinoma

- Iron deficiency anemia, B12 deficiency, ITP
- Eradication of Hp neither causes nor exacerbates GERD
- Hp poss. **reduces** risk for Barrett's esophagus/esophageal CA

HP is classified by WHO as a Class 1 carcinogen.
MALT = mucosal-associated lymphoid tissue

Maastricht V. Gut 66:6, 2017
Kasahun GG, Infect Drug Resist 13:1567-1573, 2020
Shah SG, et al. Gastroenterology 2021;160:1831–18

Question #3

PREVIEW QUESTION

A 25-year-old woman complains of 6 weeks of symptoms consistent with dyspepsia unrelieved by current use of antacids & an OTC PPI.

The best approach to the diagnosis of *H. pylori* infection in this patient is:

A. Immediate Hp serology
B. Immediate Hp stool antigen EIA
C. Endoscopy with rapid urease test (RUT)
D. Immediate ^{13}C Urea Breath Test
E. D/C PPI for 2 weeks then Hp stool antigen EIA

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E. D/C PPI for 2 weeks then Hp stool antigen EIA *

Who Should Be **Tested** for Hp?

Patients with:

Do Not Test for GERD Symptoms

- Suspected Hp infection (e.g., active DU)
- Current or past GU or DU
- Uninvestigated dyspepsia
- Gastric MALT lymphoma
- Family members in same household of pt w/ proven, active Hp infection
- Family hx of PUD or gastric cancer
- 1st generation immigrants from high-prevalence areas
- Higher prevalence groups (Latino, Black/AA, indigenous populations)
- Regular user of NSAIDs
- Long-term PPI use
- Fe deficiency anemia (unexplained)
- ITP (low evidence base)

Lee Y, *et al. Annu Rev Med* (2022)

Diagnosis of Hp Infection

NO:

Noninvasive (global)	Sensitivity	Specificity	
Urea Breath Test UBT (^{13}C)	> 90 – 95%	> 90 – 95%	Live Hp
Stool Antigen (monoclonal)	> 90 – 95%	> 90 – 95%	Live & dead Hp
Serology	85%	79%	Detects exposure

Biopsy-based (sampling error)	Sensitivity	Specificity	
Rapid urease test	90%	95%	2-5 bx recommended
Histology	90 – 95%	95 – 98%	
Culture	73%	100%	Difficult

Serology is not useful. UBT considered 'best test'. Antigen test is usually less expensive.
Use only monoclonal stool Ag tests.
Histology requires 10^4 organisms to visualize

Lee Y, *et al. Annu Rev Med* (2022)

Testing Limitations for Hp

PPI
Antibiotics
Bismuth
Bleeding

Interfere with all Hp tests because they reduce bacterial load

False negatives due to decreased Hp burden
Recommend delay diagnostic testing until:

- PPI stopped for > 2 weeks (**OTC antacids & H2RA do not affect UBT/SA testing**)
- Antibiotics, bismuth stopped for > 4 weeks
- Bleeding stopped for 4-8 weeks

Lee Y, et al. Annu Rev Med (2022)
Crowe SE, UpToDate (2018)
Crowe SE, NEJM 380:1158-65 (2019)

Initial Diagnosis of *H. pylori* with Dyspepsia

MOST = NONINVASIVE

- Stool antigen test (SAT)
- Urea Breath Test (UBT)

- Endoscopy mandatory if ≥60 years old or '**alarm symptoms** or signs':
  - Unexplained iron-def anemia
  - GI bleeding
  - Unintentional weight Loss
  - Palpable mass
  - Severe abdominal pain
  - Persistent vomiting
  - Progressive dysphagia / odynophagia

Crowe SE. UpToDate (2018)
Crowe SE, NEJM 380:1158-65 (2019)

Question #4

- Which of the following is the most appropriate next step for evaluating a 29-year-old previously healthy but overweight male patient with typical retrosternal heartburn symptoms?
  - A. Stool antigen test for *H. pylori*
  - B. Urea breath test for *H. pylori*
  - C. No testing for *H. pylori*
  - D. Serological testing for *H. pylori*
  - E. Empiric therapy for *H. pylori* regardless of testing

