**C. difficile Infection (CDI) Testing Algorithm: PCR/Reflex Toxin EIA (5/14/2021)**

- **Alternate explanation (i.e. laxative, PO contrast)?**
  - YES: ORDER Stool *C. difficile* PCR
    - NEG PCR: C. difficile PCR NEGATIVE
      - CDI unlikely
      - Consider other etiologies of diarrhea.
    - POS PCR: C. difficile Toxin EIA NEGATIVE
      - Indeterminate result
        - In most cases, do not treat for CDI. Consider the patient colonized with *C. difficile* bacteria. Reevaluate for alternative causes of diarrhea.
        - If strong clinical suspicion for CDI persists, treat and consider ID consultation.
        - Stop unnecessary oral/IV antibiotics.
        - Order Contact Plus isolation
  - NO: C. difficile PCR previously sent within 7 days?
    - YES: DO NOT ORDER C. difficile PCR
      - If diarrhea-causing medication present, stop medication and re-evaluate in 24-48 hours
    - NO: Was prior test positive?
      - YES: DO NOT SEND C. difficile PCR FOR TEST-OF-CURE
        - If diarrhea improving, continue current management. If diarrhea worsening:
          - Escalate therapy
          - Consider ID consult
      - NO: ORDER Stool *C. difficile* PCR
        - PCR Indeterminate → submit new sample

- **C. difficile Toxin EIA POSITIVE**
  - Order Contact Plus isolation.
  - Treat for *C. difficile* infection
  - Stop unnecessary oral/IV antibiotics

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**Key Points:**
- Identify new onset of unexplained large-volume, frequent, liquid diarrhea and consider a broad differential diagnosis. This process of medical decision-making is unchanged.
- If testing is appropriate, order **stool C diff PCR**. (In summer 2021, we will be announcing that this order name will change to *C. difficile* PCR/reflex toxin EIA.)
- Avoid unnecessary testing. The first test, the *C. difficile* PCR, is a very sensitive test. C diff PCR+ means the sample carries *C. difficile* organisms with the genetic material capable of producing toxin. A positive PCR test could mean CDI or could mean *C. difficile* colonization. The latter does not need CDI treatment.
- Reflex testing for *C. difficile* toxin EIA differentiates between CDI, which warrants treatment, and colonization, which does not.
- CDI is a toxin-mediated disease, so diarrhea in patients with *C. diff* PCR+/toxin EIA+ confirms the diagnosis of CDI. On the other hand, diarrhea in most patients with *C. diff* PCR+/toxin (-) do not have CDI and do not warrant CDI treatment. If strong clinical suspicion of CDI remains for a patient with a *C Diff* PCR+/toxin (-) result, however, treat...