The mind-gut connection: the bi-directional communication between our gut and our brain and its impact on mental health

With Professor Emeran Mayer

The MindHealth360 Show

Episode Transcript
Host: Kirkland Newman
Guest: Professor Emeran Mayer

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Kirkland Newman:

Welcome to the MindHealth360 Show. I'm Kirkland Newman and if you, your loved ones or clients suffer from mental health issues such as depression, anxiety, insomnia, poor memory, poor attention, mood swings, exhaustion, et cetera, I interview the leading integrative mental health practitioners from around the world to help you understand the root causes of these symptoms, many of which may surprise you and suggest solutions to help you heal. If you like this interview, please do subscribe and forward to others who might find it helpful. If you want further information, please go to www.mindhealth360.com or find us on social media.

Kirkland Newman:

Dr. Emeran Mayer, thank you so much for being here for the MindHealth360 Show. I really appreciate your time. By way of introduction, you are a distinguished research professor in the department of medicine, physiology and psychiatry at the David Geffen School of Medicine at UCLA. You're the executive director of the G. Oppenheimer Center for Neurobiology of Stress and Resilience and the co-director of the CURE: Digestive Disease Research Center at UCLA. You've made major scientific contributions to the area of basic and translational enteric neurobiology with wide ranging applications in clinical GI diseases and disorders, gastrointestinal. You've published more than 370 scientific papers and co-edited 3 scientific books. You've spoken at UCLA Tedx on the mysterious origins of gut feelings in 2015 and you've been interviewed on national public radio, PBS and by many national and international media outlets including the Los Angeles and New York Times, Atlantic Magazine and Stern and Spiegel Online. You're the author of the best selling book, The Mind-Gut Connection which came out in 2016 and the upcoming Gut-Immune Connection which is being published in 2021. I'm looking forward to seeing that. And in the meantime, this is the one that you brought out in 2016 which is a fantastic book on the gut-mind connection.

Kirkland Newman:

And I'm really excited to interview you because as you were saying before we started, there's been a renewed interest in this gut-mind connection. Probably the reason being I think that there's a lot of research that's been coming out. But the research has been there for a while. I mean since the 1980s there's been a lot of research on the gut-brain connection. I think over 50,000 papers were published on PubMed on this issue and yet it's only recently that there's been a real increase in interest in this area in the public domain and also in mainstream medical

practice, which at the moment it's still to my mind not getting enough concrete application in practical medical treatment. I don't know why that is. In my view in 10 years time you'll go to a psychiatrist and they'll probably order stool samples and they'll order blood tests, et cetera. I'm hoping. That's certainly what we try to promote at MindHealth360. But in the meantime, I don't know if it's a question of the feeling that there's a slight lack of enough research on it, or why do you think there's been a disconnect between the research that's been done and its application in mainstream medicine?

Emeran Mayer:

Yeah. I mean you expressed this really accurately. I mean in my career I've been involved for 30 years in studying brain gut interactions and this was always an outlier in science and definitely in the medical field. And it really took the ascendancy of microbiome science in the last 10 years or so that all of a sudden this topic has become popular. Initially popularised by some spectacular studies in mice and rats and this has been picked up by the lay media, it's been in my opinion really exaggerated because we had very few human studies that would corroborate these amazing findings in animals. And it's pretty much stayed the same way. 95% of the information comes from animals. What comes from humans is a lot of what we call cross sectional or association studies that you look at a population, a disease population, and look at, for example, their gut microbiome and you compare this population with another one that is healthy. So that doesn't really tell you anything about the causality. There's quite a few of those studies now. The clinical studies are very difficult. I stopped doing animal studies about seven years ago. Mainly because I found the ability to translate it to relevant human findings has always seemed very limited.

Emeran Mayer:

We've done many studies of different aspects of the brain gut axis that we could not reproduce in human subjects. For a variety of reasons I won't get into this. So having now been involved primarily in human studies, I'm fully aware of how difficult this is. Every human is different. The microbiome of most people is different from each other. More than our genes. There's all these other factors that we can't control in humans which we can control in animals. And then most of all, it's very expensive to do the human studies because you need large numbers. So you need a consortia of investigators, international consortia that study thousands of patients then use artificial intelligence to tease out relevant findings.

Emeran Mayer:

One thing I forgot, one thing that definitely is a big challenge to overcome, the mouse brain compared to the human brain is like a HP calculator from the 1980s to a super computer today that can beat somebody to the big blue--the IBM super computers that can beat somebody in a chess game. So big conclusions from such a simple device as a mouse brain to our extremely complex machine that we have for the most sophisticated computational machine in the universe is very difficult. So I think that explains the science. The human studies have lagged behind considerably. They will for a while. But what has not lagged behind is that a lot of people have populated that space where we don't have the human scientific evidence and have extrapolated from animal studies and have created , I mean I shouldn't call it a fake science environment, but a lot of it is fake science. You can claim that what somebody has found in a very artificial mouse

experiment is the reason why you have to eat such-and-such food. I hope I don't sound too negative because I'm very excited about this area and hopefully in our conversation this will come out. But just to answer your question, why we are where we are right now.

