

# *Clostridium difficile* infection:

## Meeting the challenge

APIC's *Clostridium difficile* Educational and Consensus Conference, March 11-12, highlighted prevention and control strategies.

BY MARY LOVE  
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While other healthcare-associated infections have declined in recent years, rates of *Clostridium difficile* infection (CDI) have climbed to historic highs and remain at unacceptable levels. Each year, more than 500,000 Americans acquire a CDI; 14,000 of them die.

On March 11-12, APIC's 2013 *Clostridium difficile* Educational and Consensus Conference brought together leading experts from across the country to discuss initiatives to prevent and control the spread of CDI. Key areas of focus were prevention strategies, antibiotic stewardship, current research findings, and new technologies to better detect and treat CDI.

### WHO IS GETTING CDI?

People most at risk for CDI are those taking antibiotics and also receiving medical care in any setting—not only in hospitals and nursing homes, but also in doctor and dentist offices, dialysis

clinics, and outpatient surgical centers.<sup>1</sup> “This is not just a hospital problem,” said conference co-moderator Stephen Parodi, MD, of Kaiser Permanente. “It is a community problem.” Almost all CDIs occur in people who recently received medical care in or out of hospitals.<sup>1</sup> Older people are at particular risk, with more than 90 percent of CDI-related deaths occurring to those 65 years of age and older.<sup>1</sup>

“The 2000s were characterized by a completely unanticipated CDI epidemic that continues in 2013,” said Dale N. Gerding, MD, of the Stritch School of Medicine, of Loyola University Chicago. This current epidemic

is due at least in part to the emergence of the BI/NAP1/027 strain of *C. difficile*, which is more severe and lethal than other strains and is now found in 30 to 40 percent of CDI cases in North America, Dr. Gerding added.

While the incidence of CDI in the U.S. is stable to increasing, rates in Europe have dropped, said Dr. Gerding. One reason may be the changing patterns of antibiotic use in that country, he said, citing a drop in the use

of fluoroquinolones and cephalosporins in the U.K. in the last five years.<sup>2</sup> Dr. Gerding also noted that the U.K.'s National Health Service investigates as soon as CDI occurs in one or two patients in an institution.

CDI “incidence” is also largely influenced by how the infection is diagnosed and reported, said Erik R. Dubberke, MD, MSPH, of the Washington University School of Medicine. With methods more sensitive at detecting *C. difficile*





but less specific for CDI, such as polymerase chain reaction (PCR) testing, a 40 to 60 percent increase in reported CDI is possible, he said. Public reporting of CDI has also expanded rapidly in the U.S. and other countries, added L. Clifford McDonald, MD, of the Centers for Disease Control and Prevention (CDC). In the U.K., he said, CDI reporting rates increased by 25 percent in 2008 after reporting went from voluntary to mandatory in 2007. Most U.S. states have instituted CDI reporting mandates and as of January 1, 2013, Centers for Medicare & Medicaid Services (CMS) requires reporting of lab-identified CDI through the National Healthcare Safety Network.

#### WHO DO WE TEST AND HOW?

"It is time to retire the EIA [enzyme immunoassay] for toxins A and B as a stand-alone primary assay for the detection of CDI," said Stephen M. Brecher, PhD, of the Veterans Administration

Boston Healthcare System. This assay may have some uses but, with an average sensitivity of about 60 to 70 percent, should not be the primary diagnostic procedure, said Dr. Brecher.

Unfortunately, there is not yet a reliable gold standard for testing for CDI. While toxigenic culture—where organisms are cultured on a selective medium and then tested for toxin production—is very sensitive, "the downside is that the turnaround time is about seven days," said Jennie Mayfield, BSN, MPH, CIC, of Barnes-Jewish Hospital/Washington University School of Medicine. The EIA test for glutamate dehydrogenase (GDH) has been a good screening test in many studies but must be confirmed, she added. And while Mayfield agreed that molecular testing with nucleic acid amplification (NAAT) or PCR has high sensitivity and specificity, she said that this testing remains expensive.

