

Alberta Health Services

## Antimicrobial Stewardship Backgrounder: Clostridium difficile Infection (CDI)

Susan Fryters, BScPharm, ACPR

Antimicrobial Utilization/Infectious Diseases Pharmacist  
Alberta Health Services  
Susan.Fryters@albertahealthservices.ca

Effective, Safe, and Sustainable Medication Use

Alberta Health Services

Laughter is the best medicine.  
Unless you have diarrhea.

www.albertahealthservices.ca 2

Alberta Health Services

## What is Clostridium difficile?

- Spore-forming bacteria
- Causes diarrhea when normal intestinal flora is disrupted, e.g. antimicrobials
- CDI can result in serious complications:
  - pseudomembranous colitis
  - toxic megacolon
  - death

60 preventable deaths in 2014 in AHS = attributable mortality rate of 3.4%

Spore form

Vegetative form

www.albertahealthservices.ca 3

Alberta Health Services

## Impact of C. difficile in Canada

Healthcare-associated CDI rate = 6.99 per 10,000 patient days (2011)

- 37,900 episodes in Canada in 2012
- 14-day increase in LOS
- Additional \$12,000 in costs per CDI episode

⇒ Total costs of CDI \$281 million  
⇒ Total hospital costs \$260 million

www.albertahealthservices.ca 4

Alberta Health Services

## C. difficile in Alberta

The provincial rate of HA-CDI is 3.3 cases per 10,000 patient-days.

Period	Zone	Total Primary Cases	Patient-days	Total Primary Rate	Last Quarter Total Primary Rate
October 1- December 31, 2014	South	11	47,422	2.3	6.2
	Calgary	65	245,943	3.5	4.3
	Central	19	104,688	1.7	1.3
	Edmonton	122	284,160	4.3	4.1
	North	8	57,865	1.4	2.6
	Provincial	244	746,177	3.3	3.8

Rates reported are per 10,000 patient-days  
Primary Cases include New CDI and Reinfections.

www.albertahealthservices.ca 5

6.7 cases

5.2 cases

4.5 cases

1.7 cases

www.albertahealthservices.ca 6

## CDI Risk Factors

- Hospitalization
  - Severe illness
  - Bowel surgery
  - Advanced age (> 65 years old)
  - Acid suppressive therapy (PPIs and H<sub>2</sub> blockers)
  - Antibiotic therapy
- \*\* NO evidence to support use of metro or vanco as prophylaxis, or for continuing anti-CDI therapy, while patient is on a non-CDI antibiotic \*\***

## CDI & Acid suppressive therapy

- Patients on PPIs:
  - **65% increase in CDI** [RR 1.69; 95% CI 1.40-1.97, p<0.001]<sup>1</sup>
  - Increased incidence of recurrence of CDI<sup>2</sup>

1. Janarthanan S, Dittah L, Adler DG, et al. Clostridium difficile-associated diarrhea and proton pump inhibitor therapy: a meta-analysis. *Am J Gastroenterol* 2012;107:1001-10.  
2. Ahmed Samee A, Traub M, Bachmann K, et al. Risk factors for recurrence of Clostridium difficile-associated diarrhea. *Hepatology* 2012;60:1351-4.

## CDI & Antibiotic therapy

- **Canadian cohort study**<sup>3</sup>
  - Inpatients on antibiotics were **60% more likely to develop CDI**
  - At the ward level, antibiotic use was the strongest predictor of CDI incidence
    - 10% increase in ward exposure to antibiotics → 1.34-fold increase in CDI incidence
    - Patients **with and without** direct recent antibiotic exposure

3. Brown K, Valente K, Fisman D, et al. Hospital ward antibiotic prescribing and the risks of Clostridium difficile infection. *JAMA Intern Med* 2015;175(4):628-33.

