Clinical Pathway for *Clostridium difficile* Infection (CDI)*

**Clinical Suspicion of CDI:**
- Diarrhea
- Recent chemotherapy
- Recent antibiotic use
- Abdominal pain and/or distention
- Fever
- Leukocytosis

- **Oral vancomycin**
- **Metronidazole**

**DNA Test = test for presence of C. difficile pathogenicity locus**

1. **Prophylaxis for CDI with metronidazole or vancomycin is NOT warranted.**
2. **Isolated leukocytosis is not an indication for testing or treatment of CDI.**
3. **Universal glove use required. Gown required for any substantial contact with the patient or environment. Soap and water hand hygiene is necessary. Environmental Services will clean the room with a bleach solution weekly and at discharge.**

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**Clinical Suspicion of CDI:**

**DNA Test (+)**
- GDH antigen (+); toxin A/B (+)
- GDH antigen (+); toxin A/B (-)
- GDH antigen (-); toxin A/B (-)

**CDI present:**
- Begin CDI treatment (See pg. 2)
- Stop acid suppressive medications and antimicrobials if medically possible
- Place patient in contact isolation

**CDI not present:**
- Discontinue CDI treatment if initiated
- Evaluate for other causes of diarrhea if appropriate

**Signs/symptoms improve:**
- Complete course of therapy
- No further toxin assays
- Continue contact isolation until 1 week after resolution of symptoms and end of therapy

**No improvement of diarrhea in 5 days & patient receiving metronidazole:**
- Discontinue metronidazole
- Begin oral vancomycin (See pg. 2)

**Progressive signs/symptoms (toxic megacolon, fulminant colitis, etc.):**
- Obtain abdominal/pelvic CT scan
- Consult Infectious Diseases
- Consult GI
- Begin therapy for severe, complicated disease (See pg. 2)
- Consider early surgical intervention

**Signs/symptoms improve:**
- Complete course of therapy
- No further toxin assays
- Continue contact isolation until 1 week after resolution of symptoms and end of therapy

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Note:

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2. **Isolated leukocytosis is not an indication for testing or treatment of CDI.**
3. **DNA Test = test for presence of C. difficile pathogenicity locus**
4. **Universal glove use required. Gown required for any substantial contact with the patient or environment. Soap and water hand hygiene is necessary. Environmental Services will clean the room with a bleach solution weekly and at discharge.**
Treatment Recommendations for CDI

Treatment for initial episode of CDI and the first recurrence* of CDI should be the same. See below for recommendations for treatment of CDI beyond the first recurrence.

Mild-Moderate Infection: Diarrhea that does not meet criteria for severe or complicated

- Metronidazole³ 500 mg PO q8h x 10 days
- Avoid IV metronidazole as data suggests inferior to PO.
- Pediatric dosing: 30 mg/kg/day PO divided q6h x 10 days; not to exceed 4 g/day

Severe Infection: CDI associated with the development of any of the following: WBC > 20,000, Scr ≥ 1.5 X baseline, albumin <3.0 g/dl, severe abdominal tenderness, or requires ICU care for CDI:

- Vancomycin 125 mg PO q6h x 10 days (DO NOT treat with IV vancomycin)
- Pediatric dosing: 40 mg/kg/day PO divided q6-8h x 10 days; not to exceed 2 g/day

Severe, Complicated Infection: (i.e., hypotension or shock, ileus, toxic megacolon, fulminant colitis):

- Consult ID Services
- Consult GI and General Surgery for evaluation for possible colectomy
- Vancomycin 500 mg PO q6h + metronidazole³ 500 mg IV q8h +/- vancomycin enema 500 mg in 100 mL of 0.9% NaCl; instill via Foley catheter q6h and retain for 1h

Recurrent CDI beyond 1st recurrence*:

- Vancomycin 125 mg PO q6h x 10 days followed by,
- Vancomycin 125 mg PO q12h x 7 days, 125 mg PO q24h x 7 days, then 125 mg PO every 3 days x 14 days
- Consider referral for fecal microbiota transplant if multiple recurrences

Discontinue acid suppressive medications and other antimicrobials if possible:

The use of acid suppressive medications (ASM) and especially proton pump inhibitors (PPI) has been associated with an increased risk of developing CDI. Also patients with CDI who are continued on ASM have a higher recurrence rate of CDI. The use of concomitant antimicrobials has also been associated with prolonged time to resolution and recurrence. It is recommended these agents be discontinued if medically possible.

