Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/gi-insights/recurrent-cdi-care-addressing-unmet-needs-with-emerging-treatments/18135/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Recurrent CDI Care: Addressing Unmet Needs with Emerging Treatments

Announcer:
You're listening to *GI Insights* on ReachMD, and this episode is sponsored by Nestlé Health Science, a leader in the science of nutrition and gut health. Here's your host, Dr. Brian McDonough.

Dr. McDonough:
This is *GI Insights* on ReachMD. I'm Dr. Brian McDonough, and here with me today is Dr. Carl Victor Crawford Jr., who's an Assistant Professor of Medicine and attending physician in the Division of Gastroenterology and Hepatology at New York Presbyterian, Weill Cornell Medical Center. We'll be discussing treatment challenges and unmet needs in the management of recurrent clostridioides difficile infections, or CDI for short. Dr. Crawford, welcome to the program.

Dr. Crawford:
Thank you, Dr. McDonough, for having me.

Dr. McDonough:
To start us off, Dr. Crawford, can you tell us about the prevalence of recurrent CDI?

Dr. Crawford:
So C. difficile infections are becoming more and more prevalent in the United States—not so much in the hospital, but on the outside. So if we think about what the true burden of C. difficile infections are, we have to think about half a million people developing a C. difficile infection every year, and out of those individuals, if I were to see them in the office, I would have to describe to them that this is one of the few infections that actually has a built-in relapse rate. So most individuals that are successfully treated—these are that half-a-million group of individuals—25 percent of them may have a recurrence, which means that despite being treated with antibiotics, at some point in the future this infection can come back. And that's what we define as a recurrence. And there's anywhere between 75,000 to 175,000 of these recurrent cases every year.

Dr. McDonough:
What factors put patients at risk for recurrent CDI?

Dr. Crawford:
So I would say antibiotics are probably the biggest risk factor that leads to a C. difficile infection, and then that's followed by age, unfortunately. So as we get older, our immune systems change. We enter a phase known as immunosenescence, where our immune system is not as robust as it should be. Sometimes our microbiome will change with age, and we lose some of that natural colonization resistance that we once had when we were "spring chickens." So with time, there's a magic age number where we start to see a takeoff of C. difficile infections, and that's about the age of 65. And if we look at data starting at the age of 65 and with each decade of life above that, we start to see more and more individuals developing a C. difficile infection.

Dr. McDonough:
With all that in mind, how can recurrent CDI impact a patient's quality of life?

Dr. Crawford:
So in addition to an individual being pulled through the ringer—having this diarrheal disease that may put them out of work or school and subject them to discomfort—there are other things that we have to do for these patients. We have to isolate them. We have to make these individuals clean their bathrooms.

And when I say isolation, and you're over the age of 65, it becomes very difficult. These individuals are sometimes isolated from their grandchildren, their spouses, and their friends. It really takes a psychological toll, not just a physical one, on these individuals. There was a survey that actually went out to about 350 individuals, and one of the surprising things were that even though individuals were treated successfully with antibiotics and had no further recurrences, about 41 percent of those individuals felt like they would never be the same. And when I say "never be the same," after a C. difficile infection, sometimes the gastrointestinal tract doesn't quite work the way that it did. People may have a change in their bowel habits that may linger for sometimes months or indefinitely, and this puts patients at an increased fear that the C. difficile infection is about to come back. Their gut doesn't feel well; they wake up thinking that they're going to end up in the hospital, and it can be very traumatizing. So it's not just the physical aspects of this infection, but it's the psychological and the social toll that it can take on individuals.

Dr. McDonough:
For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Brian McDonough, and I'm speaking with Dr. Carl Victor Crawford Jr. about the ongoing burden of recurrent clostridioides difficile infections.

So now that we know about the challenges associated with recurrent CDI, let's discuss how we can address them. Dr. Crawford, are there any new and emerging treatments being explored?

Dr. Crawford:
So C. difficile infections are tricky to deal with, mainly because they are by nature, antibiotic resistant, and that's one of the reasons why we started to see this take off on C. difficile infections as well as its recurrences starting around the year 2000-2001. People have experimented with different strategies using antibiotics—there's two main antibiotics that one could use to treat C. difficile infections—but also other kinds of novel strategies using different doses of an antibiotic and different frequencies of giving an antibiotic to reduce the chance that this infection can come back a second time. So the American College of Gastroenterology as well as the Infectious Disease Society of America have guidelines in order to prescribe the right antibiotics for a first-time infection as well as different strategies to use these antibiotics for second or more infection.

Now there are some other strategies that are a bit novel—not using antibiotics. One such strategy is actually targeting the immune system. So we know that C. difficile infection really causes the disease by secreting a toxin that attaches to the colon cell. And once this toxin attaches to the colon cell, it then gets taken into the cell and causes cell destruction. One company actually decided to see what would happen if we were to boost someone's immune system against this toxin, and there's actually an antibody infusion that one can get as a one-time dose that can neutralize this particular toxin that we call toxin B. And that's shown to be protective in individuals in getting a recurrence of the C. difficile infection up to 12 weeks after that infusion has been given. So that is a strategy. I think that many individuals have found that it's sometimes difficult to administer because it requires an infusion center. Sometimes it may not be covered by insurances, and it has a high out-of-pocket cost. But it is a strategy that can be used in individuals that may have a compromised immune system, and it's one of the strategies that we use here.

