CLINICAL PATHWAY:
Evaluation and Management of Suspected Clostridioides Difficile (C. difficile) Infection in pediatric patients with cancer and hematopoietic cell transplantation recipients

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Inclusion Criteria:
Suspected C. difficile infection due to:
(1) Prolonged or worsening diarrhea (at least 4 liquid stools in 24 hours; **Appendix A**, **Appendix B**) AND
(2) Risk factors for C. difficile infection (antibiotics in prior 3 months, hospitalization in prior 3 months, immunocompromised patients due to chemotherapy/humoral immunodeficiency/solid organ transplant, chronic inflammatory bowel disease, G-tube or J-tube need, use of acid suppressive therapies – PPI or H2 blockers, or prior C difficile infection)

Exclusion Criteria:
Soft or formed stools (**Appendix A**), < 4 liquid stools in 24 hours, no risk factors for C. difficile infection

Place on contact precautions. Send C.difficile testing ONLY if appropriate (see below).

Considerations for testing for C. difficile:

- **<1 years of age:** Generally colonized
  - DO NOT test; Treating for C. difficile is not indicated
- **1-2 years of age:** High likelihood of colonization
  - Evaluate/empirically treat for other infectious/non-infectious causes before testing for C. difficile
    - Add fiber to the formula of tube-fed patients
    - Stop medications associated with diarrhea; Laxatives/stool softeners should be stopped at least 48 hours prior to testing
- **>2 years of age:**
  - Test ONLY if patient has not received laxatives or other medications associated with diarrhea (or diarrhea persists after 48 hours of stopping the medication) AND if no alternative reason for diarrhea exists.

Confirmed C. difficile disease:
Positive C. difficile Ag and Toxin is consistent with infection, and treatment should be initiated/resumed. If only one of either the C.difficile Ag or Toxin are positive, the C.difficile PCR should be ordered and if positive, treatment should be initiated/resumed.
Positive C. difficile PCR and negative C. difficile Ag/Toxin represents colonization (NOT infection) and should NOT be treated.
Repeat testing of the same episode is NOT recommended.

Initial Disease
(1st episode, or repeat episode >8 weeks from prior episode)

Non-Severe Disease:
[diarrhea may contain some blood, WBC and SCr normal for age]

- <18 yrs old: **Vancomycin PO**: 10 mg/kg/dose (max 125 mg/dose) QID **OR** **Metronidazole PO** (if vancomycin PO not available): 10 mg/kg/dose (max 500 mg/dose) TID **OR** 7.5 mg/kg/dose (max 500mg/dose) QID x10 days
  - If no improvement within 5-7 days, considered treatment failure. Follow guidelines under Recurrent Disease.

Severe Disease:
[ill-appearing, diarrhea usually bloody, elevated WBC likely due to C. diff]

- **Vancomycin PO**: 10 mg/kg/dose (max 125 mg/dose) QID x 14 days
- If no improvement within 5-7 days: consult ID

Fulminant Disease:
[hypotension/shock due to C. difficile, Ileus, Megacolon; serum lactate ≥ 5 mmol/L and peripheral WBC ≥ 50,000 higher rates of mortality]

- **Metronidazole IV**: 10 mg/kg/dose (max 500 mg/dose) q8h **OR** 7.5 mg/kg/dose (max 500 mg/dose) q6h AND
- **Vancomycin PO** 10 mg/kg/dose (max 500 mg/dose) QID
- Duration of treatment: 14 days
- Consults:
  - ID
  - GI
  - Consider Surgery

NOTE: Consider discontinuation of proton pump inhibitors/H2 blockers.

Recurrent Disease
(Repeat episode up to 8 weeks from prior episode)

Treatment Options:
[See disease severity under Initial Disease for clarification.]

If failure with metronidazole:

- **Vancomycin PO** 10 mg/kg/dose QID (max 125 mg/dose for non-severe disease and severe disease; max 500 mg/dose for fulminant disease) x 14 days

If failure with vancomycin PO:

- Consider alternate cause of diarrhea
- Consult ID
- Begin **Vancomycin**:
  - Vancomycin PO 10 mg/kg/dose (max 125 mg/dose) QID for non-severe/severe disease x 14 days OR
  - Vancomycin PO 10 mg/kg/dose (max 500 mg/dose) QID for fulminant disease x 14 days *followed by taper:*
    - Vancomycin PO 10 mg/kg/dose (max 125 mg/dose) BID x 7 days *followed by*
    - Vancomycin 10 mg/kg/dose (max 125 mg/dose) once daily x 7 days *followed by*
    - Vancomycin 10 mg/kg/dose (max 125 mg) every 2-3 days x 2-8 weeks as directed by ID

If failure with vancomycin taper:

- Consider alternate cause of diarrhea
- Consult ID
- Consider **Fidaxomicin** 16 mg/kg/dose BID for children 6 months to 5 years and 200 mg/dose BID for children 6 years and older. X 10 days; if using Fidaxomicin, please contact Antimicrobial Stewardship Program for up-to-date dosing recommendations.

NOTE: Consider discontinuation of proton pump inhibitors/H2 blockers.

Discharge Criteria: clinically stable, cleared by ID and GI (and surgery, if involved), medication available prior to discharge
Discharge Instructions: Ensure insurance coverage/medication availability prior to discharge, follow up with PCP and/or GI (if involved in hospitalization)

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Appendix A: Nursing Flowchart for Appropriate C.difficile testing

Does the patient have diarrhea? (Diarrhea is defined as ≥ 4 **liquid** stools in 24 hours.)

