Stanford University Hospital Recommendations for Collection of *C. difficile* testing:

- **Is this a test of cure?**
  - NO: AVOID testing
  - YES

- **Does the Patient have Antibiotic Associated* Diarrhea?**
  - NO: AVOID testing
  - YES

- **Is the stool truly unformed? (ie. Does it take the shape of a container?)**
  - NO: Sample will be REJECTED by lab
  - YES

- **Is chronic diarrhea or ostomy present?**
  - NO: AVOID testing
  - YES

- **Were Laxatives given within the last 48 hours?**
  - NO
  - YES: Sample will be REJECTED by lab

- **Alternative causes of diarrhea present?**
  - NO
  - YES: Consider not testing

- **Send Stool Sample for *C. diff* testing**

*ALTERNATIVE CAUSES OF DIARRHEA:*
- Delayed response to Laxatives used over 48 hours ago
- Tube feeds initiated, volume changed, or preparation changed within the last 24 hours
- PO Contrast usage within the last 24 hours
- Other medical conditions causing diarrhea, including:
  - Viral gastroenteritis
  - Toxigenic bacteria causing diarrhea (ie. E coli, salmonella, etc.)
  - Colon ischemia
  - Opioid withdrawal
  - Overflow diarrhea from fecal impaction
- **Medications with diarrhea** as a side effect

*Antibiotic Associated = Antibiotics given at any time within the last 3-6 months*
Introduction: *Clostridioides difficile* (C. diff) is the leading cause of nosocomial diarrhea in the United States.\(^1\) Each diagnosed case of C. diff infection (CDI) has a significant impact on Medicare reimbursement, hospital length of stay, and cost, with the average cost for CDI case management and average CDI-attributable costs estimated to be $42,316 for each case in the United States.\(^2\) While several testing modalities are available to test for C. diff infection (CDI), there is no gold standard of testing, and limitations exist for every testing method available.\(^3,4\) As an example, the C. diff PCR test cannot successfully distinguish clinically relevant C. diff infection from asymptomatic C. diff colonization.\(^5\) Stanford hospital utilizes a modified variation of the C. diff PCR test to mitigate this issue, but without a diagnostic gold standard for comparison, no test is perfect. National clinical guidelines on CDI as well as the “Choosing Wisely” campaign recommend that testing for C. difficile should only be done in patients with diarrhea, as the presence of diarrhea would increase the pre-test probability that a patient has clinically relevant CDI.\(^3,6\) Diagnostic stewardship focused on decreasing the overutilization of lab services has been implemented at SHC and other hospitals as a novel method of reducing C. diff infection (CDI) rates.\(^7–10\) Retrospective review of Stanford’s hospital onset cases of C diff starting in early 2019 by our hospital epidemiologist suggest that a sizeable proportion of patients may have had an alternative cause of diarrhea present when tested for C. diff. As such, infectious disease experts at Stanford remain concerned that there is a sub-population of patients diagnosed with C. diff who did not require testing.

A. General Considerations:
- Stool testing for C. diff alone cannot perfectly differentiate individuals who are colonized with C. diff and do not require therapy from those with clinically relevant disease needing treatment. The patient’s clinical scenario should also be taken into account.
- Efforts should be made to consider alternative etiologies of diarrhea before testing is ordered.
- Avoid testing stool for C. diff to evaluate response to treatment (ie. As a “test of cure”).\(^3\)
  - Response to therapy for CDI may take several days. If the patient continues to have diarrhea despite many days of treatment, please re-evaluate alternative causes of diarrhea.
  - If recurrence is suspected (ie. Recurrence of symptoms AFTER a full course successful treatment occurred with cessation of diarrhea), then it is reasonable to perform repeat testing.

