Mayo Clinic Q&A podcast Dr. Faubion IBD

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SPEAKERS

Dr. Sanj Kakar, Narrator, Dr. William Faubion

N **Narrator** 00:00
Coming up on Mayo Clinic Q&A:

D **Dr. William Faubion** 00:03
It's actually quite a common disease. If you take a look at all forms of inflammatory bowel disease, both Crohn's disease and ulcerative colitis, the incidence has actually been increasing.

N **Narrator** 00:12
Right now, there is no cure for IBD. But treatment can help control the symptoms. Therapies can include drugs, surgery, even artificial intelligence.

D **Dr. William Faubion** 00:22
There is tremendous enthusiasm and optimism in the research community. I think a lot of partnership between industry and academia. I think that the future is bright for this disease as therapies get better. That's my hope anyway.

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Dr. Sanj Kakar 00:34

Welcome, everyone to Mayo Clinic Q&A. I'm Dr. Sanj Kakar. Inflammatory bowel disease, or IBD, is an umbrella term used to describe chronic inflammation of your digestive tract. Some of the common types of IBD include ulcerative colitis and Crohn's disease. While IBD usually isn't fatal, it's a debilitating disease that can lead to life threatening complications, if left untreated. Joining us to discuss this today is inflammatory bowel disease expert at Mayo Clinic, Dr. Bill Faubion. Thanks for joining us today Dr. Faubion.

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Dr. William Faubion 01:04

Thank you very much. My pleasure to be here.

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Dr. Sanj Kakar 01:07

So, we're talking about IBD Dr. Faubion. Can you tell us how common this actually is?

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Dr. William Faubion 01:13

So, it's actually quite a common disease. If you take a look at that, all comers, all forms of inflammatory bowel disease, both Crohn's disease and ulcerative colitis, the incidence has actually been increasing. And, the most recent estimates would be that as many as, depending on where you live and what region in the world you live, as many as 1 in 250, to 1 in 300 people may be affected with inflammatory bowel disease. The most recent numbers emerging also from Canada, for example, shows the incidence continued increase, meaning the number of new cases every year. So, the incidence is continuing to increase, and that increase is actually largest in young patients. So, this is still an emerging public health problem. But the short answer is, is depending on where you live, maybe as many as 1 in 300 people are affected.

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Dr. Sanj Kakar 02:04

So, why is it increasing?

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Dr. William Faubion 02:06

Well, we don't know. That's a great question. So, I always tell people, when they ask me this question about why do I have the disease or why is the disease my family, I would say that most of us that do research in this space believe that it's a combination of three events. One is you have to have the right genes, okay. But, that does not mean that you're

going to get this disease. This is what we would call a complex genetic disease, meaning that the genes that contribute to this disease are likely many, many, with each gene contributing a very small amount. Okay, so having the right genes is not that uncommon, but you have to have the right set of genes, then generally, there's some type of environmental trigger. And whether that is a particular bug that lives in my gut, whether that's the way that I eat, or the population eats, or something else that we just don't know. But, there's generally something else, some environmental trigger. And at the end of the day, this is an immunologic disease, an immune system disease. So, the convergence of those three things, we think, induces the disease and those that have the right genes. Why the incidence is increasing? Lots and lots of guesses, right, a lot of grants and funding in that space, but no strong answers yet. Probably one of the most interesting things, though, that the audience may find interesting is this disease was initially thought to be a disease of developed nations, if you will, right. But that's just simply not true. And there are spiking incidence rates in rapidly developing nations. But something that's really interesting, that's been observed probably 20 years ago, is the first inflammatory bowel disease to emerge in developing countries tends to be ulcerative colitis, then that tends to level off. And then following that you see the emergence of Crohn's disease. So, really interesting, a lot of really interesting environmental clues there, but we don't really have the answer yet.

D Dr. Sanj Kakar 04:02

I'm glad you touched upon developed versus developing countries. When I was in medical school, you're absolutely right, we were taught that in developing countries where the diet may be higher in roughage content, you didn't quite see as much inflammatory bowel disease. So, does diet have a role to play here?

