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 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

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, amox-clavulanate, carbapenems)*

RISK FACTORS FOR RECURRENCE

- Recent CDI (i.e. ≤ 12 weeks after completing the first line regimen),
- Age > 65 years old
- Severe immunosuppression, eg:
  - On chemotherapy for active malignancy;
  - Recipient of Solid organ or Hematopoietic Stem Cell Transplant (SOT or HSCT);
  - Untreated HIV or HIV with CD4<200;
  - Prednisone > 20mg per day for >2 weeks;
  - Severe Primary immunodeficiency (CVID, Combined Immunodeficiency, other)
  - On TNF-blocker or other biologic agent that is immunosuppressive or immunomodulatory;
  - Trisomy 21

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

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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 **Low risk for recurrence**	**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:* Fidaxomicin 200 mg PO BID x 10 days
Severe, uncomplicated CDI **Low risk for recurrence**	**Vancomycin**[2] 500 mg PO QID; reduce dose to 125 mg PO QID once clinically improved, total x 14 days *If documented severe allergy (hypersensitivity reaction) to vancomycin:* Fidaxomicin 200 mg PO BID and consult ID
Any uncomplicated CDI and ≥ 1 risk factor for recurrence *(see box above)*	**Fidaxomicin** 200 mg PO BID x 10 days (RAMQ Code AI582)
Severe, complicated CDI	**CONSULT ID + GENERAL SURGERY for possible colectomy, and start** **Vancomycin** 500 mg PO/PT QID[1] x 14 days AND **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	*If first recurrence:* *can consider re-treatment with* Vancomycin 125 mg PO QID x 14 days + Enroll in clinical trial (if available) + tapering regimen: Vanco 125 mg PO TID x 1 week then 125 mg PO BID x 1 week then 125 mg PO diey x 1 week then 125 mg PO q48h x 1 week then 125 mg PO q72h x 1 week then stop *If multiple recurrences:* Fidaxomicin 200 mg PO BID x 10 days AND consult ID + enroll in clinical trial if available Prolonged vanco taper can be considered (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[3]	**Vancomycin** 125 mg PO BID for up to 1 week after completion of systemic antibiotic therapy (Consider ONLY for *severe CDI* or with recurrences in previous year AND currently requiring 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
[3] Evidence on secondary prophylaxis is limited to small case series

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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