

LOS ANGELES

COLON AND RECTAL SURGICAL ASSOCIATES

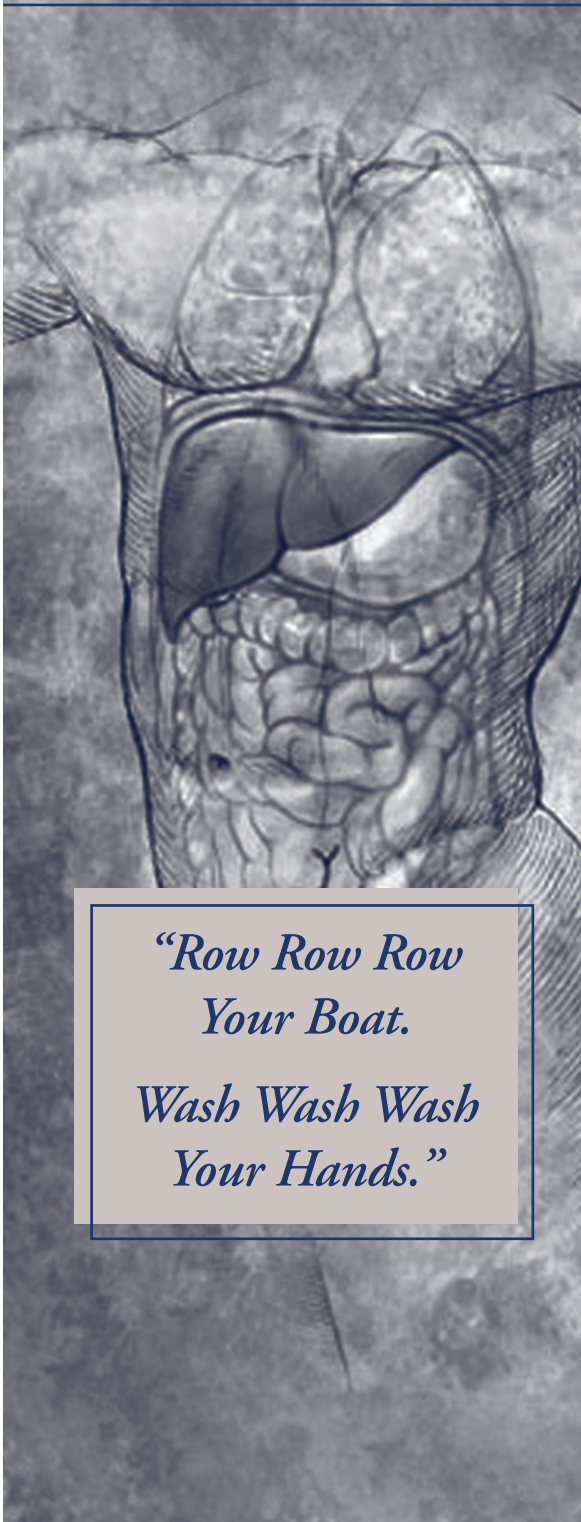
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CLOSTRIDIUM DIFFICILE INFECTION

What can we do?

*“Row Row Row Your Boat.
Wash Wash Wash Your Hands.”*



Clostridium difficile (*C. diff*) is an anaerobic, toxin-producing, gram positive, spore forming bacteria, and is the world-wide leading cause of hospital acquired diarrhea. In the United States, over 250,000 patients require hospitalization and 14,000 people die yearly as a result *C. diff* infections. What can be done about this vexing infection?

is invariably related to prior antibiotic use which suppresses the normal colonic flora, thereby allowing selective growth of *C. diff*. While nearly all antibiotics have been associated with causing a *C. diff* infection, the most frequent offending antibiotics include cephalosporins, penicillins, and clindamycin.



Particularly at risk are individuals over

age 60, those who have had prolonged antibiotic treatment, and patients who have undergone irradiation or have obstructive pulmonary disease, malignancy, mechanical bowel preparation prior to colonic surgery, enteral feeding, ICU care and those who are immunosuppressed.

THE PATHOLOGY OF THE INFLAMMATORY RESPONSE.

C. diff causes colitis and subsequent diarrhea by release of exotoxins referred to as Toxin A (enterotoxin) and Toxin B (cytotoxin). Toxin A causes increased colonic permeability and fluid secretion, while toxin B causes colonic inflammation. This process leads to a secretory diarrhea, with an inflammatory reaction which can culminate in cell death. A macrophage response leads to release of tumor necrosis factor and Interleukins 1 and 6, which are responsible for the systemic septic reaction. Clostridium difficile is a normal minor inhabitant of the intestinal microbiome. *C. diff* infection

FROM PATIENT TO YOU AND ON AND ON. ROW ROW ROW YOUR BOAT...PLEASE!!

Infection can be spread through the fecal-oral route when spores are ingested. The spores may survive for weeks or months on inanimate objects and may account for

continued on back...

*“Row Row Row
Your Boat.*

*Wash Wash Wash
Your Hands.”*

COLON AND RECTAL SURGICAL ASSOCIATES

...continued from front

widespread outbreaks within hospitals and nursing facilities. If inanimate surfaces are not properly cleaned, reinfection becomes a real possibility and problem. As the *C. diff* spores have an inherent resistance to alcohol and alcohol-based hand sanitizers, hand washing with soap and water by medical staff and family members is important. The quality of the handwashing is important. Simply slapping a little bit of soap on the hands and then wiping, will do nothing to eradicate *C. diff*. The hands must be lathered with soap, and the soap must stay in contact with the hands for as long as it takes to twice slowly sing Row Row Row Your Boat. If you have trouble remembering the words, then you may substitute Happy Birthday To You.

