Behind the Breakthrough Podcast - University Health Network

Season 5 - Dr. Bryan Coburn

Transcript

BTB

Hello and welcome to Behind the Breakthrough the podcast all about groundbreaking medical research and the people behind it at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host Christian Coté with us on the podcast today, Dr. Bryan Coburn, the clinician at UHNs division of infectious diseases, and a scientist at the Toronto General Hospital Research Institute. Dr. Coburn is a leading researcher in advancing our understanding of the microbiome, how it affects us, and how to harness its potential to become a tool to treat patients and improve health. Dr. Bryan Coburn, welcome to Behind the Breakthrough.

DR. BRYAN COBURN

Well, thank you very much for having me, this is really an amazing opportunity.

BTB

So first off, what is the microbiome?

DR. BRYAN COBURN

You know, I thought of about 20 different answers to this question over the last 10 years, and none of them are perfect. But I think that good encapsulation, or summary of what the microbiome is, they're the organisms that live on and in us, and their wide variety of organisms, bacteria are the ones that we think of the most often because probably, they're the most easy to study, but it includes things like viruses, fungi, even parasites are protozoa. So we are an environment that is home to all of these organisms. And early on in my career, I used to make the analogy that the microbiome was like a human organ. But actually, it's sort of a domesticated part of the environment. Over 450 million years of evolution, we've learned to live with these organisms, and adapt to their coexistence with us. And now they live on us as if they're part of us.

BTB

I think a lot of people would be surprised to hear that we are hosts to bacteria and parasites and things like that as part of the structure of our human bodies. And they in some ways, keep us healthy. So talk to us about that. What's the job of the microbiome? What's it doing?

DR. BRYAN COBURN

Well, you know, it's interesting, that sort of skepticism that why would we be covered and filled with these organisms? And how can that be possible? And how can it be good for us, is a pretty logical gut response, we've spent so long thinking about germ theory of infectious diseases and identifying bacteria, viruses and fungi as pathogenic disease causing entities. But if you think about it in an adaptive or evolutionary terms, we got big, meaning we came out of the ocean from being small micro organisms to being big organisms with limbs, and big bodies about 450 million years ago. And at the same time, we got big, we had to consume calories from our environment, in order to survive, you can't just absorb things passively when you're 30 kilos or 10 tonnes like a dinosaur. So you start eating your environment.

DR. BRYAN COBURN

And along with the plants and animals that you eat, you also eat the microorganisms that are in that environment. And over 450 million years of evolution, we've learned to use those organisms, they evolved with us. And we evolved all of our big complicated systems that make us function like our nervous system, our digestive system, or endocrine system. We evolved all of these systems at the same time as we were consuming these environmental organisms. So they evolved as we evolved, and we evolved to live with them. In the strictest sense, they're not part of us. They don't come from our genomes, for example, the map for those organisms, the genetic code for those organisms doesn't reside in our genome, but we have adapted to their presence. Consequently, they've become integrated into our physiology and how our systems function.

DR. BRYAN COBURN

So it makes sense when you think about it over that timescale, and that kind of evolutionary scale, the innate response, that kind of ooh, bacteria bad, can really flip. And you can really think about it the opposite way, when you think about that CO adaptation over 450 million years.

BTB

So give us a sense of the scope and scale of the microbiome in the body. Like, I think a lot of us think it's all in the gut. But that's not the case, right?

DR. BRYAN COBURN

No, every surface that is exposed to the outside environment, including our gut, is potentially colonized with organisms. So the skin has a microbiome, the nose, the mouth, the lungs have a microbiome high up in the airway, a really well functioning lung probably doesn't have many bacteria in the lower airway. We are coated with and covered in these organisms, and also filled with them. The greatest number of organisms is in our gut. There are about one to one and a half times as many bacterial cells in our gut as there are human cells in our body. So there's more of them than there are of us. They weigh about between one and three kilograms, probably. And the vast majority of them are in our gut, but they're also all over our skin. Every surface that you can contact has been in contact with bacteria, fungi, yeast, or viruses at some point, and so they're covered in those organisms.

BTB

And so what's it doing for us?

DR. BRYAN COBURN

Many things, and that's kind of the fun part of it. We're learning a lot of this as we go actually. And you can grow and thrive theoretically in a completely sterile environment. And we know that mammals can exist in an environment that completely lacks organisms because we grow mice in what are called germ free facilities where they're born in the absence of microbes, and they grow and they look normal and they behave normally and they eat normally, some things don't work quite as well as they do if they grow in the presence of organisms. So in that sense, they're not strictly required for us to be normal and healthy, but we have adapted them to do things on our behalf. Nutrient metabolism is one of the things that's kind of neat is there are things that we eat, that we don't digest that bacteria do digest, there are things that they produce that stimulate and coax our immune system into being sort of normally functioning. They produce metabolites that we use ourselves, and they protect our external and internal surfaces from colonization with disease causing organisms.

BTB

Okay, so Bryan, when we spoke prior to your interview, you were helping me understand how the microbiome works. And what I loved as you you use this analogy, a visual analogy of you likened it to the rainforest, and how the slightest perturbation can knock it out of balance, and how that in turn affects our health. Can you explain that for us?