Kirkland Newman:

It's very interesting and it's slight disheartening, but it's interesting, because when I read your book, which I've now read cover to cover and it's fascinating, there is so much in there. And so I think okay, well did you use the human, I mean I know you speak a lot about the mouse studies, et cetera, but you certainly extrapolate a lot. And because you're such a rigorous scientist you obviously were very careful about what you did extrapolate and what you say in that book. But there are some very powerful conclusions in your book, which I'd like to discuss, of the relationship between the gut and the brain and the gut and mental health, which is what I'm particularly interested in. And so we trust that the studies that you used were convincing enough for you and that's why I'm very happy to interview you, because I think what you say we can take as gospel in some ways. And so moving on, what I'd really like to understand is this relationship between our mental health and the gut. And you talk about fascinating things in this book about the effect of the gut and also the gut microbiome. So they're two different things. There's the gut and then there are all the bacteria that inhabit and all the other organisms that inhabit the gut.

Kirkland Newman:

And I think we tend to think of the gut without separating the two and that's one distinction I took from your book, which was very interesting. And you talk of the effect of the gut and the microbiota on things like neurodegenerative diseases such as Parkinson's and Alzheimer's, neuro development disorders such as autism spectrum disorders, maybe ADHD, anxiety. Obviously there's IBS. And then more common mental health disorders such as anxiety and depression. There's so many mechanisms which impact our mental health from the brain and I know it's very complex. But if you were to sort of say okay, there are the key mechanisms of how our gut and/or our microbiota impact our mental health and your degenerative diseases in particular, common mental health disorders and your developmental disorders.

Emeran Mayer:

Yeah. That's relatively easy to answer. So I refined this in my new book. So let's start out with the brain-gut microbiome was called the brain-gut microbiome axis. I like to call it now the brain-gut microbiome system because you have to use this concept of systems biology to understand something that has circular loops built into it. It's not a linear process that something that happens in your brain does something in your gut and vice versa. It's always a circular interaction. So that's really important to realize. Whatever happens in our mind, in our brain, will be transmitted to the gut. It will in extreme emotional states or with extreme or chronic stress will definitely change every gut function significantly and thereby change the environment in which the microbes live in. So that's one important mechanism.

Emeran Mayer:

Another one is that even some of the stress chemicals that our brain sends down through the sympathetic nervous system can directly talk to receptors on the gut microbiota and change their behavior. So two ways that the brain can do this. One is by directly influencing the behavior and the gene expression of microbes, and the other one by just changing the habitat and the microbes will adapt to this change by changing their relative abundances and changing their diversity richness. So that's one important part. The other part is that the microbes, we have learned a lot about this, they do play a big role. Give you one example, the whole complex of metabolism of tryptophan. So tryptophan, essentially amino acids that we all have to consume as humans to stay healthy, but there's various ways that this molecule gets transformed in the gut. Some by cells within the gut, but the microbes always play a big role in influencing that process. So it's well known that one metabolite is serotonin, so the microbes play a big role in stimulating certain cells in the gut. An enzyme that's there that transforms tryptophan into serotonin, so then it's stored in the gut.

Emeran Mayer:

And then the microbes also have an influence of how much of the serotonin is being released. Another metabolite of tryptophan is kynurenine. Unpronounceable name but very important function. Where serotonin is the good guy, kynurenine is the bad guy. And again, the microbes have a big influence on how much of the tryptophan is converted to serotonin versus the tryptophan. So under chronic stress for example, you get a decrease in a particular group of microbes, the lactobacilli. And that lactobacilli play an important role in regulating this conversion from tryptophan to kynurenine and serotonin. So if you decrease the lactobacilli that will influence, there will be more kynurenine produced. And kynurenine can get into the bloodstream, can get through the blood brain barrier and cause neuroinflammation and neurodegeneration if it's chronic.

Emeran Mayer:

And then there's the third one which is the so called indoles, it's the third main metabolite. And that's a family of chemicals that have now been implicated, and that's really interesting, in several of these brain diseases. So from autism spectrum to Alzheimer's disease and possibly even Parkinson's disease and also depression. So a similar chemical that only the microbes can produce that has now been implicated in a variety of these brain diseases. And the reason I find this interesting because it may be this relationship between what the microbes do and a particular psychiatric disease. It may be less specific for a disease, it may be that it just compromises our brain homeostasis and makes it more vulnerable. And depending on your genetics that it breaks down in some ways, either depression or in older age, neurodegenerative diseases. And there's a third thing that the microbes are involved in the regulation of gut permeability and that has to do with the mucus layer that the microbes can produce which insulates the immune system from the microbes in the gut. And so if that barrier is compromised, there's immune activation in the gut first, and then that can spread systemically throughout the body to the brain.

Emeran Mayer:

So now we have several mechanisms that probably interact with each other and it's really just the beginning. I would predict in 10 years from now we don't only have two mechanisms, we're

going to have 10 or 50 that all interact with our brain and with our genetic vulnerabilities to cause certain diseases. So it's very exciting. I think we have made a big progress in this field. But it's too early to say, well let's take this one supplement and that will take care of it, or let's take this probiotic and that will cure our autism spectrum disorder.

Kirkland Newman:

Unfortunately yeah, there are no quick fixes. So just to recap, essentially you were saying that depending on, you were saying, under stress or due to different genetic conditions, the same amino acid, so tryptophan, can either convert to serotonin or to kynurenine or to indole. And depending on which way it converts, it'll have a different effect on your brain. Either a positive one or a negative one. And that mechanism is mediated by stress. So the stress affects your gut microbiome, reduces the number of lactobacilli, which then creates that change in the way that amino acid is metabolised.

