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

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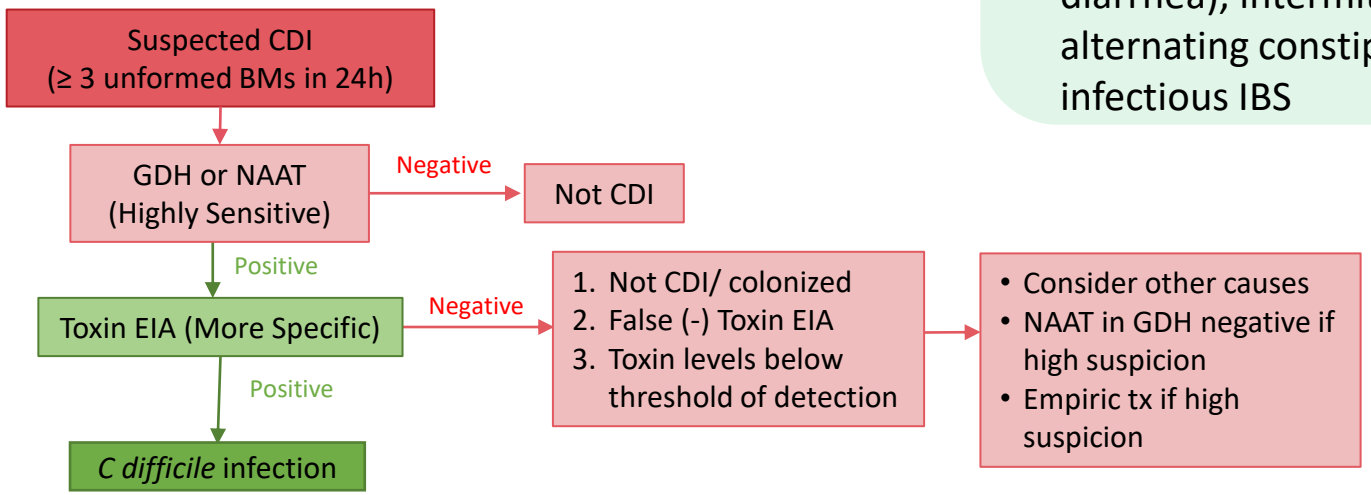
Epidemiology

- Colonization= organism detected w/o symptoms
  - 4-15% healthy adults, up to 21% hospitalized adults, 15-30% long term care facility residents
- Colonization at time of hospital admission ⇒ 6x ↑ risk *C difficile* infection (CDI)
  - RF: contact with healthcare environment, age ≥ 65, antibiotic use, IBD
- Community-associated infections
  - RF: antibiotic use, white race, cardiac disease, CKD, IBD



Diagnosis

- Only test if symptomatic (**≥3 unformed BMs** in 24h)
- Two step testing: Highly sensitive NAAT or GDH ⇒ specific toxin EIA
  - Nucleic acid amplification testing (NAAT)- PCR and loop-mediated isothermal amplification → confirms presence of toxigenic strain but *not* toxin
  - Glutamate dehydrogenase (GDH)- enzyme made by toxigenic & nontoxigenic *Clostridiodes* strains → positive GDH requires confirmation of toxigenic strain (NAAT or EIA)
- Think alternate cause w/ symptomatic colonization if lack of response to PO Vanc in non- severe cases, atypical course (ie, long hx chronic diarrhea), intermittent/ nonprogressive symptoms w/o treatment, hx alternating constipation, and symptoms more suggestive of post-infectious IBS

Prevention

- Enteric precautions for suspected/ confirmed CDI
- No recs re: precautions for asymptomatic carriers
- ⊘ probiotics for prevention if on abx (PLACIDE trial) *or* for CDI recurrence (PICO trial)

Kelly CR, Fischer M, Allegretti JR, LaPlante K, Stewart DB, Limketkai BN, Stollman NH. ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of Clostridioides difficile Infections. Am J Gastroenterol. 2021 Jun 1;116(6):1124-1147. doi: 10.14309/ajg.0000000000001278. PMID: 34003176.