DR. BRYAN COBURN

Yeah, you know, this is my favorite analogy, because it's so accurate, and it's conceptually so easy. From kindergarten, we're taught about ecosystems and the health of ecosystems. And these concepts are really now ingrained in our minds. And, you know, if you ask somebody to picture a healthy environment or a healthy ecosystem, it's typical for them to picture or imagine the equatorial rainforest. And if you think about what a healthy ecosystem is, its diverse meaning there are many different types of organisms there. It's interconnected, meaning the organisms live and thrive together because they've adapted to live and thrive together. It's resilient, meaning when something bad happens, it can recover. So imagine a flood in a healthy rainforest, the plants and animals recover that disturbed space really quickly. It is resistant to change.

DR. BRYAN COBURN

So erosion, you think about a riverbank, a really healthy, diverse riverbank is more resistant to erosion than one that's been depleted through fire or deforestation. And the microbiome operates in a very similar way. And it is analogous to the way a large ecosystem works, the organisms interact together, and they interact in a way that maintains health and stability. And microbes work in exactly the same

way they interact with us as a host. They trade things amongst themselves, nutrients and metabolites, and they feed one another. And that creates a resilient and resistant environment to perturbation.

DR. BRYAN COBURN

However, as you pointed out, just like a large ecosystem, if something disastrous happens, it affects the composition and function of that ecosystem in a disastrous way. And right now, it's devastating to think about wildfires happening around the world. And wildfires are a great example of an ecological perturbation that can completely change a landscape, can wipe out multiple species, and it can have devastating long term impacts. And then the diversity of that ecosystem has to recover. And it can take a long time, healthy ecosystems recover more quickly, but it can take a long time for that ecosystem to recover. And our microbiome is susceptible to similar types of perturbation. And I'm happy to talk about what those are. And I think there's some that we can prevent. But that's certainly an appropriate analogy.

BTB

We'll get into that, of course, with your research, but there's one more step I want to take here in terms of our awareness, or the context of the microbiome, and that is, it seems it's very much become popularized the last several years, like it's having a scientific moment. What's your sense of why that is? Because my understanding is the study of the microbiome is still in its scientific infancy.

DR. BRYAN COBURN

Yeah, or maybe it's toddlerhood. And I think that the answer to that question is complicated, like anything that is having a moment, there's multiple factors that lead into it. One of the main ones is technical. So the Human Genome Project, advanced a technology type of sequencing that allowed us to sequence a lot of DNA all at once, right? That technology also allowed us to do broad surveys of the organisms that live on and in us. So in the early 2000s, the Human Genome Project technical advancements allowed us to study and discover and better characterize the Human Microbiome or microbiomes. And so that first step was really technical. Conceptually, we knew that we were covered in organisms, there’s centuries really, if you dig back of literature in which people kind of acknowledge this, and we knew that there were healthy organisms on our skin, but the advancement of sequencing enabled us to really characterize them and survey these organisms extremely thoroughly in in quite a lot of detail.

DR. BRYAN COBURN

So that technical advancement allowed us to first characterize them and then start to link them to our understanding of human biology and disease. Another reason I think that it's having a moment, aside from the scientific novelty of it, is it occupies a very interesting kind of intersection of biology. ick factor. Neat, cool talk to your kids about poop.

BTB

I knew we'd have to mention that at some point in this conversation.

DR. BRYAN COBURN

Yeah and you know, stool is important, that's where we've learned a lot about the microbiome, and science. And if I'm totally honest, there's a little bit of opportunism and even frank charlatanism. It's a different type and domain of biomedical manufacturing, and health food products overlap. And I think that allows some space to be occupied by people who want to take advantage of it. And you know that probiotic world is kind of an interesting one where there's real science and scams all rolled into one, and for some people, it allows you to externalize things that happen to you. This is not me, this is my microbiome that's perturbed, and that gives you a target to try and do something about it. And people will take advantage of that.

BTB

What I find fascinating about trying to wrap my head around the microbiome is from what you're saying, in terms of its origins, our bodies, the human body became hosts for all of these organisms, parasites, bacteria, etc. But over time, our bodies have adapted them to us as the host. And these micro organisms are now part of keeping us healthy. Is that right?

DR. BRYAN COBURN

Yeah, they perform functions that benefit us. And some of them are really easy to conceptualize. And I like to use those as examples, because I think it makes sense. So the first is and I'm going to use macro ecology examples, again, is just colonization resistance to pathogens. So pathogens are organisms that cause infection or disease. If you think about, again, a rainforest or a riverbed or a reef, healthy ecosystem is full, it's really physically full. And it's also occupying all of the functional niches that are required to maintain that environment. And if you think about a microbiome in the same way, the ability to resist colonization with a pathogen, which means acquiring a pathogen is partly dependent on how full your microbial environment is how complete your microbiome is.

DR. BRYAN COBURN

And so it just prevents other organisms that can cause disease from interacting with you as a human. And it can be just physical occupation of amnesia and anatomical space. It can be functional, it can prevent those organisms from being able to adapt. And that's one of its key functions is that it allows us to resist acquiring organisms that cause disease. It also does things for us, like, make things that we don't make. There are vitamins and nutrients that we don't produce, there are dietary components that we can't metabolize that those organisms do. But that colonization resistance, idea that resistance to pathogens is a really neat concept that I think illustrates how a microbiome can be health associated.