D Dr. William Faubion 04:20

Probably. What I tell people, everybody has a question about their diet, and they should, right. Diet is really important. What I tell folks is this. We have bugs that live in our intestine, right? And those bugs, they live there, but they also do things called metabolism. So, they can adjust some of the nutrients that we eat, they can metabolize some of those nutrients and pass off such things called metabolites that can interface back with our own immune system and our own GI tract. So, these bugs live in our gut. The types of bugs that live in our gut, and perhaps equally important, what they're doing, heavily depends upon what we eat. So, I do think that within, hopefully my professional lifetime of taking care of patients with this disease, we will be able to recommend particular diets for particular cohorts of patients, particular groups of patients. It may be different depending on the type of disease that a patient has. There have been some successes, though, I think that the last five years have really brought to fore a variety of clinical trials that are focused on

diet. They're difficult trials to do, because they're hard to control. Meaning it's hard to know exactly what someone is eating when they go home. Some of these diets can be expensive, that could be hard too. So, there are some challenges, but I do think that what we eat drive what types of bugs live in our gut and what those bugs are doing, and that most certainly has to do with our immune response.

D Dr. Sanj Kakar 05:46

And Dr. Faubion, before we really dive into inflammatory bowel disease, I just want you to clear up, there's some other acronyms one hears, for example, IBS or irritable bowel syndrome. Can you explain to our listeners what the difference is between the two?

D Dr. William Faubion 06:02

Yeah, so inflammatory bowel disease, what we're talking about today, is a disease that if I were to pass a scope into the bowel and take a look at the bell, you'll see bleeding, you'll see ulcers. These can lead to narrowing, they can they can lead to penetrations of the bowel called a perforation or a fistula. So, they're a chronic inflammatory event that I can see, that I can touch, that I can feel, that many times leads to surgery, right? That's inflammatory bowel disease. Irritable bowel syndrome is entirely different. If you were to pass a scope, or do an X ray, you don't see anything visually wrong with the intestine. That doesn't mean though, that irritable bowel syndrome is not physiologic, meaning that there's not some cause that one can measure. It's trickier. It's an entirely different subject. It's far more common. I tell young people sometimes that if I have to give a talk, that I'm not prepared for, I may feel sick, I may throw up, I may have diarrhea, okay. That actually are some of the symptoms of irritable bowel syndrome. So, we do think that there's an enteric, there's a loop between the intestine and the neurologic system, the brain, right that all of us are familiar with the butterflies that we get. That probably has something to do with irritable bowel syndrome, that is very different from inflammatory bowel disease.

D Dr. Sanj Kakar 07:20

Great, thank you for explaining that difference. Now, you did touch upon some of the symptoms there of you know, feeling those feelings in your stomach, for example. Can you just go into the actual symptoms of inflammatory bowel disease.

D Dr. William Faubion 07:36

Right. So, I'll break them up between ulcerative colitis and Crohn's disease. So, ulcerative colitis is simple, the inflammation involves the colon, it never leaves the colon, right? It

always stays in the colon, which is the large intestine, that's the last four to six feet of bowel. All the colon does it absorb water, that's all it does, okay. And it's a reservoir for stool. If it becomes inflamed, people pass blood. And when they pass blood, they can have urgency. They have to go to the bathroom right now, right? They can have something we call tenesmus, meaning that one goes to the bathroom, you feel like you've really got to go, and you have a bad cramp but nothing comes out but a little bit of blood or mucus, or as soon as you stand up, you feel like you have to go again. That's called tenesmus. So, cramping, bleeding, pain, urgency, those are mainly the symptoms of ulcerative colitis. Crohn's disease can be a little bit more widely variable, depending upon where in the bowel the Crohn's disease is involved. If it's in the colon can be just like ulcerative colitis. But if the Crohn's disease is in the small bowel, which happens in probably two thirds of patients, one can get diarrhea, one can simply just get cramping. One can feel obstructed, like your belly kind of distends, and you feel like you need to throw up. You can hear loud noises in your small bowel, or sometimes it can be silent, and all that may happen as you just don't gain weight, if you're young. You may have fever, you may just feel nauseous and not feel well. So, Crohn's disease is a little bit trickier to pick up sometimes.

D Dr. Sanj Kakar 09:06

You mentioned bloody stools, and when I hear bloody stools, one thing so, for example, growth in the intestinal cancers. Can you describe those and how's the difference there made?