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  - C. No testing for *H. pylori* *
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  - E. Empiric therapy for *H. pylori* regardless of testing

Explanation for Q#4

- Hp is not implicated as an etiological factor in gastroesophageal reflux disease (GERD)
- Treatment for (eradication of Hp) can **increase** the risk for Barrett's esophagus & esophageal adenocarcinoma
- Serology is **not** a recommended test for *H. pylori*

Siddique O, *et al. AJM* 2018

Question #5

A 23 yo woman presents with persistent epigastric discomfort diagnosed as Hp+ gastritis by endoscopy. Fecal Hp antigen is also positive. Last year she was treated with azithromycin for a respiratory tract infection. As a child, she was treated repeatedly with PCN/amoxicillin for recurrent tonsillitis.

What do you recommend for therapy?

A. Clarithromycin + amoxicillin + PPI
B. Metronidazole + erythromycin + PPI
C. Bismuth subsalicylate + TCN + metronidazole + PPI
D. Metronidazole + amoxicillin + PPI
E. PPI therapy alone given her age

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Who should be treated for *H. pylori* infection?

Houston Consensus Conference on Testing for *Helicobacter pylori* Infection in the United States

Hashem B. El-Serag,[*,†] John Y. Kao,[‡] Fasiha Kanwal,[*,†,‖] Mark Gilger,[§,#] Frank LoVecchio,[**] Steven F. Moss,[††] Sheila Crowe,[‡‡] Adam Elfant,[††] Thomas Haas,[§§] Ronald J. Hapke,[##] and David Y. Graham[*,†]

- "We recommend that all patients with active *H pylori* infection be treated"
- "Infection causes chronic progressive damage to the gastric mucosa that in 20%–25% of individuals will result in life-threatening clinical outcomes such as peptic ulcer or gastric cancer"

El-Sarag HB, *et al. Clin Gastroenterol Hepatol 2018;16:992–1002*

Treatment of Hp

- Cure rates of most Hp therapies are **relatively low** (<80%)
- Antibiotic resistance is a HUGE challenge, provoking quadruple therapies
- **Ask about prior antibiotic exposure** hx (especially clarithromycin & fluoroquinolones)
- Discuss the critical importance of **adherence to treatment**
- Use **high dose PPI** (BID dose; increase gastric pH>4-5)
  - Hp grows optimally at pH 6-8 & low pH hinders stability & activity of macrolides, amoxicillin
  - Fast metabolizers of PPIs (CYP2C19 genotypes) reduce levels of omeprazole/lansoprazole
  - Vonoprazan: new potassium-competitive acid blocker appears promising

Lee YC, Annu Rev Med (2022)

11 – Helicobacter and Clostridium Difficile

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Treatment of Hp

- Triple therapy with a PPI, clarithromycin, & amoxicillin or metronidazole is **not favored** due to increased prevalence of macrolide resistance (but might still be an option on boards!)
  - Clarithromycin resistance in the US now ≥ 15%
- Use a bismuth-based **quadruple therapy for 14 days** as 1st-line therapy:
  - Bismuth subsalicylate or subcitrate
  - Tetracycline (**not** doxycycline: results are inferior)
  - Metronidazole
  - PPI

Shah SC, *et al. Gastroenterology* 2021;160:1831–1841
Cho J, *et al. Gastroenterol Clin N Am* 50 (2021) 261–282
Hulten KG, *et al. Gastroenterology* 2021
Lee YC, *Annu Rev Med*: 2022

Treatment of Hp Continued…

- Consider antibiotic susceptibility testing after multiple relapses
  - Culture-based & non-culture-based (NGS) techniques can determine resistance
- Success should always be confirmed by a **test of cure** after treatment of every patient (*e.g.*, UBT performed 4 or more weeks after therapy)

Lee YC, Annu Rev Med (2022)

Eradication of *Helicobacter pylori*

- Fluoroquinolone resistance is common now (>50%)
  - They are not recommended in 1st-line treatment regimens
- Resistance to amoxicillin, tetracycline & rifabutin is **uncommon**
- Clinical significance of resistance to metronidazole not straightforward