BTB

Okay, so let's turn to your work. Bryan, one of your primary research focus is to somehow leverage the microbiome, so big picture for it to become a therapeutic agent. Walk us through the principle here of how you might do that.

DR. BRYAN COBURN

Yeah, this is fascinating. And, you know, I think that this is why I'm so excited to be working on what I'm working on right now is that science moves quickly. You know, this is a science that's really maybe two decades old, if we think about it in a high degree of detail. But we're now at the point where we're thinking about applying it directly to human health, and trying to augment health outcomes make things better by therapeutically targeting, treating our microbiomes. And that's very exciting. But it means we have to be very careful. We have to be meticulous, we have to be scientific and rigorous about how we approach targeting the microbiome. And that's kind of the phase that I'm in right now.

DR. BRYAN COBURN

And I spent the first few years of my career really doing benchmarking work benchmarking, meaning just figuring out how the tools that we have work so that I can use them in clinical studies in humans. So I had to know how the sequencing performs as a technique and different assays that we use, what information that gives us and now we're using tools to directly augment or therapeutically change microbiomes. That means using well structured human clinical trials where we give people interventions that are designed to target or change the microbiome, and finally linking those changes in the microbiome to outcomes that we care about like survival or response to therapies, different types of treatments for different types of diseases. And we have to do that systematically. And we're doing that in clinical studies that are ongoing right now and things that we're planning in my group.

BTB

Okay, so in terms of recent papers, maybe you could walk us through the one about microbiome modification. What did you set out to do there?

DR. BRYAN COBURN

We've completed a clinical trial called the MET-4-IO trial, like all clinical trials, it has an obnoxious acronym, but MET-4-IO was a trial of a microbiome ecological therapeutic MET called MET4 number four, in immuno oncology, which is a cancer treatment class. There's some really brilliant and very exciting literature linking the composition of one's microbiome prior to starting cancer immunotherapy to their outcomes. And the observational data is very high quality so perturbed or altered microbiomes are associated with worse outcomes in a therapy. And we sought to find out whether we could repair, restore or change micro biomes in the context of immunotherapy.

BTB

To assist the cancer treatment.

DR. BRYAN COBURN

Yeah.

BTB

So it improves the health outcome.

DR. BRYAN COBURN

And that's the ultimate goal. Our first few questions, and this is work done with some very close collaborators Anna Spreafico and Lillian Siu at Princess Margaret. This first study that we did was really designed to make sure that the microbiome targeting therapeutic we were using, which was a pill full of bacteria was safe. It was tolerable to patients, and that it didn't make outcomes of immunotherapy worse, like it didn't create new toxicities or worsen side effects that we know occurred during immunotherapy. And finally, that it changes their microbiome at all. And this may seem like a baby step. But this is an essential first step. And this was intended to be an alternative to fecal transplant, which is where we give people stool from another healthy donor.

DR. BRYAN COBURN

This was designed to be something that we could use in a very large number of people reproducibly, scalably and safely and we had to figure out whether we could do that. And this trial showed that we could give this agent called MET-4, which is an oral bacterial consortium, a whole bunch of bacteria, it was safe, it was tolerable. It didn't make side effects of immunotherapy worse, and it did change some people's microbiomes not everybody's but it changed some people's microbiomes. And so that was a really interesting and exciting first step because it represented the first time anyone had tried to do this in the context of cancer immunotherapy.

BTB

What was the scope and scale of the trial?

DR. BRYAN COBURN

It was a relatively small number of people. So it was less than 40. And the main goals were just to try and figure out safety tolerability. And then we did some microbiome assays at the end to see if their microbiomes changed. And about 25 to 30% of people had a significant measurable change in their microbiome at the end of the treatment.

BTB

So then is there a way to discern which patients on immunotherapy for cancer are candidates for microbiome therapy using this pill?

DR. BRYAN COBURN

This is really an interesting question. And I am an infectious diseases doctor. I'm not an oncologist. And it's very easy for me to point exactly at the culprit that I'm most often responsible for, which is antibiotics. And the observational data I was alluding to where microbiome composition, what's in your microbiome was linked to outcomes of immunotherapy. One of the main risk factors for a bad outcome was antibiotic exposure immediately prior to immunotherapy. And so I am an antibiotic doctor, I kill your microbiome for a living. And to me, that's one very promising and interesting stratification tool, identify people where they've had the harm. And if you think about this, this is back to the macro ecology example, the forest fire has just occurred, the flood has just occurred. Can we go in there and replace what was lost in order to help the microbiome function through the immunotherapy. So that would be one way of stratifying. It's based on a clinical factor.

DR. BRYAN COBURN

There are tests that we can do to ascertain whether somebody's microbiome is favorable or unfavorable. Right now, those tests are probably not available rapidly enough to be clinically usable, but we're getting there. People are solving that problem. I'm not but other people are.

BTB

What was the reaction to the MET-4 study?

DR. BRYAN COBURN

Our reaction was excitement. Having completed it, to be honest, it was the first in our type. It was fun to speak with other cancer researchers who saw the potential of using a pill as opposed to a fecal transplant and a fecal transplant. I'm going to digress or go on a bit of a fecal transplant tangent everybody wants to know about it. But alternative studies have used stool derived from a donor that has responded to immunotherapy and then that stool was provided either as an enema or as capsules to immunotherapy recipients and people who've previously failed immunotherapy or had their disease progress on immunotherapy, have then had a response, which is an amazing thing. So there's this moment in the immuno therapy world where we understand that augmenting the microbiome can probably have beneficial effects on outcomes.

