

Helicobacter pylori Microbiology

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

Urease + → Survival, Colonization, Diagnosis
Urea → CO₂ + NH₃ → ↑pH

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20 Helicobacter and Clostridioides

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 diagnose Hp
- NEVER TEST WITH SEROLOGY

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Endoscopy for diagnosis if alarm symptoms

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

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 (BQT)** = bismuth/metronidazole/tetracycline/PPI (double dose PPI)
 - Treat for 14 days

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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 suppressive effects of PPI on Hp urease & some concerns about antibacterial actions of PPI

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

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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.

What are 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

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 inflammationdriven 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

Shah SC, et al Gastroenterology (2021

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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% 0.1-3% Gastric cancer 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

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H. pylori: Disease Associations

- #1 cause of chronic gastritis
- PUD: 90% of DU, 80% of GU

• MALT lymphomas (72 – 98%)

• Gastric Cancer (60 – 90%)

causal

- 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;160:1831-1841

H. pylori is a World Health Organization-designated

carcinogen & the strongest known risk factor for non-cardia

gastric adenocarcinoma

Question #3

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

What is the best approach to the diagnosis of *H. pylori* infection in this patient?

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

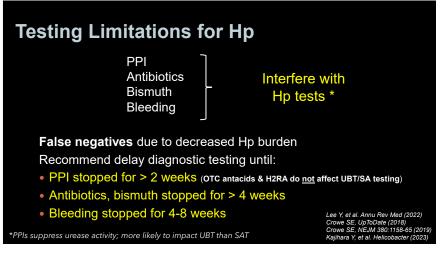
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Do Not Test for Who Should Be Tested for Hp? **GERD** Patients with: **Symptoms** Suspected Hp infection (e.g., active 1st generation immigrants from DU) high-prevalence areas Current or past GU or DU • Higher prevalence groups (Latino, Black/AA, indigenous populations) · Uninvestigated dyspepsia Regular user of NSAIDs · Gastric MALT lymphoma Long-term PPI use • Family members in same household of pt. w/ proven, active • Fe deficiency anemia (unexplained) Hp infection • ITP (low evidence base) · Family hx of PUD or gastric cancer Lee Y, et al. Annu Rev Med (2022)

Diagnosis of Hp Infection Noninvasive (global) Sensitivity Specificity Urea Breath Test UBT > 90 - 95% > 90 - 95% Live Hp (13C) Stool Antigen > 90 - 95% > 90 - 95% Live & dead Hp (monoclonal) No: Serology 85% 79% Detects exposure Sensitivity Biopsy-based (sampling **Specificity** error) 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 104 organisms to visualize Lee Y, et al. Annu Rev Med (2022)

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Initial Diagnosis of *H. pylori* with Dyspepsia

MOST = NONINVASIVE

• Stool antigen test (SAT)

• Urea Breath Test (UBT)

• Unexplained iron-def anemia

• GI bleeding

• Unintentional weight Loss

• Palpable mass

• Severe abdominal pain

• Persistent vomiting

• Progressive dysphagia / odynophagia

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Speaker: David Aronoff, MD, FIDSA, FAAM ©2025 Infectious Disease Board Review, LLC

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

Question #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

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Question #5

A 23-year-old 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

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

CLINICAL CUIDELINES

ACG Clinical Guideline: Treatment of *Helicobacter*pylori Infection

William D. Chey, MD, FACG¹, Colin W. Howden, MD, FACG², Steven F. Moss, MD, FACG³, Douglas R. Morgan, MD, MPH, FACG³, Naturals B. Greer, MD, MSEG¹, Snipa Grove, MD, MPH² and Stalija C. Shah, MD, MPH²

ABSTRACT

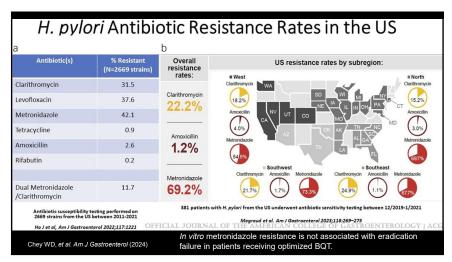
Helicobacter pylori is prevalent, elobal infectious disease that causes dyspeptia, peptic ulter disease of particle Conn.