C Diff Treatment

Initial Episode

Non- Severe
(WBC < 15K, Cr < 1.5)

- Vancomycin PO 125mg 4x/d x 10d
- Fidaxomicin PO 200mg BID x 10d
- Metronidazole PO 500mg TID x 10d in low risk (younger patients with minimal comorbidities)

Severe
(WBC > 15K, Cr > 1.5)

- Vancomycin PO 125mg 4x/d x 10d
- Fidaxomicin PO 200mg BID x 10d

Fulminant
(Severe + hypotension/ shock/ ileus/ megacolon)

- Volume resuscitation!
- Vancomycin PO 500mg q6hr x 48-72hrs ⇒ Vancomycin PO 125mg q6hrs x 10d
  - No improvement ⇒ reevaluate w/ multidisciplinary team
- Consider + metronidazole IV 500mg q8hr
- Ileus ⇒ + Vancomycin PR 500mg q6hr

Medical Treatment Failure

- Surgery ⇒ total colectomy w/ end ileostomy & stapled rectal stump *or* diverting loop ileostomy w/ colonic lavage and intraluminal vancomycin
- FMT, especially if poor surgical candidate
  - Repeat FMT q3-5d until resolution of pseudomembrane
  - Continue vancomycin PO 125mg q6hr or fidaxomicin PO 200mg q12hr as long as pseudomembrane present

Recurrent CDI (rCDI)
(Recurrent diarrhea + positive NAAT or EIA w/in 8 wks after treatment of initial episode)

First Recurrence

- Tapering/ pulsed-dose vancomycin if initial course of fidaxomicin, vancomycin, or metronidazole
  - Vancomycin PO 125mg 4x/d x 10-14d ⇒ BID x 7d ⇒ QD x 7d ⇒ q2-3d x 2-8 wks
- Fidaxomicin if initial course vancomycin or metronidazole

Second or Subsequent Recurrence

- FMT via colonoscopy or capsules >> enema
- FMT failure= recurrence of CDI w/in 8 weeks
  - Repeat FMT
    - Restart anti-CDI abx to control symptoms before repeat FMT
  - Prolonged/ indefinite vancomycin, taper down to 125mg QD

- ⊘ Antimotility agents in untreated CDI & fulminant infection, but OK PRN *after* anti-CDI tx initiated
- ⊘ Bile acid-binding agents (ie cholestyramine) → binds abx
- Psyllium and fiber OK
- Don't discontinue antisecretory tx (ie PPI) in CDI if there's appropriate indication for their use

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Predictors of Poor Outcomes

- Severe or fulminant CDI
- Low albumin (from protein-losing colopathy & host defense mechanism that secretes albumin into gut lumen to bind toxin A & B to promote proteolytic cleavage external to gut epithelium)
- FCP >2000
- Peripheral eosinophilia or undetectable eosinophils
- Fever >38.5°C
- Pseudomembranes on colonoscopy

CDI in IBD

- Test for C diff if p/w acute flare w/ diarrhea
- 4.8x ↑ risk developing CDI
- RF: corticosteroids, infliximab or adalimumab, previous hospitalizations, more frequent ambulatory care visits, shorter duration IBD, higher rate comorbidities
- Can be harder to dx ⇒ rarely have pseudomembranes (only mucopurulent exudate)
- Tx- Vancomycin 125mg 4x/d x **14d minimum**
- Do *NOT* hold immunosuppressive IBD tx during anti-CDI tx during flare ⇒ consider escalation of tx if no improvement with CDI tx after 3d
- Consider FMT for recurrent CDI in IBD

Suppression & Prophylaxis

- Recurrent CDI who aren't FMT candidates, relapsed after FMT, or require ongoing/ frequent courses abx ⇒ long term suppressive PO vancomycin
- Consider oral vancomycin prophylaxis (OVP) during subsequent systemic abx use in those with hx CDI and high risk recurrence
  - Vancomycin 125mg QD until **5d *after*** completion systemic abx
- Consider bezlotoxumab (BEZ) to prevent CDI recurrence in high risk
  - ≥ 65 + one additional RF (2nd ep CDI w/in past 6mo, immunocompromised, or severe CDI)
  - BEZ= human monoclonal Ab that binds toxin B → prevents entering GI cell layer & subsequent cell damage
  - Caution use in CHF and severe underlying CVD

CDI in Pregnancy, Peripartum, & Breastfeeding

- Recommend using vancomycin
- Fidaxomicin *if* vancomycin failure
- Avoid FMT 2/2 procedural risks & lack of data in pregnancy ⇒ Can maintain on PO vancomycin and perform FMT postpartum
- Cautious fidaxomicin use & avoid metronidazole in breastfeeding

CDI in Immunocompromised

- Vancomycin or fidaxomicin as 1st line
- Organ transplant= **highest** risk CDI
- Screen for CMV & EBV before FMT & if seronegative, consider transmission risk