August 2015 Issue | Gerard Mullin, MD, MS

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Welcome to August 2015 *Functional Medicine Update* and the first of an extraordinary mini-series on the functional microbiome. I think this is a revolutionary concept that you are all familiar with, but over the course of the next few issues of *Functional Medicine Update* you're going to learn a lot more news-to-use as it relates to that. So let's move into our discussion with our clinician and researcher of the month.

INTERVIEW TRANSCRIPT

Clinician/Research of the Month

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Well here we are at that extraordinary time in each of our issues of Functional Medicine Update, with a clinician/researcher that we think is really doing an extraordinary job and cutting edge in moving the whole field of healthcare forward. We're not disappointed, obviously, this month at all because our lead off speaker in this little mini-course that we're doing on the functional gut microbiome is a very long-standing colleague, friend, and associate of mine who has done tremendous work in our field over the last 30-plus years. Yes, our history actually does go back that far. Dr. Gerard Mullin, who is a medical doctor, did his medical degree at Rutgers New Jersey Medical School, residency at Mount Sinai, fellowships at Johns Hopkins and University of Arizona in the Andy Weil Integrative Medical Program. He is certified by the American Board of Internal Medicine and is on faculty as the co-director of the Nurse Practitioner Fellowship Program at Johns Hopkins University and is an Associate Professor of Medicine there. And more than all of those things, Dr. Mullin is an incredible seeker. He has been a pioneer. Our relationship, as I mentioned, goes back to the 1970s when we first met and he was one of the early-on people that I

invited to participate in our early formative years at the Institute for Functional Medicine.

Gerry, it's wonderful to have you as our lead-off speaker in this mini-course that we're going to be doing and I can't think of anyone more appropriate to tip it off, so thanks for being with us.

GM: It's my pleasure. Thank you for inviting me, Jeff.

JB: This is also, I think, an auspicious time for you personally because you have a new book out, which I have had the privilege of reviewing briefly, which is called The Gut Balance Revolution. I think that just the title alone illustrates how far we have come in the last 35 years in a general understanding of the importance that the gastrointestinal system plays in overall systemic health. I mean, if you would have had that title of a book 35 years ago it probably would have sold one copy to you, the author, so this is really coming a long way in the general understanding of the role that the gut plays in overall health.

I'd like, if you could, for our listeners, just to give a thumbnail biography as to what led you into this path, down this trail less traveled, and now you are really one of the leaders in functional gastroenterology.

Honor the Gut: An Ancient Concept Gains Acceptance in Western Medicine

GM: All very good questions, Jeff. I think from a personal vantage point, I was a heavy kid, believe it or not, and I had a mother who suffered from irritable bowel. She found her way through holistic nutrition, which eventually led you and I to hook up many, many years ago. She owned her own health food store, and I remember she listened to Paul Frederick, she would go to different conferences, and then I would take her along. In fact, I think she might have been at one of yours early on when you were in the New York City area. But in any event, I was a heavy kid and I found my way through by really what turned out to be this program, more of a microbiome-shifting endeavor. And it really wasn't so much about I was having bad foods, it was about the fact that they were not feeding my microbiome. So from a personal journey point of view, from more of a science point of view, as you know, for many years, the Ayurvedic systems and the traditional Chinese medicine systems, they honor the gut in terms of knowing that that's the center and core of our physiology, and naturopathic/functional medicine practitioners also follow the same rubric, and now is the time for the gut, in the last five or so years, because of the genome project leading to technology of the human microbiome project. We now have the tools to explore what the microbiota are doing for our physiology, and clearly understand that there are different axes in the body, such as the gut-brain axis, which show reciprocity, and we know now that the gut has so much controlling influence over the body. This book really describes this influence on metabolism and the ability to have sustainable weight loss just by fixing the gut.

Connecting Pancreatic Insufficiency to Gastrointestinal Disease

JB: So I want to—with that intro—go back to, believe it or not, 1979 with you, here, for a moment. I think that this will be a little walk down memory lane, but I believe this is an important part of the history of this evolution that a lot of our listeners probably are unfamiliar with and I know that, for you and I, we shared this a-ha-ism way back then. I'm going back to an article in the New England Journal of Medicine that was actually in 1977 on exocrine pancreatic insufficiency and it was written by Regan and DiMagno at Mayo, who were gastroenterologists, on the difference between pancreatic exocrine acute pathology

and insufficiency and they were discussing the use of exocrine pancreatic replacement aids in this paper for improving protein digestion.[1] This was kind of novel because I think in gastroenterology up to that point people thought about just complete lack of pancreatic enzymes as being the trigger for oral replacement with porcine or bovine pancreatic enzyme replacement, but this really talked about the state of chronic insufficiency seen as maybe a partial steatorrhea or undigested protein in the stool. So it started staking the difference between acute and chronic and functional differences. Do you recall that paper at all? I remember we discussed it way back when, but it kind of opened up the window for the difference between pathology and chronic insufficiency.