Emeran Mayer:

Yeah. And then these metabolites send feedback to the brain. This is what I said in the beginning. You have to always look at it as a circular system. And that makes it also hard to study because if you intervene at one point it will affect all the other nodes within that system. So almost a revolution has happened through the microbiome science that you have to look at microbes as not individual players that act independently like a pathogen, like an toxigenic E.Coli organism, but it's a network of microbes that interact with each other and with other parts of this brain-gut microbiome system. And my prediction is, and this is happening fairly rapidly, in about 10 years all the research will go this direction. That we try to understand these complex systems in our body in terms of systems biology and we will be dependent on artificial intelligence of making sense of all these enormous quantities of data that we now can collect. That's partially the reason why this field is moving rapidly, because the technologies to analyze things have become cheaper and cheaper, more and more sophisticated and you can no longer publish a paper with a sort of simplistic approach that you could have done 10 years ago. And then that's going to be even more so in the future.

Kirkland Newman:

Take everything into account. And then the other mechanism you were talking about was how depending on your gut microbiota that can impact the permeability of the intestinal barrier, which can then cause systemic inflammation, which can then cause neuro inflammation. I heard you in another podcast say that you don't believe in this concept of leaky gut and yet in your book you do talk about leaky gut and intestinal permeability. So what is your view? Because leaky gut has been adopted by a lot of the naturopathic community as a big cause of health issues. So what is your view on this leaky gut?

Emeran Mayer:

Yeah. It's an interesting phenomenon. This term leaky gut was mentioned to me by patients long before there was any science. It always surprises me how prescientific concepts come up before science is actually looking at it closely and before there's really good evidence. It's a general phenomenon. And I've learned to be open minded when I hear a new concept like this. To not

immediately reject it. I think what I've rejected is gut permeability is relatively easy to measure in animal models. When isolated system, you take a piece of gut and you put it into a, it's called an Ussing chamber, and then you can quantitate how much goes through the lining. So there's been that science we've had, and I think a lot of the practitioners have jumped on this early science. It's much more difficult to demonstrate this in human subjects.

Emeran Mayer:

The tests that we have in humans that have been used in animals for example, do not allow you to differentiate where this leakiness is. Is it in the small intestines, in the large intestine? So no regional separation. We also cannot say is it, as many practitioners would say that you have these holes in your gut where the microbes get through and then get into your bloodstream, so that's not the case. I think the much more likely phenomenon is, as I said earlier, that the change in the thickness and quality of the mucus layer is the key determinant because that layer separates your trillions of microbes from the lining of the gut which has these sensors from certain immune cells, dendritic cells. So you don't even have to get through the epithelial layer. Microbe doesn't have to get through it. It's just if it comes in contact with these sensors, then these sensors will transfuse that across the gut wall into the immune system of the gut. So there's probably all these stages. The earliest stage, just the thinning of your mucus layer that allows some microbes to get in contact. So you have mild low grade immune activation.

Emeran Mayer:

But as a gastroenterologist we're dealing with patients who have inflammatory bowel disease, which is a true inflammatory, or celiac disease, is a true inflammatory changes in the gut. You see ulcers and inflammation of the biopsy. White cells. You don't see that with a leaky gut. You don't see holes and ulcers. I think you have to be very careful to differentiate this from what happens with a compromised diversity and richness of the gut microbiome. Then the transduction of information from these microbes to the gut based immune system. It's not that simple. Always when I give a talk to an audience, we know about 60% of people now in the US are overweight or obese and a significant percentage of these people have metabolic syndrome. So type 2 diabetes, hypolipidemia and others. I always say there's a good percentage in this room that have metabolic syndrome, that probably have a compromised mucus layer of the gut, compromised microbiome diversity and richness, but that doesn't mean all these people have inflammation in the body.

Emeran Mayer:

They just have this compromised gut health problem, which in combination with the wrong genes and the severity and the duration will produce these downstream health effects on the brain.

Kirkland Newman:

That's very interesting. And then in terms of the ways that our gut and our brain communicate, because one of the key takeaways from your book to me was this sort of bidirectional communication between the gut and the brain, which is fascinating. And there are different ways that this happens. Now, through essentially the types of microbes that the metabolites produce by

these microbes, inflammation, the vagus nerve, endocrine cells. So hormones, neurotransmitters. So there are all these different signaling mechanisms between the brain and the gut. And I think if you can explain to us, what are the key signaling mechanisms that you see to be the most significant from our gut to our brain? And one of fascinating facts that you mentioned is that 90% of the communication for instance from vagus to the brain is afferent, so from the gut to the brain. And only 10% is from the brain to the gut. So what are the key sort of signaling mechanisms and ways that our gut and brain communicate?

