September 2015 Issue | Martin Blaser, MD

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Welcome to *Functional Medicine Update* for September 2015. This is the second in a four-part series on the gut microbiome, and we're very pleased to have, as our clinician and researcher of the month, Dr. Martin Blaser. Let's move directly to our discussion with Dr. Blaser that I think you'll find fascinating as it relates to the microbiome, antibiotics, and gut immunity.

INTERVIEW TRANSCRIPT

Clinician/Researcher of the Month

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I am so excited because I just finished reading a book that was a life-changer for me and that's a book by Dr. Martin Blaser titled Missing Microbes: How the Overuse of Antibiotics is Fueling Our Modern Plagues.[1] For those of us who have been tracking this field of gut microbial physiology and its interrelationship with the gastrointestinal associated immune system and how that influences systemic health, this book is one of those ah-ha books that is a must read for everyone. Dr. Blaser brings an incredible background and history and a range of experience in this field as an expert. Let me just tell you a little bit about him before we get into the discussion.

He's the Muriel and George Singer Professor of Medicine, Professor of Microbiology, and Director of the Human Microbiome Program at the New York University School of Medicine. He served as a Chair of the Department of Medicine at NYU from 2000 to 2012. He is both a physician and microbiologist. He has an extensive publication record covering a wide range of topics within medical microbiology. He is

interested in understanding the relationships between persistently colonizing bacteria and health. His work over the past 30 years has focused on human pathogens, including Campylobacter and Helicobacter pylori. He uses those as model systems for understanding the interactions of residential bacteria with their human hosts, and over the last decade he's been actively studying the relationship between the microbiome with health and important diseases such as asthma, obesity, diabetes, and allergies that we'll be hearing more about in this discussion with him. Over the course of his career, he has served as the advisor for a large number of students, postdoctoral fellows, and junior faculty, and has been actively involved in national scientific organizations, many of which are very prominent in steering policy decisions as it relates to medicine and medical therapies.

I found his book to be one that takes a very complex topic and distills it down into a reader-friendly format in ways that are really going to guide us in how the microbiome is interrelated to our health and the impact that antibiotics have, both positive and negative, on this whole evolution of human society.

With that as a quick, rapid-fire introduction, Dr. Blaser, I welcome you to Functional Medicine Update. Thank you so much for your time and willingness to discuss this topic with us.

MB: Yes, thanks for having me and thank you for your very kind words.

JB: You know, your resume reads like a lexicon of the history of the last, say, 30 years of this whole evolving field of microbiology as associated with infectious disease, but also as it relates to pharmacotherapy and antibiotics. What was your early education and experience that led you to becoming this world expert in infectious disease and antibiotic use?

The Paradox of Microbes

MB: Well, I am a medical doctor and I trained in internal medicine, which is a very broad training in medicine, and then I did a sub-specialty training in the field of infectious diseases. That was really when I began to get the first inklings about the tremendous diversity of the world of microbes, and mostly we were focused on the bad microbes—the ones that were making people sick, causing infections in people in the hospital. In fact, I was involved in the very early days of AIDS. I took care of some of the very first patients in the United States, because it was happening on my watch. I took care of the patient with hemophilia who had AIDS. But over the years, as I kept studying the microbes and how they made us sick, I began to appreciate that there was a lot more complexity out there, and that some of the microbes that were dangerous to us also had some benefit, and that's kind of a paradox, but the more I studied it the more I found it. And that kind of brought me to the present.

JB: One of the things that comes across, of the many in your book, is this understanding that in your life as a professional you witnessed the global change in illness and death going from infectious disease to non-infectious disease. And so a lot of people might say why has this occurred? Is it because we've been so successful in the use of antibiotics? Why has non-infectious disease now globally exceeded that of infectious disease as cause of both morbidity and mortality?