D Dr. William Faubion 09:19

Right? So something like ulcerative colitis, or Crohn's disease typically causes frankly bloody stools, right? You may pass nothing but blood. Most cancers, when they're diagnosed, they don't pass frank blood. Most patients that are diagnosed with colorectal cancer never knew they were losing any blood in their stool. And for medical students that need to take exams, the classic case would be somebody that comes in with a low blood count, an anemia. So, they're chronically losing microscopic amounts of blood in their stool. And one of the earliest tests to diagnose colon cancer was a stool blood test to look for blood in the stool. But most people can't see it. To have a frankly bloody stool, that would be a little unusual in colorectal cancer, quite common for inflammatory bowel disease.

D Dr. Sanj Kakar 10:06

Thank you. So, we have the signs, we have the symptoms, how do you actually diagnose

inflammatory bowel disease and the differences between the two main types, Crohn's disease or ulcerative colitis?

D Dr. William Faubion 10:19

Most of these diagnoses are going to include some type of lighted camera, either a camera passed from below, a so-called colonoscopy, or a camera passed above, an upper endoscopy, and then some imaging of the small bowel. That imaging of the small bowel, most folks do some type of what we call cross sectional imaging, most people know what a CT scan is, or an MRI. If you have ever, you know, had a joint problem or heard about an athlete with a joint problem to get an MRI, we can do those at the intestine also. And those are called MRI enterographies or CT enterographies, meaning that we're focusing on the bowel. So, you've got 15 to 20 feet of small bowel, and that can be imaged with these cross-sectional studies. That can allow us to see if there's inflammation of the small bowel, it can allow us to see if there's these penetrating complications, the so-called fistulae. It can allow us to see if there's any narrowing, something called a stricture. And then the scopes, the lighted scopes, can help us visually look at the bowel and look for ulcers. Those are the typical ways it's diagnosed. There are some blood tests that are emerging, because sometimes somebody will come with some very, very minor symptoms, and they may have a family history of inflammatory bowel disease, and you don't feel like that you need to do all of the studies, however, you may just want to do a blood test. So, there are a variety of blood tests that have been designed to look for inflammatory bowel disease. Those are not very sensitive or specific, generally, they're followed-up, they can just raise your level of suspicion, generally, or followed up with one of the tests that I described, or both.

D Dr. Sanj Kakar 11:56

Now, if you've never had this camera being passed, I'm sure listeners are thinking, what does that look like. Can you describe what that looks like?

D Dr. William Faubion 12:05

Sure. So, the first thing you need to know is most people prefer to be sedated for the test. And so, if you're going to have that lighted camera pass from below, a colonoscopy, you would drink the night before and the morning of, a volume of fluid, you know, probably to about this size or kind of the low volume prep to clean the colon out so it's cleansed. And then somebody like myself, after you've been sedated, would pass the scope in from your bottom from the rectum through the four to six feet of colon, and then slowly we withdraw it and we visualize the colon on the way back. We can also take little pieces of tissue,

called biopsies, at that point to look at it under the microscope and see if we can see signs of microscopic inflammation. We can also do that from above, pass the scope into the stomach and the first part of the small bowel. And now they also have something called a capsule enteroscopy, where a patient can swallow a capsule, and that lighted capsule will pass all the way through the small bowel, storing images all the way. And then we can review those images and scroll through them on the computer to take a look at the entire small bowel to look for ulcers also. That's called a capsule enteroscopy.

D Dr. Sanj Kakar 13:14
Wow, I've never heard of that before. That's really high tech.

D Dr. William Faubion 13:18
Yeah, it's fun.

D Dr. Sanj Kakar 13:19
Now in terms of the treatment, can you tell us about the different forms of treatment? You mentioned earlier about surgery and other medical treatments for inflammatory bowel disease.

