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/catching-complications-in-ibd-how-to-id-those-at-risk/12781/

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

Catching Complications in IBD: How to ID Those at Risk

Dr. Buch:
Predicting which patients with inflammatory bowel disease will develop complications is a goal that allows for much better medication choices. But how exactly do we go about predicting that risk?

This is *GI Insights* on ReachMD, and I'm your host, Dr. Peter Buch. Today we are honored to be joined by Dr. Corey Siegel. Dr. Siegel is Section Chief of Gastroenterology and Hepatology at Dartmouth-Hitchcock Medical Center and professor at the Dartmouth Institute. Dr. Siegel's research has been pivotal in the IBD field. And we're very happy to have him with us today.

Dr. Siegel, welcome to the program.

Dr. Siegel:
Thank you for having me. I really appreciate it.

Dr. Buch:
To start us off, Dr. Siegel, what are the limitations in just using the clinical risk stratification of Crohn's disease and ulcerative colitis when making decisions on therapy?

Dr. Siegel:
Well, sure, thank you for that question. You know, seeing patients in the clinic, it's a challenge when you're sitting with patients, even when you review all the data that we have about them, whether it be colonoscopy reports, imaging, blood tests, and certainly hearing the history from patients and physical exam. It's hard because that gives us a snapshot of time of how patients are doing right at that moment. But it really doesn't help us that much in predicting what things are going to look like in the future for them. And that's where it becomes very important to help us make treatment decisions is not only how are you feeling today, but what might happen to you in the future and giving treatments to prevent those complications from occurring as opposed to waiting for them to occur.

Dr. Buch:
And along those same lines, what are the risks of using serologic and genetic markers alone?

Dr. Siegel:
So there are a lot of evolving data now about certain genetic markers and serologic markers and thinking about how they play into Crohn's disease, and again, using them as tools to predict the future. However, they're not quite good enough individually to be used to really give us a precise prediction of what might happen in the future. They're helpful, and they're helpful to show us which patients may have complications over time or have might have a more severe disease course. But again, on their own, they're not highly predictive. That's when you start trying to put these factors together and use them in combination that we learn more and really become more precise about who might have a higher risk versus a lower risk of disease complications.

Dr. Buch:
And what role does the microbiome play in risk stratification?

Dr. Siegel:
We're learning about this. Right now, from a practical standpoint, it doesn't really help us too much. We don't know exactly, with a patient coming into the clinic, running some microbiome analyses to use those results to guide us. But we're definitely learning, and a number of groups are working on this. Probably one of the most interesting papers that came out on this pediatric population, published in *The Lancet* in 2017, Subra Kugathasan was the first author on this, and he called it the RISK cohort. And they were able to identify

certain bacteria that are in the patient's gut that are more predictive of certain complications. And they were specific. Specific bacteria associated with either strictures or penetrating disease, such as fistulas or abscesses, that really helped identify which patients might go in one direction or the other. So if you want to fast forward a little bit to the future, you can imagine that at baseline, we're meeting patients, we're getting an array of information about them, including assessing their microbiome and using those results to think about which patients might have specific disease phenotypes and address those upfront and proactively try to protect against that with treatments.

Dr. Buch:
And I understand there's even some research at this point of using the microbiome as a treatment for inflammatory bowel disease.

Dr. Siegel:
Yeah, that's right. There's something different about the microbiome of patients with inflammatory bowel disease. The big question, the age-old chicken and egg question is: is the microbiome changing because of IBD, or is IBD occurring because of the microbiome? We think it's probably the latter, which is IBD may be occurring because of the microbiome. In which case, if you can change it, or alter it in some way, then we might be able to change disease course. And for instance, the proof of principle and this is with fecal transplantation, which is used in ulcerative colitis more so than it has been in Crohn's disease from a research angle. And in fact, they have been able to change the course of a flare of disease using a change of microbiome through fecal transplant. So a lot of work to do in this. Again, fast forwarding to the future, you can imagine that we find a patient who's at risk for certain complications, or even if you want to go back in time a little further, at risk for having inflammatory bowel disease. And can we change the microbiome through different techniques that are being developed now to help prevent IBD completely, or even just trying to prevent certain complications that occur as a result of Crohn's disease or ulcerative colitis?

