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CONTAGIOUS COMMENTS
Department of Epidemiology

Clostridioides difficile: New Name and New CHCO testing and Treatment Clinical Pathway

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Clostridioides difficile (C. diff)

Microbiology. Clostridioides difficile (formerly known as *Clostridium difficile*) is a spore-forming, anaerobic, Gram-positive bacillus that is primarily acquired from the environment or by the fecal-oral route. *C. difficile* spores can survive for years in the environment and are resistant to heat, radiation, drying, chemicals, and oxygen.

Epidemiology. C. difficile is now the most common cause of antimicrobial-associated diarrhea. It is also a common health-care associated pathogen, with the incidence of *C. difficile* infection (CDI) in hospitalized children increasing dramatically over the past decade. Community-acquired CDIs in children are also rising and now represent most CDIs in the pediatric population. Essential components for development of CDI include exposure and acquisition of *C. difficile* accompanied by disruption of the normal colonic microbiome. The primary risk factor for development of CDI is previous antibiotic exposure. Other risk factors include contact with the healthcare environment, use of gastric acid-suppressing agents, receipt of cytotoxic chemotherapy, inflammatory bowel disease, presence of a gastrostomy tube, and/or underlying immunocompromising conditions.

Clinical presentation. Asymptomatic carriage with non-toxin and toxin bearing strains is common in the general population. CDI is primarily caused by new infection or overgrowth of strains that elaborate toxins A or B, which damage intestinal epithelial cells. Clinical disease due to toxigenic (toxin-producing) *C. difficile* varies from mild or moderate watery diarrhea to pseudomembranous colitis with bloody diarrhea, fever, and abdominal pain. Rarely, patients may present with ileus or toxic megacolon.

Testing

Current tests available at CHCO. The CHCO microbiology lab currently offers two tests that detect *C. difficile*: the monoplex *C. difficile* PCR (Xpert® C. diff, Cepheid) and the Film Array® Gastrointestinal Pathogen Panel (GIP, Biofire). If risk factors or the clinical scenario warrant testing only for toxigenic *C. difficile*, the monoplex *C. difficile* PCR should be used. The charge for the monoplex *C. difficile* PCR is about half of the multiplex GIP PCR. If more comprehensive testing is indicated (e.g., if one of multiple organisms could be the cause of disease), then the GIP should be utilized. The GIP is a multiplex PCR assay which detects the 22 most common bacterial, parasitic, and viral causes of gastroenteritis/colitis, including *C. difficile*. Both of these tests target the toxin A (tcdA) and/or the toxin B genes (tcdB), although tcdB is considered the major virulence factor. The sensitivity of the *C. difficile* component of the monoplex C. diff PCR and multiplex GIP assays are comparable and estimated at 99 and 97%, respectively.

Issues with current testing. The specificity of either of these *C. difficile* tests varies by the patient being tested. Patients may have positive test results unrelated to the cause of their diarrhea due to asymptomatic carriage of toxigenic strains of *C. difficile*. Asymptomatic carriage in some patient populations creates difficulty in interpretation of positive *C. difficile* PCR results. This is particularly problematic in pediatrics. The rate of asymptomatic colonization in children under 1 year of age ranges 30-60%. By 2-3 years of age, colonization rates begin to decline to rates in adult populations (3-10%). Colonization rates are also elevated in certain high-risk patient populations, such as those with underlying gastrointestinal disorders or malignancies. There is currently no test to distinguish asymptomatic carriage from true disease.

New testing changes. Increased diagnostic stewardship for stool pathogen testing and stool documentation is needed. Through the work of the *C. difficile* steering committee at CHCO, several changes have been implemented utilizing the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) clinical practice guidelines for *C. difficile* infection[1] and addressing needs specific to CHCO. Namely, a *C. difficile* testing and treatment clinical pathway was created to aid in decision support for testing and treatment of *C. difficile* that will be available to all CHCO locations except CHCO-Colorado Springs, which will be using the UC Health microbiology laboratory that utilizes a two-tier testing method for *C. difficile*. All other guidance provided within the pathway is applicable to CHCO-Colorado Springs providers. This document is available on MyChildrensColorado.org on the Clinical Pathways page.

Documentation of inpatient stool consistency is now required in nursing flowsheets using the Bristol Stool Form Scale (see Right), which defines diarrhea as ≥3 Bristol 6-7 stools in a 24-hour period. This documentation plays a key role in determining whether a patient is having diarrhea that warrants further workup.

To improve diagnostic stewardship, as of April 2019, providers can now order GIP with *C. difficile* **OR** GIP without *C. difficile* **OR** the *C. difficile* monoplex PCR. The GIP without *C. difficile* order allows providers to order a GIP without reporting *C. difficile* results if they are not suspicious for *C. difficile* (low pre-test probability) as the cause of diarrhea in a patient (e.g., has not been on recent antibiotics).