MB: I think there are a couple of answers to your question. The first is that the decline in infectious diseases actually began before antibiotics. It began in the late 19th century. We can prove sanitation, clean water, saved untold millions of lives. Better prevention, vaccines saved millions of lives. Things

were coming down even before antibiotics started, but certainly antibiotics have contributed as well. And in terms of non-infectious disease growing, one of the realities of life is that all of us are going to die, and when you die you have to die of something. So if you're not going to die of an infectious disease you're going to die of a non-infectious disease. In part, that's what's happening: people stopped dying of infection and then other things began to emerge. And then we found that some of these things began emerging more and more and more—illnesses related to obesity and diabetes, for example, immunologic diseases.

The Birth of the Antibiotic Age

JB: I really like the way you've written your book because it is a string of very interesting stories, some of which are your own personal experiences with your patients and others of which are stories about leaders in the field that have helped advance our understanding. One of those stories is about Alexander Fleming. Maybe you could just remind us all as to how this whole antibiotic age was initiated.

MB: Yes, thank you. One of the reasons that I wrote Missing Microbes is to acquaint the general reader—not just scientists—with some of the relevant history, and the discovery of penicillin is really important. The story of Fleming is that he was a bacteriologist. He had been a doctor during World War I and he saw the terrible injuries and how soldiers died from infections, and he was interested in finding better cures. He was working with an organism called Staph aureus, which is an organism that causes a lot of disease even today. He was working with Staph aureus. He had plated the colonies of Staph on a petri dish and he went off on vacation, and when he came back a month later, there were the plates sitting in the corner; he had forgotten to throw them out. And as he was throwing them out, he saw that on this lawn of Staph—what you might think of as a lawn—there is this big clear area, a big bald spot, and right in the middle of the bald spot was a mold. And he immediately understood that that mold was producing something that was killing Staph. He found what that mold was producing and he called it penicillin, because the mold was Penicillium. Now it turns out that peasants had been using moldy bread to treat wounds for centuries, so they actually kind of knew it, but it took a scientist like Fleming to find out exactly what the active ingredient was. And it took another decade for a team of scientists to be able to produce it in large enough amounts so that it would be useful, and of course it has been enormously useful ever since.

A Census of Cells in the Human Body

JB: Yes, and then from that begins your story of Missing Microbes because the feature set of this story, I believe, is that within residence in our body is this fairly large "organ" called the microbiome that's not connected to our body by the vasculature but through the absorption, across the GI border, of various types of substances that are produced by this, say, two pounds of living organisms that we call the microbiome. So we've got these eukaryotic cells—our own cells—living with these prokaryotic organisms, so tell us a little bit about how this microbial world in our gut connects to this whole antibiotic story because it seems like it's another paradoxical part of our emerging understanding.

MB: Sure, sure. First off, start with the facts, and the fact is that if you did a census of all the cells in the human body, you would find that there are more bacterial cells in our bodies than we have human cells—somewhere between 3-to-1 to 10-to-1 more bacteria than humans. And if you did another census of how many unique genes we have in the human body, then it's about 100-to-1, favoring the bacteria. So

ever since there have been animals on this planet, which is at least 500 million years, they have had residential microbes—microbes that call them home—going back deep into time and continuing to the present. Every plant, every animal on Earth has their own residential organisms, and it's become increasing clear that these organisms are not just passengers—we're not just carrying them—but they are actually beneficial to us; they help us digest our food, they help us make vitamins, they train our immune system, they keep out bad bacteria (pathogenic bacteria) and viruses as well. There's a lot of benefit, and the story of penicillin is very important because now we had a tool that we could treat infections, but we kept using antibiotics more and more and more for every different purpose, and no one really considered the possibility that these antibiotics might be having an effect on our microbiome, that they could have some short-term or long-term effects on the organisms that were really present.

Antibiotic Use in Animals: Implications for the Obesity Epidemic

JB: This may not be a logical segue, but let me jump over to a topic that you discuss quite a bit in your book, which is the sub-therapeutic use of antibiotics in animal feed to enhance weight gain, particularly in cattle. We look at these as ruminant organisms with multiple stomachs and all sorts of microbiological activity going on and fermentation of their vegetable-based diets, and yet we're giving them low-level antibiotics over the course of their lives. Tell us a little bit about how that interrelates to this whole story of antibiotic use and antibiotic sensitivity.

