CHLOSTRIDIUM DIFFICILE INFECTION (CDI)

2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA)

DIAGNOSIS:

- A key clinical manifestation is diarrhea accompanied by abdominal pain as well as by systemic inflammatory response. In very severe cases, diarrhea ceases due to development os severe ileus.
- Antibiotic exposure within 3 months. Amoxicillin, cephalosporins, clindamycin, and fluoroquinolones are the antibiotics that are most frequently associated with the disease, but almost all antibiotics have been associated with infection.
- Other documented risk factors for CDI include:
    - ❖ Advanced age.
    - ❖ Inflammatory bowel disease
    - ❖ Organ transplantation
    - ❖ Chemotherapy
    - ❖ Chronic kidney disease
    - ❖ Immunodeficiency
    - ❖ Exposure to an infant carrier or infected adult

- Laboratory detection and identification of C. difficile alone does not diagnose CDI as 4% of healthy adults are colonized by C. difficile, and 20–25% of the C. difficile strains may be non-toxigenic.
- Stool testing for *C. difficile* toxins should be confined to patients with diarrhea, or rarely, in pts with suspected CDI that develop severe ileus. The testing and treatment of persons with solid stools is not recommended.
- Highly sensitive PCR testing should not be ordered in patients with a low probability of infection (i.e., a patient without risk factors; a patient has a soft or formed stool; a patient with diarrhea who is using stool softeners or laxatives).
- CDI is currently diagnosed either by DNA-based tests that identify the microbial toxin genes in unformed stool or by enzyme immunoassay for toxins in stool along with the presence of clinical symptoms and signs.
- The final confirmation of CDI may require a combination of tests (the highly sensitive nucleic acid amplification test - NAAT and the toxin enzyme immunoassay (EIA) confirmatory test).

SEVERITY:

- Indicators of severe *C. difficile* infection:
    - ❖ White-cell count greater than 15,000
    - ❖ Acute kidney injury (sCr >1.5)
- Indicators of fulminant *C. difficile* infection:
    - ❖ Toxic megacolon, peritonitis, hypotension, sepsis/septic shock

TREATMENT:

For all pts with CDI any current antibiotic therapy should be discontinued if possible. Pts should be hydrated accordingly along with monitoring of clinical status.

Initial episode, non-severe:

- Oral vancomycin 125 mg q6h for 10 days or oral metronidazole 500 mg q8h for 10 days if vancomycin not available.

Initial episode, severe:

- Vancomycin 125 mg orally or NGT q6h for 10 days

Initial episode, fulminant:

- Vancomycin 500 mg orally or NGT q6h and metronidazole 500 mg IV for 10 to 14 days.
- The use of additional vancomycin therapy via rectal retention enema, 500 mg in 100 mL normal saline every 6 h, is recommended if complete ileus is present.
- Surgery should be considered if the patient's clinical status is not improving. Consider toxic megacolon if the patient develops abdominal distention with lessening of diarrhea, which strongly suggests paralytic ileus due to loss of colonic muscular tone.

First recurrence:

- Oral vancomycin 125 mg q6h for 10 days if metronidazole was used for the first episode.
- Vancomycin in a tapered and pulsed regimen* or oral fidaxomicin 200 mg q12h for 10 days if vancomycin was used for the first episode.

*Tapered and pulsed regimen of vancomycin as follows:

- 125 mg q6h for 10 to 14 days
- 125 mg q12h for 1 week
- 125 mg daily for 1 week
- Then every 2 or 3 days for 2 to 8 weeks

Second or further recurrence:

- Vancomycin in a tapered and pulsed regimen or fidaxomicin 200 mg q12h for 10 days or vancomycin 125 mg q6h by mouth for 10 days followed by rifaximin 400 mg 3 times daily for 20 days.
- Fecal microbiota transplantation (appropriate antibiotic treatments for at least 2 recurrences (ie, 3 CDI episodes) should be tried prior to offering fecal microbiota transplantation.

Second and subsequent recurrences can be difficult to cure, primarily because of the persistence of spores in the bowel or environment and the inability of the patient to mount an effective immune response to *C. difficile* toxins, rather than to antibiotic resistance.

Posttreatment testing has no role in confirming eradication. Many successfully treated patients will continue to test positive for weeks or months after the resolution of symptoms; additional treatment is neither required nor effective.

More difficult is the decision of when to test and treat patients who have mild ongoing or recurrent diarrhea after initial treatment. In such patients, stool testing can be helpful in differentiating recurrent *C. difficile* infection from postinfectious irritable bowel syndrome or inflammatory bowel disease that can be triggered by acute enteric infections.

Monoclonal antibodies aimed at preventing the cytotoxic effect of these toxins is a sensible strategy for controlling the disease. In 2016, the US FDA approved Merck's ZINPLAVA™ (bezlotoxumab) to reduce the recurrence of CDI in adult patients receiving antimicrobial therapy for CDI who are at high risk of CDI recurrence.

Fecal microbiota transplantation (FMT) is designed to restore the normal gut microflora for patients with CDI. The use of FMT to treat recurrent/relapsing cases of CDI has proven to be safe and effective. Although FMT has an 80–95% success rate with long term durability, a number of disadvantages still exist. In particular, the manipulation of feces and the classical enteral administration methods are not only laborious, but tend to make the procedure rather unattractive for physicians and patients alike

Although there is an epidemiologic association between proton pump inhibitor (PPI) use and CDI, and unnecessary PPIs should always be discontinued, there is insufficient evidence for discontinuation of PPIs as a measure for preventing CDI.

There are insufficient data at this time to recommend administration of probiotics for primary prevention of CDI.

CHLOSTRIDIUM DIFFICILE INFECTION (CDI)

2018 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA)

- Patients with a high likelihood of CDI manifested by unexplained new-onset watery diarrhea can have a nucleic acid amplification test (NAAT) as a single diagnostic test. For inconsistent results, an institutional multistep testing strategy to diagnose CDI should be in place incorporating a toxin enzyme immunoassay (EIA) confirmatory test.

- In adults with a nonfulminant initial CDI episode, treat with vancomycin or fidaxomicin rather than metronidazole.

- For fulminant CDI, vancomycin 500 mg orally or NGT q6h and metronidazole 500 mg IV for 10 to 14 days. Use additional vancomycin therapy via rectal retention enema, 500 mg in 100 mL normal saline every 6 h if complete ileus is present.

- For first CDI recurrence, avoid repeating the initial treatment regimen. Use vancomycin or, potentially, fidaxomicin if metronidazole was used initially. Use pulse-tapered vancomycin or fidaxomicin if vancomycin was used initially.

- For a second or subsequent recurrence, treat with pulse-tapered vancomycin or vancomycin for 10 days followed by rifaximin or fidaxomicin or use fecal microbiota transplantation (FMT) to treat adults in whom antibiotic therapy has failed.