

PACAH

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“Better Out than In”

A Review of the new Clostridium Difficile Infection (CDI) Guidelines

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“Better Out than In”

Objectives

At the completion of this activity, the participant will be able to:

- Explain why CDI is a burden in Long-Term Care (LTC) settings
- Identify major risk factors for CDI
- Discuss the management of initial recurrent CDI
- Discuss Infection Prevention and Control measures
- Describe the role of Antibiotic Stewardship in controlling CDI rates

Complications and Costs of CDI

- Morbidity, mortality, and cost
 - Incidence
 - Historically 3.4-8.4 cases/1000 hospital admissions¹
 - Outbreaks with 22.5 cases/1000 hospital admissions²
 - Estimated 500,000 cases/year in US³
 - Complications: toxic megacolon, sepsis, colectomy, death
 - Mortality: 6-30%⁴
 - Estimated up to 30,000 deaths/year in US³
 - Estimated cost is over \$4.8 billion per year⁵

1 Hyland M, et al. Can J Infect Dis 2001;12:81-8.

2 Loo VG, et al. N Engl J Med 2005;353:2442-9.

3 Lessa FC, Mu Y, Bamberg WM, et al. N Engl J Med 2015;372:825-34.

4 Miller MA, et al. Infect control Hosp Epidemiol 2002;23:137-40.

5 Dubberke ER, Olsen MA. Clin Infect Dis 2012;55(Suppl 2):S88-92

Epidemiology

- Long Term Care Facilities (LTCF)
 - Of estimated 300,000 health care- associated cases, approximately 105,000 (36%) had a nursing home onset¹
 - 5% of LTCF residents have asymptomatic colonization²
 - Prevalence in LTCF residents is 22.4%³
 - LTCF residents 7 times more likely to develop CDI vs. community residents³
 - 3 times more likely to develop severe diseases³

1 Lessa FC, Mu Y, Bamberg WM, et al. N Engl J Med 2015;372:825-34.

2 Rivera EV, Woods S. J Gen Intern Med 2003;18(2):27-30.

3 Karanika S, Grigoras C, Flokas ME, et al. J Am Geriatr Soc 2017;65(8): 1733-40.

Risk Factors

- Antimicrobial exposure during the previous 1-8 weeks (90% of cases)
 - Most commonly seen with
 - Clindamycin
 - Ampicillin/amoxicillin
 - Cephalosporins
 - Fluoroquinolones
 - Takes up to 3 months after antimicrobial exposure for the normal flora to fully recover



Risk Factors (continued)

- Advanced age (≥ 65 years)
- Gastrointestinal surgery
- Immunosuppression
- Underlying debilitating condition
- Nasogastric tube feeding
- Prolonged hospitalization
- Acid suppressive therapy
- Lower concentrations of antibodies against toxins A and B

McDonald LC, Gerding DN, Johnson S, et al. Clin Infect Dis 2018;66(7):987-94.

Bassetti M, et al. Expert Rev Anti Infect Ther 2012;10(12):1405-23.

Cohen SH, et al. Infect Cont Hosp Epidemiol 2010;31(5):431-55.

Dial S, et al. JAMA 2005;294(23):2989-95.

Dial S, et al. Can Med Assoc J 2004;171(1):33-8.

Dial S, et al. Can Med Assoc J 2006;175745-830.

Dial S, et al. JAMA 2005;21:2989-95.

Clinical Presentation

- Diarrhea
- Fever
- Malaise
- Abdominal cramps/pain
- Anorexia/nausea/vomiting
- Leukocytosis
- Elevations in serum creatinine
- Hypoalbuminemia
- Leukocytes in the stool

Diagnosis

- Definition of CDI
 - ≥ 3 unformed stools over 24 hours or fewer consecutive hours in conjunction with positive stool test results or pseudomembranes

Diagnostic Tools

- CT scan of the abdomen
- Mild CDI: diffuse or patchy colitis
 - Pseudomembranous colitis: mucosal edema, thickened colon, pancolitis, or pericolonic inflammation
 - Can identify ileus and megacolon
- Sigmoidoscopy or colonoscopy
- Mild CDI: diffuse, patchy colitis
 - Pseudomembranous colitis: raised, adherent, yellow plaques
 - Erythema, edema, friability, or erosions

Bassetti M, et al. *Expert Rev Anti Infect Ther* 2012;10(12):1405-23

Hurley BW, et al. *Arch Intern Med* 2002;62:2177-84.

