

CONTAGIOUS COMMENTS

Department of Epidemiology

Clostridium difficile

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C. difficile (CD) is an anaerobic spore-forming bacillus that is present in soil and the environment. Hospitals have become major reservoirs of the organism. Estimates are that 20-40% of hospitalized patients become colonized or infected with CD during their hospital stay. Children less than 2 years old have high CD colonization rates (up to 70%) however normal healthy individuals more than 2 years old have a 1 - 3% colonization rate. Healthy healthcare workers are reported to have a 13 – 15% CD colonization rate. This is thought to be due to their constant exposure to CD cases.

Patient exposure to antimicrobials is a major risk factor for colonization or disease. Antibiotics, especially broad spectrum antibiotics such as clindamycin, penicillins, cephalosporins and fluoroquinolones allow for overgrowth of CD by suppression of the normal flora of the colon. CD toxins A and B alter the colonic mucosal cell's cytoskeleton by disrupting F-actin microfilaments. CD overgrowth also elicits an inflammatory response syndrome, secondary to CD toxin A and B production, which induces pro-inflammatory cytokines within in the colonic mucosal surface. Other risk factors are advanced age, prolonged hospital stay, having a CD infected roommate, prolonged nasogastric tube placement, GI surgery, use of gastric acid suppressing agents, and repeated enemas.

The organism has been implicated in *C. difficile* associated diarrhea (CDAD), pseudomembranous colitis, toxic megacolon, and sepsis, sometimes resulting in patient death. CD is acquired through fecal-oral transmission of CD spores, mainly via the contaminated hands of healthcare personnel, or direct environmental acquisition. Patients shed large numbers of organisms that readily sporulate and survive in a dormant state for long periods in the hospital environment. CD spores are readily recovered from hospital toilets, bedpans, rectal thermometers, floors and room furniture.

US national estimates of hospital associated CDAD held steady at about 40 cases /100,000 discharges from 1996 to 2000. The data for 2001-2004 has demonstrated a remarkable shift in the epidemiology of CDAD, with rates effectively doubling, with increased severity of disease that has mainly been concentrated in large northeastern hospitals and in patients more than 64 years of age. For this age group, rates of CDAD have gone up 5 fold and severe disease rates gone up 4 fold. There have been recent reports of peripartum and community-acquired CDAD, with bloody diarrhea in younger patients having no antibiotic exposure. These recent increases

in CDAD rates have been associated with the emergence of a CD strain in Europe and North America, and possibly world wide, with increased virulence, and increased antimicrobial resistance.

Molecular epidemiology studies looking at strain typing of thousands of CD isolates, molecular markers for virulence and antimicrobial resistance have shown the following:

1. The new epidemic CD strains have DNA that is very similar by Pulse Field Gel Electrophoresis (PFGE), and represents a new emerging clone. DNA from non-epidemic CD strains is diverse by PFGE.
2. Toxinotyping using Restriction Fragment Length Polymorphisms (RFLP) of the pathogenicity locus (PaLoc) which contains the genes encoding toxins A (*tcdA*) and B (*tcdB*), demonstrates that the new epidemic CD strains are all of the relatively uncommon toxinotype III.
3. In addition to CD toxins A and B, all the new epidemic CD strains make “binary toxin” (the Iota toxin common in *Clostridium perfringens*) which is uncommon in the non-epidemic CD strains.
4. The new epidemic CD strains have an 18 base pair deletion in the DNA of the *tcdC* gene, which is a negative regulator of the PaLoc locus. This results in 5-20 fold hyperproduction of CD toxins A and B, starting in log phase growth, compared to non-epidemic CD strains, which produce lower levels of toxin A and B only during stationary phase growth.
5. The epidemic CD strains have increased high level resistance to clindamycin and levofloxacin. The data are unclear if antibiotic use has selected this epidemic CD strain, but many experts feel that over use of fluoroquinolones has been a contributing factor. Because of concerns about selecting for Vancomycin Resistant Enterococcus (VRE), metronidazole rather than vancomycin is recommended as the first line therapy for CDAD. Some cases of CDAD with the new CD epidemic strain are clinically refractory to therapy with metronidazole, however there is no *in vitro* laboratory evidence of metronidazole resistance among these new CD strains.

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The good news is that this new CD strain has not yet moved into the pediatric population. What can we do? We can take the following proactive steps:

1. Restrict unnecessary use of antibiotics, especially clindamycin, ceftriaxone and fluoroquinolones.
2. Conduct surveillance for CDAD patients and track positive lab results for CD Toxin A or A/B. Early diagnosis and treatment can reduce adverse events. Use laboratory information system to link positive lab results to initiate contact precautions. At TCH, we routinely monitor CD infections in our patients and we have not had any significant increase in CDAD in the last 5 years.
3. Maintain infection control efforts such as contact precautions for all CDAD patients, intensive environmental cleaning with bleach for all CDAD patient rooms (at TCH we use the bleach product DISPATCH[®], Caltech Industries, Inc.), and hand washing with either soap-and-water or alcohol hand

washes for all routine healthcare worker contacts with CDAD patients or their room environments.

This is the only way to limit colonization of healthcare workers.

In CD outbreak situations, soap-and-water hand washing is recommended by the CDC, as alcohol hand washes do not kill CD spores.

If we rigorously follow these steps we may limit endemic CD disease (estimated to cost the US healthcare system 1 billion dollars per year) and have a good chance at preventing the spread of this new epidemic CD strain to our pediatric patients.