Dr. Dubberke said some investigators have looked at inflam-

matory markers, such as fecal lactoferrin and fecal calprotectin, as adjunctive methods to identify patients with symptomatic infection while a confirmatory test is pending, but that these inflammatory markers lacked sufficient sensitivity and specificity.

So, what are acceptable strategies for testing? Dr. Brecher recommends either: (1) EIA for GDH with or without toxins A and B, combined with a molecular assay for discrepant results, or (2) a molecular test with or without a confirmatory toxin assay. He added that testing should be limited to at-risk patients with clinically significant diarrhea after ruling out other causes such as laxatives or other infections. "With any test you have to include data from the patient," said Dr. Brecher. Testing should not be used as a "test of cure" or repeated if not clinically necessary, he said.

#### IS THERE HOPE FOR BETTER INFECTION PREVENTION?

Although many infection prevention and control guidelines are readily available, the conference speakers agreed that more innovative ways are needed to really engage people. "It's one

thing to post a sign or a guideline," said conference co-moderator Barbara DeBaun, RN, MSN, CIC, of Cynosure Health. "It's a completely different thing to actually have people demonstrate good practices."

Nancy Corbett, RN, BSN, MHA, of Kaiser Permanente, described her organization's two-year evolution of standardized workflows to improve infection prevention behaviors. "We wanted to make infection prevention engaging and part of everything all of us do," she said. "We wanted to do something different, change the culture, and understand each other's workflow."

Recognizing that the best learning strategy is to teach others, Kaiser challenged 420 representatives from its network to work in multidisciplinary teams to create 20- to 30-minute modules to share at their medical centers. The very creative solutions incorporated hands-on demonstrations, role-play scenarios, and videos such as "Holey Glow—Hand Hygiene and Glove Etiquette." Staff members also signed pledges to speak up if they saw a coworker miss a hand hygiene opportunity.



**FAR LEFT.** Nancy Corbett, RN, BSN, MHA, leads an isolation role playing demonstration during her session titled "Deliberate Practice: Improving the Reliability of Hand Hygiene and Isolation Practices." **LEFT.** Conference attendees engaged in peer-to-peer roundtable discussions on best practices and the challenges and barriers to *C. difficile* prevention. **ABOVE.** Moderator Stephen Parodi led the summary panel discussion on day two of the conference with L. Clifford McDonald, MD; Phenelle Segal, RN, CIC; Stephen Brecher, PhD; Vickie Brown, RN, MPH, CIC; and Julia Moody, MS, SM(ASCP).



**“Mayfield acknowledged that although much has been done to understand CDI, much more science and research is still needed.”**

The majority of respondents in APIC’s recent CDI Pace of Progress Survey<sup>3</sup> reported more healthcare personnel participation in CDI education efforts, along with an increased emphasis on environmental cleaning and equipment decontamination efforts, said Mayfield. However, 64 percent of respondents relied on observations to monitor the effectiveness of cleaning, rather than more accurate methods like adenosine triphosphate (ATP) or fluorescing products, she said.

“Multiple studies have shown that 50 percent of high-touch surfaces are not cleaned during terminal cleaning of a patient room,” said Vickie Brown, RN, MPH, CIC, of WakeMed Health & Hospitals. Spores can remain viable on environmental surfaces for long periods of time—up to five months according to some studies. Routine hospital disinfectants such as quaternary ammonium compounds are

ineffective in eradicating *C. difficile* spores.

Steam cleaning has been found to be effective, reducing bacterial levels by more than 90 percent in one 2011 study<sup>5</sup>, said Mayfield. Techniques that use hydrogen peroxide vapor have also shown promise in decreasing multidrug-resistant organisms, she added, but have long cycle times—from two to three hours for a single room. Ultraviolet (UV) radiation devices have also been effective in decreasing environmental contamination, but may require a two-step process for bathrooms as well as long cycle times, said Mayfield, noting that UV units are also expensive—priced from \$40,000 and up.

