CD Summary

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OREGON PUBLIC HEALTH DIVISION • OREGON HEALTH AUTHORITY

CLOSTRIDIUM DIFFICILE INFECTION: OUR BIGGEST NOSOCOMIAL PROBLEM?

Clostridium difficile infection (CDI) is the most common cause of healthcare-associated infections (HAIs) in the United States, and it can be severe and even fatal. This issue of the *CD Summary* delineates the burden of CDI, offers recommendations on how to prevent transmission and suggests educational resources for healthcare providers.

BACKGROUND & RISK FACTORS

C. difficile is a hardy, anaerobic Gram-positive bacillus that can encapsulate itself as a thick-walled, highly resistant spore. It is spread by the fecal-oral route, and ingested spores can survive passage through the acidic stomach to reach the small intestine, where they germinate and thereafter elaborate two exotoxins: toxin A, which recruits inflammatory mediators, and toxin B, which has cytotoxic effects on the intestinal mucosa. Together, they cause the inflammation and mucous secretion that characterize *C. difficile* colitis.[1]

The intestinal flora normally keep *C. difficile* in check, but antibiotic disruption of this microbiota enables its proliferation and resultant pathology. Fluoroquinolones have been associated with *C. difficile* disease most commonly.[2] Restricting fluoroquinolone use has been effective in truncating outbreaks.[3] Risk factors associated with CDIs are shown in the Box.[4]

Risk factors for *C. difficile* infection[4]

- antibiotic exposure
- proton pump inhibitors
- gastrointestinal surgery or manipulation
- long length of stay in healthcare settings
- serious underlying illness
- immunocompromising conditions
- advanced age

CDI may be asymptomatic or present as watery diarrhea; or typical, pseudomembranous or fulminant colitis with toxic megacolon and colonic perforation.[1] Diagnosis is typically made by looking for the toxins or their genes via cytotoxin assay, enzyme-linked immunosorbent assay, or polymerase chain reaction. Anaerobic culture is possible — but "difficile."

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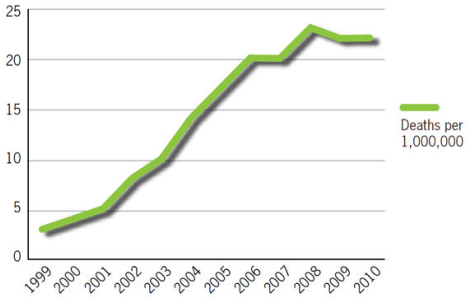
An estimated 80,400 hospital-onset CDIs occurred in the U.S. in 2011.[5] On average, a single episode of CDI increases the length of hospital stay from 2.8 to 5.5 days and costs from $3,006 and $15,397 — resulting in cumulative costs of $1.0 to 4.9 billion annually in the U.S.[2] Five to ten percent of CDI patients die of the illness .[2] U.S. CDI deaths increased steadily in the U.S. from 1999 to 2008 (Figure).[6]

Figure. Deaths caused by *C. difficile* infections,* 1999–2010[6]



* Age-adjusted rate of *C. difficile* as the (primary) underlying cause of death

TREATMENT OF CDI

Oral metronidazole, 500 mg orally, three times daily* for 10–14 days, is the standard first-line treatment of initial episodes of mild-to-moderate CDI.[7] Oral vancomycin, 125 mg four times daily for the same duration, is recommended to treat severe initial CDI episodes or initial episodes that do not resolve with metronidazole. In 2011, the FDA approved fidaxomicin for treatment of CDI. Fidaxomicin is a minimally absorbed macrocyclic antibiotic noninferior to, and associated with fewer recurrences than, vancomycin[8]; the dose is 200 mg p.o. twice daily for 10 days.