- All patients with active H pylori infection should be treated
- Infection causes chronic progressive damage to the gastric mucosa
- 20%–25% of individuals will get life-threatening problems such as peptic ulcer or gastric cancer

Chey, WD, et al. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Am J Gastroenterol 119(9):p 1730-1753, September 2024

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Treatment of Hp

- Cure rates of most Hp therapies are relatively low (<80%)
- Antibiotic resistance is a HUGE challenge, provoking quadruple therapies
- AVOID CLARITHROMYIN & 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
- Vonoprazan: new potassium-competitive acid blocker that is more potent than PPIs appears promising

Lee YC, Annu Rev Med (2022), Chey WD, et al. Am J Gastroenterol (2024)

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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 1stline therapy:
 - Bismuth subsalicylate or subcitrate
- Tetracycline (**not** doxycycline: results are inferior)
- Metronidazole
- PPI

enterology 2021;160:1831–1841 Perol Clin N Am 50 (2021) 261–282

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)

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| irea | Treatment | | n in North Ameri | Penicillin |
|--------------------------------|---------------------------|-------------------------------|-------------------------------------|---------------|
| | Naïve | | -Experienced Ivage) | Allergy |
| Regimen | | Empiric | Proven antibiotic sensitivity | |
| Optimized Bismuth Quadruple | | | | ✓ ✓ ✓ * |
| Rifabutin Triple | \square | \square | \checkmark | |
| Vonoprazan Dual | \checkmark | 0 | 0 | |
| Vonoprazan Triple | | | \checkmark | |
| Levofloxacin Triple | | | | |
| ☑ ☑ Recommended | ☑ ☑ Suggest | ed May be consider | dered when other treatments ar | e not options |
| * When Bismuth Quadruple T | herapy not an option, con | sider referral for formal per | nicillin allergy testing and/or des | ensitization |

| Table 5. Recommended regimens for treatment-naive patients with <i>H. pylori</i> infection | | | | |
|--|---|----------------------------|-----------------|---|
| Regimen | Drugs (doses) | Dosing frequency | FDA approval | Recommendation |
| Optimized bismuth quadruple ^a | PPI (standard dose) ^b Bismuth subcitrate (120–300 mg) or subsalicylate (300 mg) ^d | b.i.d. q.i.d. | No ^c | Strong (moderate quality of evidence) |
| | Tetracycline (500 mg) ^e Metronidazole (500 mg) | q.i.d. t.i.d. or q.i.d. | | |
| Rifabutin triple (Talicia) ^f | Omeprazole (10 mg) ^b Amoxicillin (250 mg) Rifabutin (12.5 mg) | 4 capsules t.i.d. | Yes | Conditional (low quality of evidence) |
| PCAB dual (Voquezna DualPak) ^g | Vonoprazan (20 mg) Amoxicillin (1,000 mg) | b.i.d. t.i.d. | Yes | Conditional (moderate quality of evidence |
| PCAB triple (Voquezna TriplePak) ^h | Vonoprazan (20 mg) Clarithromycin (500 mg) Amoxicillin (1,000 mg) | b.i.d. | Yes | Conditional (moderate quality of evidence |

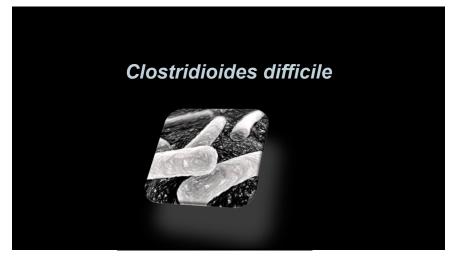
After treatment of this patient for Hp gastritis, when should the *H. pylori* stool antigen test be repeated?