#### **CAN WE DO MORE TO STOP ANTIBIOTIC MISUSE?**

Antibiotic exposure is the single most important risk factor for developing CDI, with up to 85 percent of CDI patients having



Moderator Stephen Parodi, MD, guides a question-and-answer session on the first day of the conference, as Vickie Brown, RN, MPH, CIC; Stephen Brecher, PhD; and L. Clifford McDonald, MD, engage in a discussion to address an attendee's question.

had an antibiotic exposure in the 28 days before infection, said Julia Moody, MS, SM(ASCP), of the Hospital Corporation of America. Almost all antibiotics have been implicated in CDI, but certain antibiotic classes—such as cephalosporins, clindamycin, and fluoroquinolones—seem to have a higher risk for causing infection, she added.

“Up to 50 percent of antibiotic use is either unnecessary or inappropriate across all types of healthcare settings,” said Moody. She cited a recent study showing that urinary tract infections and pneumonia are the leading indications for unnecessary antibiotic use in patients with current or recent CDI.<sup>6</sup>

Moody discussed strategies for implementing antibiotic stewardship programs, which have had an impact on reducing CDI. A stewardship team typically features a clinical PharmD and a physician champion at its center. “The physician champion needs to be someone who is respected in the medical community and is able to have discussions on a peer-to-peer basis and work collaboratively to make change,” Moody said. The champion need not be an infectious disease specialist, she added. Sometimes a pathologist, pediatrician, or hospitalist may be a more appropriate choice.

Stewardship programs are slowly increasing, with 60 percent of APIC CDI survey respondents reporting programs at their facilities, compared to 52 percent in 2010.<sup>3</sup> Tools for

understanding and establishing stewardship teams are available in APIC’s recently updated *Guide to Preventing Clostridium difficile Infections* and on the Get Smart: Know When Antibiotics Work for Healthcare site of the CDC ([www.cdc.gov/getsmart](http://www.cdc.gov/getsmart)). “Antibiotic stewardship really needs to be a team approach,” said Phenelle Segal, RN, CIC, of Infection Control Consulting Services. “We cannot practice effective infection prevention and control without a multidisciplinary team.”

#### **WHAT DOES THE FUTURE HOLD?**

With new diagnostic tests and mandatory reporting, reported rates of CDI are expected to increase in the short term, said Dr. Gerding. However, these measures should eventually drive improved infection prevention and an ultimate reduction in CDI rates, he added. Dr. Gerding said that experts expect the current BI/NAP1/027 frequency to decline in North America over the next decade, although new epidemic strains will emerge.

New treatments in the pipeline include fidaxomicin, which is approved for CDI. It is a narrow-spectrum macrocycle antibiotic with no activity against gram negatives. “It is the first new CDI treatment antibiotic in 25 years,” said Dr. Gerding. Monoclonal antibodies directed against toxin A and toxin B are in phase III trials, he said, after showing significant reductions in CDI recurrence rates in phase II trials.<sup>7</sup>



Attendees participate in a personal protective equipment exercise on day two of the conference.

Dr. Gerding said that vaccines and other biotherapeutics are also showing promise. He added that a toxin A/B vaccine is currently in a Phase II trial to assess effectiveness in preventing primary CDI. Treatment with non-toxicogenic *Clostridium difficile* spores to prevent recurrent

CDI has completed a Phase II trial and results will be available soon. For prevention of multiply recurrent CDI, a randomized trial of fecal microbiota transplantation (FMT) versus oral vancomycin has shown a highly significant improved outcome for FMT.<sup>8</sup>

Although some studies suggest good results with probiotics, said Mayfield, there have been no randomized controlled trials that included treatment of CDI as the primary outcome.<sup>9</sup> A limitation of probiotics is that the complex gut microbiome has hundreds of bacteria species, while most probiotics contain only one or two organisms, she said.

Fecal transplantation remains a viable treatment option with high rates of success reported in treating recurrent CDI, said Mayfield, citing a 2011 study that reported more than 90 percent efficacy.<sup>10</sup> However, standardization and safety testing are lacking, she said. Dr. Gerding added that the effectiveness of fecal transplants in clinical trials has varied with the route of instillation, relationship to the stool donor, volume given, and treatments given before infusion. Suggested areas of future research include stool banking from healthy donors and the use of stool isolates, said Mayfield.