MB: For now almost 70 years, farmers have been giving antibiotics to their livestock in low doses because they found that giving them antibiotics would make the animals grow faster and use their feed more efficiently and this is what's called growth promotion. In fact most of the antibiotics used in the United States today are used on the farm for growth promotion, and the reason that farmers use it is because it works. About 10 years ago, all of a sudden the question popped into my mind: Well, why does it work—why does giving low-dose antibiotics work? By the way, it's not just cattle; it's cattle, it's swine, it's chickens, turkeys, sheep, just about all the animals we use for food production, more than just mammals. It works across all of them. The earlier in life they start the antibiotics the more profound the effect. And so I thought, well, if giving antibiotics to farm animals is fattening them up, is it possible that that's what we're doing to our children by giving them antibiotics for good purposes, is the inadvertent side effect that we may be destining them to become fatter later in life? And in fact, we've found more and more evidence that supports this.

Defining the Scope of the Microbiome

JB: Yes, I want to come back to that in some greater detail. I think your work is just pioneering and as I read about it and went back and looked at some of your publications it was like oh my word, this is information everybody needs to be aware of. I'd like to, however, go back a step and talk just briefly about the microbiome. It's a term that's being used a lot more now, but I think there's some confusion about what organisms are included within the microbiome and where do they reside. Is it just in the gut? Is it just bacteria? When we talk microbiome, what are we really talking about?

MB: Well, the term microbiome refers to all the microbes—these are forms of life that we can't see with the naked eye; they are microscopic—all the microbes that live in and on the human body, and how they're interrelating with us. That's the microbiome. We mostly focus on bacteria, but it also includes the fungi, the yeasts that live in us, the viruses that live in us, and even the protozoa and the worms that live

on us. So we have a very diverse zoo of microbes living in the human body, and my zoo is different from your zoo.

JB: Does that include things like the lungs, the skin, the epithelia?

MB: Yes, it includes, as you mentioned, the gastrointestinal tract, from the mouth at the front end to the back end. It includes, in women, their vagina. In all of us it includes our skin—everywhere on the skin there are microbes, and the populations in microbes in one area of skin are different from the populations in another area (although the left side and the right side are pretty similar).

JB: And as we start to think of this microbiome, what number of different species would be the order of magnitude that people would have that colonize their bodies?

MB: We think there are somewhere [between] several thousand to ten thousand species on all of us, and we might say that the average zoo in the United States has about a thousand species. So each of us is carrying a zoo much bigger than the average zoo.

Diversity is Important in Microbial Ecosystems

JB: That's really interesting. I recall studying, years ago, ecology, and there was a principle in ecology that said that diversity means stability in ecosystems. Is that similar with the microbiome—the more diverse the ecosystem the more stable, the more friendly it is to the body?

MB: We don't know whether that's true, but I believe that it is true. That hasn't been proven, but as you point out, that's a principle of ecology, whether we're talking about the ocean, or forests, or prairies, and probably the bodies of animals as well. So diversity has been beneficial, and again, one of the reasons I wrote Missing Microbes is to point out to the average person that we used to have a very diverse zoo of microbes in the human body, and there is more and more evidence that our diversity is going down, and so we have lost microbes. That's why I call it Missing Microbes—we have lost some of our ancient organisms that our ancestors have had since time immemorial and now, in the last 50 years and perhaps even more recently, we seem to be losing them at a pretty alarming rate.

JB: As I kind of reviewed—at least at a high level—the emerging literature on the microbiome, there is this discussion that there are two major families—Firmicutes and Bacteroidetes—that seem to predominate in the literature. What's the story of these two families in the context of the full complexity of the microbiome?

MB: What you are referring to, in taxonomy they are called phyla. Those are the two major phyla in the gastrointestinal tract. It's not just in humans. If you look at any mammal, those two phyla—Firmicutes and Bacteroidetes—are the predominant organisms in the GI tract. In the skin, the phyla are a little different. Actinobacteria are very predominant, and Firmicutes as well. In the mouth it's a little different as well. So each zone of the body has a different census—different populations that are present. You could think of it like you looked at a map of the world and you'd see different populations in different countries. There is some overlap, and of course the biggest country is the GI tract. That's where the biggest population of microbes is, but there are untold billions on the skin and in the mouth, etc.