Emeran Mayer:

So starting with your last point that you mentioned, the reason that we have only 10% of the vagus nerve and a small percentage of the sympathetic nervous system going from the brain to the gut is because the gut has its own nervous system. The enteric nervous, or little brain of the gut, which is the third branch of the autonomic nervous system. And that system can pretty much run all the gut functions by itself. It doesn't need the big brain. The brain kicks in if there's some situation going on in the body or outside of us that turns on the alarm bells and then the brain basically interferes with the gut's own nervous system. So that's why it doesn't need this constant input from the brain. But if you're chronically stressed or if you're depressed, this top down effect will be altered chronically. So on the other direction signaling from the gut to the brain, the vagus nervous has received most of the attention because in animals it's sort of easy. You cut the vagus nerve and then you'll see the defects that you've observed before, are they gone? So for most phenomena the vagus nerve has been implicated. We now know from most recent science, it's not just one nerve. The vagus nerve has multiple different subtypes of fiber, all of which have different receptors.

Emeran Mayer:

Some fibers in this bottom to top signaling component of the vagus nerve have receptors for this chemical that is produced by a certain microbe. So there's probably hundreds of these different fibers. So it's very complex. It's not just that everything goes in the same pathway. And then all this different information gets to the vagus' nucleus in the brain stem where all of this is then synthesized. It's a little computer that synthesizes and integrates everything. And then it sends it off to higher centers within the brain. So the vagus nerve, clearly a big component. The second one I would say are these, what you could call, endocrine pathways where the microbes basically piggyback onto or use the cells in our gut, these enterochromaffin cells and enteroendocrine cells. Gut is the biggest endocrine system in the body. And the microbes have receptors for their own chemicals on these cells. So 10 years ago if you'd asked me how our gut-brain communication's happening I would say yes, we have all these cells in the gut and they signal to the brain and that can explain everything that we need to know for our gut health.

Emeran Mayer:

So in the meantime we know the microbes take advantage of all these mechanisms and use them for their own signaling. These endocrine pathways are another one. And then the third one is the immune pathway, as we talked about. So microbes can activate the gut based immune system. That may be a fairly general effect that's not a specific microbe but it's just a decrease in the diversity and the abundance of certain, for example, mucus producing stimulating microbes,

akkermansia and prevotella have been implicated in this. Microbes or microbial taxa that in developed countries have decreased in their relative abundance as compared to in Africa or in South America. The decrease of these microbes that play a role in this mucus production and prevention of immune activation is clearly the third pathway. I'm convinced that all three of them interact with each other. So these are not channels that are insulated by a cable and don't cross communicate. They're all cross communicating with each other and it's the integration of these signals that-

Kirkland Newman:
That matters.

Emeran Mayer:
Yeah. That matters.

Kirkland Newman:
And just to recap, so the three systems, the three main ways of the gut communication with the brain is through the different nerves that go from the gut to the brain. The most popular or well known being the vagus nerve. The largest essentially. And then the endocrine cells which are essentially, and you say in your book, it's fascinating, that if you take all these endocrine cells and if you put them altogether it makes an endocrine organ which is larger than all the other endocrine organs such as the thyroid and the adrenals and the ovaries and testes, et cetera. So I found that fascinating. All the different endocrine receptors and cells in the gut. And then the third system is the immune system and inflammation. Is that correct?

Emeran Mayer:
Yeah. I may add something to it because this has become a hot topic in brain health. So there's another type of signaling where the microbes, we know diet is a big influence and the microbes do a lot with our diet and that influence is there, but another pathway is converting molecules that our body produces. For example, bile acids. Bile is produced, we learned in medical school, that this is mainly for better digestion and absorption of fat, but bile acids and bile acid receptors are everywhere in the body and the brain. And the microbes play a big role in that, so the bile that we produce, secreted into the small intestine. First stored in the gallbladder and then the small intestine. Then the microbes convert those bile acids with a certain enzyme that they possess into bile acids that are being reabsorbed in the small intestine and get back into circulation.

Emeran Mayer:
And so you have probably hundreds of different types of these bile acids. Some of which get into the brain. Some are beneficial. Others are harmful. And the ratio of some of these bile acids to each other have been implicated, for example, in cognitive decline in Alzheimer's disease both in animal studies but also in postmortem tissues in the brain. Where people have found these secondary bile acids that only the microbes could have affected because the brain does not have these enzymes to do it. So that's a similar principle in other body produced substances. Sex hormones, estrogen obviously metabolises in the liver, then excreted with the bile into the small

intestine. Microbes have another enzyme that they can modulate certain of these estrogen molecules so they're re-absorbable and get into the systemic circulation. The amount of this liver-gut microbiome brain circulatory system is dependent on what types of microbes you have. So not everybody has that same effect. Somebody may have a high ability to convert these estrogen molecules into absorbable signalling molecules to get back into the blood, whereas other women may not have that mechanism so the level in your blood of estrogen particularly post-menopausal is influenced by what type of microbial community that you have. And the same for the bile acids.

Emeran Mayer:

So we get all of a sudden a full integration of our own biology and physiology with the microbial ecosystem that we have inside of us. These are things I find extremely exciting because they get us way beyond just a simple concept of leakiness of the gut.

Kirkland Newman:

Absolutely. And so would you say, listening to you, that all the different mechanisms, the most influential factor really is the microbiota. So whether it's the vagus nerve, or the endocrine system, or the immune system and inflammation, the main mediators of this are the gut microbiota and the main sort of variables which will impact how these systems respond and how they influence our bodies and our brains, the main factor is this gut microbiota and the nature of it?

Emeran Mayer:

I said several times, in combination with our genetic makeup.