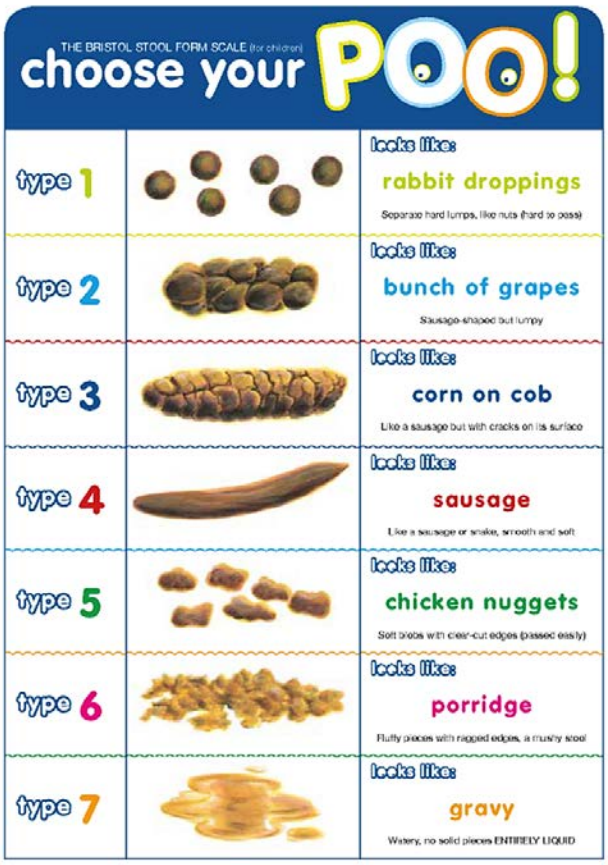
Additionally, certain testing restrictions have been implemented with alerts to assist clinicians in ordering the appropriate test, including:

- No testing for *C. difficile* in **children < 1-year-old** (high rate of colonization, difficult to interpret positive). Choose GIP *without* C. difficile.
- No repeat *C. difficile* testing if **within 14 days** of last positive *C. difficile* or **within 7 days** of last *C. difficile* test (if negative).
- No testing unless **≥3 Bristol 6-7 stools** are documented within the last 24 hours to ensure only patients with diarrhea are tested.
- No testing if **laxatives** have been given within the past 24 hours.
- No GIP testing if patient has been **hospitalized for > 72 hours**, since it is unlikely to acquire another pathogen other than *C. difficile* while in the hospital. In this case, order *C. difficile* monoplex PCR.

If the GIP or *C. difficile* monoplex PCR is ordered in these scenarios above, a red stop sign will appear to inform the provider that there is a recommendation against testing due to one of these restrictions. If the test is still desired by the provider, the provider may call either the ID or GI fellow on call (between 7AM and 7PM) to request a "second sign" of the order and discuss the rationale for testing despite the restriction. ID and GI are not automatically notified of this request, so a call is required. Nursing will not see the order until it is signed by ID or GI (whomever was called).

Treatment

The new *C. difficile* testing and treatment clinical pathway provides guidance for treatment regimens stratified based on a patient's underlying medical conditions and severity of clinical presentation. Metronidazole remains the treatment of choice for mild CDI in low-risk patients. Oral vancomycin is recommended as first-line therapy for high-risk patients, patients presenting with severe disease, or for recurrent disease. Recommendations for when to consider Fecal



Microbiota Transplant (FMT) in patients with severe or fulminant disease or recurrent CDI are also discussed.

Prevention

To prevent transmission of *C. difficile* within the healthcare environment any patient with GI symptoms (vomiting, diarrhea) should be placed on contact precautions. If testing is positive for *C. difficile*, the patient should be placed on contact precautions "+bleach", since bleach cleaning is required in these rooms. All rooms (inpatient/outpatient) of patients with *C. difficile* should be terminally cleaned and treated with UV light following discharge or moving rooms.

All staff entering the room should use alcohol-based hand rub (ABHR). Staff that will be touching the patient or any part of the patient environment should wear gowns and gloves. Gloves should be changed if moving from a dirty to a clean procedure or if the gloves are visibly soiled. If a dedicated stethoscope is available in the room, it should be used to examine the patient. If one is not available, any personal stethoscope that is used should be cleaned thoroughly with a bleach wipe following use and should be allowed to dry completely. Gown and gloves should be removed upon leaving the room and ABHR used on hands after exiting. If hands are visibly soiled, soap and water is recommended for hand hygiene.

References:

1. McDonald LC et al, "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)". CID. 2018; 66(7):e1-e48.

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