B. Alternative Etiologies of Diarrhea
- Efforts should be made to rule out other causes of diarrhea, especially in patients who have no evidence of colonic/systemic inflammation (ie. Fever, leukocytosis, abdominal pain/distension). These include the following:
  - Laxative/Enema usage AT LEAST within the last 48 hours
    - If the patient was recently heavily constipated or recovering from post-operative ileus, diarrhea may persist beyond 48 hours after stool output has begun
  - Tube feeds initiated, volume changed, or preparation changed within the last 24 hours
  - PO Contrast usage within the last 24 hours
  - Recently diagnosed alternative medical conditions causing acute diarrhea, including:
    - Known alternative infectious cause of diarrhea (e.g. viral gastroenteritis or toxigenic bacteria such as E coli/salmonella/etc.)
    - Colonic ischemia (usually bloody diarrhea)
    - Opioid withdrawal
    - Overflow diarrhea with fecal impaction
  - Medications with diarrhea as a known side effect should be evaluated

C. Medications with diarrhea as a common side effect\(^1\): NOTE - clinical situation should be taken into account (i.e. Was the medication recently started or has this been a chronic medication unlikely to cause new acute diarrhea? Is there evidence of other toxicitidfes from this medication?)
- Acarbose
- Antiarrhythmics - digoxin (as a sign of digoxin toxicity), quinidine
- Beta blockers – e.g. carvedilol
- Colchicine
- Cholinergic drugs – donepezil, pyridostigmine
- Cytotoxic Chemotherapy – Irinotecan, 5-fluorouracil, capecitabine
- Docusate
- Immunosuppressants - mycophenolate, tacrolimus, or cyclosporine
- Metformin
- Magnesium containing drugs (antacids, magnesium citrate)
- Octreotide
- Promotility agents – Metoclopramide, erythromycin
- Oral electrolyte replacement solutions
- Oral solution medications in which sorbitol is an additive
  - Please check with pharmacy if patient is on oral solutions to determine if a significant amount of sorbitol is present
- Probiotics
- Prostaglandin analogues - Misoprostol
- Selective Serotonin Reuptake Inhibitors – e.g. sertraline
- Ticlodipine
- Tyrosine Kinase inhibitors

### D. Stanford University Hospital Criteria for CDI:

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<thead>
<tr>
<th>Clinical Symptoms of CDI</th>
<th>Diagnostic Testing Positive for CDI</th>
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<tr>
<td>ONE of the following should be present</td>
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<tr>
<td>1) Diarrhea:</td>
<td>1) Positive stool test for ( C. ) difficile toxin B PCR</td>
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<td>ONE of the following:</td>
<td>AND</td>
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<td>- ( \geq 3 ) unformed stools over 24 hours</td>
<td>AND</td>
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<td>- Significant worsening in patients with chronic diarrhea (e.g. inflammatory bowel disease)</td>
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<td>- Increased output from any ostomy site compared to baseline in the setting of recent antibiotic use</td>
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**Alternative causes of diarrhea** are evaluated and deemed unlikely the cause of the current clinical presentation

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<tr>
<th>2) Imaging consistent with CDI</th>
<th>2) Colonoscopy findings consistent with CDI</th>
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<tbody>
<tr>
<td>- Active colitis on CT scan</td>
<td>• Visualization of pseudomembranous colitis on endoscopy, if other causes of pseudomembranes are felt to be less likely</td>
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<td>OR</td>
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<td>- Unexplained Ileus or Toxic megacolon</td>
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<td>o Ileus and toxic megacolon are rare manifestations of CDI.</td>
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<tr>
<td>o In patients with uncomplicated ileus, other causes of ileus should be considered before testing for CDI</td>
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C. Microbiology Lab Testing Criteria for C. difficile PCR (Must be met for lab to accept sample)

1. ≥3 loose or watery stools per 24 hr.
2. Unformed stool specimen (conforms to the shape of the container).
   Exceptions include patients with ileus or toxic megacolon, which requires front-line provider override.
3. No previous PCR test within the last 7 days.
4. No use of laxatives (excluding docusate) within the past 48 hours
5. Patient < 1 year old (C. diff colonization is frequent in this population)

References:


