
Overuse of Antibiotics Causing Severe Illness and Fatalities in U.S. and Canada

The overuse of antibiotics is long known to have caused the emergence of drug-resistant bacteria, and now things are much worse. Last month, a federal agency reported outbreaks of a particularly virulent strain called *Clostridium difficile* which is causing a severe form of diarrhea and an increased rate of fatalities. The use of antibiotics can disrupt the normal flora of the bowel and promote the overgrowth of *Clostridium difficile*. More cases of pseudomembranous colitis, a complication of antibiotics that causes severe inflammation of the colon, have been reported.

Although seriously ill or elderly people in hospitals or long-term care facilities are the most likely to be afflicted, now birthing women have been added to the list. Most alarming, cases of *Clostridium difficile*-associated diarrhea severe enough to require hospitalization were reported in otherwise healthy adults and children who had not taken antibiotics but were in close contact with someone diagnosed with *Clostridium difficile*-associated diarrhea. Only certain antibiotics are implicated in all these outbreaks.

Three Reports Published Simultaneously

The U.S. Centers for Disease Control and Prevention detailed the most recent outbreaks early last month in its Morbidity and Mortality Weekly Report. Knowledge of its impending publication prompted an early release of two related studies by The New England Journal of Medicine.

In the first one, Canadian researchers conducted a study of 12 hospitals in the province of Quebec to determine the incidence of hospital-borne *Clostridium difficile*-associated diarrhea. Between January and June of 2004, there were 1703 patients diagnosed with this infection. This represented 22.5 cases for 1000 hospital admissions. Within 30 days of a diagnosis of *Clostridium difficile*, this infection caused the death of nearly 7% of these hospital patients and contributed to the deaths of another 7.5%. Elderly patients were more likely to be infected than younger patients. Two families of antibiotics were identified as the primary culprits—fluoroquinolones and cephalosporins (see next page).

In the other study, American researchers reported outbreaks in eight health care facilities in six states (Georgia, Illinois, Maine, New Jersey, Oregon, and Pennsylvania) between 2000 and 2003. The research team led by L. Clifford McDonald, MD, U.S. Centers for Disease Control and Prevention (CDC), reported that *Clostridium difficile*, which used to be uncommon, has now morphed into a far more toxic version of itself. The CDC has received alarming reports, such as this from the University of Pittsburgh Medical Center where outbreaks of severe *Clostridium difficile*-related infections were nearly twice as high between 2000 and 2001 as they were during the entire 1990s. Twenty-six patients with severe infections required colectomy (the surgical removal of all or part of the colon) and 18 patients died.

Outbreaks Increasingly Dire

The CDC-led research team concluded that in some areas of the country, there is an epidemic of a virulent form of *Clostridium difficile* which has become resistant to the fluoroquinolones family of antibiotics. In an editorial that accompanied both studies reported in the December 8, 2005 New England Journal of Medicine, John G. Bartlett, MD, and Trish M. Perl, MD, described how antibiotic-associated colitis began to be reported early in the antibiotic era. For example, researchers reported in 1974 that a study of 200 consecutive patients given clindamycin (see next page) showed that 41 had diarrhea and 20 had pseudomembranous colitis.

Bartlett and Perl of Johns Hopkins School of Medicine described the changing pattern of disease severity as each new class of antibiotic drugs was introduced and overprescribed. *Clostridium difficile* developed a resistance and doctors would turn to another class of antibiotics. The editorialists had specific advice for physicians who were warned that the standard stool test available in most laboratories will not identify the virulent strain of *Clostridium difficile*. Doctors are advised to suspect this epidemic strain based on the number and severity of cases in their locale.

Treatment, advised Bartlett and Perl, should start with prompt discontinuation of the antibiotic if it is one of the

Antibiotic Overuse continued

many that are implicated in *Clostridium difficile*-associated diarrhea. Doctors should then prescribe oral metronidazole, a drug that can treat some anaerobic bacterial infections (sold as Flagyl and numerous other brand names). Careful hand washing with soap and water is recommended for all medical personnel and home caregivers as a supplement to the use of alcohol-based sanitizer because such sanitizers do not eradicate *Clostridium difficile*.

What you can do:

-Do not request antibiotics for a viral illness. Colds, flu, and bronchitis are examples of viral illnesses for which antibiotics are frequently and inappropriately prescribed.

-Wash your hands often. This is the most important means of preventing the spread of infection, according to the U.S. Centers for Disease Control and Prevention. For more information, go to the Alliance for the Prudent Use of Antibiotics (www.tufts.edu/apua).

-Seek medical attention for diarrhea lasting longer than three days or accompanied by blood or high fever. This advice from the Morbidity & Mortality Weekly Report is based on the fact that outbreaks of *Clostridium difficile*-associated infection have been reported in people previously thought to be at low risk—that is, healthy, young, and not recently hospitalized. Also, diarrhea and pseudomembranous colitis have been observed to begin up to several weeks following cessation of antibiotics therapy, according to Worst Pills, Best Pills, A Consumer's Guide to Avoiding Drug-Induced Death or Illness.

-Rethink the chronic use of heartburn medicines like Nexium, Prilosec, Prevacid, and others in the drug class known as proton pump inhibitors. Use of these drugs, which suppress stomach acid, is linked to a higher incidence of *Clostridium difficile* in non-hospitalized people, according to a study published last month in the Journal of the American Medical Association. Apparently, stomach acid protects against invading pathogens. To a lesser extent, use of another class of heartburn drugs called H2 blockers (Tagamet, Pepcid, Axid, and Zantac) is also linked to an increased risk of *Clostridium difficile*. ±

Antibiotics Implicated In Recent Outbreaks

Nearly all antibiotics can cause pseudomembranous colitis in a small minority of people. Its severity can range from mild to life-threatening. Only the following antibiotic families and clindamycin, however, are implicated in the recent outbreaks of the most virulent *Clostridium difficile*-associated infections.

In their editorial for The New England Journal of Medicine, John G. Barlett, MD, and Trish M. Perl MD, advised doctors to use restraint in the use of second- and third-generation cephalosporins, fluoroquinolones, or a combination of the three:

Fluoroquinolone Antibiotic Family

The family includes Ciprofloxacin, Gatifloxacin, Levofloxacin, Lomefloxacin, Norfloxacin, Ofloxacin, Sparfloxacin, and Trovafloxacin. Each is known by one or more brand names. Ciprofloxacin, for example, is sold under four brand names: Ciloxan, Cipro, Cipro Cystitis Pack, and Cipro HC. The first drug in this family was introduced in 1984.

Cephalosporins Antibiotic Family

Each drug in this family can have one to three different brand names. Some brand names for second- and third-generation cephalosporins include: Vantin, Zinacef, Ceflor, Suprax, Lorabid, Ceftin, and Cefzil. The first drug in this family was introduced in 1974.

Clindamycin

Introduced in 1973, clindamycin has been reserved for life-threatening infections that do not respond to penicillin or other antibiotics. It is sold under the brand names of Cleocin, Cleocin Pediatric, Cleocin T, Cleocin Vaginal Cream, Dalacin C, and Dalacin T. ±

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