Growing Concerns About Antibiotic Resistance

JB: And in your book, you talk about antibiotic resistance even being seen in infants these days. How does antibiotic resistance get produced and why is it so prevalent?

MB: Actually, when Fleming won the Nobel Prize for the discovery of penicillin, in his speech he talked about that resistance was inevitable. So it turns out that Charles Darwin was right: there is natural selection and there is survival of the fittest. If you have any question about that you just have to study bacteria and how they respond to antibiotics. So if I have a culture of bacteria on a petri dish or in a test tube and I put in an antibiotic, that antibiotic will kill most of the organisms, but a few will survive, and they survive because they are naturally resistant. And now, those organisms are going to grow up. They are going to become the main population because all their competitors are dead from the antibiotic, so that's the survival of the fittest. When the antibiotic is present, organisms that have resistance have a big advantage, and so the more we use antibiotics, the more we select for resistant organisms. And over the decades, we are selecting more and more for resistance. This organism, Methicillin-resistant Staphylococcus aureus—or MRSA, as it's called—this essentially wasn't present before the discovery of antibiotics, but somewhere it emerged and then with all the antibiotics we are using we're killing off its competitors and MRSA is getting more and more numerous.

JB: One of the really great things that you've done in the book, I believe, is to talk about the evolution of your own research and your knowledge accrual over the decades you've been in this field. Could you just summarize with the extraordinary amount of work that you've done, the ah-has that you've had as you have gotten into this field more deeply?

Lessons from the Story of Helicobacter Pylori

MB: Yes, right. To summarize 30 years of work in one paragraph? I'll do my best. I think what might be most interesting is to talk about Helicobacter pylori, which is the organism that lives in the human stomach. There are several amazing stories about this. The first is that this organism was discovered in the late 1970s/early 1980s living in the stomach, and that was surprising because most of us were taught that the stomach was sterile, that there were no organisms, that nothing could survive in the acid. But two scientists in Australia, Robin Warren and Barry Marshall found these organisms, they cultured it for the first time, and they showed that people who had those organisms were at higher risk for getting stomach ulcers and they showed that if you treated the ulcers with antibiotics you could cure them.

So this is a big revolution. This changed our whole concept of ulcers and it created a new treatment. And based on their work—and I was present at some of their earliest scientific meetings—we went on to look at the relationship between H. pylori and stomach cancer, and we found there was a strong relationship there. So everybody began to look at Helicobacter pylori as a typical pathogen—a bad organism causing ulcers and causing stomach cancer. And I was one of the leaders of that. But the more I studied Helicobacter the more it became clear that that wasn't the whole story; that's part of the story, but not the whole story. A more complete story, in fact, is that Helicobacter pylori has been present in humans for at least one hundred thousand years, and that's about how far we can go back with our current method. We believe it's actually been present for millions of years but we can't prove that yet. But in essence we can say the Helicobacter has been present in humans for time immemorial, and it's now clear that Helicobacter is disappearing. It's going away very rapidly and as a result we now have people who have

it or who don't have it, and that's how Marshall and Warren could see that people who have it have a certain cost. One of the costs of carrying it is there is a risk of getting an ulcer and then there is a risk of getting gastric cancer as well. But more recent work, including our work, has shown that people who have the organism are more likely to get ulcers, but they're less likely to get diseases of the esophagus, like reflux esophagitis, or what's also called GERD. That's important because GERD has just been skyrocketing. It was a rare disease and now, in almost every household there is somebody who has GERD. The question is where did this disease come from? When we started looking at GERD we began to understand that as Helicobacter is disappearing, ulcer disease is disappearing and gastric cancer is disappearing. Both are great things, but new diseases are arriving, like reflux and its consequences, which is a form of esophageal cancer. All of a sudden it was clear that Helicobacter—an ancient organism—when it disappears there is some benefit and there is some cost, and gradually we've been finding that's a general paradigm for the microbiome in general. We can't lose our ancient friends so readily without there being some consequences.

