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HealthLine

Focus on *Clostridium difficile* Infection – Part 1: Diagnosis and Treatment

- by Mary Mehrabian and Allen Lefkovitz

Clostridium difficile is a Gram positive, toxin-producing bacteria that attacks the intestinal wall lining causing inflammation and diarrhea. *Clostridium difficile* is one of the most recognized healthcare associated pathogens, and results in significant morbidity, mortality and health care costs. Each year *Clostridium difficile* infection (CDI) affects half a million Americans, leads to more than 250,000 hospitalizations, and results in 15,000-30,000 deaths. Disruption of normal intestinal flora by the use of antibiotics is the most common cause of CDI. Elderly individuals in long term care (LTC) settings are believed to be at a higher risk for CDI due to a decline in immune function, frequent hospitalizations, increased antimicrobial usage, and communal living. For those with CDI, timely diagnosis and treatment is crucial.

In February 2018 the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) published their first updated guidelines on CDI since 2010. This month's focus article will cover diagnosis and treatment of CDI, while next month's focus article will address risk and risk reduction (concentrating on antimicrobial stewardship/infection control) as well as the use of probiotics.

Diagnosis

Only individuals who experience three or more unformed stools in less than 24 hours should be assessed for CDI. If the individual is not receiving laxatives, nucleic acid amplification testing (NAAT) is a suitable diagnostic test. However, if any laxatives have been used, a multi-step testing process involving glutamate dehydrogenase (GDH) plus toxin as well as a nucleic acid amplification test (NAAT) plus toxin should be considered. Repeat testing should not be performed within 7 days during the same episode of diarrhea or for asymptomatic patients. In addition to fecal diagnostic testing, a white blood cell count (WBC) and serum creatinine (SCr) may be helpful in the determination of the severity of the infection.

Treatment

In addition to providing supportive care, prior to initiating treatment for CDI, discontinuation of the inciting antimicrobial agent(s) should be considered whenever possible. Likewise, a reevaluation of antiperistatic agents (e.g., loperamide, opioids, anticholinergics) may be appropriate. Empiric treatment should be started only if diagnostic testing cannot be done in 48 hours or if the individual presents with severe, fulminant (complicated) infection.

Severity of CDI may be characterized as follows:

Non-severe	• WBC less than 15,000 AND • SCr less than 1.5 mg/dL
Severe	• WBC greater than or equal to 15,000 OR • SCr great than or equal to 1.5 mg/dL
Fulminant	• Evidence of hypotension, shock, ileus or megacolon

WBC = white blood cell; SCr = serum creatinine

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The decision of which treatment to initiate should be based on both severity and whether or not it is an initial or recurrent episode. LTC facilities should defer to prescriber judgement and individual facility policies as applicable to manage CDI, including the use of emergency medical services or transfer to a high acuity setting when appropriate.

A summary of recommended treatment options for initial cases and based upon severity are provided in the table below.

Initial CDI	• Vancomycin 125 mg orally every 6 hr x10 days OR • Dificid (fidaxomicin) 200 mg orally every 12 hr x10 days
Initial Severe or Fulminant CDI	**Initial Severe CDI:** • Vancomycin 125 mg orally every 6 hr x10 days OR • Dificid (fidaxomicin) 200 mg orally every 12 hr x10 days • If at high risk for recurrence (e.g., chronic kidney disease, inflammatory bowel disease): May add as adjunct: Zinplava (bezlotoxumab) 10mg/kg IV infusion x1 dose **Initial Fulminant CDI (complicated):** • Vancomycin 500 mg orally (or 500 mg rectally in 100 mL NS for ileus) every 6 hr x10 days **plus** metronidazole 500 mg IV every 8 hr x10 days

Metronidazole is no longer recommended as initial treatment for non-severe infection, unless vancomycin and fidaxomicin are unavailable. Additionally, metronidazole therapy should not be repeated or prolonged due to risk of irreversible neurotoxicity.

Severe CDI can be treated with the same agents and duration as non-severe episodes, but if there is a concern for recurrence in the treatment of severe infection, one dose of Zinplava (bezlotoxumab) IV may be considered for adjunctive therapy.

Recurrent infection

Following an initial case of CDI, there is up to a 30% risk of recurrence. Recurrence is defined as another episode of symptom onset and positive assay result **following** a confirmed episode in the previous two to eight weeks. Treatment options for first, second, and subsequent recurrences are outlined in the table below; however, metronidazole, cholestyramine, colestipol, and rifampin are not recommended for recurrent CDI.

First Recurrence	Second or Subsequent Recurrence
If metronidazole was used for initial episode: • vancomycin 125 mg orally every 6 hr x10 days **If vancomycin was used for initial episode:** • Dificid (fidaxomicin) 200 mg orally every 12 hr x10 days OR Vancomycin in a tapered and pulsed regimen*	• Vancomycin in a tapered and pulsed regimen* OR • Vancomycin 125mg orally every 6 hr x10 days followed by rifaximin 400 mg orally every 8 hr x20 days OR • Dificid (fidaxomicin) 200 mg orally every 12 hr x10 days OR • Fecal microbiota transplantation

*Tapered and pulsed regimen: vancomycin 10 mg/kg with max of 125 mg every 6 hr x10 to 14 days, then 10 mg/kg with max of 125 mg every 12 hr x7 days, then 10 mg/kg with max of 125 mg daily x7 days, then 10 mg/kg with max of 125 mg every 2 or 3 days x2 to 8 weeks. Other taper and pulse regimens exist and may be used at the discretion of the prescriber.

Infection with *Clostridium difficile* increases morbidity, mortality and healthcare cost. As treatment modalities vary depending upon presentation, severity of symptoms, and prior history of CDI, appropriate diagnostic testing, treatment, and ongoing monitoring are crucial.

The full CDI guidelines are available for free at: http://www.idsociety.org/Guidelines/Patient_Care/IDSA_Practice_Guidelines/Infections_By_Organ_System-81567/Gastrointestinal/Clostridium_difficile/

NEW Generic Medications

- by Allen Lefkovitz

Generic Name	Brand Name	Date Generic Available
Ritonavir 100 mg Tablet	Norvir® Tablet	3/20/18
Drosperinone/Ethinyl Estradiol/Levomefolate Calcium 3 mg/0.03 mg/0.451 mg	Safyral™ Tablet	3/12/18

NEW Drug

ZTlido™ (lidocaine) Topical System

- by Dave Pregizer

Brand Name (Generic Name)	**ZTlido [ZEE-TEE-LIE-DOH] (lidocaine) [LYE-doe-kane]]**
How Supplied	Lidocaine 1.8% in a single-use topical system
Therapeutic Class	Amide local anesthetic
Approved Indication	Relief of pain associated with post-herpetic neuralgia
Usual Dosing	Apply to intact skin to cover the most painful area and apply the prescribed number of topical systems (up to three) only once for up to 12 hours in a 24-hour period. May be cut into smaller sizes prior to removal of the release liner.
Select Drug Interactions	Class I antiarrhythmics (e.g., mexiletine) may have additive toxic effects. Additive effects when used concomitantly with other local anesthetic agents.
Most Common Side Effects	Application site reactions such as irritation, erythema, and pruritus
Miscellaneous	One ZTlido (lidocaine topical system) 1.8% provides equivalent lidocaine exposure to one Lidoderm (lidocaine patch 5%). Avoid application to larger surface areas, to non-intact skin, for a longer duration, or with external heat sources due to risk of increased absorption.
Website	www.ZTlido.com

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