Tracking an Emerging Infectious Disease: Clostridium difficile-Associated Disease

Clostridium difficile (*C. difficile*) is the leading infectious cause of antibiotic-associated diarrhea in hospitals. It causes mild to moderate self-limiting diarrhea to severe inflammation of the colon, which may require surgery or result in death. Since 2000, cases of *C. difficile* associated disease (CDAD) have increased significantly, with many patients experiencing severe inflammation of the colon [Gelone et al. ICAAC 2006 K1006].

Eng and colleagues presented results from a case-control retrospective study of antibiotics used and patient diagnoses in the VA New Jersey Health Care system from January 2004 to December 2005 to determine the relationship between CDAD increases and a formulary change from levofloxacin to gatifloxacin. Results presented at the 2006 ICAAC conference showed that CDAD occurred in 117 patients, 76 of which occurred after the formulary switch to gatifloxacin (p=0.049).

Another study reported by Van Dissel and colleagues evaluated the use of immune whey protein concentrate (Anti-CD-WPC) to prevent CDAD relapse after an outbreak of *C. difficile* in several hospitals in The Netherlands. Twenty one different PCR-ribotypes of *C. difficile* were distinguished; 8% of CDAD cases were associated with toxin A negative/toxin B positive strains. The most prevalent non-O27 PCR-ribotypes were 014 (19%) and 002 (11%). After completing antibiotic treatment, patients received Anti-CD-WPC 5gm tid for 2 weeks, with a 60-day follow-up. Relapse occurred in 13/109 (12%); most of the relapses were due O27 PCR-ribotypes (16%) vs. 8% for other strains, suggesting that Anti-CD-WPC aids prevent of relapse of *C. difficile*-associated diarrhea.

Increased virulence of CDAD is associated with high toxin production by fluoroquinolone-resistant strains belonging to ribotype 027. Nord and colleagues presented results from a study that investigated whether new drugs for Gram-positive infections select for colonization of *C. difficile* in humans. Twelve (12) subjects received one 1 gm dose of dalbavancin as an IV infusion and 12 received tigecycline (50mg) as IV infusions bid/10 days. Serum and fecal samples were collected before, during, and after drug administration to determine drug concentrations and for microbiological analysis.

Fecal concentrations of dalbavancin were 6.8-73.4 mg/kg (Day 5) and 7.4-26.4 mg/kg (Day 14). Dalbavancin was not detected on day 60. There was some impact on the numbers of enterococci and *Escherichia coli* but no changes in lactobacilli, clostridia, or bacteroides. No *C. difficile* strains were recovered. Tigecycline fecal concentrations were 1.0 to 11.3 mg/kg (Day 5) and 3.0 to 14.1

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mg/kg (Day 8). No concentrations were found on days 18 to 31. The numbers of enterococci, *E. coli*, lactobacilli, and bifidobacteria were reduced, while other enterobacteria and yeasts increased. There was no impact on bacteroides. No *C. difficile* strains were isolated. The investigators concluded that dalbavancin and tigecycline do not select for intestinal colonization of *C. difficile*.

In most parts of the world CDAD is not required to be reported to public health authorities, resulting in a limited understanding of its epidemiology. To gain a better understanding of what is occurring with this disease, Dr. Steven Gelone and colleagues launched the first global, web-based surveillance project of CDAD (wwww.rmhca.com/cdadproject/) in October 2005. As of May, 2006 there were 775 clinician respondents. A total of 630 (81%) were from the US and 145 (19%) were from the rest of the world (Table 1) [Gelone et al. ICAAC 2006 K1006].

Increased participation in this worldwide surveillance project would contribute to a better understanding of the epidemiology of CDAD.

Table 1: US versus Rest of World (ROW) Results

	US (n = 630)	ROW (n = 145)
Increased # of cases of CDAD	315 (50%)	34 (24%)
Increased # of severe cases of CDAD	316 (51%)	46 (32%)
Increased treatment relapse	353 (56%)	48 (33%)
Attributable colectomy	220 (35%)	33 (23%)
Attributable death	189 (30%)	35 (24%)

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resistant SP isolates collected in year 5, compared with 1.1% (9/825) in year 1 and 8.5% (60/710) in year 3. All *erm*(B)+*mef*(A) serotype 19A isolates in year 5 were MDR (resistant to ≥2 antibacterial classes), with high rates of resistance to amoxicillin-clavulanate (83.1%), cefuroxime (100%), erythromycin (100.0%), cotrimoxazole (100%), and tetracycline (100.0%). Resistance to telithromycin was rare (0.7%) and no isolates were levofloxacin resistant.

Type 19A has steadily increased in prevalence, as well as in resistance to common drug classes. The multiresistant *erm*(B)+*mef*(A) SP 19A clone continues to spread in the US. Common among patients aged 0-2 years, this SP 19A clone exhibits a high degree of MDR, particularly to the β-lactams and the macrolides. Results of the studies presented at the 2006 ICAAC conference in San Diego point to a growing need to include this serotype in future vaccine formulations.

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into the air as did female volunteers. No significant alteration of the airborne spreading patterns under different clothing conditions was found. Thus, the most efficient reduction in the airborne spread of *S. aureus* was obtained by changing into sterilized surgical scrubs. However, even under the most effective clothing regime 0.12 CFUs/m3/min of *S. aureus* were spread into the environment.

Special accommodations such as isolation procedures for *S. aureus* carriers suffering from these conditions appear unjustified in view of the airborne dispersal of this pathogen. However, patients and staff should be encouraged to practice basic hand washing techniques, which may include antiseptic washes and shampoos and the application of topical antibiotic ointments to the anterior nares of the nose. The use of disposable aprons and gloves by staff reduces skin-to-skin contact and may therefore further reduce the risk of transmission. The spread of *S. aureus* is of particular concern as it has become resistant to many commonly used antibiotics [Stucki et al. *Antimicrobial Agents and Chemotherapy* 2006].