JB: That is a really remarkable story, and as you said, that's a model for the whole ecology of our body. I think it's a good specific example of a more general theme as it relates to species diversity and stability. With that in mind as a context, you've done a really excellent job in Missing Microbes talking about how the microbiome, then, and this diverse population relates to metabolic diseases such as diabetes, arthritis, and obesity. Can you take us a little bit down that path because that's an extraordinary chapter in our evolving understanding?

Why Are Microbes Going Missing? A Discussion of Changing Birth Practices and Antibiotic Use

MB: I can but I think before I do that I'd like to discuss why our microbes are missing. What's causing them to disappear?

JB: Great.

MB: And I want to talk about two issues. The first issue is that a big fraction of the microbes that we have in our body, we got from our mother, and she got from her mother, and she got from her mother, and so on and so forth, all the way back in time. And what is now clear is that when a baby is born they are pretty much sterile, but as soon as they begin the birthing process they start acquiring microbes from their mother, and that's the way we humans have been doing it for millions of years and all other mammals have been doing it. That's the nature of mammals; we're born from a womb and we are given birth as a live birth (we're not born in an egg).

But now we're doing things that are changing that intergenerational transfer of microbes. For example, more than half the women in the United States are getting antibiotics during pregnancy, and now a third of the babies born in the United States are born by Caesarian section. In some countries it is fifty percent of the babies are born by C-section. Both of these interfere with that normal intergenerational transfer of microbes, and there's evidence that the microbes that come out are different (the babies born by C-section or their moms were on antibiotics are different). And there are new studies that are suggesting that these kids have increased risk for certain diseases, like diabetes, like celiac disease and allergies in childhood.

The second thing we're doing is that we're giving kids a lot of antibiotics. Sometimes the antibiotics are

absolutely necessary: that child must have antibiotics or they will become seriously ill or even die. But most of the time that kids are getting antibiotics, it's unnecessary. That's been recognized for many years, but everybody's reluctant. They thought, well, it might help, but it won't hurt. But now we're getting more and more evidence that it could hurt, so we have to recalculate whether all these courses of antibiotics that kids are getting are really necessary, and we see that there are big differences. In Sweden they are only using 40 percent of the antibiotics we're using, and their kids are growing up just fine. So our microbes are missing—they are disappearing—in part because of things that we're doing that are] well-intentioned, but that have unintended consequences.

The Role of the Microbiome in Developmental Processes

JB: Wow, that's really a powerful insight. You know, it was very interesting to me—you described one of the unintended consequences could be changes in various types of growth stimulating hormones that are related to alteration of the gut microbiome and you even raised a question about changes in height of various girls and boys as a consequence of the interrelationship they have with their microbiome, not to mention these other metabolic diseases. It sounds like a very complex network that we're discussing.

MB: Well, for a long time pediatricians understood that a child's height at the age of about two-and-a-half is a very strong determinant of what their final height will be as an adult. They've known that for generations. And that first two-and-a-half years of life is really important, and it turns out that's when the microbiome is getting its shape, its structure. All kids begin with a relatively sparse microbiome and then it fills out, and how it fills out appears to be a determinant of height and weight, and so this leads back into your other question, which I didn't answer before. If farmers give low doses of antibiotics and their farm animals gain weight more rapidly, what about kids? Well, we began to do studies in the laboratory in mice, and we could recreate in the lab what the farmers have found: giving antibiotics to the mice made them fat. And in another experiment, if we put mice on a high fat diet they got fat, if we put them on antibiotics they got fat, but if we put them on both together they got very fat, and we think that that's a paradigm for what's going on in our kids. And sometimes in the mice the fatness didn't occur until much later in life. They were growing normally and then all of a sudden they started getting much fatter, and that might be the equivalent to somebody who is relatively normal and in their 20s and 30s start gaining a lot of weight.

JB: Is there a putative explanation at a mechanistic level for this relationship or is it still work in progress?