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: 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 injury

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

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- Recurrence risk reduced by stopping other antibiotics, using fidaxomicin, bezlotoxumab, live biotherapeutic products, or FMT
- No test of cure should be performed

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Facts about C. difficile infection (CDI)

- Not all antibiotic-associated diarrhea (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 Pathogenesis of CDI

Pseudomembrane

Vegetative form produces toxins A and B

Colonization

Toxins cause disruption of epithelial barrier

Inflammatory response with release of cytokines

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

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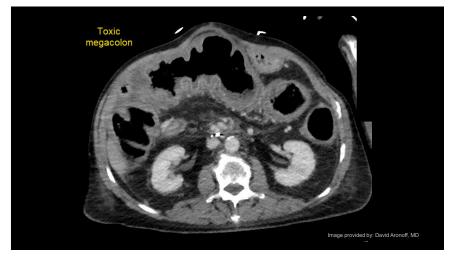
Common Clinical Manifestations

- 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



Clinical Supportive Clinical **CDI Severity Definition Data** Leukocytosis with a Leukocytosis WBC count of ≤15,000 Nonsevere cells/mL and a **AKI** serum creatinine level Sepsis/shock <1.5 mg/dL Megacolon Leukocytosis with a WBC count of ≥15,000 Severe cells/mL or a serum Stool frequency is not part creatinine level >1.5 mg/dL of severity assessment Hypotension or shock, Fulminant ileus, megacolon Table from Wilcox M, IDSE (2018) McDonald LC, et al. Clin Infect Dis. 2018 Mar 19:66(7):987-994

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C. difficile Diagnostic Testing

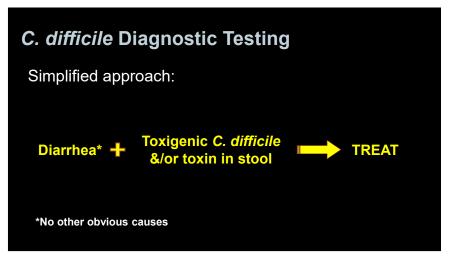
Whom to test?

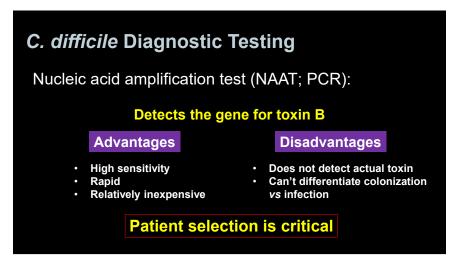
- Appropriate epidemiology/ill with diarrhea/endoscopic findings
- No laxatives within last 48 hrs (board exam vs. real world caveat)
- · Chemotherapy, enteral tube feeds, IBD flare should make you think twice
- Test diarrheal stools (unless ileus). Test only one stool sample.
- >3 liquid stools over 24h
- Only test specimens if patient > 1 year old

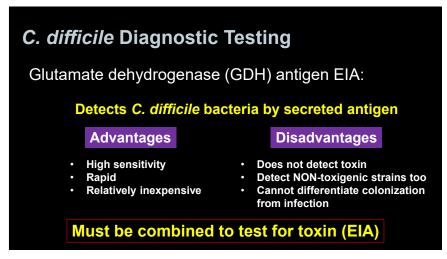
McDonald LC, et al. Clin Infect Dis. 2018 Mar 19;66(7):987-994 L'Huillier JC, et al. J Trauma Acute Care Surg 2024

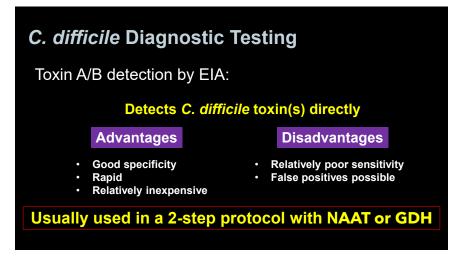
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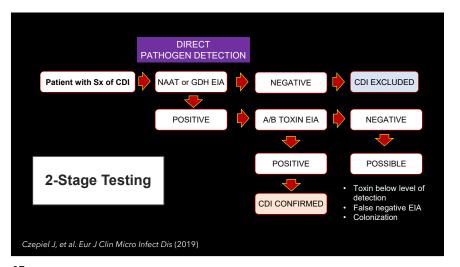