Now one of the more novel strategies—doing what's called a fecal microbiota transplant, or an FMT for short, was found to confer colonization resistance in a heartbeat. And there are a multitude of studies that have shown how efficacious this is in breaking the cycle of recurrent C. difficile infections, better than any antibiotic or any antibiotic strategy that we've been using over the last 20 years.

There are two major ways that we can perform this now that actually work really well. One is using the full complement of what's in the microbiome. So it's basically sourcing microbiome from healthy human individuals—screening these individuals for communicable diseases as well as screening the stool for particular pathogens. And once individuals have really passed, the stool is then analyzed for its fitness to prevent recurrent C. difficile infections. This product is called RBX 2660 from those studies, and it's actually marketed to be delivered via a rectal retention enema in the office. So there's about 150 cc's of this microbiota solution that we're able to give individuals with recurrent C. difficile infections after they've been adequately treated with antibiotics for that CDI, and it's done in the office over about 3 minutes. And the patient waits in the office for about 15 more minutes just to make sure that they're OK, and then they're home. And basically, that's the end. That breaks that cycle.

There is another product that's been shown to be efficacious, which is a little bit of a take on this particular therapy. And this particular product in the studies was called SER-109. And the researchers who developed this product decided to say, well, is there a consortia or a main group of microorganisms that are responsible for colonization resistance that can just fight off C. diff? And they were able to isolate the particular microorganisms that could form a spore, or a very hardy form of a bacteria, almost like an egg, if you will. And they were able to filter out everything else inside of the microbiota. They were able to destroy all of the viruses, all of the archaea, all the protozoa and the yeast, and they were just left with these spores. And they purified these spores in an alcohol wash, put these spores in pills, and they basically took individuals that had recurrences of C. difficile infections, treated them with the standard of care, had them drink a bottle of magnesium citrate after that completion of antibiotics to help rinse out some of the antibiotic from the system, and they

had individuals take four of these pills for three consecutive days. And they were able to achieve very high success rates at preventing recurrences of the C. difficile infection.

Now these are both FDA-approved products that are approved for use as soon as the first recurrence in individuals that have C. difficile infections. And right now, these are not in the guidelines because these products were approved after the last ACG and IDSA guidelines. However, whether you're an internist, infectious disease specialist, gastroenterologist, or surgeon, you can actually prescribe these for your individuals that you're seeing that have these multiple recurrences.

Dr. McDonough:
These are some fascinating options and excellent research. And kind of going off on that, how can we address antibiotic-resistant strains of recurrent CDI? And I know you're looking at some of those options even as you just discussed.

Dr. Crawford:
Right. So one of the benefits of using live microbes or microbiota therapy is that it doesn't require antibiotics. And C. difficile infection is resistant to many antibiotics, and there are a couple of studies that have looked at, well, what is the likelihood that C. difficile infections are going to become resistant to the antibiotics that we use to treat it?

There are two main antibiotics that we use: fidaxomicin and vancomycin. And currently, we're not seeing a lot of resistance in the East Coast. However, there was a group that actually studied C. difficile found in routine clinical care in Texas as well as in Kenya. And they saw that there's a growing number of, I would say, non-susceptible or intermediately susceptible strains of C. diff against vancomycin. And vancomycin is probably one of the mainstays of antibiotics that we use for C. diff.

Now based on the significant morbidity and mortality that C. diff has, you can only imagine what would happen if this started to migrate from Texas to the rest of the United States, if it's not already in other parts of the United States already. What happens if this kind of infection starts to spread across other geographic locations in Europe or Africa, et cetera? Because we do use antibiotics, which is one of the big risk factors for C. difficile infections for a variety of other conditions. Having some other strategies, such as appropriate antibiotic prescribing practices and using the appropriate antibiotics to treat C. diff or true C. difficile infections, will help slow that down. But when individuals are coming down with recurrences of C. diff, it may actually be more important for us to use these microbial therapies to break that cycle of recurrence on the sooner side rather than exposing our patients and the gut microbiome to more and more vancomycin.

Dr. McDonough:
We've covered a lot today, Dr. Crawford, but before we close, do you have any final thoughts about managing recurrent CDI?

Dr. Crawford:
So in all of my patients that have C. difficile infections, as I'm helping them recover, I use this as an opportunity to help them adopt a healthier lifestyle because after antibiotic therapy, there is diminishment of good bacteria inside of the gastrointestinal tract. There has to be a fuel source for these bacteria to feed on so that they can grow and multiply and take back up the spots that they once had inside of the gastrointestinal tract. So I have my patients increase the amount of fiber that they get in their diet. I have them vary the sources. I have them experiment with other kinds of plant-based foods. I have them eliminate ultra-processed foods. I have them shy away from meats that may be antibiotic treated just to be able to nourish the gut microbiome.

Dr. McDonough:
With those key takeaways in mind, I'd like to thank my guest, Dr. Carl Crawford, for joining me to discuss how the current CDI affects patients and how emerging therapies may help us lessen that burden. Dr. Crawford, it was great having you on the program.

Dr. Crawford:
Thank you so much for inviting me, Dr. McDonough.

Dr. McDonough:
Thank you.

Announcer:
This episode of *GI Insights* was sponsored by Nestlé Health Science, a leader in the science of nutrition and gut health. To access this and other episodes in our series, visit *GI Insights* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!