MB: Well it's definitely a work in progress. We're working on it, but we think that what happened over the millions of years is that human development is choreographed by the microbiome. The organisms are there—those ancient organisms are talking to our cells as babies are developing, and that's the way it's always been and so there has been a normal developmental pathway for metabolism and for immunity. But now the microbes are different, and in essence the language that they are talking to our cells in is different, and the consequences of that altered conversation are different. That's how we're thinking about it. We're interested in some particular chemical mechanisms that are involved.

Looking for Solutions to Stop the Loss of Microbes

JB: Thanks to you we've outlined a pretty interesting perimeter of a playing field of a problem, clearly,

because we're all living in a similar environment, here, at some level in the developed world, so what do we do about this, where do we go from here, how about probiotics, does our diet play a role, what factors can we modulate to really do something in response to this changing ecology?

MB: Yes, well, I'm glad you asked that question because that's chapter 16 of Missing Microbes: solutions. Where I try to go into what are some of the things that we can do to improve health. The first stage, which is Public Health 101, is stop the damage, try to limit the use of antibiotics, limit the use of C-sections to those cases where it is really necessary (it's not an elective item). So if we can decrease the damage, that will be very important. Another possibility is that when a child, for example, has to be on an antibiotic, we might want to give them a probiotic that will help them avoid the damage. The problem is we don't know what those probiotics are yet. I don't think it's the ones that you can buy in the health food store; I think they are going to be new ones that we are going to understand scientifically and those are the ones that we're going to use. Another very interesting issue is that when you look at people in the jungle who haven't had modern life, their microbiota is much more diverse than ours, and the possibility is that we might use some of the microbiota from those people living in the jungle to help restore what we have lost. Both my wife, Maria Gloria Dominguez, and I are working on this very problem.

JB: We've heard recently of some pretty remarkable responses that various people have had from microbial transplants through instillation of fecal material into people from people with healthy microbiomes. Do you think this is a therapeutic trend in medicine? Any thoughts on that?

MB: Well, I have to give your listeners some background; I also discuss this in Missing Microbes. There's a very terrible disease called Clostridium difficile infection; it's also called C. diff infection. And typically this occurs after someone has had antibiotics. This organism, C. diff, overgrows and can be very damaging to the intestinal tract. Sometimes people die from this, and it can be very a severe disease. The typical treatment is with antibiotics, but the treatment is not always effective. In fact, there are often recurrences of this. A number of years ago some doctors found that if they gave people with C. diff infections a fecal transplant, either from the top end or from the bottom end they gave them normal fecal material, they would cure that disease. Now remember this is a bad disease; this is a life threatening disease, people die from it. And that therapy actually has been curative. It was a big randomized clinical trial to test fecal transplant versus conventional therapy, and in fact they had to stop the trial because the fecal transplant was so much better.[2] So that's now become established: for that infection, the fecal transplant works. Now scientists are working on trying to improve it so that it's not fecal transplant but maybe give certain specific probiotic organisms, but again that's work in progress. Could fecal therapy be a pillar of medicine in the future? It's possible, but I think it's unlikely. I think if we find that there are conditions where restoring the microbiota in the GI tract are important, maybe for a while such fecal therapy will be used, but scientists will try to come up with something a little cleaner, a little better defined.

JB: So there are people, obviously, who necessitate the application of antibiotics for—as you pointed out—certain medical needs. Are there any antibiotics that are more friendly to the microbiome than others or is it just a class effect?

MB: Well, I think that all antibiotics are pretty unfriendly to the microbiome, but some are more unfriendly, and we've actually just had a paper published. Again this was studies in mice, but when we compared the two major classes of antibiotics that are used in children—we studied beta lactams (that's

the class that includes penicillin and amoxicillin) versus macrolides (that's the class that includes erythromycin and azithromycin—that's the Z-Pak—and clarithromycin). So we compared the beta lactams and the macrolides and we found that the macrolides were much more damaging than the beta lactams.[3] I was at a meeting in Europe last month and there was a presentation at that meeting looking at children in Finland, and they found the same thing in human children as well, suggesting that the macrolides, which have been increasingly popular in recent years, may be more damaging to our gut ecology than the penicillin and amoxicillin and the more standardly used items.[4]

