

# Attack on *C. difficile*: How can we combat this serious health issue

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In five different studies presented at the American College of Gastroenterology's (ACG) 75th Annual Scientific meeting in San Antonio, researchers explored the impact of various factors on increasing rates of *Clostridium difficile* infection (*C. difficile*), such as the use of proton pump inhibitors (PPIs) and the substantial increase in antibiotic use due to new National Hospital Quality Measures; strategies to combat high rates of *C. difficile* infections; and cutting-edge treatments for this potentially deadly—and quite common—infection.

Five studies were featured during an ACG press briefing on Tuesday, October 18, 2010 entitled: "Attack on *C. difficile*: A GI Perspective - How We Can Combat this Serious Health Issue."

*C. difficile* associated diarrhea (CDAD) is a major cause of morbidity and increasing health care costs among hospitalized patients, as *C. difficile* infections have dramatically increased in recent years, with 500,000 cases in the United States annually and approximately 15,000 deaths each year, according to the U.S. Centers for Disease Control & Prevention.

## **Proton Pump Inhibitors Linked to Incidence of *C. difficile* Associated Diarrhea**

While antibiotic use is the most documented risk factor for CDAD, attention has been directed towards a plausible—but controversial—link with [proton pump inhibitors](#) (PPIs). Researchers today unveiled results

of a meta-analysis of 16 observational studies, which explored the association between CDAD and PPIs. The study, "A Meta-analysis of 16 Observational Studies on Proton-Pump Inhibitor Use and Risk of *Clostridium difficile* Associated Diarrhea" investigated the association between PPIs and CDAD from 1980-2010 and involved more than 1.2 million hospitalized patients.

The investigators extracted adjusted risk estimates from the studies and used a random effects meta-analysis. The summary risk estimate showed a 65 percent increase in the incidence of CDAD among PPI users, according to Sailajah Janarthanan, M.D., who co-authored the study. Researchers also conducted a stratified analysis by study design and when looking at both prospective and retrospective studies, found that there was still a significant increase in *C. difficile* among PPI users.

### **The Introduction of National Hospital Quality Measures Linked to Rising *C. difficile* Rates**

In 2004, the Joint Commission on Accreditation of Health Care Organizations (JCAHO) and the Centers for Medicare and Medicaid Services (CMS) introduced National Hospital Quality Measures (NHQM) to improve pneumonia and surgical infection outcomes. However, these new quality measures have resulted in a substantial increase of antibiotic usage, which researchers hypothesized has led to an increase in *C. difficile* associated diarrhea and colitis in an inner city hospital in New York. As a result, researchers reviewed charts of all patients with confirmed *C. difficile* infection admitted to the Bronx Lebanon Hospital Center from January 1, 2003 to December 31, 2008. Antibiotic usage for all inpatients during the same time was also reviewed.

The study, "National Quality Measures and *Clostridium difficile* Infection in an Inner City Hospital," found a total of 439 patients with

confirmed *C. difficile* infection from January 1, 2003 to December 31, 2008.

"We observed significant increase in *Clostridium difficile* infection rate between 2003 and 2006," said Ariyo Ihimoyan, M.D. The number of cases per 10,000 admissions was 16 in 2003; 20 in 2004; 50 in 2005; 36 in 2006; 40 in 2007; and 58 in 2008. The total number of antibiotic doses uses per 1000 admissions was 3268 in 2003; 3536 in 2004; 4585 in 2005; 5150 in 2006; 5848 in 2007; and 5867 in 2008.

"From these findings, we conclude that the introduction of National Hospital Quality Measures have led to a substantial increase in antibiotic usage," said Dr. Ihimoyan. "We believe this resulted in an increase in *Clostridium difficile* infections in our patient population. Antibiotic usage-related quality measures may have resulted in unintended complications and should be re-evaluated."

### **How Can We Combat *C. difficile*?**

Another study unveiled during the October 18 press briefing addressed the ways hospitals, gastroenterologists and other health care practitioners could combat *C. difficile* entitled, "Aggressive Attack on *C. difficile* Results in Significant Decrease in Hospital Infection Rate: the INTEGRIS Baptist Medical Center Experience."

