**Clostridium difficile Infection (CDI) Management Guideline**

- **Do not test all patients with loose or watery stools for CDI**
  - CDI is responsible for <10% of nosocomial diarrhea
  - Consider other causes of diarrhea first (e.g. tube feeds, oral contrast, bowel regimens, antibiotic side effects, etc.) unless symptoms strongly suggest CDI
- **Patients with mild-moderate nosocomial diarrhea without other CDI features (see below) should have non-CDI causes treated (stop inciting meds especially laxatives, add fiber to tube feeds, etc.) and be monitored for resolution before CDI testing is considered**
- **Infants <12 mo. are likely to be colonized with *C. difficile* and should not be routinely tested**
- **Never** test formed stool, asymptomatic patients, or perform a “test of cure”
- **Unformed stool is the only acceptable specimen (i.e. stool conforms to shape of the container)**
  - Order only one CDI test and await results before initiating therapy (exception: If severe disease with typical symptoms, reasonable to initiate therapy before results)

Reserve CDI testing for patients who meet the following criteria:

1. **Significant diarrhea (>3 watery bowel movements in <24 hours) and at least one feature suggestive of CDI including:**
   - Unexplained elevation in WBC count or fever
   - New onset abdominal pain and/or distention with diarrhea
2. **Severe diarrhea (>7 bowel movements or >1.5L over 24 hours)**
3. **Persistent diarrhea = significant diarrhea for >24 hours which is not resolved with conservative treatment and does not have another explanation**

**Clostridium difficile test interpretation algorithm:**
Interpret test results and make treatment decisions after considering patient symptoms

- **Antigen (+); toxin A/B (+)**
  - **CDI Present**
  - Initiate severity-based CDI therapy
  - Stop acid suppressive medications and concomitant antimicrobials if possible
  - Place patient in contact isolation

- **Antigen (+); toxin A/B (-)**
  - **CDI Present**
  - Initiate severity-based CDI therapy

- **Antigen (-); toxin A/B (-)**
  - **CDI Not Present**
  - Discontinue CDI treatment and isolation
  - Evaluate for other causes of diarrhea

- **PCR Test (+)**
  - **CDI Present**

- **PCR Test (-)**
  - **CDI Not Present**
  - **CDI May Be Present**
    - PCR positive, toxin negative patients have lower levels of *C. difficile* colonization and may not need therapy
    - Place patient in enteric isolation
    - Treatment decision should be individualized; consider treatment with severe, non-resolving, or otherwise unexplained diarrhea strongly suggestive of CDI
Treatment Recommendations for CDI

Base treatment choice for CDI on an assessment of infection severity. It is reasonable in mild infections to discontinue the inciting antibiotics and monitor for diarrhea resolution over the next 24-48 hours without initiating antibiotic therapy.

**Treatment Recommendations for All Patients with CDI:**
- Replace fluids and electrolytes as needed
- Discontinue acid suppressive medications (ASM) if possible. Continued use is associated with increased risk of CDI and recurrence
- Discontinue concomitant antibiotics if possible. Continued antibiotic use is associated with prolonged time to CDI symptom resolution and CDI recurrence. Narrow antibiotic spectrum as much as possible and discontinue necessary antibiotics as early as medically safe.
- Discontinue both anti-motility and pro-motility medications
- Monitor for clinical worsening and adjust therapy as needed

**Mild-Moderate Infection:** Diarrhea that does not meet criteria for severe or complicated
- Vancomycin 125mg PO q6h x 10 days (preferred, but more expensive)
- Metronidazole 500 mg PO q8h x 10 days
  - Avoid IV metronidazole as data suggests inferior to PO.
  - If no improvement by day 5 change to vancomycin

**Severe Infection:** CDI associated with the development of any of the following: WBC > 15,000, SCr ≥ 1.5 X baseline, acute decrease in albumin <3.0 g/dl, severe abdominal tenderness/pain, or requires ICU care for CDI:
- Vancomycin 125 mg PO q6h x 10 days (DO NOT treat with IV vancomycin)

**Severe, Complicated Infection:** (i.e., hypotension or shock, ileus, toxic megacolon, fulminant colitis):
- Consult ID Service to assist with therapy management
- Consult GI and General Surgery for evaluation for possible colectomy
- Vancomycin 500 mg PO q6h + metronidazole in 100 mL of 0.9% NaCl; instill via Foley catheter q6h and retain for 1h

**Recurrent CDI:** CDI recurrence defined as the re-appearance of signs/symptoms of CDI with a positive *C. difficile* test within 8 weeks of a previous CDI episode for which signs/symptoms had resolved. Recurrence of diarrhea is frequent in patients with previous CDI, reserve testing for those meeting previously described testing thresholds. In early, mild diarrhea, it is reasonable to hydrate and monitor symptoms for 24-48 hours to determine if they resolve spontaneously. If symptoms worsen or do not resolve, initiate CDI testing.

- **All Patients with recurrence:**
  - Stop acid suppressive medications and concomitant antibiotics if possible
- **First Recurrence:**
  - Can use same agent as treatment of first episode
  - Consider fidaxomicin 200mg BID X 10 days in high risk *outpatients* (elderly, stem cell transplant, early solid organ transplant) as decreased risk of recurrence *(very expensive)*
- **Second Recurrence:**
  - Vancomycin 125 mg PO q6h x 10 days followed by, vancomycin taper of 125 mg PO q12h x 7 days, 125 mg PO q24h x 7 days, then 125 mg PO every 3 days x 14 days
• >2 Recurrences:
  o If has not received vancomycin taper attempt this first; if CDI recurs after vancomycin taper proceed as below
  o Referral to ID or GI for fecal microbiota transplant (FMT) or Bezlotoxumab
    1. **FMT preferred** – cure rate 70-90%
    2. Bezlotoxumab 10 mg/kg IV once
      • Decreases recurrence roughly 40%
      • Consider where FMT is not an option
        o i.e. likely to receive additional courses of antibiotics in near future or unsafe/unwilling to undergo FMT
      • No benefit in resolution of acute symptoms, avoid inpatient use
# CDI Test Interpretation

## 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 and symptoms</td>
</tr>
<tr>
<td>Negative</td>
<td>Positive</td>
<td>Indeterminate</td>
<td>Repeat test x 1.</td>
</tr>
</tbody>
</table>

## Testing Interpretation:

**GDH and toxin negative:** No *C. difficile* is present (Negative Predictive Value >99%)
- Repeat testing is not recommended due to poor yield
- Repeat testing could be considered if ≥5 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 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
- PCR test will be performed on all GDH +, toxin negative stools
  - **PCR Test (+)**
    - *C. difficile* with toxin gene is present and symptoms may be due to CDI
    - PCR positive, toxin negative patients have low levels of *C. difficile* colonization and may not require therapy
    - Treatment decision should be individualized with treatment considered in those with severe, strongly suggestive, non-resolving, or otherwise unexplained symptoms
  - **PCR Test (-)**
    - No toxigenic CDI present with positive GDH test due to one of 2 possibilities:
      - 1) Non-toxigenic *C. difficile* detected or 2) false positive GDH
    - No treatment indicated
CDI Isolation/Infection Control

- All patient care units will use the same procedures for testing, treatment, and isolation
- Presumptive isolation upon testing for CDI is recommended
- GDH and toxin negative patients AND GDH positive, toxin negative, PCR test negative patients = No isolation necessary
- GDH and toxin positive patients AND GDH positive, toxin negative, PCR 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), whichever is longer
- Environmental Services will perform routine bleach cleaning of rooms of all patients with C. difficile infection (CDI) weekly and at patient discharge along with terminal UV disinfection

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