DR. BRYAN COBURN

But we need to think about ways that we can do that, for the 1000s of immunotherapy recipients that are out there. And fecal transplant, although it has been scaled for use, for example, for treating infections in the United States using a stool banking system, it's very difficult to do safely, it's very difficult to do reproducibly, it relies on a donor that provides the same product over and over again. And that can be very difficult to…

BTB

Scales.

DR. BRYAN COBURN

And so the opportunity that we tried to seize was to use an intervention that was scalable, that was reproducible, that did allow us to give the same thing to 1000s of recipients over and over again. And so that was the main advance of our approach. And that, for me, is very, very exciting.

BTB

I'm sorry to be so based, but when you're telling patients that you recruited for this trial, that you're gonna give them a pill form of bacteria and other organisms like this that have a taste like how did you convince them?

DR. BRYAN COBURN

The capsules are encapsulated in multiple layers, it's like taking any other capsule, and there have been multiple studies of acceptability of stool in capsules, given for other indications. And it's almost always well tolerated. Remembering that this is a population that's highly motivated to try and do something beneficial. So the motivation is there. Side effects are generally pretty mild in most cases, for both the MET-4 intervention, that type, then there's lots of trials of different encapsulated bacteria, but also for fecal transplant.

BTB

Okay, so let's look at one of your next research steps. I know it's early days, but I find this one fascinating because it will be a first of its kind clinical trial.

DR. BRYAN COBURN

That's pretty much it. And here's what the study design is. People who have bloodstream infection, meaning bacteria in their blood get treated with antibiotics, the antibiotics wipe out or massively affect their microbiome. At the end of that antibiotic treatment, which they needed, because they had a severe and potentially life threatening infection, we're going to give them organisms back, we're giving those organisms back like going in and replanting a forest after a forest fire. So the intervention, the antibiotic was there to treat the infection, they had to have that it was life saving. So they had that treatment of infection. And at the end of that treatment, when their microbiome is highly disrupted, we are giving them back organisms in the form of a capsule full of bacteria to try and restore their microbiome and help eradicate or get rid of the infection causing organism that they had.

DR. BRYAN COBURN

So after treatment for an infection, believe it or not, the organism usually doesn't go away, it still lives in our body, and it hides out. And so our goal is to try and get rid of those disease causing antibiotic resistant infections by giving them this intervention.

BTB

So with patients with this blood disease that had to be treated with an antibiotic, maybe backup, how would they typically have been treated?

DR. BRYAN COBURN

They would be given the antibiotic, and then that's it, they wouldn't get anything else afterwards. And their microbiome would have been disrupted, and it would have just had to recover.

BTB

On its own.

DR. BRYAN COBURN

On its own. And, again, that's sort of like a forest fire. And as a clinician, I sometimes think, okay, you know, what this person is young and healthy, they had kind of a one off infection, they might have had an infection that was not likely to come back or be reproduced. And I would say, Fine, your microbiome can recover on its own, I'm not worried we can take time, the time is not the enemy here. But other people who are highly vulnerable to having recurrent infections, having the infection come back again, or to have infections persist, those people are the ones who are most likely to benefit from getting rid of these hard to treat organisms. So that's our goal is they got an infection once, we want to see whether we can get rid of the hard to treat infection causing organisms.

BTB

So the premise here also would be to help speed up their recovery so that there's less time that they're vulnerable in terms of their immune system?

DR. BRYAN COBURN

Exactly. That's exactly right is this idea that there's a post infection vulnerable window, where being colonized having a bad organism in your body is risky. And our goal is first just to see whether we can get rid of that organism and in longer term studies are future goals to see whether we can prevent infections completely prevent them from recurring or decrease the risk of recurrence. And the wrinkle here is that we've selected a population in which the infection, the organism that they got was resistant to multiple antibiotics. So it was harder to treat than usual. And this study is designed in part to try and get rid of those hard to treat organisms. So if they do get another infection, the hope would be that it would be with an easier to treat organism.

BTB

What's the scope and scale of this trial going to be?

DR. BRYAN COBURN

So this is a 100 patient pilot study, the goal is to see whether again, we can do this safely, feasibly, recruit enough patients, get the samples we need to make sure that we know what we're doing is safe. And then if the pilot and feasibility study, we meet our aims, which are safety feasibility, then we proceed to a larger full scale trial.

BTB

And this will be also administered as a pill form?

DR. BRYAN COBURN

Yep, yep.

BTB

Yeah. So give us a sense of next steps, then Bryan on this trial?

DR. BRYAN COBURN

So we're just going through our final approvals with ethics. And then we have to be approved by Health Canada. And that's happening now. Our goal is to recruit our first patient into the trial before the end of 2023. And finish the pilot feasibility study by the end of 2024.

BTB

There's a quote of yours I read, where you talk about the many patients you see who have infections caused by antimicrobial resistant organisms, and you say, quote, our hope is that this new line of research leads to therapeutic interventions that can be widely and cheaply available to people in Canada and around the globe. Unquote. I'm curious, what's your take on the scope of leveraging the microbiome to treat patients? Where can this go?