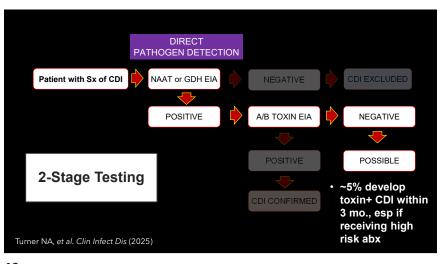


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Speaker: David Aronoff, MD, FIDSA, FAAM ©2025 Infectious Disease Board Review, LLC





| Question #7 |
|--|
| 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 <i>C. difficile</i> 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 |

| | IDEA/SHEA | ACG | ESCMID |
|-----------------------|---|--|---|
| | P | referred Regimens for an Ini | itial 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 |
| | Pr | eferred Regimens for Recurr | rent 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 beziotoxumab, if not used previously (tailored based on past treatment regimens) |

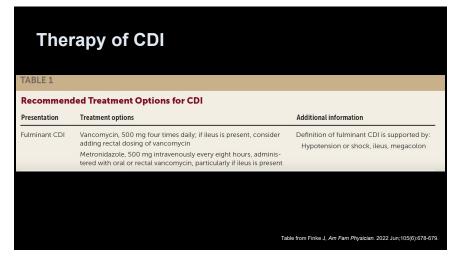
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| Treatment | Contents | Dose/route | Recurrence rate (active treatment) | Recurrence rate (placebo) | Absolute risk reduction | FDA Approval | Ref. |
|-----------------------------|----------------------------|-------------------------------|------------------------------------|---------------------------------|-------------------------------|------------------|------|
| 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) |
| Package Insert; 2. Packag | e Insert; 3. Package In | sert; 4. Louie T, et al. JAM. | A (2023); 5. Tariq R, et al. Cl. | D (2019) | | | |
| *Phase I | l study data | | 12 or (b) 8 week | s post treatmen | t | | |

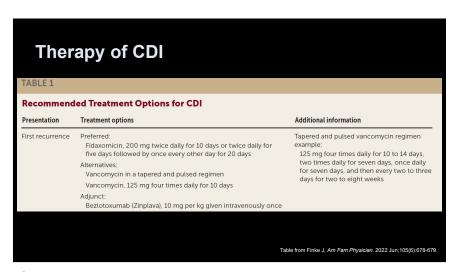
| | TABLE 1 | | |
|---------------------------|---------------------------|---|--|
| | Recommend | led Treatment Options for CDI | |
| | Presentation | Treatment options | |
| Thorany | Initial case | Preferred: Fidaxomicin (Difficid), 200 mg twice daily for 10 days Alternative: Vancomycin, 125 mg four times daily for 10 days Alternative for nonsevere CDI if above agents not available: Metronidazole (Flagyll, 500 mg three times daily for 10 to 14 days | |
| Therapy of CDI with | First recurrence | Preferred: Fidaxomin, 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 lour times daily for 10 days Adjunct: Bezlotoxumab IZinplaval, 10 mg per kg given intravenously once | |
| drug doses | Subsequent recurrences | Preferred: Fidaromicin, 200 mg twice daily for 10 days or twice daily for fide 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: Bezoldoxumab, 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 roal or rectal vancomycin, particularly if ileus is present | Table from Finke J, <i>Am Fam Physician</i> . 2 Jun:105(6):678- |

| 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 μ mol per L) | | |



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Therapy of CDI **Recommended Treatment Options for CDI** Presentation Treatment options Additional information Subsequent Infectious Diseases Society of America Fidaxomicin, 200 mg twice daily for 10 days or twice daily for quideline panel recommends appropriate antibiotic treatments should be tried for five days followed by once every other day for 20 days at least two recurrences (i.e., three CDI Alternatives episodes) before offering fecal microbiota Vancomycin in a tapered and pulsed regimen transplantation Vancomycin, 125 mg four times daily for 10 days, followed by rifaximin (Xifaxan), 400 mg three times daily for 20 days Bezlotoxumab, 10 mg per kg given intravenously once Table from Finke J, Am Fam Physician. 2022 Jun;105(6):678-679.

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