GM: It's a very good point. The particulars of the paper I do not recall. You know, we have our GI modules at IFM, and now we have stool elastase as a marker for insufficiency, but it goes to the point that we look at things more functionally. We're now able to have a functional marker that people years ago did not honor, and now we understand that there are many patients, and studies actually show in about 5 to 7 percent of people with irritable bowel have functional pancreatic insufficiency that may be a contributor, right?[2] So if you have pancreatic insufficiency, you need those pancreatic enzymes not to only prevent maldigestion, but also to help clear the upper GI tract of bacteria. So we know that there is a strong link of SIBO (small bowel overgrowth) to IBS, and also it appears that pancreatic insufficiency, although subtle or subclinical, you need a functional marker to detect it; it may be part of that pathogenesis. So that's where, you know, a paper like that…you reflect back that people in 1977 were having that kind of thinking is really incredible.

Identification of Exorphins was a Key Event in the History of Gastroenerology

JB: So let's take that a step farther—this is really fun for me, by the way—and that is let's go to another what I consider landmark paper that probably a lot of the individuals who come into the field now would not be aware of, and this was in the Journal of Biological Chemistry and it was titled "Opioid Peptides Derived from Food Proteins."[3] This was the first time that the term "exorphins" was used—this was actually defined in this paper. The principal author was a woman who was at the Laboratory of General and Comparative Biochemistry at the National Institutes of Mental Health, Christine Zioudrou, who went on to publish 20-some other papers over the course of the last few decades. This was actually in 1979, volume 254 of the Journal of Biological Chemistry, and in this particular paper what she demonstrated was that peptides with opioid activity were found in pepsin hydrolysates of wheat gluten and alpha-casein. This, to me, is a fairly remarkable first-level discussion. That really started this whole field that we've seen advance over the last 30 years, and I think that this paper was the seminal paper that really started this whole thing going because it was the first use of the term "exorphins." These are proteins that have biological activity that are derived from partially digested food that mimic endorphins, and so they produce this state of hyperendorphemia. Do you recall that step in history and how it has evolved over the last 30 years?

GM: It's amazing the way we now link different food clinical reactions to physiological outcomes. That's a very nice example. Even looking at the endorphins, but looking at this whole gluten issue that you just brought up and the fact that this was something that, for the person who thought that they had a gluten issue was categorized as being schizophrenic for raising the issue, but now the evidence is becoming so clear that even the experts in my field acknowledge that there is something out there with gluten, although they fail to acknowledge what the possible connectors are, as you just raised. What I find to be interesting, such as in the Gluten Summit, is that you're taking a lot of different people who are

doing really interesting work together and linkages, because of the fact that we know that our gluten has changed—it has shifted in so many ways in terms of our wheat being so gluten rich, the fact that we're using GMOs and you're heading Round-Up and herbicide residues that can damage the gut, and so on and so forth. We're seeing an explosion in gluten-sensitivity in people, and also the fact that celiac disease is clearly on the rise as well and people cannot offer a good explanation. Part of that, I think, takes us back to the gut microbiome because people clearly, in the last 20 to 30 years, their biome is clearly shifting. Those are my thoughts on that.