Dr. Buch:
For those just joining us, this *GI Insights* on ReachMD, I'm Dr. Peter Buch, and today we are discussing how to identify IBD risk factors with Dr. Corey Siegel.

Continuing our discussion, Dr. Siegel, what are microRNAs and why are they important?

Dr. Siegel:
Let's think about why people get IBD, and then that might help us understand why microRNA is important.

So we don't understand exactly the pathogenesis of IBD, but we know it's some combination of genetics and the microbiome that are in your body, the environment, and then your immune system. And then genetics, we've been studying for decades now in inflammatory bowel disease, but it doesn't really sufficiently explain the pathogenesis. We know that genes are different in people with IBD, for the most part, compared to people who do not have IBD. But just having those genes or not having those genes doesn't really explain at all.

MicroRNA are pretty much how it sounds. They're small RNA particles that regulate gene expression. So when did those genes turn on and off? And how did the genes behave? Which might be more important than, “Do you have the genes or do you not have the genes?” And when you think about how that might play a role, we know that microRNA are involved in a couple of really important processes in the body. One is around intestinal barrier function, so your intestine protecting you and not allowing certain antigens or certain things you eat or certain bacteria to stimulate your immune system. And the other then is around inflammation. So if the microRNA are acting differently in people with IBD versus those who don't have IBD, or those with active IBD versus inactive IBD, then that might give us an opportunity to think about how to intervene, and either treat or prevent the inflammation from inflammatory bowel disease. So more specifically, if you have a disruption in your mucosal barrier, and you're stimulating the immune system more than you should be, and then therefore, that leads to inflammation, if we can help repair that process in some way, we could really help make some progress.

So again, not ready for primetime. It's not something that we can test in the clinic and understand what to do with it. But at least in animal models, there's some really exciting work being done, even using microRNA to think about how to treat patients using enemas that use certain microRNA to help with repair of the bowel.

So more to come in the future on this, but I would bet that over the next 5, 10 years this will become a big part of our conversation about not just pathogenesis, but about treatment.

Dr. Buch:
Thank you. Can you please discuss how CDPATH helps with risk stratification of Crohn's disease?

Dr. Siegel:
Oh, sure. CDPATH is a product that we help develop and really proud in the progress it's made. CDPATH is a computer prediction tool to help us risk stratify patients, determining which patients are at low, medium, or high risk of having complications of Crohn's disease.

Complications being defined as strictures or internal penetrating disease or fistulas. More plainly said, which patients are at risk for requiring surgery

And if we were able to predict which patients are at high risk versus low risk, that can really help guide our therapies. And to me as a clinician, this is one of the most challenging things we deal with. And I mentioned this earlier, when we see patients in clinic, it's hard to tell which way they're going and it's hard to tell if they're gonna do okay for 5, 10 years and really have symptoms but not complications versus those who might rapidly progress and be in the operating room within 6 to 12 months.

So CDPATH was a tool developed, combining many of the things we've already talked about. It combines clinical markers, serologic markers, and genetic markers and puts them together in a risk algorithm or risk tool to stratify patients, again, from low, medium, to high risk of having complications over the next three years.

It uses a technique called system dynamics analysis, which is used in various other fields, actually not very much in medicine. But it creates this very simple output of this tool that you get a graph that shows patients exactly what their risk would be over the next three years and shows the trajectory toward that risk. So you could say, “Oh, somebody’s at a 30% risk of having a complication in three years,” but you really want to know if that 30% happens right away or if you slowly get there. Or even worse, if there's an 80% risk of having a complication of three years, does that happen between year two and three? Or does it happen within the first few months?