Kirkland Newman:

Okay.

Emeran Mayer:

Somebody may have a very compromised microbiome but have very healthy genes and longevity genes and with parents that lived into their hundreds. That individual is unlikely to develop any serious disease from it. And I think we tend to forget this. It's the combination of the vulnerability of genes with, you could almost say, with the microbial genome. That is this determinant.

Kirkland Newman:

Despite the sort of emphasis on epigenetics and how we're now finding more and more that epigenetics is actually more important. So gene expression is more important than our genetic makeup. So presumably the microbiota is incredibly important in that epigenetic expression of our genetic makeup.

Emeran Mayer:

Absolutely. Again, from animal studies we know that early on in the developing gut and developmental phase of the in the first thousand days in life. A lot of epigenetic programming is happening. And yeah, so when I say genetic vulnerability factors, it's genetics and epigenetics. I don't separate that. Good example, we worked in this area for some time in the past. This early adversity which has been shown to have epigenetic effects on the glucocorticoid receptor. And so whatever happened to you early on with trauma early on in life in combination in humans with the support systems and the systems that foster resilience which also probably act through epigenetics determine then your vulnerability later in life. It's the genetics and the positive and negative influences that modify this gene expression through epigenetic mechanisms.

Kirkland Newman:

Fantastic. And so I think that brings us nicely to the key factors that can disrupt our gut microbiome and you name them in your book incredibly well but you harp on about two main ones, and there are a whole bunch of other ones. So tell us, what are the key disruptive factors to our gut microbiome and to our gut?

Emeran Mayer:

I think it's important to separate this into different phases of human life. So clearly early in life I would say fundamentally these first thousands days. Within the terms of brain development in humans that goes on age of 18 and even into the early 20s. So that early phase, these first thousand days, play a huge role and starts in utero. It starts with the health and the diet and the stress level of the mother. All of which have been shown to influence the development of the infant's gut microbiome. The mechanisms, all of them affect the mother's gut health, which then has effects either through immune activation on fetal development, or when the infant is born. So the vaginal microbiota of the mother, together with some of the intestinal microbiota that the newborn comes in contact with during going through the birth canal, all of these are influences that shape and program the microbiome early on.

Emeran Mayer:

And you often forget it does start in the mother. Like in autism spectrum disorders. This doesn't develop in a child after delivery. There are already brain changes in the fetus and in the developing brain in utero, which may be related to these mechanisms I just mentioned. Then we have a fairly stable phase until puberty, always a big time of change for all the bodily systems with sex hormones kicking in and changing. The tuning of the autonomic nervous system and gut microbiome, as well our diet. And then in the adult, I would say diet and the ingestion of xenobiotics, all the chemicals that we ingest. And the number of these chemicals is obviously enormous from medications to all kinds of things; pesticides that are in our diet, in our air, in our water. That's probably the main influence that we are exposed to, which can be influenced fairly easily with a healthy diet. So that’s why I always say, we can't reverse the damage that has been done early on, and we can't blame our mothers for the things that happened to them during pregnancy. They had no idea. Still today there's no educational effort to teach mothers before they become pregnant or during pregnancy of all the potential influences that obesity or an unhealthy diet has on their developing child.

Emeran Mayer:

But we can do a lot about the adult diet. I forgot, in the early phase, in this program phase in the first thousand days, antibiotics obviously play a huge role as well. There's studies that have shown that in the first two years of life the typical child in the US is exposed to something like eight courses of antibiotics, which all of them, or 99%, are unnecessary because these children had viral infections. The parents are very concerned that this is something more serious and got their pediatrician to prescribe antibiotics. This is a huge influence in a developmental phase of the microbiome, if you basically provide toxins that suppress the normal development. But I think it's extremely important to say there are things that happened early in life that in retrospect we can't change. We can do it through education. But what we can change as adults in our diet.

Kirkland Newman:

Absolutely. And I think you mentioned in your book that essentially our diets and the intake for instance of diets high in animal fat can be detrimental to our microbiome and that plant based diets are much preferable. You have a large chapter on sort of the Mediterranean diet and the importance of the Mediterranean diet. But in terms of other things that disrupt our microbiome you talk about stress, sort of chronic stress, trauma, adverse childhood circumstances, even negative emotions such as sorrow, anger and fear which I thought was very interesting. Obviously genetics, toxins and pollutants, antibiotics you mention. And also modern agriculture and farming methods, monoculture, pesticides, antibiotics. And then you also mentioned pathogens such as viruses, fungi, parasites, et cetera. So talk about sugars and artificial sweeteners, emulsifiers, processed food products which are very disruptive to the microbiome. So this seems like a whole list of things from our modern life which are damaging to our microbiome. What would you say are sort of the key ways that we can protect ourselves from all these disrupters?

Emeran Mayer:

So first of all I would say, listening to you rattling down this list that I brought up in my book, you would think that it's hopeless. We are being bombarded with all these negative influences. But I think we always have to keep in mind the microbiome is an incredibly resilient system. If you imagine there's trillions of organisms communicating with each other and all kinds of chemical, biochemical loops of regulation. It's incredibly resilient. Most adults can take a 10 course of antibiotic and it will make a dip in their diversity and after a couple weeks it's back to normal which is amazing. Same thing. We can go through a gastroenteritis. We think we're dying, our gut is completely emptied and gotten rid of everything good in it, and it's not the case. I think that's an important point. It's very resilient. If you look at it as sort of a larger perspective, many of these influences have been exaggerated during the last 75 years of the changes developed societies have gone through. On top of that, industrialised agriculture, the massive influences of what I call the medical pharmaceutical industrial complex. It always has to do with industry.

