Clostridioides difficile infection (CDI) in adults

C. difficile infection (CDI) is one of the most common causes of healthcare-associated infections globally and leads to significant morbidity and mortality. Although the proportion of the virulent subtype (NAP1 strain) has been decreasing in Quebec (from 62% of strains in 2005-2015, to 29% of strains in 2017), the incidence of CDI in community settings has increased. Prompt recognition and management is critical to reduce morbidity and transmission within the hospital setting.

DEFINITIONS

CDI: presence of symptoms (generally diarrhea; more rarely ileus or toxic megacolon) AND stool test positive for *C. difficile* toxin or presence of toxigenic *C. difficile* [or colonoscopic or histopathologic findings of pseudomembranous colitis]
Diarrhea: **≥ 3 diarrheal stools in 24 hours**
Recurrent CDI: re-occurrence of symptoms ≤ 8 weeks after previous episode
Asymptomatic colonization/carriage: stool test positive and no symptoms (asymptomatic patients should generally NOT be tested nor treated)

LAB TESTING for *C. diffcile*:

- ONLY for symptomatic (diarrhea) or high clinical suspicion (e.g. toxic megacolon)
- Repeat testing to document cure is NOT recommended

RISK FACTORS FOR CDI

Recent antibiotic use*, age > 65 years, previous episode of CDI, GI surgery, inflammatory bowel disease, immunocompromise (SOT, HSCT, chemotherapy, HIV with CD4 < 200), CKD, continuous PPI use

**Antibiotics associated with higher risk: broad-spectrum antibiotics with activity against enteric flora (e.g. clindamycin, fluoroquinolones, cephalosporins, clavulin, carbapenems)*

CLINICAL STAGES OF DISEASE

CLINICAL DEFINITION	PARAMETERS
Mild to moderate	WBC < 15 x 10^9 Serum creatinine within normal range (< 133 µmol/L)
Severe, uncomplicated	WBC > 15 x 10^9 Serum creatinine > 133 µmol/L (or > 50% increase from baseline)
Severe, complicated	Hypotension or shock, ileus, megacolon

PHARMACOLOGIC THERAPY

- Discontinue causative antibiotic(s) as soon as possible
- Reassess proton pump inhibitors (pantoprazole, lansoprazole) and D/C if possible[1]
- Avoid antimotility agents (loperamide, diphenoxylate, opioids)

INDICATION	TREATMENT RECOMMENDATIONS
Mild to moderate CDI	**Vancomycin**[2] 125 mg PO QID x 10 days (can extend to 14 days if improving but not resolved) *If documented severe allergy (hypersensitivity reaction) to vancomycin:* Metronidazole 500 mg PO TID x 14 days
Severe, uncomplicated CDI	**Vancomycin**[2] 500 mg PO QID; reduce dose to 125 mg PO QID once clinically improved, total duration 14 days *If documented severe allergy (hypersensitivity reaction) to vancomycin:* Fidaxomicin 200 mg PO BID and consult ID
Severe, complicated CDI	**CONSULT ID + GENERAL SURGERY for possible colectomy, and start** **Vancomycin** 500 mg PO/PT QID[1] x 14 days **PLUS** **Metronidazole** 500 mg IV q8h x 10-14 days If vancomycin PO/PT not feasible and/or paralytic ileus: Vancomycin retention enema (x30 min) 500 mg/100 mL NS PR QID
Recurrent CDI: first recurrence	*Re-treatment* with **Vancomycin** 125 mg PO QID x 14 days + Enroll in clinical trial (if available) + consider tapering regimen: 125 mg PO TID x 1 week then 125 mg PO BID x 1 week then 125 mg PO daily x 1 week then 125 mg PO q48h x 1 week then 125 mg PO q72h x 1 week then stop
Multiple recurrences	CONSULT ID + Enroll in clinical trial (if available) + **Fidaxomicin** 200 mg PO BID x 10 days ***OR*** **Vancomycin** prolonged taper (125 mg po QID for 14 days; 125 mg po TID for 7 days; 125 mg po BID for 7 days; 125 mg po once daily for 7 days, and then every 2 or 3 days for 2–8 weeks Fecal microbiota transplantation (FMT) may be considered in select cases
Secondary prophylaxis	Evidence is limited to small case series; consider ONLY for *severe CDI* or with recurrences in previous year AND currently requiring systemic antibiotic therapy: Vancomycin 125 mg PO BID for up to 1 week after completion of systemic antibiotic therapy

[1] https://deprescribing.org/wp-content/uploads/2018/08/ppi-deprescribing-algorithm_2018_En.pdf

[2] Vancomycin IV is NOT effective for CDI and should NOT be prescribed; vancomycin PO can be systemically absorbed especially if presence of severe colonic disease; it would be prudent to monitor serum concentrations in cases with severe disease (on high doses) in the context of advanced CKD

ADDITIONAL CONSIDERATIONS

- Use of other antibiotics for salvage may be considered in collaboration with ID.
- There is insufficient evidence to recommend the use of probiotics for primary prevention of CDI, but these might be beneficial in certain high risk individuals (routine use not recommended).

REFERENCES

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