Shah SC, *et al. Gastroenterology* 2021;160:1831–1841
Cho J, *et al. Gastroenterol Clin N Am* 50 (2021) 261–282
Hulten KG, *et al. Gastroenterology* 2021

RIFABUTIN-Based Combinations

- 2020: The FDA approved **fixed-dose combination** of omeprazole, amoxicillin & rifabutin (Talicia) for *Hp* treatment in adults
- Omeprazole 10 mg, amoxicillin 250 mg, & rifabutin 12.5 mg
  - The recommended dosage is 4 capsules (with food) every 8 hours for 14 days
- For salvage; not amazing

Summary: Omeprazole/Amoxicillin/Rifabutin (*Talicia*)

- A fixed-dose, rifabutin-based, 3-drug combination FDA-approved for treatment of *Helicobacter pylori* infection.
- First rifabutin-based product to be approved for treatment of *H. pylori* infection.
- Rifabutin-based triple therapy has been used for years as a salvage regimen for treatment-refractory *H. pylori* infection.
- Approval was based on the results of two trials in treatment-naive patients; *H. pylori* was eradicated in about 80% of those treated with the combination.
- How the efficacy of *Talicia* compares to that of other regimens used for first-line treatment of *H. pylori* infection is unknown.
- Rates of *H. pylori* resistance to rifabutin have been low; whether more widespread use as part of a first-line regimen would result in higher rates of resistance remains to be established.
- Common adverse effects include diarrhea, headache, rash, and dyspepsia.
- Has the potential to interact with many other drugs.

The Medical Letter (2020)
Smith SM, *et al. European Journal of Gastroenterology & Hepatology* (2024)

Question #6

After treatment of this patient for Hp gastritis, the *H. pylori* stool antigen test should be repeated:

A. On the final day of *H. pylori* therapy
B. Two weeks after completion of *H. pylori* therapy
C. Four weeks after completion of *H. pylori* therapy
D. The test should not be repeated to assess cure

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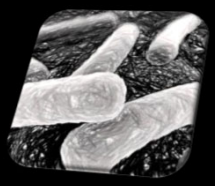
CLOSTRIDIOIDES DIFFICILE



Clostridioides difficile: Take Home Points

- Community-onset disease increasingly common
- Diagnosis of *C. difficile* infection (CDI) relies on combination of appropriate clinical syndrome plus evidence of toxin B
- Not all *C. difficile* organisms are toxigenic/disease-causing
- Severe disease is based on leukocytosis &/or renal injuf‰

Clostridioides difficile: Take Home Points

- Fidaxomicin is a favored first-line option, & oral vanco is good (more recurrences, but often more available/less $)
- Metronidazole is no longer a preferred option
- Recurrence is a major challenge
- Recurrence risk reduced by stopping other antibiotics, using fidaxomicin, bezlotoxumab, live biotherapeutic products, or FMT
- No test of cure should be performed

Facts about *C. difficile* infection (CDI)

- Not all antibiotic-associated diarrhrea (AAD) is due to *C. difficile* (probably <40%)
- Nearly all AA **colitis** is CDI
- ~500,000 cases & ~30,000 deaths per year in the US
- Healthcare-associated CDI rates are declining
- Community-associated CDI rates are increasing
- Recurrent CDI (rCDI) is a major problem, accounting for 75,000-175,000 cases of CDI each year in the US

Feuerstadt P, *et al. BMC Infectious Diseases* (2023) 23:132
Selvaraj V & Alsamman MA. Antibiotic-Associated Diarrhea Beyond *C. Difficile*: A Scoping Review. *Brown Hospital Medicine*. 2022

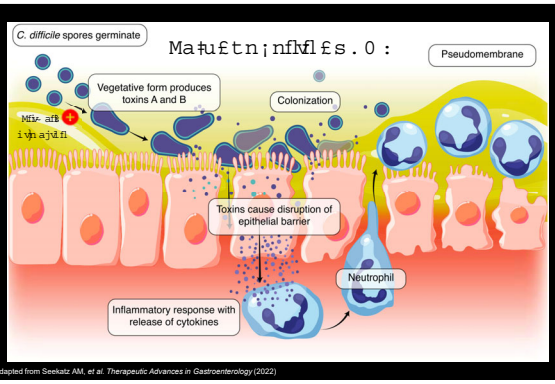
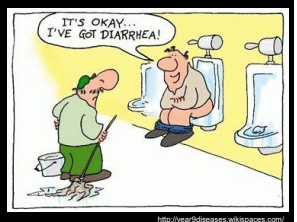