JB: So the next step in this sequence of events is Zioudrou and her colleagues came back in 1983 with a follow-on paper. Again, she was still at the National Institutes of Mental Health. This one was published in Biochemistry.[4] What they did is they actually chemically isolated these peptides that were involved in the partial digestion of wheat and milk protein and they chemically sequenced them. They found out that they were fairly small peptides that had structures that you could easily manufacture in the lab by synthesis. One of those structures was arginine-tyrosine-leucine-glycine-tyrosine-leucine and glutamic acid. And when you synthesize that particular small peptide that was a remnant of the partial hydrolysis or partial digestion of the food protein, and then you tested that in brain slice assays for endorphin activity, it had very, very high endorphin activity, demonstrating the kind of proof of concept that these bioactive, partial hydrolysate peptides could in fact have mimetic activities to endorphins. The question that remained, however, up to that point, was how do these fairly large molecules—these proteoids that are composed of something like 9 or 10 amino acids—how could they get across the GI barrier or the blood-barrier because it was felt that these are semipermeable membranes and they don't allow peptides, they just allow amino acids to come across? And then it was about that same period of time that a variety of gastroenterologists started publishing papers on M cell vesicle formation of micropinocytosis in the uptake of proteoid structures across membranes. You can actually find that maybe five percent of dietary protein was being absorbed not as intact amino acids, but as these proteoids that may have residual biological activity. So we started to really witness, in your field, a plausible mechanism by which certain remnant, partially digested protein fragments could actually have biological activity all unto themselves and influence immune system, nervous system, and other functional capabilities of the body. Now this seems to me—this is the early 80s—to be a revolutionary period in changing the whole perception of gastroenterology. Do you recall how that all developed in your field?

Immune Reactivity to Incompletely Digested Proteins

GM: One of the docs here, Mark Donowitz, who was an AGA president or president of the American Gastroenterology Association, I think he did early work along these lines (him and his group when they were up in Boston). I think it's very important work because we were taught in medical school wrongly that ultimately all proteins that are digested no matter what, even without stomach acid and so on and so forth. I think it's an important concept to keep in play, is that these incompletely digested proteins are presented to our immune system is because we look for plausible mechanisms for immune reactivity to these various foods that you've been walking down memory lane and alluding to. These mechanisms actually explain some of these phenomena that we're discussing.

JB: So that leads us to the next step in my chronology as we're walking down this trail, and that is the gut has been found—about middle 80s—to not be as impermeable as we thought—that there can be changes in these tight junctions that we later labeled early on as leaky gut. Everyone was calling us crazy back then—that this was a very bad term, there's no such thing as leaky gut. It's interesting now that term is

being used in all sorts of publications in gastroenterology and other fields. Tell us a little bit about how that concept of gut mucosal permeability evolved as part of the field.

GM: That's very hard to pinpoint because it just—like the microbiome—became an explosion, I'd say in the last five years as well. And it may be in part related to the microbiome, knowing the microbiome does cause loosening of the tight junctions. But when you look at transport and you look at barrier integrity, somehow you're looking very much in the same models. I think the same group of scientists, including Mark Donowitz, looked at this, and I think what they were finding is that even though there is variability in the junctions, I think once they start to link inflammation to loosening of the tight junctions, then next step—because there is such profound loosening of the tight junctions in the setting of, let's say, ulcerative colitis or Crohn's disease and so on and so forth, is to begin looking at subclinical physiology and find that you can have loosening of the barrier and endotoxemia even without overt disease. So I think that in the last five years in particular this became so reproducible that the scientists adopted the term leaky gut, which is more of a functional medicine term.

JB: Yes, I think that is really a beautiful insight, and I know that in your book, Gut Balance Revolution, you really have done a nice job of kind of making this user friendly (these concepts) to the reader. These are pretty profound basic and medical science discoveries that were made, and as they've gotten translated now into the clinic, they've actually become user friendly in the way you're describing them in the book, so I want to really compliment you because I believe that sometimes these important concepts can be lost because they don't get properly communicated. I think you're doing a very good job of getting these concepts across so they can be seen as clinically valuable.

So once we've opened a portal of entry to these molecules, which may have residual biological activity, and they are now exposed to the other side of the GI, what's sitting over there is this extraordinary diverse gut-associated or mucosal-associated lymphoid tissue, which is where more than 50 percent of the immune system is clustered. Why is it that the field of gastroenterology was seemingly so slow to really pick up on the fact that they were the seat of immunity and not just a piece of plumbing?

GM: I really don't know because I guess many are of the mindset that—like a plumber mindset—you just go in and you see something broken and you go in and fix it with a medication, and I guess the rest seemed irrelevant to some extent. Thankfully now, with all the science, and even at the meeting they had last month in Washington (Digestive Disease Week), the amount of science on the microbiome was profound and even permeability, so I think docs are starting to get it, but I think—again—because they kind of ride the wave and the wave now is microbiome permeability, but this is something we've been talking about for decades in functional medicine, right?

JB: Yes, about 30! It's amazing.