D Dr. William Faubion 13:31
Absolutely. So, as I mentioned early in the program, this is an immunologic disease, meaning most of the therapies designed to treat inflammatory bowel disease affect the immune system. And I would say they broadly affect the immune system in sort of three different ways. If people have colitis, just inflammation localized to the colon, they may start with a medication, and the active ingredient is something called 5-ASA, and there's about 25 different formulations of this product. This type of product has been around for over 60 years. And so, a 5-ASA drug works almost like rubbing a salve on a burn. It's a local anti-inflammatory, it doesn't affect you body wide, what we would call systemically, it doesn't suppress your immune system. It just works locally. If you're a lucky patient that just has inflammation localized to the colon, and you're one of the 4 in 10 patients that respond to this type of agent, that may be all you ever need. Beyond that, though, the drugs begin to affect the immune system body wide, okay. And there's some older products that we took by mouth, the so called thiopurines, those have also been around for at least 40 years. And they broadly affect the immune system in sort of a nonspecific way. Those can be effective in maybe 3 to 4 in 10 patients. Many newer therapies, though, have moved beyond that and have become more specific in how they affect the immune

system. These we call biologics, okay. And the reason they're called biologics is simply because rather than making the medication synthetically in a test tube in a laboratory, the agent requires a biologic platform or a living platform, okay. And that's because the product is designed as what I'll call an antibody. Alright. So, an antibody is a protein that lives in our bloodstream. It's made by our immune system, and its sole purpose is to recognize other proteins and do something with it. So, antibodies have been designed against a variety of targets in the immune system. And things that you'll hear about your listeners may be familiar with our so-called anti TNF agents, right? The oldest one of these was infliximab, that's the generic name. Then there was Adalimumab, Certolizumab, Golimumab. All of these affect TNF, we call them anti TNF. And now we've moved on beyond this particular target to a handful of other targets. And then also even biologic agents to block how an immune cell moves in the body. Does it traffic to the colon or not, the so-called anti-trafficking agents. So, that could be a subject of an entirely new podcast on the types of different therapies. But, I would say just to reiterate, there's the older therapies that can work just like rubbing a salve on a burn, don't act throughout body wide, then an older set of medications that act body wide that are pill form, and then newer agents, the so-called biologics that are much more specific, okay. And with those come, perhaps I think, some increasing ability to work, so-called increasing efficacy. And I know, probably what we'll get into is, how do you select the right medication for the right patient? There's a lot of really interesting science in that. And we can move on and talk about that, too. But, I'll turn it back over to you.

D Dr. Sanj Kakar 17:01

No, no, no, I'm glad that you mentioned that. Because as you said, 4 of the 10 patients may do well with a certain treatment and others may not. So, how do you determine and individualize your treatment plan on the patient?

D Dr. William Faubion 17:14

I would say that's one of the most exciting parts about academic research right now in this space. Not only is it really exciting to try to discover new targets, right? But part of that discovery of new targets is why the heck does a patient have the disease anyway. So, defining what the actual molecular cause is in a unique individual patient, that's what a lot of us are spending a lot of our time doing. And I think what we're going to learn right now, we say there's Crohn's disease and ulcerative colitis. We already know that there's probably well, there's Crohn's disease that looks more like ulcerative colitis than Crohn's disease, right. So, I think over time, the more in depth that we get into the molecular cause of an individual patient's disease, the more we're going to say, there may be 10 types of Crohn's disease, right? There's probably not 50. But, there's certainly more than one. And

so, when we start to cluster patients by what's wrong with this type of molecular pathway that leads to this type of Crohn's disease, will be much more specific about why I want to choose this medication then for this pathway. And that's why, when you basket them all together, and you run a clinical trial, and only 4 in 10 responded, it's likely because you've got one mechanism for one type of disease, but we're throwing everybody over the wall into the same trial. And that's really where we're moving. That's where a lot of research is moving into.

D Dr. Sanj Kakar 18:42

So, can you talk about, I understand that you're using artificial intelligence and machine learning? Is this how it's helping you?

D Dr. William Faubion 18:48

Yes. So, these data sets are really complicated, right. So, I already mentioned that bugs live in our intestine, and the bugs do things, right. The so-called microbiome, if you will, and the metabolome. We can measure those things on an individual patient, but that's going to be billions of data points, right. Because we've got trillions of bugs that live in our gut, way more bugs actually than cells in our body. And those bugs are all making hundreds of different metabolites. So that math starts to multiply up pretty quick, and you end up with a lot, a lot of data points. Well, if you couple that with the genetics, right, that's a lot of data. If I couple that with immunologic outputs, right, what my immune system is doing. Well, that's a lot of data, right. And that's just three. There's probably many more. So, how do we take all of that data and organize it in a way that predicts, well this patient belongs over here in this group, this patient's not at all like this group they're more like this group. How do I do that? That's where we really need what we would call machine-based learning, right. Because there are mathematical models that will allow us to cluster patients by likeness or by differences using complex data, but it's a lot of math and a lot of computer power. So, that's really where machine-based learning is being utilized to integrate these complex data sets, and output, well, Bill, your patient is like patient A, and not like patient D, and I may never know why, but the algorithm tells us so.