Emeran Mayer:

From the last 75 years we have taken things we have done on a small scale and amplified and multiplied them hundred fold. And I think that influence has caused damage. Possibly

irreversible. So gradual decrease in diversity, gradual extinction of certain strains and species that we still have. If you look at the stool samples from primal people that live on the Orinoco river or in the Rift Valley in Africa, we've lost some of these strains permanently because of all these negative influences. We don't know which one is the most important one. But certainly this has had a damaging effect on our microbiome. And probably the reason that we're currently in this, we all talk about the pandemic, because I think our attention span can only sort of focus on one disaster at a time so now we've pushed away climate change and we pushed away, so the current disease epidemic that the western world is living in is amazing. Even though we live longer, we're sicker and sicker with all these diseases that are related to obesity and metabolic syndrome and hypertension.

Emeran Mayer:

I recently read an article. I think it was in The Lancet or in The New England Journal that based on the current practice guidelines for the intake of statins, 100% of men over 65 years should be on statins. So the way we keep ourselves alive, but not dealing with the root cause of these problems, is inundating everybody with medications. So we don't die from these diseases anymore as often as we did in the past, including cardiovascular disease, but more and more people have it.

Kirkland Newman:

Completely. And one of things I love is your analogy of the ecosystem, and the fact that we're losing diversity in our ecosystem outside, that we're losing species, that we're losing forests, that we're losing the balance in our ecosystem. And in the same way in a parallel we're losing the balance in the ecosystems of our gut. And you talk a lot about diversity. Just as we know that diversity is essential for the wellbeing of the planet and agriculture and the bees and the birds, et cetera, we also know that diversity and abundance of microbes is essential to our health. And in the same way that we've been destroying our planet, we've also been destroying our microbiota. And it's interesting if you look at the parallel for the last 75 years as you mentioned, the increase in antibiotics, NSAIDs, the birth control pill, pollutants, chemicals, all these toxins, whether they're pharmaceuticals or whether they're pesticides, have really disrupted the microbiota. And I wonder, you mentioned the increase in chronic disease, absolutely, but also from a mental health perspective, there's been a complete increase in mental health issues, whether it's autism, Alzheimer's, which is sort of epidemic proportions. Depression. Anxiety.

Kirkland Newman:

Now some people will argue, well that's because they're more diagnosed. But there is no doubt that there's an increase in numbers as well. And if you track that against the health of our microbiome and the aggressors to our microbiome, there's a very clear correlation I would think.

Emeran Mayer:

The autism spectrum disorders, that's a particularly striking example because of the increase. I think now one in 50 newborns is diagnosed with autism spectrum disorder. Yes, the diagnostic criteria have changed and maybe that number is not quite as high if you did it with the old definition, but there's absolutely no question that there is a relationship. It is interesting that

autism risk genes are present in about about 10% of the population. It's so striking. So there must be something advantageous that these genes have had during evolution, otherwise they would have disappeared. But the fact that this has been, again, in the same time period, the last 75 years, has been increasing continuously. And we know now at Caltech, we've done some key research in this area, there's some amazing findings that we can link microbial factors with brain changes and behavioral changes. Again, this research in my opinion has not done enough looking at this in the pregnant mother, where I think a lot of this damage starts.

Emeran Mayer:

There's no question. It's harder with something like anxiety because we're also living in a world that is, particularly with this interconnectedness and the 24 hour news cycle and what we have gone through in this country with the political news in the last four years and still going through. If that's not anxiety creating, you would have to be a total stoic individual not to be affected by this.

Kirkland Newman:

But the resilience of our guts. There will be anxiety. And there's an increase in anxiety. But I mean I've read some studies that say that different types of microbes in the gut can help increase our resilience to stress. Whether it's I think bifidobacteria, infantis, lactobacilli, I can't remember, but you might know. But I agree, we're bombarded by stress. But would we not have an easier time of being resilient to that stress if our gut microbiota were in better shape?

Emeran Mayer:

Yes. I would say it's easy for me to give a definitive answer if you ask me anything about a specific diet and the consequences, for example on these bile acids in the brain and the cognitive decline. So we have more solid evidence that that's the case.

Emeran Mayer:

We have some evidence. The latest type of studies are being done that you take a fecal microbial transplant from a depressed patient into a germ free mouse and then this mouse model will develop depression-like behaviors. We have several of these studies now, and the microbes that are responsible for this have been identified. There are some discrepancies within studies but we're getting closer to that. That there's clearly that influence. But because depression's such a complex disease, to tease out what's the most important piece to it, I certainly think that, and this is more a gut feeling than really evidence -- There's some evidence from Australian scientist Felice Jacka about this, she created this whole new field of nutritional psychiatry -- that a largely plant based diet has a beneficial effect over and above the conventional treatment of patients with depression.

