


Clostridioides difficile

(formerly known as *Clostridium difficile*)

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Learning Objectives

- Appreciate that testing for *Clostridioides difficile* (*C. difficile*) is an example of diagnostic stewardship: using the right test in the right patient in the right time.
- Recognize situations where *C. difficile* testing is NOT recommended
- State treatment for initial and subsequent occurrences of diarrhea caused by bona fide *C. difficile* infection (CDI) in the outpatient setting
- List at least two ways in which advanced practice providers can help parents understand:
 - When *C. difficile* testing is not appropriate
 - How to minimize the risk of *C. difficile* infection by practicing antimicrobial stewardship


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Relevant Guidelines



Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA)

Clinical Infectious Diseases 2018;66(7):e1-e48



RED BOOK: 2021-2024 REPORT OF THE COMMITTEE ON INFECTIOUS DISEASES - 32nd Ed. (2021)

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Recommendations for Diagnosis of *C. difficile* Infection (CDI)

- **Infants ≤12 months:** Testing for CDI is never routinely recommended due to high rate of asymptomatic carriage
- **1-2 years of age:** CDI testing should not be routinely performed in children with diarrhea unless other infectious or noninfectious causes have been excluded
- **≥2 years of age:** as part of a full diarrhea workup, test for CDI if patient has prolonged or worsening diarrhea AND risk factors (immunocompromised, underlying inflammatory bowel disease) or relevant exposures (contact with healthcare system or recent antibiotics)

Clinical Infectious Diseases 2018;66(7):e1-e48

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Recommendations for Diagnosis of *C. difficile* Infection (CDI)

- Order CDI testing only on patients with unexplained and new onset of **≥ 3 loose or unformed stools in ≤ 24 hrs**
- In general, testing for *C. difficile* should not be ordered on a patient:
 - With formed stools (unless ileitis or toxic megacolon suspected)
 - On laxatives or stool softeners
 - With evidence of a viral or non-infectious cause of diarrhea
- No role for “test of cure” in patients treated for CDI whose symptoms resolve

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Recommendations for Outpatient Treatment

Severity	First Occurrence	First Recurrence (Up to 30% of cases)	Second Recurrence	Notes
Mid-moderate	*Metronidazole, 30 mg/kg/day, PO, every 6 hr (max dose 500 mg/dose) *If fails to respond in 5-7 days consider switch to vancomycin, 40 mg/kg/day, PO, every 6 hr for 10 days (maximum 125 mg/dose)	*Metronidazole, 30 mg/kg/day, PO, every 6 hr (max dose 500 mg/dose) *If fails to respond in 5-7 days consider switch to vancomycin, 40 mg/kg/day, PO, every 6 hr for 10 days (maximum 125 mg/dose)	*Vancomycin, PO, as pulsed or prolonged tapered dose (consult Redbook or expert in pediatric infectious diseases) *Do not use metronidazole	*Oral vancomycin must be used. IV vancomycin does not concentrate in the intestinal lumen and is ineffective for treatment of CDI.
Severe ^a	*Vancomycin, 40 mg/kg/day, PO, every 6 hr for 10 days (maximum 125 mg/dose)	*Vancomycin, 40 mg/kg/day, PO, every 6 hr for 10 days (maximum 125 mg/dose)	*Same as above	*Severe CDI is not well defined in pediatrics; consider with leukocytosis, leukopenia or worsening renal function. Monitor for complications requiring admission (dehydration, ileitis, megacolon etc).

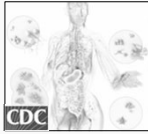
Clinical Infectious Diseases 2018;66(7):e1-e48

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When to Seek Subspecialty Consultation

- Outpatient prolonged or recurrent CDI
- Inpatient hospitalization
- Assess need for Fecal Microbiota Transplantation (FMT):
 - Multiple recurrences with failure of taper
 - ≥2 hospitalizations with significant morbidity
 - Fulminant *C. difficile* colitis with no response to therapy after 48 hours



Davidovics et al. JPGN 2019

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Recommendations for Management

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Prevention of *C. difficile* Transmission at Home and in the Community

- *C. difficile* exists in spore form outside the body on hands and surfaces
- Soap does not kill *C. difficile* spores
- However, the friction of hand washing with soap and water removes spores from hands
- Hand gel is not effective against *C. difficile* spores




<https://www.cdc.gov/cdiff/prevent.html> <https://www.cdc.gov/handwashing/when-how-handwashing.html>

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Prevention of *C. difficile* Transmission at Home and in the Community

C. difficile is spread through the “fecal-oral” route; asymptomatic people can spread it to others.

- Wash hands with soap and water
- Clean surfaces with solution of 1 part bleach to 9 parts water



<https://www.cdc.gov/cdiff/prevent.html>


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Daycare Setting

Exclude child from daycare until:

- Stools are contained in the diaper, OR
- Child is continent and stools no > 2 stools above normal per day


Emphasize meticulous hand hygiene and infection-control measures



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Common Myths




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Myth: One Loose Stool Constitutes Diarrhea

Definition of diarrhea:

- World Health Organization: Passage of three or more loose or watery stools per day
- However, any deviation from child's usual pattern should raise concern especially if ill appearing, or with blood or mucous in stool



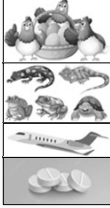
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Myth: *C. difficile* is the Most Common Cause of Diarrhea in US Children