Following treatment, CDI recurs in as many as 35% of patients. Risk factors for recurrence include older age and duration of hospitalization.[9] Intestinal microbiota transplantation (IMT), a.k.a. "fecal transplant," holds promise for treatment for severe or recurrent CDI. In a 2011 meta-analysis, IMT was followed by full resolution of CDI 92% of cases.[10] The treatment has not been approved by FDA, so its use would typically be restricted to "Investigational New Drug" (IND) protocols; but in July of last year, FDA announced that it would exercise "enforcement discretion" so long as the treating physician obtained adequate informed consent from the patient before performing fecal transplantation for CDI that was not responding to standard therapies.[11]

OREGON DATA

Since January 2012 Oregon hospitals have been required to report all positive *C. difficile* specimens to CDC's National Healthcare Safety Network (NHSN). Each year, the Oregon Health Authority (OHA) reports healthcare-onset CDI (HO-CDI) data as "standardized infection ratios" (SIRs), which are calculated by dividing the number of observed infections at a hospital by the number of "expected" infections — the latter being predicted from data derived from all U.S. hospitals that reported to NHSN during 2008. In 2013, Oregon had 24% fewer HO-CDIs than the national experience. Here in Oregon, however, the HO-CDI SIR increased by 10% between 2012 and 2013.

As a part of OHA's Emerging Infections Program, we have conducted population-based surveillance for CDI among residents of Klamath and Deschutes Counties. Surveillance began in Klamath County in January 2010 and in Deschutes County in 2012. In this surveillance effort, 23% of CDIs were associated with admission to a healthcare facility. Fifty-two percent of CDIs were defined

* And don't even think about writing "t.i.d."

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as community-associated (CA), meaning CDI without known exposure to a healthcare facility. Seventy-seven percent of cases had received antibiotics at some point during the 12 weeks before symptom onset. Infections recurred in 14% of individuals, and 3% died within 30 days of CDI. In Oregon, 75% of CDI cases have occurred in individuals >50 years of age.

PREVENTION OF CDI

CDI is common, potentially severe and preventable. Antibiotics play a pivotal role in CDI pathogenesis. A recent multisite survey of hospital inpatients found that 51.9% of hospital inpatients were receiving or scheduled to receive antimicrobial agents.[5] A meta-analysis found that antimicrobial stewardship programs reduce CDI incidence by an average of 52%.[12] Outside the hospital, Oregon's Alliance Working for Antibiotic Resistance Education (AWARE) has crafted materials for clinicians and community members to help reduce the prescribing of antibiotics for viral infections.

C. difficile spores turn up on the hands of healthcare workers and in hospital surfaces. Gloves reduce *C. difficile* spread, and because alcohol-based hand sanitizers do not inactivate the spores, healthcare workers should wash their hands with soap and water after doffing the gloves.[13,14] Gowns are also recommended for those entering patient rooms of patients with CDI. †

C. difficile spores can remain viable on surfaces for up to 5 months.[15] Environmental surfaces should be disinfected with a sporicidal agent such as a 1:10 dilution of household bleach solution.[2]

† or any diarrheal disease, for that matter

Communication among healthcare providers is essential for instituting contact precautions, ordering confirmatory testing, initiating cleaning procedures and adhering to hand hygiene practices. Oregon Adminstrative Rule 333-019-0052 requires written communication of infection or colonization with *C. difficile* (or multidrug-resistant organisms) to receiving facilities upon patient transfer or discharge. To support this effort, OHA has created webinars, toolkits and samples of interfacility transfer forms.

Healthcare facilities should consider establishing internal surveillance for CDI to understand better their local risk factors and infection patterns.

FOR MORE INFORMATION

- OHA's Alliance Working for Antibiotic Resistance Education (AWARE) website includes CDI tools and resources for clinicians and communities: *http://public.health.oregon.gov/PreventionWellness/SafeLiving/AntibioticResistance/Pages/GetAwarePublications.aspx*.
- Interfacility transfer communication: visit *http://public.health.oregon.gov/DiseasesConditions/CommunicableDisease/HAI/Prevention/Pages/Interfacility-Communication.aspx*.

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