Waging "an all out war on *C. difficile*," researchers implemented a number of measures over a three-month period at INTEGRIS Baptist Medical Center, a tertiary care facility in Oklahoma City which admits approximately 26,000 patients per year and experienced an increase in *C. difficile* cases.

"Aimed at reducing the incidences of *C. difficile* infections, these measures consisted of a multi-faceted attack on *C. difficile*, including

improved prevention, early detection, review and full implementation of national infection control guidelines, and aggressive treatment measures," explained Mark H. Mellow, M.D., FACG, Center for Digestive Health, Oklahoma City, OK. "In addition to standard isolation procedures, we also elicited suggestions from physicians and nurses to best ensure compliance, such as placing a trashcan near the door to avoid traversing the room after de-gowning; keeping an uncluttered sink area; using appropriate size gloves; and making stethoscopes easily accessible," said Dr. Mellow.

Dr. Mellow and his team also initiated a campaign to limit proton pump inhibitor use outside of critical care units and encouraged nursing staff to send stool for *C. difficile* toxin (CDT) testing if *C. difficile* was suspected, without waiting for physician order.

"In the 12 months prior to our interventions, the incidence of CDT positive hospitalized patients was 11.3 per 100 admissions," said Dr. Mellow. "After a 3-month implementation period, the ensuing 12-month positive CDT incidence fell to 6.9 per 1000 patients, a decrease in *C. difficile* infection incidence of 40 percent. As a result, a 'war on *C. difficile*' can have a significant positive impact on a hospital's rate of infection," said Dr. Mellow.

### **Cutting Edge Treatments Help Patients with *C. difficile***

Up to 25 percent of patients will have a recurrence of *C. difficile* infection, and a proportion will be refractory to [antibiotics](#). Additional therapies for this difficult-to-treat subpopulation include antibiotics, probiotics, toxin-binding medications, active vaccination, intravenous immunoglobulin, and fecal bacteriotherapy (FB).

"Fecal bacteriotherapy, more commonly known as fecal transplant, has been slowly gaining ground as a rescue for recurrent and refractory cases

of *C. difficile* associated diarrhea," said C. Brock Miller, M.D., University of North Carolina at Chapel. Dr. Miller and his research team today reported findings from their initial experience using FB via colonoscopy, "Fecal Bacteriotherapy via Colonoscopy for Refractory and Recurrent *Clostridium difficile* Associated Diarrhea," which showcased two patients.

The first patient, a healthy 34-year old woman who developed CDAD after eight courses of [antibiotics](#) over six months, and had ongoing recurrences of CDAD, had an immediate improvement in symptoms and has been infection-free for nine months after fresh stool donated from her healthy 40-year old sister was liquefied and delivered throughout the terminal ileum and entire colon via colonoscopy.

A second patient, a healthy 50-year old female, who also developed recurrent *C. difficile* toxin positive diarrhea, elected to undergo FB via colonoscopy after testing and donation by her husband. She has been cured of *C. difficile* associated diarrhea to date, according to Dr. Miller.

"While further clinical studies and long-term follow-up of patients are required, fecal bacteriotherapy appears to be a viable, safe, and inexpensive option for cases of recurrent and refractory disease," said Dr. Miller.

The goal of another study unveiled today was to explore novel and inexpensive antimicrobial agents commonly found in nature in an effort to combat *C. difficile* in hospitals.

"For more than 2000 years in the Indian subcontinent, indigenous people have been using turmeric in their daily food," explained Rattan Patel, M.D. "Traditional Indian medicine, Ayurveda, has been using this spice to help decrease the rate of gastrointestinal infection."

In the study, "Inhibiting Hospital Associated Infection of Toxigenic *Clostridium difficile* Using Natural Spice – Turmeric (Curcumin)," Dr. Patel and his research team found that all strains of *C. difficile* were inhibited by turmeric extract (curcumin).

"Turmeric has been shown to be relatively safe in clinical studies, with more than 40 clinical trials already performed in the United States using curcumin as an intervention as per the Clinical Trail database," said Dr. Patel. "It's likely that daily use of turmeric in hospital settings, in food products like curry or soup, can potentially decrease the incidence of *Clostridium difficile* associated diarrhea. But more studies are needed to determine the mechanism of action of turmeric and the physiological effects of turmeric in animal models of pseudomembranous colitis," said Dr. Patel.

Provided by American College of Gastroenterology

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