DR. BRYAN COBURN

I think that this is the next three decades or five decades, or however long, I am hoping to keep going before I retire decades of microbiome science. The truth is that there are many, many ways that this can go and the fun part of thinking about targeting the microbiome is to think about the many ways that we can do it. Giving organisms back is just one way. And when patients now ask me when I see them, after they've had antibiotics, people walk in and say, you know, I'm worried about my microbiome, I just

had all these antibiotics, what should I do? Should I take a probiotic? Should I get a fecal transplant, should I eat something different, and what I tell them is that they eat what we eat. The Canada Food Guide is actually a picture of a plate, half of that plate is fresh fruits and vegetables, a quarter of it is grains, and legumes. And that's a fairly fiber rich diet.

DR. BRYAN COBURN

One of the ways we can target our microbiome or modify our microbiome is through diet, they eat what we eat. And we can use a healthy microbiome promoting diet. And we can be very specific about it by giving things that certain microbes eat and will make those specific microbes grow. Or we can think about it in a holistic sense, a healthy diet, particularly a fiber rich diet has been associated with good health outcomes in many, many, many studies independent of the microbiome. So that's one way we can target the microbiome, we can give organisms back we can give just a single organism like a probiotic. Or we can give lots of different organisms, like we do in these trials that I've been doing, we can give a whole human ecosystem back like a fecal transplant, we can give products that the microbiome makes. So those are sometimes called post biotics. These are compounds that are only produced by bacteria or fungi in the gut. And we can give those products back if they have a specific health effects.

DR. BRYAN COBURN

So the next two or three decades is going to be figuring out in what people what intervention is required and when. And I heard one of my colleagues, actually my division director, man named Rupert Kaul, say, if you went to a doctor and said, I have an infection, and they said, Okay, well then take some antibiotics, you would think they were a pretty bad doctor, because they didn't ask you what your infection was. They didn't try and figure out what the organism was. They didn't tell you what antibiotics to use. They just said, oh, yeah, go to the pharmacy pick up some antibiotics take those antibiotics. And I think that we're in the phase now where we have to figure out how to do what we do with antibiotics, where we identify the disease and the problem, we match that disease or problem to a specific therapeutic intervention. We measure whether that therapeutic intervention works for that disease, and then we provide or prescribe the intervention to the patient with that specific problem, we have to start thinking about it that way.

DR. BRYAN COBURN

And I think that that is the next phase of microbiome research. I'd like to say that there's a you know, just one big button, reset microbiome, and you press that and everything's gonna be fine. But for some conditions, it's going to be modifying diet. For others, it's going to be giving a fecal transplant, and for yet others, it might be using a single species probiotic during an at risk window to prevent other organisms from growing. And we're gonna have to figure out all of that stuff through rigorous, well structured clinical trials over the next few decades. And I think that's the fun part. The global scalability part, I think, which I alluded to, in that quote, I feel strongly that what we do in my research group or with my collaborators, be freely available or at least cheaply available everywhere. Diet is the cheapest intervention we can use in modern medicine. And that's part of the appeal of studying microbiomes is

that organisms are very difficult to patent. That's part of the appeal is that we can do things that can be freely disseminated and available worldwide, relatively inexpensively growing bacteria is relatively easy. And so part of my hope is that as identify these interventions, they're easily available to anyone who needs them. And I try and keep that as central part of my core mission.

BTB

A final thought on potential here, because earlier, you mentioned things like opportunism and charlatanism. Can you maybe help listeners temper or just maybe give some advice on maybe what not to pursue when it comes to the popularity of the microbiome these days?

DR. BRYAN COBURN

Yeah, you know, this is such a difficult and important question. And right now, the state of the science is that there are a few indications for which giving a specific probiotic has been tested in a clinical trial, there aren't many. There are many, many, many, many more commercially available.

BTB

Yes.

DR. BRYAN COBURN

Probiotics for things that will promise X, Y, and Z based on poor quality science or complete absence of science. I have to say that three or four years ago, I used to say, You know what, the main toxicity of buying a probiotic is its cost. It's sometimes…

BTB

There’s not a lot of harm if you ingest it.

DR. BRYAN COBURN

I used to say that and now in ecological terms, I have to admit, I'm thinking more about the forest fire analogy, or the flood analogy, if you have a forest fire, that single species, probiotic, for example, is basically the equivalent of going in and planting a field of wheat. While it's maybe good to have something there, for some people during a high risk window, it's still not the ecosystem that you started with. And so I've tended to think of myself as an ecologist, my goals therapeutically. And the advice I give is, you know, the best thing you can do is try and repopulate a healthy microbiome, which is a diverse microbiome. And the best thing you can do for that is to have a healthy diet and a high fiber diet has been associated with a high diversity microbiome.

DR. BRYAN COBURN

So as a general rule, I tend to say, You know what Probiotics have not been shown to improve outcomes outside of a very limited number of circumstances, the best thing you can do for your microbiome is diet. And I described the Canada food guide a lot, actually the new Canada food guide a lot because I like it quite a bit. It's easy to sort of conceptualize and I say, if you want to help your microbiome, picture a plate, make sure that the food on your plate or your grocery cart is mostly full of vegetable based or plant based foods that have fiber in them, and minimize processed foods, red meat and other components of your diet. And that's the healthiest thing you can do for your microbiome.