D Dr. Sanj Kakar 20:25

Yeah, no, I love the way that you're being able to now individualize your treatments for these patients. And looking forward to seeing how that research translates into clinical practice. You mentioned medical treatments. Are they the mainstay for inflammatory bowel disease, or does surgery have a role?

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Dr. William Faubion 20:40

So historically, if you just look back over the decades, 80% of patients with inflammatory bowel disease have come to some form of surgery within 20 years of their disease, okay. So, we work in partnership, hand in hand with our colorectal surgical colleagues. That's one of the things that I enjoy most about practicing here at Mayo Clinic is that sort of integrated multi-specialty care. You really can't take care of an inflammatory bowel disease patient without a surgical colleague, because so many of these patients will require some type of intervention, some type of interventional procedure. There's some data emerging that that's getting less common, right as therapies get better. That's my hope anyway, and I think there's some emerging data to suggest that's the case. If you have ulcerative colitis, some of our patients go on and have their entire colon removed. That's called an ilio-anal pouch procedure or J pouch procedure. And the end of the small bowel is actually fashioned into a new rectum that sewn down to the anal canal. And then patients go off all their therapies and can live their entire life eating whatever they want to eat. The food traffic's who their small bowel is retained in this internal kind of new rectum and then pooped out whenever they need to go. Patients with Crohn's disease can't do that. The chronic disease will involve the pouch in the small bowel. So, you really can't do that operation for Crohn's disease. What happens far more likely with Crohn's disease, because about two thirds of patients get the disease at the end of their small bowel right where it enters into the colon, that many times leads to narrowing something called a stricture. And that'll lead to symptoms where people can't eat well, they'll feel distended like a balloon. And so, that has to be operated on sometimes and then reconnected. Also, patients with Crohn's disease can develop something called a peri-anal fistula. And that's a problem right around the bottom, a little swelling or an infection. And that requires surgical care sometimes as well. That occurs in about 1 in 5 patients with Crohn's disease. It's kind of a passion of mine as well, in research.

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Dr. Sanj Kakar 22:36

So, Dr. Faubion, let's talk about the future. You know, you've talked about some really innovative types of research moving forward. Do you foresee a day where inflammatory bowel disease will be cured, with say, for example, medical treatments? What do you see coming down the road?

D

Dr. William Faubion 22:52

So, I'll tell you probably the next 3 to 10 years, I think we can give what we would call a medical cure, meaning I've identified the pathway that's abnormal, and I can specifically treat that pathway. And people go on and live a full healthy life, and they will pass away of something else. I think that's the reality for many patients now, okay. But if I were to

think a little bit further downstream, about a true cure, I think of the patient that truly has an environmental cause to their disease, okay. It is an aberrant community of organisms that live in their intestine. And it's the chronic, metabolic function of this unusual colony of organisms. Well, if I could treat those with an antibiotic and put them on the right diet, and they no longer get bowel inflammation, that sounds like a cure to me. Similarly, how celiac, you know some patients have celiac disease or an allergy to gluten. As long as they avoid gluten, they have no symptoms and their small bowel looks normal. I would like to have that as sort of the intermediary goal, right to a cure. So, I think that's absolutely attainable.

D **Dr. Sanj Kakar** 24:04

Dr. Faubion, that's a lot of information. That's really great stuff. What didn't we cover today that you would like to share with us?

D **Dr. William Faubion** 24:14

I think I'd like to share that there is tremendous enthusiasm and optimism in the research community, I think a lot of partnership between industry and academia. There are a variety of different academic consortia that are interested in this, a lot of sharing of resources. And so, I think that the future is bright for this disease.

D **Dr. Sanj Kakar** 24:39

Wonderful. Our thanks to Dr. Bill Faubion, a gastroenterologist at Mayo Clinic for discussing inflammatory bowel disease with us today. Thanks for joining us today, Dr. Faubion.

D **Dr. William Faubion** 24:49

Thank you very much.

N **Narrator** 24:51

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