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## Antibiotics for acute uncomplicated diverticulitis: Time for a paradigm change?

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For years, acute uncomplicated diverticulitis (AUD) has been considered a relatively straightforward disease to treat. Patients typically present to the Emergency Department (ED) or their primary care provider (PCP) with new onset abdominal pain, often (but not always) in the left lower quadrant. After a presumptive clinical diagnosis is made, or with a confirmatory CT scan, even a fresh-faced July intern knows that the only real clinical management question is deciding on inpatient or outpatient treatment. If the patient can take liquids, has tolerable pain and a supportive home environment, we send them home with oral antibiotics. If not, we admit them for IV antibiotics, fluids and pain control. Either way, the prescription of antibiotics have always been a given in the management algorithm, a practice uniformly advocated in practice guidelines, book chapters and review articles.

In this month's issue of *Gastroenterology*, the American Gastroenterological Association (AGA) has made things a little more complicated for that intern, as well as for the ED provider, the PCP, and the potential GI consultant. New guidelines for the management of acute diverticulitis suggest that antibiotics be used *selectively*, rather than routinely, in patients with uncomplicated acute diverticulitis.<sup>1</sup> The guidelines are accompanied by a detailed technical review.<sup>2</sup>

The recommendation itself is based on two large multicenter trials. The first, from Sweden and Iceland, included 669 inpatients with imaging confirmed acute uncomplicated diverticulitis.<sup>3</sup> Patients were allocated to either 7 days of antibiotics or intravenous fluids only. The trial found no difference in time to resolution of symptoms, complications, length of hospital stay or risk of recurrence.

The second trial included 528 patients in the Netherlands with a first occurrence of imaging confirmed acute uncomplicated diverticulitis.<sup>4</sup> Patients were allocated to either 10 days of antibiotics or observation. The trial found no difference in time to resolution of symptoms, complications, length of hospital stay or risk of recurrence.

The guidelines committee rated the quality of this evidence as “low” because the first trial had a high risk of bias and the second trial is only available in abstract form.

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A rationale for these new trials was the observation that there has never been any direct high-quality evidence that patients with AUD benefit from antibiotics (simply non-inferiority of one antibiotic versus another) as well as the increasingly accepted concept that AUD might be more of an inflammatory process than an acute bacterial infection.

Despite the relatively low quality of these new trials, several national health systems in Europe have moved away from the obligate use of antibiotics for acute uncomplicated diverticulitis: (i) The Danish Surgical Society has concluded that antibiotics are not routinely recommended;<sup>5</sup> (ii) A working group from the Netherlands recommended that antibiotics not be routinely administered;<sup>6</sup> (iii) An Italian consensus report found that antibiotics may not improve outcomes but should be used on a case-by-case basis;<sup>7</sup> and (iv) A multidisciplinary German group recommended that antibiotics be omitted in patients without risk factors for complicated disease but only with “close monitoring”.<sup>8</sup>

Contrary to these international guidelines, a recent Cochrane review, while echoing the interpretation that “the newest evidence from one RCT (randomized clinical trial) says there is no significant difference between antibiotics versus no antibiotics in the treatment of uncomplicated diverticulitis” also cautioned explicitly that “This new evidence needs confirmation from more RCTs before it can be implicated safely in clinical guidelines”.<sup>9</sup> Moreover, a recent systematic review began with the observation that before effective broad-spectrum antibiotics were available, diverticulitis was a devastating disease associated with substantial morbidity and mortality and that now most cases resolve with antibiotics.<sup>10</sup> They also, however, concluded that recent studies demonstrate a lesser role for ‘aggressive’ antibiotic intervention.

So which is it? Are antibiotics beneficial in our patients with acute uncomplicated diverticulitis, or are we simply being hypercautious and conservative, and perhaps ‘treating ourselves’. While not the subject of this commentary, it is clear that overuse of antibiotics is causing significant harm, both to individual patients, with potentially life-threatening complications such as *C difficile* infection, and communally, with emerging bacterial resistance. In fact, the United States White House recently released its National Action Plan for Combating Antibiotic-Resistant Bacteria<sup>11</sup> and the Center for Disease Control (CDC) has budgeted over –250 million dollars in FY2016 to implement this program. Antibiotic stewardship and restraint are major cornerstones of these efforts.

We’ve now confused our intern, of course, who will likely ask “well, which patients can avoid antibiotics?” In the absence of perfect data, we can start by saying that there is complete agreement that some patients with uncomplicated diverticulitis should certainly still be treated with antibiotics. Patients who are immunosuppressed, pregnant or have significant co-morbid disease should receive antibiotics, as should any patient with evidence of systematic inflammatory response syndrome or sepsis.<sup>12</sup> For the otherwise healthy patient with AUD, it is probably best to say that we are uncertain which course is best. The trials to date are suggestive but still preliminary, and it is unclear how the evolving European experience applies to our own patients. At the moment, the final decision becomes both a matter of clinical judgment and perhaps also a reflection of treatment values.

One could, appropriately, and in good conscience, withhold antibiotics and ensure close follow up of their patient. Another provider might instead rationally choose to prescribe antibiotics, arguing that the trials to date are low quality and our decades of experience treating patients with antibiotics and obtaining good outcomes are truly the best evidence to date. For those torn between these two alternatives, it might be best to lay out the facts as we understand them and allow the patient a role in this decision.

Clearly, there is urgent clinical trial work remaining to be done to better define the appropriate use of antibiotics in AUD. Until that work is done, the new guidelines are best seen as allowing the clinician to consider withholding antibiotics from select uncomplicated patients with mild disease.

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