BTB

So why is it for consumers out there to be cautious about the notion of probiotic as this panacea, restoring your microbiome, not the case?

DR. BRYAN COBURN

No. And I think that that is really the most useful advice I can give people who are seeking information is think about an ecosystem. If somebody told you that they could restore rainforest after a fire by giving a single species it would seem ridiculous. And so that lens that framework, I think is a useful starting point. And knowing that a lot of information on the internet is of low quality and is trying to sell you something, it's probably the most important piece of information I can give.

BTB

You're listening to Behind the Breakthrough, the podcast all about groundbreaking medical research, and the people behind it at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host Christian Coté. And on the podcast today we're talking with Dr. Bryan Coburn, a clinician in UHNs division of infectious diseases, and scientist at the Toronto General Hospital Research Institute. Dr. Coburn is a leading researcher in advancing our understanding of the microbiome, and how to harness it to treat patients and improve health. So Bryan, you were born and raised in Toronto, both your parents come from social science backgrounds, your dad was a professor of Public Health Sciences at the U of T and your mom, an English and arts teacher. Their reaction when you told them you were drawn to science and medicine was?

DR. BRYAN COBURN

Oh you know, this has become a Coburn, family apocryphal story, it's a phase. That's what I usually say it's a phase. I don't really know if that was true, I can tell you that that's my anchoring memory at the node where I was deciding between the biological sciences, medicine, engineering, I think, because I like to tinker with things, and the social sciences. That's what I remember. They were incredibly supportive, of course, when I kind of focused my goal and have always been supportive of my career as it’s progressed. But I do admit that that was the anchoring memories like Now why would you want to do that?

BTB

Bottom line working in healthcare is essentially about being in the service of others. What is it about service that draws you to this vocation?

DR. BRYAN COBURN

It's funny, 10 years ago, when I was just starting out, I had this model of my career in which around the age of 45-50, I would start to phase out my clinical practice, which is where I am now, I would start to phase that out. And I would focus on research because that's where the compelling new questions are. And I felt that clinical work was about questions I knew the answers to, that's why I was there. That's why doctors are good at their job as they've seen it before.

DR. BRYAN COBURN

But I have to admit that over the last two or three years, and maybe it was the pandemic, maybe it was me just getting older, I've come to value that moment of, I use the term unearned intimacy, you get to be part of somebody's life at a highly vulnerable moment. When you have no right to be there, and you're not just tolerated, you're sought and included. And you see people when they're vulnerable, you provide them with answers, not always positive ones, but answers to questions that are essential to how they approach the rest of their life, or their life during a tough moment. And that is immensely, immensely gratifying. And the customer service, that moment where you face the person and the patient has become its own reward for me. It's an incredibly privileged moment. And I've come to enjoy it immensely. And I think that that part of clinical work is really driving a lot of my motivation, both clinically and in research.

BTB

What a wonderful take. You mentioned, you like tinkering too growing up, you've, you like fixing things like you operated at a bike store to help fund your university academic training. And you like figuring out getting from point A to point B, do those attributes translate in terms of your career path and medicine?

DR. BRYAN COBURN

I think so. It's funny, because you know, it was a pretty rinky dink bike store. And I worked in the bike industry for probably 10 years. And the other guy that he and I owned this thing I should, if you could put air quotes in it, it was a pretty, it was a pretty small affair. He's now a neurologist in Alberta, after having been an a Olympic cross country skier, a guy named Gordon Jewett, he's an amazing guy. But he and I did this and then both went on to medicine serendipitously enough, he took 20 years to do it and started at the age of 40. But yeah, that sort of problem solving aspect of the kind of getting from A to B, I often used to joke that in science, if you gave me a bag of Lego blocks, said Your job is to solve a problem with these now I would say okay, well, let's, let's have a go at this. And I like that uncertainty.

DR. BRYAN COBURN

And this has come up before I often use this analogy of being plopped in the middle of Antarctica as a metaphor for problem solving. If you don't know where you're going, you don't know what's out there. You don't know whether you're gonna succeed, you don't know whether somebody's been the direction you've been before, and either succeeded or failed miserably. It's exciting. It's fun, that really stimulates me. And I like this idea of not knowing where I'm going. And one of my clinical supervisors, when I was a clinical trainee, he said, Well, you know, good for you, you're putting your brick in the wall of knowledge. And at the time, I was immensely insulted, I couldn't believe he would say such a condescending thing. And now that is my only goal in life.

BTB

Wow!

DR. BRYAN COBURN

Is just to take that brick and put in, it was Murray Krahn actually, who died recently and was a scientist here. And, and I remember being so deeply insulted when he told me that my most narcissistic and egotistical I think, and now that is my goal in life is just to put a brick in the wall of knowledge, not necessarily even knowing that I've done it or where it goes.

BTB

Every brick is important, right on the shoulders. I read where Elizabeth Blackburn, who is a Nobel Prize winner was asked about the virtues of successful scientists. And she mentioned you know, resilience, persistence, as well as being opportunistic and creative. Does that resonate with you?