Figure adapted from Seekatz AM, *et al. Therapeutic Advances in Gastroenterology* (2022)

Common Clinical Manifestations

- Watery & mucousy diarrhea up to 10 - 15 times daily
- Lower abdominal pain & cramping
- Low grade fever (15%+)
- Leukocytosis (> 15,000 cells/ml = severe)
- Nausea
- Anorexia
- Malaise



http://year9diseases.wikispaces.com/

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CDI Severity

- **Leukocytosis**
- **AKI**
- **Sepsis/shock**
- **Megacolon**

Stool frequency is not part of severity assessment

Clinical Definition	Supportive Clinical Data
Nonsevere	Leukocytosis with a WBC count of ≤15,000 cells/mL and a serum creatinine level <1.5 mg/dL
Severe	Leukocytosis with a WBC count of ≥15,000 cells/mL or a serum creatinine level >1.5 mg/dL
Fulminant	Hypotension or shock, ileus, megacolon

Table from Wilcox M, *IDSE* (2018)
McDonald LC, *et al. Clin Infect Dis.* 2018 Mar 19;66(7):987-994

C. difficile Diagnostic Testing

Whom to test?

- Appropriate epidemiology/ill with diarrhea/endoscopic findings
  - No laxatives within last 48 hrs (board exam vs. real world caveat)
- Test diarrheal stools (unless ileus). *One stool.*
  - >3 liquid stools over 24h
- Only test specimens if patient > 1 year old

McDonald LC, *et al. Clin Infect Dis.* 2018 Mar 19;66(7):987-994

C. difficile Diagnostic Testing

Simplified approach:

Diarrhea* + **Toxigenic *C. difficile* &/or toxin in stool** → **TREAT**

*No other obvious causes

C. difficile Diagnostic Testing

Nucleic acid amplification test (NAAT; PCR):

Detects the gene for toxin B

Advantages

- High sensitivity
- Rapid
- Relatively inexpensive

Disadvantages

- Does not detect actual toxin
- Can't differentiate colonization *vs* infection

Patient selection is critical

C. difficile Diagnostic Testing

Glutamate dehydrogenase (GDH) antigen EIA:

Detects *C. difficile* bacteria by secreted antigen

Advantages

- High sensitivity
- Rapid
- Relatively inexpensive

Disadvantages

- Does not detect toxin
- Detects NON-toxigenic strains
- Cannot differentiate colonization from infection

Must be combined to test for toxin (NAAT or EIA)

C. difficile Diagnostic Testing

Toxin A/B detection by EIA:

Detects *C. difficile* toxin(s) directly

Advantages

- Good specificity
- Rapid
- Relatively inexpensive

Disadvantages

- Poor sensitivity
- False positives possible

Usually used in a 2-step protocol with N% %S £fi8 0 9

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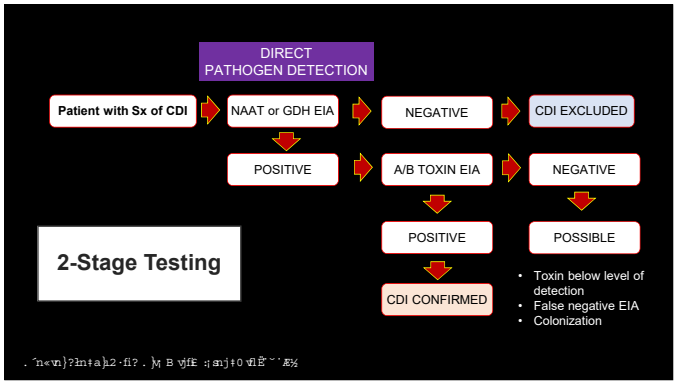