And you can imagine that sitting in a clinic with a patient if you had that information, if you are armed with that information to share with a patient and use this as a tool to communicate with patients about their disease, it really helps guide the decision-making process. Patients might have minimal symptoms but really be at high risk for progression, or have significant symptoms but might be a low risk for progression. And those different scenarios may really guide how we think about which medications are right for them at that time.

So we developed this over a number of years. We're really thrilled to have recently partnered with Takeda, that they working together with Prometheus Laboratories have allowed CDPATH to get to the market. And actually with Takeda’s support, this is available completely free to patients. So there's no charge for eligible patients. There's some restrictions of who can use it and who can't use it. But adult patients with Crohn's disease who were in the earlier part of their disease course, so relatively soon after diagnosis, can now have free access to CDPATH that they and their providers can use together to help guide treatment decisions.

Dr. Buch:
So Dr. Siegel, if one of our listeners wants to start using CDPATH, how do you suggest that they acquire that ability?

Dr. Siegel:
Yeah, there are two different ways. One, they can talk to their Takeda representative who will probably know all the information on how to access that. But easier even would be to go to the website, which is CDPATH.com. And they can see which patients are eligible, how they can get free access to this tool, and their participating laboratories that they can talk to their local representatives about how to get this done as efficiently as possible.

Dr. Buch:
But of course, with any positives come negatives. So what are the limitations of using this platform?

Dr. Siegel:
Yeah, I'll be the first to admit that nothing's perfect, particularly a tool that I was part of creating. The tool has pretty good predictive ability, but it's certainly not perfect. And to rely on any test alone, even colonoscopy, imaging tests, laboratory tests, we really have to keep it as a piece of the puzzle in our decision making. So I think the biggest risk would be to rely on this completely and ignore other factors that we're learning both from our patients on physical exam, from their history, or other ways that we're understanding the disease. An example of where you can make a mistake, is if CDPATH shows that a patient's at low risk over the next three years of complications, and if they're minimally symptomatic, to say, “Hey, you look to be a pretty low risk, call me if you get into trouble.” And that's not what we want to do. I still think we should closely follow our patients, even those at low risk, because low risk isn't no risk, and they may progress over time. And with Crohn's disease, it's really important to treat these diseases before complications occur and not wait for them to occur, and then use good treatment. So I would suggest that CDPATH is really a very valuable tool to help in decision making and risk stratification, but it shouldn't be used on its own. It should be combined with your clinical judgment, and all the other factors that we learn from patients.

Dr. Buch:
Before we wrap up, Dr. Siegel, is there anything else you would like to share with our audience?

Dr. Siegel:
Well, thank you, I think all the questions you asked are around this concept of really proactive management for Crohn's disease. And the

biggest mistake we make with our patients with Crohn's disease is waiting for patients to feel sick and to feel that they deserve the appropriate treatments. And the mistake is made on both sides. I think both patients and providers are waiting too long. We have very, very effective treatments for Crohn's disease, but they don't treat complications of the disease, they prevent complications and treat inflammation. So anything that we can do to try to treat our patients earlier, to understand which patients are at the highest risk, and to communicate that clearly with patients so they understand we're not just treating symptoms, but we're treating them so that we can prevent complications, which in many cases can be irreversible. So to me, and I appreciate all of your questions, it really leads to this idea that we have to stay ahead of these diseases and not chase the disease. And when we do that, we have a much better chance of improving the quality of lives of all of our patients.

Dr. Buch:
I want to thank Dr. Cory Siegel for sharing his insights on how we can identify those IBD patients who are at risk for complications. Dr. Siegel, it was great speaking with you today.

Dr. Siegel:
Thank you for having me.

Dr. Buch:
For ReachMD, this is your host, Dr. Peter Buch. To access this episode as well as others from the series, visit ReachMD.com/GIInsights, where it can Be Part of the Knowledge. Thanks for listening, and see you next time.