Emeran Mayer:

It's definitely something if patients come to me with depression, I would always include diet in it. I would tell them we don't have as much data from human studies as we have from mouse studies, but I would say right now, given what we know how unhealthy the western diet is and how much it's related to this systemic immune activation and generation of these unhealthy

tryptophan metabolites. I would say you have to include the dietary part. If that dietary recommendation also includes fermented foods. Again, the studies with probiotics are not as solid as you would need for registration of a new drug, or the vaccine now. It's far from that rigor. But the consumption of fermented foods has been with humans for thousands of years, and I would bet my money on it -- and again, it's like many things, our gut feelings -- that the incorporation of multiple naturally fermented foods, including fermented dairy products, fermented plant products should be part of a therapeutic approach to a compromised gut microbiome.

Kirkland Newman:

That's great. And I think what I'd love to do is ask you for your key recommendations for how to nourish our gut so that we can then nourish our mental health. What are the sort of tried and true pieces of advice you can give our listeners? And just before that I also wanted to talk about the Parkinson's study that you mention in your book which I thought was fascinating showing that Parkinson's, they found, starts in the gut essentially. Or at least one important study showed that it started in the gut with the disrupted gut microbiome. Then that impacts the brain and they think there might be a mechanism where it goes really from a disruption in the gut to the brain. And I wonder if they've found similar mechanisms for instance in Alzheimer's, or is it just Parkinson's?

Emeran Mayer:

Well, there are certain similarities. Early changes in the nervous system occur in the brain stem. There's an area called locus coeruleus. It's the main noradrenergic center within our brain. And both in early Alzheimer's and in Parkinson's disease, early changes in that brain stem area have been identified. And they can occur years before other neurological symptoms come. Now, the unique thing about this part of the brain stem is it's very close to the vagus nucleus within the brain and so it's the site of the brain that first receives these signals from the gut and from the gut microbes. So my feeling is, even though it's been worked out the best for Parkinson's disease, the evidence is the strongest that a subset Parkinson's disease patients it clearly starts as a gut problem and enteric nervous system problem and is then transmuted. So these Lewy bodies, these molecules then migrate through the vagus nerve from the gut to the brain.

Emeran Mayer:

Certainly in Alzheimer's disease, I was telling you about, there's also been these brain stem changes been identified. But also we have these other mechanisms, like this bile acid signaling. But I would say for both of these diseases that, or probably for all the neurodegenerative diseases, I think the gut microbiome plays a major role. My guess is we're closer to understanding this for Parkinson's. The good thing is it could be 12 or 14 years from your first symptoms in the gut, like new onset chronic constipation or the sleep abnormality which is related to the brain stem changes. You have 12 to 14 years before this whole syndrome develops. So the possibility for intervention is enormous. So if we found that a dietary intervention, going onto a Mediterranean type diet, it doesn't have to be vegetarian or vegan, there should be some fish and poultry in the diet as well. But if we found that that intervention, if you're really rigorous and combine it with other things like exercise, always comes up as another way of influencing the health of the gut microbiome.

Emeran Mayer:

If you could delay the onset of the neurological findings by even five years or 10 years, it would be enormous. So we may not be able to cure but we could delay the onset and that, I think, is very realistic even now.

Kirkland Newman:

Which is great. And then in terms of the things that improve the health of our gut microbiome, you mentioned exercise and I've heard that before. And I've always been curious, why is exercise good for our gut? I mean, I can see diet, but why is exercise so good for our gut? What's the mechanism?

Emeran Mayer:

So exercise, you have to differentiate. Extreme exercise, endurance exercise, ultramarathons, triathlons, I don't know if you do any of those exercises yourself.

Kirkland Newman:

As little as possible.

Emeran Mayer:

They're actually unhealthy. Athletes that do this, I have a few in my practice, they get gut symptoms. They get bleeding, colitis. It's been shown their gut permeability increases so they develop a leakier gut. There's immune activation. So all the negative things, the body basically perceives that as a chronic stressor, as a severe stressor, and reacts in that way with sympathetic nervous system activation. So it's not healthy, even though a lot of people think running marathons will necessarily have a health benefit.

Kirkland Newman:

So it's due to the stress response essentially because it creates a stressor on the body which the body interprets in the same way as it could a psychological stress.

Emeran Mayer:

Exactly. If you don't know about exercise, it's the regular moderate exercise that has been shown to have a beneficial effect on the diversity and the richness of the gut microbiome. And the changes are actually very similar to a healthy diet. It's interesting that somehow the microbes get the same message from if you exercise regularly as if you eat healthy. So if you do both together, obviously that will synchronise the beneficial effect. What exactly the mechanism is, if people that exercise regularly eat healthier, have less systemic inflammation, send a more balanced autonomic signal to the gut, which I think is likely.

Kirkland Newman:

Understood. So in terms of really healing our microbiome, you mentioned diet, diet, diet, and especially the Mediterranean diet because of its antiinflammatory and antioxidant properties. Is that correct? And also its high fiber?