DR. BRYAN COBURN

Yeah, absolutely. I like to think that I'm good at seeing opportunities. I think if I'm especially good at anything, as a scientist, it's making connections that other people might not see. And understanding how those connections can be fruitful avenues for exploration. And the best way to do that is to seek and create opportunity. And one of the ways that I think I've been good at that, or we've been good at that, as a team is involving lots of people in discussions about stuff we don't know, and talking to people and interacting with people who are not working in my area at all. And then surrounding myself with people or being in a team where everybody's thinking about opportunity, and then seizes it when it comes. So not just being solely responsible for recognizing and pursuing an opportunity, but surrounding yourself with people who are also thinking about opportunity so that they might see something you don't. And that I think is one of the great joys of science is that you get to pursue opportunities by using the word privilege once already, but this idea that I get to do that is actually insane. You know, this idea that if somebody shows me something that might be fun to do and interesting to do and has potential future benefit that I get to go after it is the good fortune I have to do that. It drives a lot of what we do in my research group.

BTB

You mentioned some mentors, Murray Krahn, who have helped shape your career journey. Talk to us about how they helped compress your learning, focus you and help you basically become successful?

DR. BRYAN COBURN

It's interesting that moment with Murray Krahn was like a moment. It was a moment in a hallway on the 13th floor of the Eaton building.

BTB

It’s seared in your memory.

DR. BRYAN COBURN

I remember everything about it, including the how wrong, I was to be insulted. But also how formative that small piece of advice was. And mentorship is like that. You don't know where you're gonna get it from, you don't know when you're gonna get it. Mentorship at its base definition, the easiest form of mentorship is just giving people information or asking them what they want to do in life, good mentorship might be asking them what they want to do in life, and why they want to do it. And the best mentors who will make you reevaluate what you want to do and why you want to do it. And I often think that the best mentors I have, it's so easy for a mentor to just reflect back to you what you've said to them. The best mentors that I've had, have not just been honest with me, but they've made me be honest with myself. And you know, you don't know where you're gonna find those moments. It takes investment. It takes thought it takes care and interest. And it doesn't have to be drawn out over a decade long of mentorship. It can be just a few moments of mentorship.

DR. BRYAN COBURN

I'm extremely fortunate to have been formally mentored by Rupert Kaul, our division head, and he's very good at reminding me who I am. There's no crap allowed. That's maybe slightly profane, but you know that he won't tolerate it. So if I say something to him that he knows is disingenuous, he knows that it's not true. He will, he will call me out on it, he will make me be honest with myself. And that is fantastic mentorship.

BTB

You're a clinician scientist, you see patients as well as do research. So you you see their need for improved treatments, cures? How do you reconcile that urgency of their need with the fact that science takes time?

DR. BRYAN COBURN

Hope, optimism, I've looked back at 150 years of incredible progress in infectious diseases. And I recently started an HIV practice 10 years into my career, I took up an HIV clinic, which I hadn't done and to this point, and this is an area where lives are totally different living with HIV than they were 20 or 25 years ago, we have incredible leadership in Canada and HIV globally. Sharon Walmsley's at our institution and is phenomenal. She's a juggernaut, high energy, productive and effective. And I know that what I see now clinically, which is often I don't like to use the word boring when referring to people's health, but it's so routine that it's all we ever hoped for 20 years ago is available right now, and HIV care is still getting better.

DR. BRYAN COBURN

But to see that kind of progress gives me hope, for the next 20 years. Reconciling that with the immediate need, I understand that I'm not gonna be able to help everybody. Now I do my best to do that, within the confines of what I'm able to do in my knowledge, but understanding that there is going to be change over the next 10 or 15 years. And if I'm lucky to put that brick in that wall that produces that change, then hopefully, in 20 years, somebody is going to be looking back at this next two decades and say, You know what, I don't know who did this, but a whole bunch of people. And look how good things are now in this domain, how much better they are now than they were 20 years ago.

BTB

So day to day do you feel pressure in your work?

DR. BRYAN COBURN

I'm a low stress individual, I like stress, maybe it's not that I'm low stress, I like it, it's a reminder that I should be doing something. So I enjoy pressure to some degree. I like the idea that failure is imminent, because it means that we're doing something. And I think I've learned to assimilate that pressure. I feel it just like anybody does. I think that that's real life. And there are certainly professional tick boxes and milestones that I feel like I have to make in order to keep my job or get promoted, or whatever. But I try not to let those bother me. I'm not especially ambitious for fame. And that's very liberating. But that liberates so much of your time, if you just want to do your job and not be known for it, you can have so much better work life balance and so much less pressure and stress.

BTB

You mentioned failure. I'm curious, you know, research involves roadblocks and challenges and failure. How do you navigate that because it's not like we're taught how to deal with failure in school?

DR. BRYAN COBURN

I deal with it just the same way as everybody else, which is I knotted up in a terrible ball with my guilt and shame. And I suppress it and I wait for it to hunt me down at three in the morning, seven nights in a row and it's torture. Yeah, if we all do that it's the truth. And you know, I ruminate on failure like

anybody, the 3am I don't know what it is about 3am that wakes us up with our failures that can be from a week, a year 10 years ago, or that day. So that still happens to me. And I think that I'm at my most effective when I'm most effective dealing with failure, I sort of swallow my pride and I blurt it out. I have a disclosure compulsion. I go to the nearest person who I think will be the most judgmental, who will have insight and I say this is what I just did, or this is my current failure. And I never received judgment. I almost never receive judgment. I almost always received sympathy and then I'm lucky enough to have colleagues with whom I can move forward to incite. It's that idea that taking failure and making it part of your story part of your history, your personal history and your professional history is essential.