Question #7

PREVIEW QUESTION

- 67 year old woman develops diarrhea while hospitalized for community acquired pneumonia. She is afebrile, WBC count is 12,000/ml, creatinine is 1.2 mg/dl (baseline 1.0 mg/dl) and she is experiencing 12 small loose stools daily with abdominal cramping. Stool PCR is positive for *C. difficile* toxin B. Which of the following therapies is recommended?
  a. Metronidazole 500 mg po TID x 10 days
  b. Vancomycin 500 mg PO qid x 10 days
  c. Fidaxomicin 200 mg PO BID x 10 days
  d. Bezlotoxumab + vancomycin x 10 days
  e. Fidaxomicin 200 mg PO BID + metronidazole 500 mg PO TID x 10 days

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  d. Bezlotoxumab + vancomycin x 10 days
  e. Fidaxomicin 200 mg PO BID + metronidazole 500 mg PO TID x 10 days

Table 1. Treatment Strategies for CDI.

	IDEA/SHEA	ACG	ESCMID
Preferred Regimens for an Initial CDI Episode			
Non-severe	Fidaxomicin	Fidaxomicin or vancomycin (metronidazole for low-risk only)	Fidaxomicin
Severe	Fidaxomicin	Fidaxomicin or vancomycin	Fidaxomicin or vancomycin
Fulminant/complicated	High-dose vancomycin + IV metronidazole	High-dose vancomycin ± IV metronidazole	Vancomycin or fidaxomicin
Preferred Regimens for Recurrent CDI Episodes			
First recurrence	Fidaxomicin	Fidaxomicin or tapered/pulsed vancomycin	First-line: Fidaxomicin or the addition of bezlotoxumab (tailored based on treatment regimen for the initial episode)
Second recurrence	Fidaxomicin, vancomycin tapered and pulsed regimen, vancomycin followed by rifaximin, FMT	Not specifically addressed	FMT or standard regimens and bezlotoxumab, if not used previously (tailored based on past treatment regimens)

Table from Bainum TB, *et al. Microorganisms* (2023)

Recurrent CDI

Treatment	Contents	Dose/route	Recurrence rate (active treatment)	Recurrence rate (placebo)	Absolute risk reduction	FDA Approval	Ref.
Bezlotoxumab (ZINPLAVA®)	Monoclonal Ab	10 mg/kg IV x 1	15.7-17.4%[a]	25.7-27.6%[a]	**10.0-10.2%**	YES	(1)
SER-109 (VOWST®)	Feces	4 caps QD PO x 3 d	12.4%[b]	39.8%[b]	**27.4%**	YES	(2)
RBX2660 (REBYOTA®)	Feces	150 mL PR enema x 1	29.4%[b]	42.5%[b]	**13.1%**	YES	(3)
VE303	8 Clostridia strains	10 caps QD x 14 d	13.8%[b]	45.5%[b]	**31.7%**	NO	(4)*
FMT#	Feces	Various	32.3%	56.6%	**23.3%**	With pt. consent	(5)

1. Package Insert; 2. Package Insert; 3. Package Insert; 4. Louie T, *et al. JAMA* (2023); 5. Tariq R, *et al. CID* (2019)

Recurrence rates are shown for (a) 12 or (b) 8 weeks post treatment
*Phase II study data only
#FMT more effective with > 1 dose