GM: I'm just saying…And then in naturopathic medicine, the rubric, we talk about Ayurvedic, Chinese medicine, everything goes back to the core of gut physiology and what's in the gut: you've got microbiome and immune, and a lot of nerves, and enteric nervous system, and hormones, and so on and so forth. It's all there. Michael Gershon actually was kind of…well, you're probably going to get to that so I'll stop there.

Neurogastroenterology: Connecting Both the Nervous System and the Immune System to the Gut

JB: Well I think that's great because the next step was really to talk about the second brain, because we have this extraordinary density of nerves as well as extraordinary activity of the immune system all intersecting at the gut level and so Gershon's book The Second Brain was really a landmark.[5] Take us down that chapter of the story.

GM: I think that, if there is a turning point…I mean I would say now, of course, the microbiome, permeability, are big turning points, but that was probably THE turning point, because that book really was the birth of neurogastroenterology. A group of docs started to come together recognizing that there is a very strong enteric connection to the central nervous system, and the book The Second Brain really was mainly about neurotransmitters and the bidirectional communication of the second brain (the gut) with the first brain and vice versa, but I think his work was truly a turning point. And now you have a whole group of docs out there who do neurogastroenterology. We have—at Hopkins—one of the largest groups in the country, led by Jay Pasricha. They have what they call a food-mind-body center. In other words, you look at the brain (they have a psychiatrist), they have nutritionists to look at food, and they have GI docs. I think that model that they have at this point is the future in dealing with irritable bowel and functional bowel diseases, and Michael Gershon's work really gave birth to that thought process in his book The Second Brain.

Metabolic Endotoxemia: The Common Pathway to Many Health Issues

JB: That's beautifully stated. That's very exciting about what's going on at Hopkins. This breakdown of gut mucosal integrity, the interrelationship with all these gut hormones, not just serotonin but all the other myriad of hormones that are produced at different regions along the GI tract and so you get regional specificity in terms of messaging to the brain and the brain back to the gut. So we can really see what we were discussing in functional medicine, as you indicated, more than two decades ago really starting to get traction now as a major theme in medicine. So that takes me a little bit on to the next step, which you have already alluded to it: post-prandial metabolic endotoxemia. When I was in school—and I hate to say now that it was in the 60s—the concept of endotoxemia was really related to sepsis and acute septic shock and really life-threatening conditions. But now we're talking about this functional chronic disorder of post-prandial metabolic endotoxemia, which went from being a sidebar conversation to where there are now papers being published on that topic in human studies. Tell us a little bit about that topic.

GM: You know, it's very interesting, let me put it in perspective. We know that metabolic endotoxemia is the final common pathway to a lot of problems. There are docs even today, believe it or not, despite the evidence, who will say, "Leaky gut, who cares? It's not going to change what you do." Well, in the book we're talking about today, The Gut Balance Revolution, we talk about weight loss, and weight gain, and diabetes. Metabolic endotoxemia is the final common pathway to that, as well as fatty liver, which is seen in about a third of our US population these days, Jeff. I think what we're looking at is a situation where you have a dysbiotic gut microbiome, which is so prevalent today due to junk food and antibiotics, etc., a breakdown in gut integrity, for a number of reasons medications, the gut microbiome, the result is metabolic endotoxemia, and that in itself turns on inflammation which is turning on a lot of diseases. We've got a hundred million people in America with a chronic disease with inflammation as a root cause, and one of the root causes is metabolic endotoxemia. So it's really profound, and the way you bring it up so elegantly makes me pause and think about one experiment that I can at least mention is that they take these mice and they infuse alcohol. You know, alcohol will not only break down the gut barrier but it will produce metabolic endotoxemia as one of the causes for liver disease. People think that, yes, alcohol

damages the liver, but it also damages the liver if you have metabolic endotoxemia. Give those rats probiotics, then give them the alcohol, and it prevents the damage. So not to say go out there and take probiotics and drink it up, but it really shows you the importance of the gut integrity and the metabolic endotoxemia to disease.[6]

JB: That's a beautiful example. Thank you. As you're saying that I'm reminded again of a paper in the Lancet magazine in which the report was on relapse rates in acute Crohn's patients. These are people that had been hospitalized from acute Crohn's episodes. They did lactulose mannitol testing to look at gut permeability in these patients before and after discharge, and they found that those individuals who were discharged with low gut permeability (in other words, normal mucosal integrity) had less relapse rate within the first year. Those that were discharged with a high mucosal permeability, meaning leaky gut, had more probability of relapse in the first year.[7] So we ask the question: how many docs measure gut permeability before they send their patients, post-Crohn's episode, out into the world? And I would say probably a very small number of individuals, which means you're almost loading the dice in favor of getting relapse of continued crises episodes because you're not asking the right questions. If you ask the right questions, then you might be able to do something—as you indicated—by specific types of therapies.

