

Community-Associated *C. difficile* - Another Traditionally Hospital-Acquired Infection Continues to Spread

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MRSA started out as a primarily hospital-acquired infection, and now it's loose in our communities. Are we headed the same way with *C. difficile*?

Dr. Bud Wiederman, MD, MA, Evidence eMended Editor, Grand Rounds

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Source: Adams DJ, Eberly MD, Rajnik M, et al. Risk factors for community-associated *Clostridium difficile* infection in children. **J Pediatr.** 2017;186:105–109; doi: 10.1016/j.jpeds.2017.03.032.

See **AAP Grand Rounds commentary by Dr. Rebecca Brady** (subscription required).

Before I go on to describe this article from a database for dependents of military families, I'd better reveal to readers the potential for bias in my review. I know the first 3 authors of this study pretty well. We've worked together in a few settings, mostly with regard to pediatric infectious diseases fellowship training. All of the pediatric ID fellows in the Walter Reed training program spend some time at my institution, and our groups have monthly joint conferences and other times for interaction, all enjoyable. So, either I'll be cowed by my feelings of good will towards this group and give them a break in my usually caustic reviews, or I'll overcompensate and trash their study unjustly. Regardless, their data provide much food for thought.

They queried the TRICARE database for diagnostic coding for *C. difficile* infection (CDI) over a 2-year period in children between 1 and 18 years of age (more on this age choice later), excluding any cases where children were hospitalized prior to the diagnosis to focus on just the community-acquired cases. They ended up with 1331 cases, and they then matched 3 control cases, matched for age, sex, and (I later found out) time period but without a CDI diagnosis, to each case. They found that cases, compared to controls, had a strong association with a number of exposures, including to various classes of antibiotics, proton pump inhibitors, and family members with CDI. These findings clearly are significant for front-line pediatric providers, again emphasizing the importance of limiting antibiotic exposure in children but also highlighting the possible risks of gastric acid suppressive medications. This latter finding isn't new, but I suspect it is not well recognized by community practitioners; think twice about continuing these medications for prolonged periods in children.

A couple of issues occurred to me while studying this article. First, I was a little uncomfortable with the authors' decision to include children down to 1 year of age, since asymptomatic colonization with CD is still somewhat common up to age 3, and the AAP urges caution in testing for CDI before that time. Given my friendship with the authors (at least, we were friends until they read this review), I decided to contact them and find out whether their conclusions would be changed if they just limited the study to ages 3 - 18 years. It turned out that 1 of the journal reviewers had already asked them this question, and they had performed a sensitivity analysis looking at just that. It revealed that some of the associations (H2 receptor antagonists,

sulfonamides, 1st generation cephalosporins, macrolides, and penicillins exposures) lost their statistical significance as associations with CDI, possibly due to loss of power with fewer numbers. However, I think the essential findings of their research were not affected by the age grouping. I wish the journal editors had decided to include this statement in the final article.

Second, I found myself wishing the authors had done a different study. Does their database allow them to query how often CDI testing was ordered in this population? If so, they could perform a similar analysis comparing CDI positive with CDI negative children, to see if the same risk factors rose to the top. I think this would be a very important analysis since clinicians (I would assume) are more likely to order testing for CDI in children with exposure to antibiotics and other traditional CDI risk factors, and thus a form of selection bias is clouding the current study data. Maybe this is the next study for this group of investigators!

At the moment, I'm left slightly depressed that CDI is becoming all too common in children. Let's all try to do our part to limit antibiotic and H2 receptor antagonist exposure in this population.

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