Clinical manifestation can range from asymptomatic to fulminant colitis and sepsis. Typically, patients report at least 3 episodes of non-bloody diarrhea per day. In more severe cases, diarrhea may be associated with fever, abdominal pain or distension, and an elevated WBC. Peritonitis or intestinal perforation can occur but are rare. Symptoms usually occur about 7 days after initiation of antibiotics for other maladies, but have been reported to occur even months after cessation of antibiotics.

EASY TO DIAGNOSE. DIFFICULT TO REMEMBER.

All patients with unexplained, non-bloody diarrhea should undergo stool testing. The gold standard is stool testing with enzyme immunoassays for the *C. diff* toxin. The assay has a 70-95% sensitivity and a 99-100% specificity. Repetitive testing is no longer recommended. While cultures for *C. diff* are more sensitive, they are significantly more expensive, time consuming and may detect healthy asymptomatic adult carries (3%), and are therefore not recommended.

Radiographic studies, including plain films and CT scanning, may be used as adjuncts in the diagnosis of more severe cases, especially in ruling out colonic perforation or fulminant colitis. Typical findings in non-perforated cases includes polypoid mucosal thickening, haustral fold thickening or colonic distension. CT scans may show pancolitis, fat stranding and ascites or early signs of fulminant colitis, which may include pneumatosis coli (air in the bowel wall).

Endoscopic findings commonly show evidence of pseudomembranes (multiple 2-5 mm raised adherent yellow or white plaques) but should be reserved for laboratory negative cases in which there is still a strong suspicion for *C. diff*, or if trying to differentiate from other types of colitis such as Inflammatory bowel disease, ischemic colitis or other infections. However, not all patients may manifest pseudomembranes, especially in mild cases. Pseudomembranes may not involve the rectum (70%) or may be beyond the reach of a flexible sigmoidoscope (10%), therefore requiring a colonoscopy to secure a diagnosis. Caution should be exercised during the performance of colonoscopy, especially in an inflamed colon, as there is higher risk of perforation.

THE CORRECT ANTIBIOTICS CAN CURE C. DIFF.

Offending antibiotics should be discontinued or minimized, and early initiation of fluid and electrolyte replacement is important. Contact precautions are begun immediately. Anti-diarrheal medication should be avoided.

Initial antibiotic therapy includes oral metronidazole, 500 mg three times daily for 10-14 day. In patients unable to take oral medications, intravenous metronidazole may also be used. Oral vancomycin, 125 mg four times daily, may be used in patients with an allergy to metronidazole or in patients who are pregnant or are nursing. For more severe cases, vancomycin should be first line choice and even higher doses (500 mg four times daily) may be indicated. For patients who are unable to take oral medication there is no role for IV vancomycin but it may be given as a retention enema. Fidaxomicin and Rifaximin have also been used as alternative antibiotic choices. Additionally, cholestyramine may be given to bind *C. diff* toxin and limit the disease, but may interfere with oral vancomycin use due to its binding effects on vancomycin.

Recurrences of *C. diff* infection may occur in 10-20% of patients within 8 weeks of successful treatment and first line re-treatment should be the same medication used previously (95% effective). Depending on frequency of recurrences, a prolonged treatment course with a Vancomycin taper is recommended (125 mg qid x 7 days, 125mg bid x 7 days, 125 mg q day x 7 days, 125mg qod x 7 days, and 125 mg q three days at 7 days).

STOOL TO THE RESCUE (WHEN ALL ELSE FAILS).

Fecal Microbial Transplantation (FMT) has been recommended in cases refractory to standard therapy for recurrences and involves instillation of normal fecal flora into the colon. The repopulation of normal fecal flora prevents overgrowth of *C. diff* and toxin production thereby clearing the infection. The process involves instillation of "healthy" stool from a screened family member or partner into the colon via colonoscopy, nasogastric administration, or rectal enema. Colonoscopic administration has been found to have the highest cure rates of over 95%. More recently, frozen encapsulated fecal capsules from unrelated donors have been developed and may allow for a wider use, given the simpler application method while maintaining success rates over 90%. It should be noted that FMT is not readily available due to regulatory issues.

Surgery is reserved for acute fulminant colitis or toxic megacolon. Patients with progressive evidence of systemic sepsis or acute abdomen will require emergent surgery. Surgery in this setting involves removal of the entire colon with preservation of the rectum, and formation of an ileostomy. In the hospital setting, early consultation is important, as delayed surgical intervention is associated with significant morbidity and mortality. Once the patient has recovered, the ileostomy can be reversed in 3-6 months to re-establish intestinal continuity.

ROW YOUR BOAT.

Indiscriminant prescription of antibiotics and poor handwashing practices are associated with an increase incidence of Clostridium difficile infection. *C. diff* infection can be a frustrating problem due to high risk of spread and recurrence for both the patient and the clinician. While a majority of cases can be managed medically, a small subset can develop life threatening infection. Early detection and treatment is key to successful eradication.