DR. BRYAN COBURN

And I think if I do one thing that I look back on with pride, maybe, is that my most embarrassing moments clinically, in my training, or in my career, are stories that everybody knows, so much so that my colleagues kind of roll their eyes, they're like, Oh, yeah this story again. And I think incorporating that failure into my personal narrative and history, makes me face it, and move on from it and also learn from it. So I think that I do that, and I get some enjoyment out of it, too.

BTB

Another challenge I'm seeing for scientists of this generation is how to amplify their work, not just within academia, but with the general public in a way that's accessible, so that it can reach a wider audience. Do you have any guidance for younger scientists in that regard?

DR. BRYAN COBURN

Talk to somebody who does it well, that sounds like a flippant statement. But no, if that's a goal, there are people who do it very well. And I think understanding that there is an audience for your work, when you're most self conscious, you don't think that's the case. Or you think that your work is not worthy of that audience. And that really is a pervasive negative thoughts like, Oh, that's true. But you know, they don't want to hear about my work, understanding that people do want to hear about your work. And actually, the best interactions I've had with audiences, when I give talks are with people who are not experts in my area, experts will nitpick and they'll find the methodological weakness or weaknesses, which are, you know, inherent in scientific work. Every approach has its limitations. And that's important. That's critical feedback. That's feedback from expert peers.

DR. BRYAN COBURN

But recalibrating what's important to people requires an audience of people who may or may not know why you're doing what you're doing. And so seek those audiences and know that your work is of interest to people. People are innately curious, they will hear what you're doing with interest and provide better feedback than many of your peers provide, and they'll recalibrate you to what's important. And so seeking those audiences will be the springboard for making your work more broadly understood.

BTB

As we all know, during the pandemic, the COVID 19 pandemic medical research and science was at an all time high in terms of being in the spotlight. And that attention revealed to what we were speaking about here how intertwined research and science are with advancing health. My question to you is, as the pandemic recedes, how do we keep medical research top of mind with the public?

DR. BRYAN COBURN

This is a very specific and interesting challenge right now. And as we emerge from the COVID-19 pandemic, one of the maybe distressing consequences has been polarization of how people interpret and value research. I think it was maybe a few days ago, in the New York Times, there was an article about eradication of three key diseases, TB, malaria, and polio, and how, during the March of Dimes, there was this great unified, understanding that this was a collective effort. This required social cohesion. This required an understanding that we're out to look after one another, and it moved the polio vaccine forward quickly, literally, by people sending in change. The March of Dimes was literally about dimes. That idea has a little bit been lost and worse than lost. It's been so polarizing that people are opposed to it. I think recognizing that we're all in this together. And starting with that foundation of looking after one another. That's a broad statement. It's grander than any scientist can meet.

DR. BRYAN COBURN

But understanding that medical research is an essential part of that. And that it doesn't necessarily mean focusing on a single disease at any given time, although sometimes it will. But it means that we focus on looking after one another, and building a community in which we focus on and we value progress in research so that we can help a generation that hasn't been born yet. That's a fundamental philosophical shift. But I think it's a conversation that needs to be had. And most importantly, when we talk about research, talking about it as part of the community of humans, not a pocket separate from that, as scientific researchers, we are not independent of society. We are part of it, it is integrated into how we progress as a society and as communities.

DR. BRYAN COBURN

And so I think that reminding ourselves as scientists that we aren't in an ivory tower, reinventing research in communities, thinking about whose communities are going to be affected by research and how to incorporate them into how we do science. This is about cohesion. And I think that that is a lesson that is easy to assimilate. And I think that that would have a little bit of a political impact to think about scientific research as an exercise in community cohesion. So I think that we need to talk to scientists like that as opposed to just asking for more money.

BTB

There's a leadership author Simon Sinek I'd love to read a quote to you and get your responses. He says people don't buy what you do, they buy why you do it. Why do you do what you do?

DR. BRYAN COBURN

I think that that social cohesion bit is part of it, I see what I'm trying to treat as a clinician, I want to help participate in the improvement of individuals' health. But also I see it as a responsible act, this is something that I am able to do, I am very generously supported to do. And that produces responsibility. Part of my motivation is just to leave something the tiniest increment that wasn't there before that advances humans as a healthy community. And I don't know whether that's going to be directly something I do, or we do in the lab, which would be phenomenally lucky. Or whether it's through creating an environment where a trainee who goes on to do something in their own group, or both, I hope both but it's that idea that I'm participating in a community activity. That's the driver for me. And it really does reflect what I do in the lab where a microbiome is really a functional community. And I think that trying to be part of a functional community is directly related to what we do thinking about microbial communities.

BTB

Dr. Bryan Coburn scientist at the Toronto General Hospital Research Institute. Thanks for sharing your fascinating research on the microbiome and continued success.

DR. BRYAN COBURN

Thank you very much. Thanks so much for having me.

BTB

For more on Dr. Coburn's work and the podcast go to uhn.ca or www.behindthebreakthrough.ca. And please let us know what you think we'd love your feedback. That's a wrap for this edition of Behind the Breakthrough, the podcast all about groundbreaking medical research, and the people behind it at the University Health Network in Toronto, Canada's largest research and teaching hospital. I'm your host, Christian Coté. Thanks for listening.