Therapy of CDI with drug doses

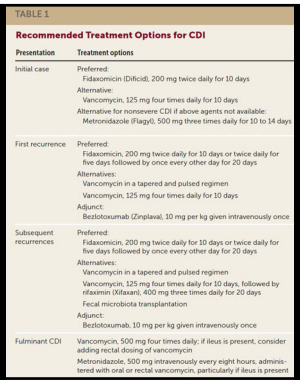

TABLE 1

Recommended Treatment Options for CDI

Presentation	Treatment options
Initial case	Preferred: Fidaxomicin (Dificid), 200 mg twice daily for 10 days Alternative: Vancomycin, 125 mg four times daily for 10 days Alternative for nonsevere CDI if above agents not available: Metronidazole (Flagyl), 500 mg three times daily for 10 to 14 days
First recurrence	Preferred: Fidaxomicin, 200 mg twice daily for 10 days or twice daily for five days followed by once every other day for 20 days Alternatives: Vancomycin in a tapered and pulsed regimen Vancomycin, 125 mg four times daily for 10 days Adjunct: Bezlotoxumab (Zinplava), 10 mg per kg given intravenously once
Subsequent recurrences	Preferred: Fidaxomicin, 200 mg twice daily for 10 days or twice daily for five days followed by once every other day for 20 days Alternatives: Vancomycin in a tapered and pulsed regimen Vancomycin, 125 mg four times daily for 10 days, followed by rifaximin (Xifaxan), 400 mg three times daily for 20 days Fecal microbiota transplantation Adjunct: Bezlotoxumab, 10 mg per kg given intravenously once
Fulminant CDI	Vancomycin, 500 mg four times daily; if ileus is present, consider adding rectal dosing of vancomycin Metronidazole, 500 mg intravenously every eight hours, administered with oral or rectal vancomycin, particularly if ileus is present

Table from Finke J, *Am Fam Physician*. 2022 Jun;105(6):678-679.

11 – Helicobacter and Clostridium Difficile

Speaker: David Aronoff, MD

Therapy of CDI

TABLE 1

Recommended Treatment Options for CDI

Presentation	Treatment options	Additional information
Initial case	Preferred: Fidaxomicin (Dificid), 200 mg twice daily for 10 days Alternative: Vancomycin, 125 mg four times daily for 10 days Alternative for nonsevere CDI if above agents not available: Metronidazole (Flagyl), 500 mg three times daily for 10 to 14 days	Fidaxomicin: Caution for use in patients with congestive heart failure Diagnosis of nonsevere cases supported by: White blood cell count < 15,000 cells per μL (15×10^9 per L) Serum creatinine < 1.5 mg per dL (132.6 μmol per L)

No more metronidazole

(unless mild disease, in young person, +/- cost constraints)

Table from Finke J, *Am Fam Physician*. 2022 Jun;105(6):678-679.

Therapy of CDI

TABLE 1

Recommended Treatment Options for CDI

Presentation	Treatment options	Additional information
Fulminant CDI	Vancomycin, 500 mg four times daily; if ileus is present, consider adding rectal dosing of vancomycin Metronidazole, 500 mg intravenously every eight hours, administered with oral or rectal vancomycin, particularly if ileus is present	Definition of fulminant CDI is supported by: Hypotension or shock, ileus, megacolon

Table from Finke J, *Am Fam Physician*. 2022 Jun;105(6):678-679.

Therapy of CDI

TABLE 1

Recommended Treatment Options for CDI

Presentation	Treatment options	Additional information
First recurrence	Preferred: Fidaxomicin, 200 mg twice daily for 10 days or twice daily for five days followed by once every other day for 20 days Alternatives: Vancomycin in a tapered and pulsed regimen Vancomycin, 125 mg four times daily for 10 days Adjunct: Bezlotoxumab (Zinplava), 10 mg per kg given intravenously once	Tapered and pulsed vancomycin regimen example: 125 mg four times daily for 10 to 14 days, two times daily for seven days, once daily for seven days, and then every two to three days for two to eight weeks

Table from Finke J, *Am Fam Physician*. 2022 Jun;105(6):678-679.

Therapy of CDI

TABLE 1

Recommended Treatment Options for CDI

Presentation	Treatment options	Additional information
Subsequent recurrences	Preferred: Fidaxomicin, 200 mg twice daily for 10 days or twice daily for five days followed by once every other day for 20 days Alternatives: Vancomycin in a tapered and pulsed regimen Vancomycin, 125 mg four times daily for 10 days, followed by rifaximin (Xifaxan), 400 mg three times daily for 20 days Fecal microbiota transplantation Adjunct: Bezlotoxumab, 10 mg per kg given intravenously once	Infectious Diseases Society of America guideline panel recommends appropriate antibiotic treatments should be tried for at least two recurrences (i.e., three CDI episodes) before offering fecal microbiota transplantation

Table from Finke J, *Am Fam Physician*. 2022 Jun;105(6):678-679.

Thank you

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