GM: Right.

JB: So let's talk a little bit about this microbiome and its connection, as you indicated, to this array of chronic conditions. It relates to obesity, and NASH (non-alcoholic steatohepatitis, and it relates to type 2 diabetes, and it relates to myocellular lipotoxicity and muscle-related problems that are associated with metabolic sarcopenia. Tell us a little bit about this microbiome, because this—to me—looks like where a lot of the action is emerging to happen.

The Gut Microbiome is the Core of Our Being

GM: The audience is becoming so familiar because of the reports out in the lay and the medical press that we have a hundred trillion organisms in our gut that outnumber us in logarithmic numbers, both in cells and DNA, and really diversity of the ecosystem inside of us really determines and impacts upon our physiology and our health outcomes. The more biodiversity we have of them, the more we improve metabolomics and the better physiological outcomes we see. Back when you were in school and I was in school, I felt that the amount of knowledge and the amount and the importance of the gut microbiome was so minimal it was almost treated like the appendix, being vestigial. And now we're finding out it's really the core of our being and we certainly understand now that if you treat your gut microbiome well, they will treat you well and the reverse is also true. Through diet, if you treat them badly by a highly refined, processed western diet they will turn rancid quickly and you will suffer, unfortunately, the consequences.

JB: One of the things that I've read recently and it would be very helpful if you could give us probably the real story, but what I've read is that these two major phyla, the firmicutes and the bacteroidetes, the balance between them appears to be very important. Those individuals that had the higher percentage firmicutes, which is generally associated with a higher meat-based diet versus those that were more vegetarian-based diet that had more of the bacteriodetes, those individuals were more subject to some of these metabolic disturbances associated with gut microbiome connections to metabolomics. I find it interesting because the bacteroidetes are more, really, the Gram negative bacteria, which we know are the

ones that have cell walls that have lipopolysaccharides that are associated with inflammatory conditions (this endotoxemia). So it almost appeared a little bit, to me, paradoxical that the firmicutes, which are not as Gram negative (they are more Gram positive) actually have the greater concern if they get predominant. Is there still some sense that measuring these two large phyla—the firmicutes and the bacteroidetes—are important or is that less seen so now?

GM: I think in animals it was important that they actually found that relationship between the bacteroidetes and firmicutes. I think between both phyla they compose 90 percent of our microbiome, so by and large you are going to see hundreds of bacteria fall under both phyla, and even—to your point about being paradoxical—even lactobacilli fall under the firmicutes, and in certain studies there is more lactobacilli in obese people, which is mindboggling, but there are a lot of different lactobacilli out there. I think in humans, maybe in those who start out with the large firmicutes-to-bacteroidetes ratio and something is not working quite right in your program for them—their diet and so on and so forth—and you want to shift the curve and you want a way of measuring it just like you want to measure permeability in the Crohn's, right, maybe there's a role for that, but I found that early when companies were measuring it, I find that if treated the SIBO or small bowel overgrowth and I fixed their dysbiosis patients got better. I didn't need the added expense or the added dataset, and I think now biodiversity, which some people are now adding to their tests, I think that's important as well, more so than looking at those ratios that we used to look at two or three years ago.

How Long Does It Take to Change the Microbiome through Diet?

JB: That's a really helpful clinical insight. It's interesting for me personally. I was just involved with a project where I was measuring a whole bunch of things as part of this Pioneer 100 project on myself each quarter. One of those is was I was doing stool microbiome analysis every quarter. I could actually see, through changes in my diet and lifestyle, very interesting changes both in the ratio of the firmicutes to the bacteroidetes, and also the diversity of my microbiome as I kind of tuned up my diet. So the question is, how long does it take, do you think, for a patient or a person, once they intervene with cleaning up a diet, to actually start changing their microbiome?

GM: You know, it's a very good question. There's a study by Gary Wu which answers the question in a negative sense, in that in 24 hours you can adversely shift your microbiome on a western diet.[8] You can lower the biodiversity, and as you pointed out before, you can really increase the firmicutes phyla. Now, in a positive way, that's going to take time. That's going to take a matter of days if not weeks. But you want it to be sustainable, right? And that's what my program really is all about is making it so it sticks.