JB: When I finished reading Missing Microbes and I put the book down and—as you do when you finish a book—you take a few moments of reflective pause to ask yourself what did you learn, I recognized that there was a kaleidoscope of different topics that were very, very well stated in the book that stuck with me. But one of the major dominant themes was the construct that this is all going to lead to significant change in medical and cultural practices and therefore we will be seeing, with this information, some sweeping changes. Maybe it will occur over a longer period of time, but as you look with the history you have and with the future-looking ability that you possess, what do you see happening in medicine and in society at large as it relates to this information as it becomes more well understood?

MB: Yes, that's a good question. Now, as I have to gaze in the crystal ball, I'm afraid that if we don't do anything it's going to get worse. So we really have to do something and that's in part why I wrote Missing Microbes: as a call to arms. It's to get our citizenry aroused with our pitchforks and try to figure out how to get out of this deep hole that we've dug. What it's going to mean is, for one thing, we're going to have to be much more restrictive in the use of certain medical practices, including antibiotics, as I mentioned. I think we're going to have to invent a whole new class of antibiotics that are narrow spectrum. The typical antibiotics used now are broad spectrum; they cover the waterfront. But if I were a parent or grandparent of a child who came in with an ear infection and they needed antibiotics, I would much rather it be an antibiotic that was just targeting the organism that's present without doing a lot of collateral damage; kind of a laser strike against that organism. We have the capabilities now in general, but we have to do a lot more work to develop those narrow spectrum antibiotics and get them on the market, and then we have to develop diagnostics so that when the parent comes in with that ill child there can be a rapid diagnostic that will help the doctor say this is due to a virus, this is due to a bacteria. And if it's due to a bacteria, is it bacteria A, B, C, or D, and if it is D, the doctor will take off the shelf narrow spectrum treatment for organism D. I think that's where medicine in the future is going to go. It's going to be expensive, it's going to take more research, and the drugs will be more expensive than the antibiotics of today, but I think right now the antibiotics we're using are a false economy. You can pay for it now or you can pay for it later in terms of the increased medical bills. I think that's what we're seeing are those delayed costs because of these epidemic diseases like asthma and obesity.

JB: Well, I think that's an incredible insightful perspective as it relates to how this concept of stratified disease treatment and personalized healthcare is evolving in the post-genomic age. I hadn't thought clearly about what you just said, but it seems like it's another really superb example of how genomic information is starting to really filter down into a different strategic approach towards healthcare by lasering in to personalized individualized care that relates to treating the specific cause and not just the broad brush of hitting all the outliers around the surrounding environment. It's a really insightful comment that you brought up.

Let me ask one last question in close, and that is clearly you're an advocate, clearly you're a leader who

is willing to step up and have their voice heard. What kind of response have you had to date from Missing Microbes as it relates to your advocacy position?

MB: I'm really pleased. People are listening. The book has been reviewed quite a bit. The reviews, in general, have been quite positive. It's gotten a lot of media attention. It's being translated into sixteen languages; I'm really happy about that. So far, though, not Spanish, Portuguese, or German; those are the big holes, so if you know any publishers who would consider those, I would like it to be read by a lot of ordinary normal people—people who are concerned about their health and about the health of their children and their grandchildren. So far there has been a lot of very good attention and actually I've gotten some awards from my work recently. I think people are beginning to listen. It's beginning to have an effect, and that's exactly why I wrote Missing Microbes.

JB: As a person who has shared this field, somewhat, with you over the last 30-plus years, a person who is a parent and grandparent I want to thank you. I think your work has been seminal. I think your book is superb, and as I mentioned it was one of those catch me by the frontal cortex of my brain and really shake me when I read it. Dr. Blaser, I want to thank you very much for being available and sharing with all of us. This will go out to health practitioners around the world who are going to make decisions about how they care for their patients and communicate to their mothers and fathers, so all we can say is thanks so much for your tireless work.

MB: And thank you for your terrific questions.

JB: Appreciate it.

MB: Thank you.

JB: Be well.

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