- Viruses account for most bouts of diarrhea in resource rich countries
 - Bacteria (Salmonella, Shigella, etc) are second
- Wide variety of acute and chronic disorders may present with diarrhea
- Thorough history and physical exam can narrow the differential:
 - Onset of symptoms
 - Stool characteristics (diarrhea frequency, duration, consistency, presence of blood)
 - Exposure history (diet, environment including farm animals/poultry/reptiles, travel history, water source, sick contacts, daycare, etc)
 - Antibiotic history
 - Exam: Abdominal distension, tenderness, guarding



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Typical Clinical Presentation of *C. difficile* Overlaps with Other Causes of Diarrhea

Typical presentation of *C. difficile*:

- Acute, watery diarrhea with lower abdominal pain, low-grade fever, and leukocytosis
- Begins during or shortly after antibiotic administration
- Community-associated infection with toxigenic strains of *C. difficile* has been reported in otherwise healthy children who had minimal or no exposure to antibiotics




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Typical Clinical Presentation of *C. difficile* Overlaps with Other Causes of Diarrhea

C. difficile produces two major toxins (A and B)



- Nontoxigenic strains exist but do not cause symptoms
- Mechanism for symptomatic CDI:

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    graph LR
    A[Perturbation of normal intestinal microbiome (Usually from antibiotics)] --> B[Acquisition of Toxigenic strain of C. difficile]
    B --> C[Growth and Elaboration of Toxins]
    C --> D[Inflammation]
    D --> E[Symptoms]
    
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Sammons et al. JAMA Pediatr. 2013

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Why Don't Infants and Young Children Typically Get Sick from *C. difficile*?



<http://www.ciker.com>

Although picture is not entirely clear, possibly because:

- Immature intestinal mucosa may lack receptors for *C. difficile* toxins
 - Even though toxin present, does not cause symptoms
- Infants' immature/blunted immune response may play a part



Intestinal Mucosa

<https://www.cdc.gov/hicpac/reviews/cdiff/nciu/index.html>

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Stool Analysis in Patients with Diarrhea

Baseline Stool Analysis:

- Stool culture including analysis for Shiga toxin and *E.coli* O157
- Viral studies for norovirus and rotavirus

Based on exposures, consider:

- Stool ova & parasite X 3 samples
- Stool *Cryptosporidium* and *Giardia* analysis



https://en.wikipedia.org/wiki/Stool_test

Consider testing for *C. difficile* in the appropriate clinical setting

- Tests vary by institution, but should include *C. difficile* toxin analysis

Clinical Infectious Diseases 2018;66(7):e1-e48

Feigin & Cherry 2019

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Stool Analysis in Patients with Diarrhea

Molecular diagnostic analysis (stool pathogen panels) can be helpful BUT:

- Should only be used in conjunction with (not a substitute for) stool culture, etc.
- Interpretation is challenging due to:
 - High rates of asymptomatic colonization (i.e. *C. difficile* reported in an infant)
 - Reporting of multiple enteric pathogens without insight into main culprit



https://en.wikipedia.org/wiki/Stool_test

Feigin & Cherry 2019

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Antibiotic Use and Stewardship

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Antibiotic Stewardship Can Prevent *C. difficile*

Prior use of antibiotics is the single most important risk factor for *C. difficile* infection

- A 2014 study showed that the majority (71%) of pediatric CDI occurred among children that recently took antibiotics prescribed in doctor's offices for other conditions (ear, sinus, or upper respiratory infections)
- Other studies show at least 50 percent of antibiotics prescribed in doctor's offices for children are for respiratory infections, most of which do not require antibiotics.

<https://www.cdc.gov/media/releases/2014/p0307-severe-diarrheal-illness.html>

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Educate Parents to Reduce Antibiotic Use

- Unnecessary antibiotics can cause harm:
 - Allergic reactions
 - Antibiotic resistance
 - ***C. difficile* infection**
 - Increased risk of inflammatory bowel disease and obesity



- When indicated, prescribe the right antibiotic, at the right dose, for the right duration
- Educate parents about:
 - Signs of harmful side effects
 - Signs of worsening infection

<https://www.cdc.gov/antibiotic-use/week/toolkit.html>

Davidovics et al. JPGN 2019

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Antimicrobial Stewardship Program (ASP) Resources



<https://pids.org/pediatric-asp-toolkit/>



Be Antibiotics Aware Partner Toolkit

<https://www.cdc.gov/antibiotic-use/week/toolkit.html>

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Managing Family Expectations

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Scenario with Families- *C. difficile* testing

Parent/Guardian: "Our neighbor's grandfather had "C. diff" in the nursing home and he was very sick. Now my baby has diarrhea and I want her tested for everything just to be sure."

- Response: "Depending on age, people's reaction to C.diff is very different. Children and adults can get sick from C. diff but babies and toddlers typically don't. Testing for C. diff can distract us away from the more common causes of diarrhea (viruses), or bacteria/parasites they may have picked up from their environment. I'm going to take a thorough history, do an exam, and then test for the most common causes of diarrhea in your baby's age group".

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Scenario with Families- Antimicrobial Stewardship

Parent/Guardian: "I worried my child needs antibiotics for his cough, congestion and fever."

- Response: "Now that I've examined him, I believe a virus is causing your child's symptoms. Things you can do to help him are making sure he gets lots of rest, fluids, acetaminophen or ibuprofen for fever, humidify the air, use saline nose drops to decrease congestion. Antibiotics don't help against viruses. They are prescribed when there are signs of bacterial pneumonia, but I don't hear any pneumonia sounds when I listen to his lungs and the oxygen level in his blood is normal. Antibiotics can have some serious side effects including *C. difficile*, which we'll discuss. We'll also discuss when to bring him back for further evaluation".
- [Using a combination of positive and negative treatment recommendations is associated with an 85% decrease in antibiotic prescribing AND significantly increased parental satisfaction].

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