Dallal RM, et al. *Ann Surg* 2002;235:363-72.

Gerding DN, Johnson S. Chapter 123. In Fauci AS, et al: *Harrison's Principles of Internal Medicine*, 17th Edition:

<http://www.accessmedicine.com>. Accessed 7/6/2009.

Diagnostic Tools

- 1-step testing
 - Nucleic acid amplification tests (NAATs)
 - Only diarrheal samples from patients not on laxatives with symptoms likely associated with CDI (at least 3 loose or unformed stools in ≤ 24 hours and history of antibiotic exposure.
- 2-step/3-step testing
 - Any diarrheal samples
 - Stool Test for *C.difficile* PLUS a stool toxin assay
 - NAAT PLUS a stool toxin assay

Testing Guidelines

- **DO NOT** test if
 - Diarrhea due to tube feeds, laxatives or other bowel regimen
 - Sepsis or leukocytosis without GI symptoms or signs
- **DO NOT** repeat testing as a test of cure
 - Molecular tests can remain positive for weeks after treatment



Management



- **Discontinue** the offending antimicrobial, if possible
- **Do not** administer antiperistaltic agents (e.g., loperamide) “Better Out than In”
- **Discontinue** proton pump inhibitors (PPIs), epidemiologic association is possible
- **Discontinue** bowel regimens!

Medical Management

Treatment Recommendations

Clinical Definition	Clinical Data	Recommended Treatment ^a	Strength of Recommendation/ Quality of Evidence
Initial episode, non-severe	Leukocytosis with a white blood cell count of $\leq 15,000$ cells/mL and a serum creatinine level < 1.5 mg/dL	• VAN 125 mg given 4 times daily by mouth for 10 days, OR	Strong/High
		• FDX 200 mg given twice daily by mouth for 10 days	Strong/High
		• Alternate if above agents are unavailable: Metronidazole, 500 mg 3 times per day by mouth for 10 days	Weak/ High
Initial episode, severe ^b	Leukocytosis with a white blood cell count of $\geq 15,000$ cells/mL or a serum creatinine level > 1.5 mg/dL	• VAN 125 mg 4 times per day by mouth for 10 days, OR	Strong/High
		• FDX 200 mg given twice daily by mouth for 10 days	Strong/High
Initial episode, fulminant	Hypotension or shock, ileus, megacolon	• VAN 500 mg 4 times per day by mouth or by nasogastric tube. If ileus, consider adding rectal instillation of VAN. Intravenously administered Metronidazole (500 mg every 8 hours) should be administered together with oral or rectal VAN, particularly if ileus is present.	Strong/Moderate (oral VAN); Weak/Low (rectal VAN); Strong/Moderate (intravenous metronidazole)



Treatment Recommendations (Continued)

Clinical Definition	Clinical Data	Recommended Treatment ^a	Strength of Recommendation/ Quality of Evidence
First recurrence	...	• VAN 125 mg given 4 times daily by mouth for 10 days if metronidazole was used for the initial episode, OR	Weak/Low
		• Use a prolonged tapered and pulsed VAN regimen if a standard regimen was used for the initial episode (eg, 125 mg 4 times per day by mouth for 10–14 days, 2 times per day for a week, once per day for a week, and then every 2 or 3 days for 2–8 weeks), OR	Weak/Low
		• FDX 200 mg given twice daily by mouth for 10 days if VAN was used for the initial episode	Weak/Moderate
Second or subsequent recurrence	...	• VAN in a tapered and pulsed regimen, OR	Weak/Low
		• VAN 125 mg 4 times per day by mouth for 10 days followed by rifaximin 400 mg 3 times daily for 20 days, OR	Weak/Low
		• FDX 200 mg given twice daily by mouth for 10 days, OR	Weak/Low
		• Fecal microbiota transplantation ^c	Strong Moderate

Abbreviations: FDX, fidaxomicin; VAN, vancomycin.