*Recurrence is defined as the re-appearance of signs/symptoms of CDI within two months of previous CDI episode for which signs/symptoms had resolved. Treatment of the first recurrence should be with the same antibiotic used for the initial episode.

³Metronidazole should not be used in pregnant/lactating women.
Testing Recommendations for CDI

Table 1. *Clostridium difficile* Assay Results

<table>
<thead>
<tr>
<th>GDH Result</th>
<th>Toxin Assay Result</th>
<th>Interpretation</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>No <em>C. difficile</em> present</td>
<td>No further action. Repeat testing is discouraged.</td>
</tr>
<tr>
<td>Positive</td>
<td>Positive</td>
<td>Toxigenic <em>C. difficile</em> is present</td>
<td>Utilize contact isolation precautions and begin therapy according to management algorithm. Repeat testing is discouraged.</td>
</tr>
<tr>
<td>Positive</td>
<td>Negative</td>
<td>Non-toxigenic <em>C. difficile</em> or false-negative toxin assay</td>
<td>DNA confirmatory test for toxin performed. Interpret based on this result</td>
</tr>
<tr>
<td>Negative</td>
<td>Positive</td>
<td>Indeterminate</td>
<td>Repeat test x 1.</td>
</tr>
</tbody>
</table>

**Specimen and Order:**
- Liquid stool only (i.e. stool conforms to the container) and only one specimen per patient in 24 hours
  - Non-liquid stool will not be processed by the microbiology lab
- Order one test for *C. difficile* at a time. **Do not order multiple tests for *C. difficile*.**

**Testing Interpretation:**

**GDH and toxin negative:** No *C. difficile* is present (Negative Predictive Value >99%)
- Repeat testing is not recommended due to poor yield
- At TNMC over the first 2 months of use of the GDH/toxin assay only 2 of 147 (1.4%) episodes of repeat testing after an initially negative stool resulted in the diagnosis of toxigenic *C. difficile*. The cost in patient charges of repeat testing was roughly $37,000 per diagnosed episode
- The likelihood of a false positive test result increases dramatically with each repeated test due to lower pretest probability in the test population. PPV of a repeated test is approximately 30 and 50% and results in more false positives than true positives
- Repeat testing could be considered if several days have passed and the clinical syndrome has changed

**GDH and toxin positive:** Toxigenic *C. difficile* is present (Positive Predictive Value ~99%)
- Treat as appropriate if symptoms suggestive of CDI are present (refer to guidelines above)
- Repeat testing after a positive is not recommended for at least 14 days and no test of cure should be performed

**GDH positive, toxin negative:** *C. difficile* may be present.
- Repeat testing is NOT recommended as this practice has not resulted in an increased detection of toxin positive stools
- DNA Confirmatory test (Illumigene™) will be performed daily on all GDH +, toxin negative stools
  - **DNA Confirmatory Test (+)**
    - *C. difficile* with toxin gene is present
    - Treat as appropriate if symptoms suggestive of CDI are present (refer to guidelines above)
  - **DNA Confirmatory Test (-)**
    - 2 possibilities: 1) *C. difficile* is present and does not have the toxin gene or 2) false positive GDH
    - No treatment indicated
Isolation/Infection Control

- All patient care units will use the same procedures for testing, treatment, and isolation
- Presumptive isolation on units where it is currently in use (SOTU, OSCHU, PICU, etc) may continue, but otherwise is not routinely necessary
- GDH and toxin negative patients AND GDH positive, toxin negative, DNA test negative patients = No isolation necessary
- GDH and toxin positive patients AND GDH positive, toxin negative, DNA test positive patients = Initiate CDI contact isolation precautions
  - Isolation procedures include: Universal glove use, gown use for any substantial patient or environmental contact, and soap and water hand hygiene after patient or environment contact
  - Patients will remain in isolation for 1 week after treatment is completed and they are asymptomatic (no diarrhea)
- Environmental Services will perform routine bleach cleaning of rooms of all patients with C. difficile infection (CDI) weekly and at patient discharge

References

Updated October 2013