Mayfield acknowledged that although much has been done to understand CDI, much more science and research is still needed. Specifically, she cited the need for identifying patients who may be carrying the organism for weeks or months. Also needed are better ways to learn where the organism goes and

exactly how it is being transmitted, she added.

There is "light at the end of the colon," said Dr. Brecher. "But there's room for more. We're getting there." **B**

Mary Love is a medical writer for Prevention Strategist.



## ACCESS PEER-REVIEWED ARTICLES ABOUT CLOSTRIDIUM DIFFICILE IN THE AMERICAN JOURNAL OF INFECTION CONTROL

**Electronic screening of patients for predisposition to *Clostridium difficile* infection in a community hospital,** Penny B. Cooper, Albert J. Heuer, Cirle A. Warren [March 2013 (volume 41 issue 3 Pages 232-235 DOI: 10.1016/j.ajic.2012.03.022)]

**Alkaline detergent combined with a routine ward bedpan washer disinfectant cycle eradicates *Clostridium difficile* spores from the surface of plastic bedpans,** Michelle J. Alfa, Nancy Olson, Louise Buelow-Smith, Brenda-Lee Murray [April 2013 (volume 41 issue 4 Pages 381-383 DOI: 10.1016/j.ajic.2012.04.326)]

**Knowledge, attitudes and practice regarding *Clostridium difficile*: A survey of physicians in an academic medical center,** Eugene Fayerberg, Jacques Bouchard, Susan M. Kellie [March 2013 (volume 41 issue 3 Pages 266-269 DOI: 10.1016/j.ajic.2012.03.013)]

**Understanding factors that impact on health care professionals' risk perceptions and responses toward *Clostridium difficile* and methicillin-resistant *Staphylococcus aureus*: A structured**

**literature review,** Emma Burnett, Nora Kearney, Bridget Johnston, Joanne Corlett, Stephen MacGillivray [March 2013 (Article in Press DOI: 10.1016/j.ajic.2012.12.013)]

**Absence of *Clostridium difficile* in asymptomatic hospital staff,** Markus Hell, Kathrin Sickau, Gregor Chmelizek, Jan Marco Kern, Matthias Maass, Steliana Huhulescu, Franz Allerberger [December 2012 (volume 40 issue 10 Pages 1023-1024 DOI: 10.1016/j.ajic.2012.01.018)]

**Improved detection of toxigenic *Clostridium difficile* using the Cepheid Xpert C *difficile* assay and impact on C *difficile* infection rates in a tertiary hospital: A double-edged sword,** Deborah A. Williamson, Indira Basu, Joshua Freeman, Terri Swager, Sally A. Roberts [March 2013 (volume 41 issue 3 Pages 270-272 DOI: 10.1016/j.ajic.2012.03.025)]

**Clinical impact of switching conventional enzyme immunoassay with nucleic acid amplification test for suspected *Clostridium difficile*-associated diarrhea,** Steven W. Johnson, Meganne Kanatani, Romney M. Humphries, Daniel Z. Uslan [April 2013 (volume 41 issue 4 Pages 373-375 DOI: 10.1016/j.ajic.2012.04.329)]

**Engaging patients in the prevention of health care-associated infections: A survey of patients' awareness, knowledge, and perceptions regarding the risks and consequences of infection with methicillin-resistant *Staphylococcus aureus* and *Clostridium difficile*,** Andrew Ottum, Ajay K. Sethi, Elizabeth Jacobs, Sara Zerbel, Martha E. Gaines, Nasia Safdar [April 2013 (volume 41 issue 4 Pages 322-326 DOI: 10.1016/j.ajic.2012.04.334)]

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## NEED ADDITIONAL CLOSTRIDIUM DIFFICILE INFECTION PREVENTION RESOURCES AND EDUCATION?

- Download the new *Guide to Preventing Clostridium difficile Infections*.
- Read the executive summary from the *Clostridium difficile* Educational and Consensus Conference.
- Access the full 2013 CDI Pace of Progress Survey.
- Order the conference proceedings.

Access these resources and more at [www.apic.org/CDIresources](http://www.apic.org/CDIresources).