^aAll randomized trials have compared 10-day treatment courses, but some patients (particularly those treated with metronidazole) may have delayed response to treatment and clinicians should consider extending treatment duration to 14 days in those circumstances.

^bThe criteria proposed for defining severe or fulminant *Clostridium difficile* infection (CDI) are based on expert opinion. These may need to be reviewed in the future upon publication of pro-spectively validated severity scores for patients with CDI.

^cThe opinion of the panel is that appropriate antibiotic treatments for at least 2 recurrences (ie, 3 CDI episodes) should be tried prior to offering fecal microbiota transplantation.



Novel Therapies: Fecal Microbiota Transplantation (FMT)

- The process of taking stool from a healthy donor and placing it into the GI tract of a patient
- Goal is to restore the healthy gut microbiota by replenishing the intestinal ecosystem of the patient with the microbiota of the healthy donor
- Increasingly popular in the clinical arena and the public media
- Introduction of detrimental microbes during fecal transplantation is a concern

Novel Therapies: Bezlotoxumab (BEZ)_(Continued)

- Monoclonal antibody
- Safe and effective in preventing CDI recurrence
- High cost

Infection Prevention and Control

Infection Prevention and Control

- Wash your hands with soap and water! 
 - Alcohol based hand sanitizers do not kill *C. difficile* spores
- Enteric pathogen isolation
 - Contact isolation with gowns and gloves – continue for at least 48 hours after diarrhea has resolved.
 - Handwashing required before and after resident visit
- Bleach-based room cleaning
- Private room or cohorting if same organism

The Role of Antibiotic Stewardship

The CMS Perspective (Continued)

- Infection Prevention and Control Program (IPCP) includes an Antibiotic Stewardship Program (ASP)
 - ASP is not a stand-alone program
- Antibiotic resistance has emerged as a national healthcare concern
- Even appropriate use of antibiotics can contribute to antibiotic resistance

Role of Antibiotic Stewardship in controlling CDI rates



- Minimize the frequency and duration of high-risk antibiotic therapy and the number of antibiotic agents prescribed, to reduce CDI risk.
- Implement an Antibiotic Stewardship Program (ASP)
- Antibiotics to be targeted should be based on the local epidemiology and the *C.difficile* strains present.
- Restriction of fluoroquinolones, clindamycin, and cephalosporins (except for surgical prophylaxis) should be considered.

Probiotics

Probiotics

- What is the role of Probiotics in primary prevention of CDI?
 - Insufficient data
- What is the role of probiotics for the prevention of CDI recurrence
 - Shown promise

Summary of Clinical Pearls



CDI Pearls



- Most common antibiotics that can predispose a resident to CDI are Clindamycin, Ampicillin/Amoxicillin, Cephalosporins and Fluoroquinolones.
- Do not repeat testing as a test of cure
- Discontinue the offending antimicrobial, PPI's and bowel regimens
- No Loperamide! Better Out than In.
- Wash hands with soap and water

Metronidazole is OUT!
Vancomycin is IN!

*Thank
You!!*

Questions

Case

MM is a 65 year old female and is a resident of a LTC facility. She is reporting frequent foul-smelling stools. 4 weeks ago she had been hospitalized for a complicated UTI. She received ceftriaxone IV for 7 days. The stool test is positive for *C.difficile* toxins A and B. Her medications are Metoprolol, Omeprazole and Escitalopram.

1. Which of the following is the MOST APPROPRIATE agent to treat MM's *C.difficile* infection?
 - a. Oral Metronidazole
 - b. Oral Vancomycin
 - c. Oral Fidaxomicin
 - d. Fecal Microbiota transplant
2. What is the recommended method for hand-washing when caring for residents with CDI?
 - a. Alcohol hand gel
 - b. Soap and water
 - c. You don't have to wash your hands
3. Which one of MM's medications should you consider discontinuing?
 - a. Omeprazole
 - b. Metoprolol
 - c. Escitoprolam