YES

Initiate contact precautions. In the last 48 hours, has the patient received any laxatives or other medications that could cause diarrhea?

NO

Contact the patient's provider. Have the following crucial information ready:

- ☐ number of liquid stools last 24 hours
- ☐ relevant symptoms (i.e. abdominal pain and/or cramps, fever, chills)

Obtain and send stool specimen as soon as possible if ordered.

Please Note:

- Vomiting is not characteristic of *C. difficile* and raises the question of other diagnoses, such as viral gastroenteritis.
- Studies have shown that there is no characteristic odor of stool from patients with *C. difficile.*

YES

Contact provider. Request that laxatives and stool softeners be held if possible. Inform provider of other meds that can cause diarrhea.

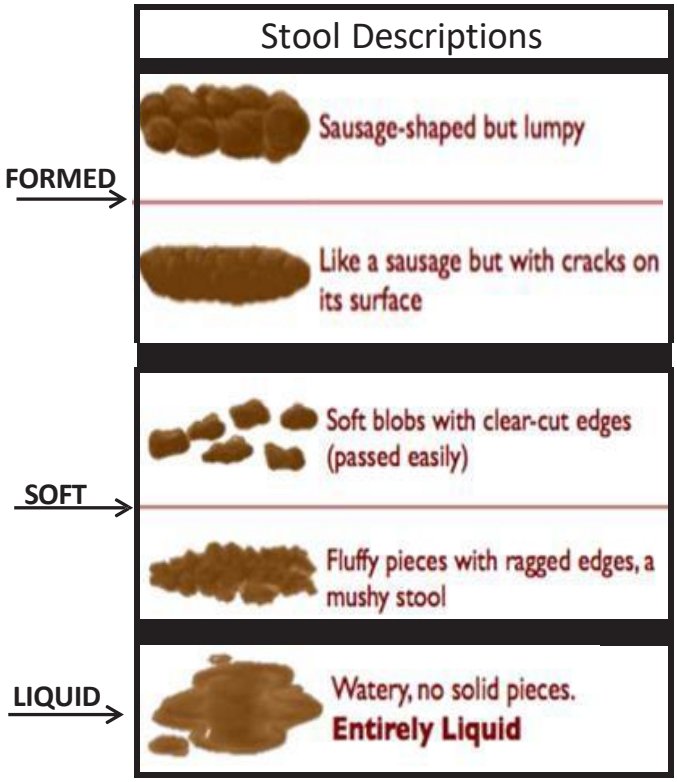
NO

Continue to monitor for signs and symptoms of infection and document consistency (**formed, soft or liquid**) of all bowel movements.

Testing for *C. difficile* is NOT recommended.
Continue to monitor for signs and symptoms of infection.

Some Medications That Can Cause Diarrhea

- **Laxatives**
  - lactulose, bisacodyl, mag citrate, docusate, Go-lytely, senna, polyethylene glycol and sorbitol, to name a few
- **Enemas**
- **Other Medications, including:**
  - Antineoplastics especially irinotecan
  - Antibiotics
  - Kayexalate
  - Octreotide
  - Metformin and other diabetic medications
  - Magnesium-containing antacids



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Appendix B: Provider Flowchart for Appropriate C.difficile testing

Does the patient have diarrhea? (Diarrhea is defined as ≥ 4 **liquid** stools in 24 hours.)

YES

Initiate contact precautions. In the last 48 hours, has the patient received any laxatives or other medications that could cause

NO

Providers should assess the following to determine if *C. difficile* testing is appropriate:

- Age
- Laxative/enema use in last 24 hours
- Number and consistency of stools (verify ≥ 4 liquid stools in 24 hours)
- Abdominal symptoms such as pain, distension
- Vital signs
- WBC
- Tube feedings
- Other medications that can cause diarrhea

Have a low threshold for seeing the patient in order to make an optimal decision about testing.

Vomiting is not characteristic of *C. difficile* and raises the question of other diagnoses, such as norovirus infection.

YES

Nurse to call provider to ask about discontinuing laxatives, enemas, etc. and to review other meds.

NO

Nursing will continue to monitor for signs and symptoms of infection and document consistency (**formed, soft or liquid**) of all bowel movements.

Testing for *C. difficile* is NOT recommended unless other clinical indications present (refer to box on left).

Some Medications That Can Cause Diarrhea

- **Laxatives**
  - lactulose, bisacodyl, mag citrate, docusate, Go-lytely, senna, polyethylene glycol and sorbitol, to name a few
- **Enemas**
- **Other Medications, including:**
  - Antineoplastics especially irinotecan
  - Antibiotics
  - Kayexalate
  - Octreotide
  - Metformin and other diabetic medications
  - Magnesium-containing antacids

Acute care hospitals are required to report all *C. difficile* LabID events to there local public health contacts.

- **Community-Onset**: LabID Event specimen collected in an outpatient location or an inpatient location **≤2 days** after admission to the facility (i.e., day 1 or 2). **TRY TO IDENTIFY ASAP AFTER ADMISSION**
- **Healthcare setting-Onset :** LabID Event specimen collected **>3 days** after admission to the facility.

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