## Antimicrobial Treatment of CDI

Mild to Moderate Infection	
First or second episode	Metronidazole 500mg PO/NG TID for 10 days <b>Failure to respond in 3-5 days, change to:</b> Vancomycin 125mg PO/NG QID for 10 days
Third or greater episode	Vancomycin 125mg PO/NG QID for 10 days then 125mg BID for 7 days, then 125mg daily for 7 days, then 125mg q2days for 7 days, then 125mg q3days for 7 days
<b>Severe Infection</b>   WBC>15 x 10 <sup>9</sup> /L, creatinine ≥ 1.5x baseline, hypotension, shock, megacolon Vancomycin 125mg PO/NG QID for 10 days If ileus/NPO: Vancomycin 500mg PR*** QID for 10 days PLUS Metronidazole 500mg IV q8h† for 10 days	
** Vancomycin 500mg in 100mL NS via colonic tube clamped x 3h. † Switch to PO/NG as soon as possible; see doses under 1 <sup>st</sup> or 2 <sup>nd</sup> episode.	

Taper regimen. Pulse therapy can also be used.

**NB: Vanco IV not effective**

## Therapeutic Interchanges in CDI

Original Order	Interchange
Vancomycin PO at any dose if patient does not meet criteria for severe CDI* or for oral vancomycin (see next slide)	Metronidazole 500mg PO TID
Vancomycin oral doses > 125mg PO QID	Vancomycin 125mg PO QID***
Vancomycin oral doses (capsules)	Vancomycin IV solution given PO at same dose

- \* Severe CDI: WBC>15x 10<sup>9</sup>/L, creatinine ≥ 1.5x baseline, hypotension, shock, megacolon.  
 \*\*\* Higher doses of oral/NG vancomycin are not needed as:  
 a. faecal levels achieved with 125mg PO Q D (using IV formulation) are 500-100Cx higher than the MIC<sub>90</sub> of vancomycin against *C. difficile*<sup>5</sup>  
 b. a recent study in patients with severe CDI showed no difference in cure rates or other outcomes with doses higher than 125mg PO QID<sup>6</sup>

5. Gonzales et al. Faecal pharmacokinetics of orally administered vancomycin in patients with suspected CDI. *BMC Infect Dis* 2010;10:363-9.  
6. Lam et al. Effect of vancomycin dose on treatment outcomes in severe Clostridium difficile infection. *Int J Antimicrob Agents* 2013;42(6):553-8.

## Oral Vancomycin Guidelines

Oral vancomycin is used solely for the treatment of *C. difficile* infection and only if there is:

- documented failure or clinical deterioration on metronidazole therapy
- clinical relapse of *C. difficile* infection with symptoms after 2 courses of metronidazole therapy
- severe *C. difficile* infection (defined as WBC > 15x10<sup>9</sup>/L, serum creatinine ≥ 1.5 times baseline, hypotension, or shock) or documented or impending toxic megacolon
- intolerance or adverse effects of metronidazole therapy

Alberta Health Services

## CDI Order Sets in AHS/CH

Order Set Name or Number	AHS Zone/ Location
C. Difficile (Clostridium Difficile Management) order set in SCM	Calgary Zone
Red Deer - #19867 Central Zone - #19868	Central Zone
Adult - Form #19718 Pediatric - Form #19719	Edmonton Zone North Zone
Form CV-0318	Covenant Health

www.albertahealthservices.ca 13

Alberta Health Services

## Why use CDI PPCO/order sets?

- Retrospective case-control study<sup>1</sup>
  - 51.7% of patients' prescribers followed the 2010 IDSA guidelines
  - Patients whose prescribers followed the IDSA guidelines experienced fewer complications (17.2% vs. 56.3%, P<0.0001)
    - > ↓ mortality (5.4% vs 21.8%, P = 0.0012)
    - > ↓ CDI recurrence (14% vs 35.6%, P = 0.0007)
  - Patients who presented with severe & complicated disease received guideline-based therapy significantly less often than patients with mild disease (19.7%, 35.3%, and 81.2%, respectively, P <.0001)

