

Possible New Treatment for C. Diff., An Old Enemy



By Josh Bloom — September 23, 2015



As if we don't have enough problems with antibiotic resistance

and superbugs, an evil entity called *Clostridium difficile* (C. diff.) continues to take its toll on patients, most commonly those who are hospitalized and already receiving antibiotics.

In fact, it is the antibiotics themselves that are largely responsible for the C. diff. problem. Especially when used over a long-time interval, broad spectrum antibiotics alter the normal gut flora, sometimes drastically. Since C. diff. is resistant to most antibiotics, in the absence of competing bacteria it can overgrow causing a full-blown infection.

The bug causes severe diarrhea. How severe, you ask?

Microbiology expert and ACSH advisor. Dr. David Shlaes has written extensively about the dangers of C. diff., including sections in his book "Antibiotics The Perfect Storm" (Springer, New York, 2010).

In his many blog pieces, and in the book, Dr. Shlaes discusses C. diff. frequently with good reason:

"[R]ates of C. diff. diarrhea have increased about 100% between 1996 and 2003 and that virtually all of this increase occurred in patients older than 64 years of age. We find the same picture when we look at deaths from C. diff. The death rate has climbed tremendously over the same time period and it is mainly coming from the older population. In 1993, C. diff was associated with an 8% chance of death, while in 2003 the death rate was between 9.5 and 10%. *Most of this mortality was among those over 64 years of age where the death rate in recent years ranges from 30 to 50% (emphasis added)*. It is estimated that the cost for C. diff alone in the U.S. is over \$1 billion per year and climbing rapidly."

Yes, C. diff. is that dangerous. And there is no good way to treat it. It responds poorly to most antibiotics, which is intuitively obvious, since the antibiotics used to treat the primary infection were probably caused by them.

Dr. Robin Patel from the Mayo Clinic recently told [MedPage Today](#) ^[1], "Treating *C. difficile* disease is a challenge. There are a small number of antibiotics that we can use. But we're *using antibiotics to treat something that is caused by antibiotics*. So the concept of looking at non-antibiotic

approaches ... is attractive."

And, as bacterial resistance a slowly ticking time bomb it continues to eat into our therapeutic options for treating infections, and this can only get worse.

That is, unless someone comes up with a new approach.

Researchers at Stanford University Medical Center may have done just this, although it's still early. Instead of using just another antibiotic to try to wipe out *C. diff.*, they are using an antibody called bezlotoxumab that targets the toxins which the bacteria create. These toxins, not the bacteria themselves, cause the symptoms. Actually, when not producing these toxins *C. difficile* can be a commensal in the gut.

It is not easy to get rid of *C. diff.* Recurrence of the infection is a big problem.

Stephen Jenkins, PhD, of Weill Cornell Medical College in New York, said, "[f]inding ways of preventing recurrence is important. In the hospital setting, refractory disease is not uncommon at all." This is even more important, since when the infection recurs it is often more difficult to treat than the first occurrence.

Two phase III studies were presented at the Interscience Conference of Antimicrobial Agents and Chemotherapy. The studies showed that patients who were treated for 12 weeks with antibiotics and bezlotoxumab had a significant reduction in the rate of recurrence.

Lead investigator Dr. Mark Wilcox, from Leeds Teaching Hospitals and University of Leeds in Great Britain said, [r]esults of these studies showed that a single, one-time infusion of the antitoxin bezlotoxumab given with standard of care *C. difficile* antibiotic treatment significantly reduced the recurrence of *C. difficile* infection compared to standard of care alone, and demonstrated this benefit over a 12-week period. These results were also demonstrated in patient subgroups known to be at high risk for *C. difficile* recurrence.

This does not appear to be a home run, but a novel approach to treating a very dangerous infection could be just what the doctor called for.

Dr. Shlaes agrees.

From a 2014 perspective piece that he and Dr. Brad Spellberg co-wrote in [Clinical Pharmacology & Therapeutics](#) [2], "*Clostridium difficile* colitis, relapsing *C. difficile* colitis is an important clinical problem. This disease results from disruption of bowel flora by antimicrobial therapy. Severe and relapsing forms of the disease are typically not the result of resistance to antimicrobial agents but reflect the extent of bowel-flora disruption and underlying host status. We therefore believe that the future of therapy for these infections will focus on restoration of bowel flora via probiotic therapy, ideally in the form of a capsule or other innocuous liquid delivery vehicle, rather than fecal transplantation. Toxin neutralization is also a desirable therapeutic goal."

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[1] <http://www.medpagetoday.com/MeetingCoverage/ICAAC/53666>

[2] <http://onlinelibrary.wiley.com/doi/10.1038/clpt.2014.106/abstract>