JB: So as I read your Gut Balance Revolution, once of the beauties, I believe, is that it nicely describes the application of what we thought of now 25 years ago, which was we called the gastrointestinal restoration program—we just gave it an acronym, the 4R Program, which was Remove, Replace, Reinoculate, and Repair. And I think you've done a really superb job of taking that esoteric concept and really weaving it into a clinically manageable implementation program. Tell us a little bit about how you came up with and how it is applied.

GM: It really goes back to what you all taught us, Jeff, many years ago. I mean, back at the foundations of functional medicine. You had started with the 4R Program, and once we got the GI Module together we added the fifth R—the Rebalance. There's a logical order and sequence to approach the gut health.

First you want to remove the triggers, right? You want to remove the allergens, you want to remove the bad foods. In the first phase of the book, talking about the removal and getting rid of the bad actors. And also what I try to promote is more of a jumpstart or a rebooting of the system, just like you want to reboot your computer. I really get people on a low net carb, meaning that these highly refined processed foods—the glutens, the dairies, which are high in FODMAPs, which are highly fermentable foods which can give people such symptomatology, but get them off the foods that they are sensitive to, and also just try to cut down on the overall carb content. And you'll see that you'll start to transform not only their microbiome, but they'll start to have this lean metabolism effect immediately. And then just like in the functional medicine model, as we try to weed out more of the less healthy bacterium, we then re-feed and re-fertilize and re-seed the good gut microbiome and get that inner garden to thrive. And then we want to maintain that through life. What I chose was the Mediterranean diet, as maybe the Andrew Weil influence on me with his anti-inflammatory diet. But the Mediterranean diet has so many positive health outcomes that we're just seeing within the two months the data on the brain and cognition and mood and Alzheimer's and so on and so forth—dementia and protection against stroke. Mediterranean and anti-inflammatory diet is a great way to live and if your biome is resilient, then you'll have the flexibility to enjoy life and be able to take breaks and socialize and eat some of the foods that you enjoy without really destroying your biome.

Beyond the Scope: How is the Field of Gastroenterology Evolving?

JB: Yes, I think you've really done a beautiful job of putting the seat of the GI tract right at the head of the table, so to speak, because from that all these messages that take us way back to the Zioudrou work on exorphins, and all through this time we start to be able to manage messaging at the gut immune level, which then has systemic effects across every organ system. So the field of gastroenterology, if I can bring this discussion to a close, has really often been woven, down at the clinical level, to scoping. Where do you see gastroenterology going? Do you think it's still going to be seen primarily as an end-stage diagnostic subspecialty, or are we really starting to see the profession modifying its diversity as to how it sees the GI tract and GI problems?

GM: I think what we need to do…I mean, it sounds profound, but I think if there was capitation in effect—in other words, that we got paid to take care of people better and have better health outcomes and not got paid, whether in money or in work RVUs for scopes, I think it would transform the profession radically and make us think differently. It would force us to think differently, and then people would take a look at this biome and it would be more than just interesting science, and I think it would really force people to partner with their dietitians like I do. Through the years many in the functional medicine community and elsewhere I have worked with. My first book was with Kathie Swift on The Inside Tract, and I've partnered with so many dietitians.[9] I think we need to really partner with people for better health outcomes. The data is there. I think that would really force the practice to move forward, and I think that's coming. And I think that day is coming because we're getting cut back on reimbursements for procedures, and everybody's getting squeezed, and there are only so many scopes you can do in a day, and I think people aren't in private practice anymore, they are in groups. The day will come—and I may be retired by that point, physically at least. But I think that day's going to come, and I think that's going to really allow us, and with this data in front of us, I think we're going to be able to take much better care of people at that point in time because we're going to be paid to do that and we're not being paid to do that now.

JB: Well I think that was a fantastic overview and it was actually very optimistic and forward-looking, I believe, for both the profession and for medicine in general. Dr. Mullin, I want to thank you personally for more than three decades of colleague-ship and your leadership and advocacy. It really is remarkable to sit here and review what has happened over these last three-plus decades. It really is transformative and I think your book The Gut Balance Revolution captures the spirit of this major change, which is redefining the role of gastroenterology in healthcare. Thanks so much for your leadership over the years.

GM: Really, thank you for having such a profound influence over my career, Jeff.

JB: It's my great privilege and pleasure and we'll wish you the best and catch up with you soon.

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