1. Brown AT, Seifert CF. Effect of treatment variation on outcomes in patients with *Clostridium difficile*. Am J Med 2014;127:865-70.

www.albertahealthservices.ca 14

Alberta Health Services

## Summary

**Guideline concordant therapy for CDI improves patient outcomes, including recurrences and mortality<sup>1</sup>**

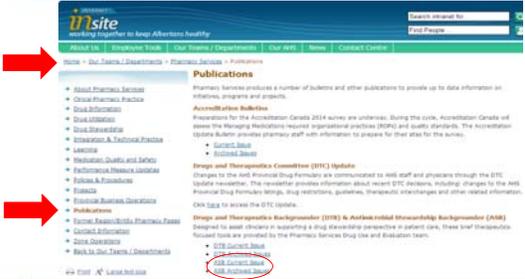


1. Brown AT, Seifert CF. Effect of treatment variation on outcomes in patients with *Clostridium difficile*. Am J Med 2014;127:865-70.

www.albertahealthservices.ca 15

Alberta Health Services

## AHS Insite

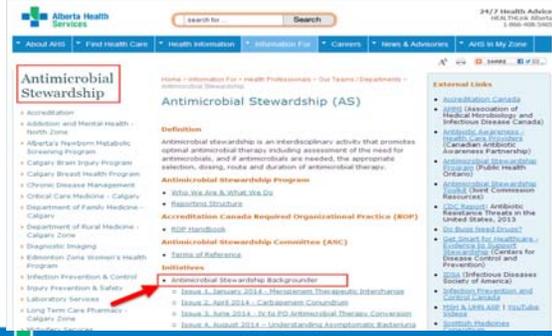


www.albertahealthservices.ca 16

Alberta Health Services

## AHS External ASP website

http://www.albertahealthservices.ca/9674.asp



www.albertahealthservices.ca 17

Alberta Health Services

## With Thanks.....

- Dr. Uma Chandran  
Associate Medical Director, Infection Prevention & Control, RAH/GRH
- DUAP

www.albertahealthservices.ca 18

## References

---

1. Brown AT, Seifert CF. Effect of treatment variation on outcomes in patients with *Clostridium difficile*. *Am J Med* 2014;127:865-70.
2. Provincial IPC Surveillance. Alberta Health Services/Covenant Health *Clostridium difficile* Infections, 3rd Quarter Report, October – December 2014.
3. Brown K, Valenta K, Fisman D, et al. Hospital ward antibiotic prescribing and the risks of *Clostridium difficile* infection. *JAMA Intern Med* 2015;175(4):626-33.
4. Blondel-Hill E, Fryters S, eds. Bugs & Drugs 2012. 2012 edition. Edmonton, AB: Alberta Health Services; 2012. p. 307-9. Alberta Health Services. Bugs & Drugs (March 5, 2015; 2.0.1) [mobile application software]. [Internet]. Available from: <https://itunes.apple.com/ca/app/bugs-drugs/id909765024?mt=3>
5. Gonzalez M, Pepin J, Frost EH, et al. Faecal pharmacokinetics of orally administered vancomycin in patients with suspected *Clostridium difficile* infection. *BMC Infect Dis* 2010;10:363-9.
6. Lam SW, Bass SN, Neuner EA, et al. Effect of vancomycin dose on treatment outcomes in severe *Clostridium difficile* infection. *Int J Antimicrob Agents* 2013;42(6):553-8.
7. Hoang H, Zurek K, Remtulla S. Covenant Health Antimicrobial Stewardship E-Newsletter, April 16, 2014, Issue 2. Available at: [http://www.compassionnet.ca/PatientResident/CHASE\\_Newsletter\\_Issue\\_2.pdf](http://www.compassionnet.ca/PatientResident/CHASE_Newsletter_Issue_2.pdf)

## Questions?

---