Emeran Mayer:
Yeah. I go into this in great detail in my new book. There's two things. There's always a lot of good things in plant based food, particularly if it doesn't necessarily have all the evils of industrial agriculture. The chemicals on it and the pesticides and the depletion of nutrients because the way it's grown with chemical fertilizers. But if you assume that diet comes from organic agriculture, ideally what we now say regenerative organic, that you actually put things back into the soil and its microbiome that enriched what the plant then can extract. You have two factors. One is the fiber molecules. And there's not just one type of fiber, there's thousands of different fiber molecules. So the more varied the plant sources are, the better for your gut microbial diversity. And that's easily understood because microbes are specialised to what they can break down and what molecules they can break down. So if you bombard them with all kinds of different fibers or vegetables and fruits, different types of seasons or the seasonal variation, the more you force that system to become more diverse.

Emeran Mayer:
The second one is fiber. Certain fibers also have a beneficiary effect on the gut itself. Like on secretion and fluid retention and transit time. So you will have an optimal transit time in food that you ingest from the stomach to the large intestine, which has a beneficial effect. So this whole thing about, it's another one of my dislike terms, SIBO, small intestinal bacterial overgrowth, which in my opinion is way, way over utilized. But the fact is, if you have stasis in your small intestine because you don't have these fasting patterns of contractions that clean out your small intestine every 90 minutes, then you will have larger populations of microbes in your small intestine where they don't belong. Fiber will have the same effect. It will expedite the transit through your GI tract.

Emeran Mayer:
The other component are these polyphenols. You mentioned antioxidants. Polyphenols are these very large molecules. Multiple rings of phenolic compounds that are composed into this very large molecule that is non absorbable in the small intestine. We don't have the enzymes that break it down, and we don't have the microbes in the proximal small intestine to break them down either. So what happens with these molecules, they go down into the end of the small intestine into the large intestine, and they interact with the microbes. There are prebiotics that are food for the microbes. The microbes convert them into smaller molecules so we then absorb and they get entire system circulation. And the third one is, we call it microcidal effects, so they have negative effects on bad gut bacteria that we shouldn't have there.

Emeran Mayer:
Unfortunately in the lay literature in the press, people always talk about antioxidants. I've talked to several experts on this. We have enough antioxidants that our body produces to keep us healthy. And the antioxidant effect is only seen if you put these polyphenols together with cells

in a test tube where there's no intestine in between. So yes, then you have an antioxidant effect, but if you measure them in the blood of people that eat a lot of fruit, you won't see them. That's called a lack of bioavailability. So only less than 5% of these plant beneficial molecules actually show up intact in the circulation. But it's a rapidly growing field. What the microbes make out of these polyphenols are highly health beneficial and health promoting. And it may be a major beneficial effect on Alzheimer's disease, cognitive decline, and all these other diseases that we're dealing with. Polyphenols are the pharmacy of the plants. They use them to defend themselves against UV light and drought and pests and infestations. And it's a wonderful thing, emphasising this holistic concept that we're all part of one health concept, that this pharmaceutical system of the plants also has these benefits for our own system.

Emeran Mayer:

So to me, that's one of the most exciting things. And definitely, if you just take fiber and polyphenols you have enough to explain the health benefits of a plant based diet.

Kirkland Newman:

And it's interesting because I was interviewing someone the other day on the mitochondria and we were talking about hormesis, which is sort of beneficial stress, and he was saying that the way polyphenols really work is through hormesis. So they create a slight stress level in us which then causes our endogenous antioxidant system to kick into place. And I thought that was fascinating.

Emeran Mayer:

That's an interesting concept, and I would say this field is at an early stage. It's very complicated because you start out with about 8,000 different molecules that would be called polyphenols from plants and then the microbes break them down into thousands of additional molecules from the parent molecule. So to understand what these individual molecules do, they act as a combinatorial system that you need hundreds of different mixtures to get the health benefit. So it's very difficult with our current scientific methods to understand exactly the mechanism. And this is an interesting one that I hadn't heard about the mitochondria, but there will be lots of potential mechanisms identified. It gets us into a totally new understanding. It's the opposite of what the pharmaceutical industry has always done, and I've been involved in this field as well in my early part of my career.

Emeran Mayer:

You want the most selective, specific molecule that targets one receptor subtype in one particular area of the brain. This polyphenols system acts exactly the opposite. It's the most diffused, generic approach to health by balancing multiple pretty antagonistic influences. Some of these things are good, others are bad, but it's the combination of those. The traditional Chinese medicine system is the closest because they have this same combinatorial understanding of medicine that it's not one substance, it's low amounts of multiple substances, partially with antagonistic effects.

Kirkland Newman:

That's why I love integrative health and functional medicine, because it really looks at the sort of whole as opposed to the individual parts, both in terms of root cause and diagnosis but also in terms of healing and treatment.

Kirkland Newman:

So I must say, you've been incredibly generous with your time and I could talk to you for hours but I guess we need to wrap up. But in order to recap, in terms of improving our gut microbiome, so plant based diet with some meat, some fish, some poultry. Exercise. Another thing that I found fascinating in your book was the effect of acute chronic and traumatic stress on the microbiota. So obviously we all know that stress is bad, but I was really interested in the impact. When you talk about cellular memory with trauma victims, people who've undergone trauma. And I was reading your book thinking, "Oh. Nobody really knows what this concept of cellular memory is." But maybe, because you talk about the microbes in your gut storing memories in a database which is then accessible to the brain. I found that fascinating and I thought, "I wonder if that's essentially how we can explain cellular memory and this memory of these traumatic experiences which is stored in our gut."

Emeran Mayer:

The memory of the microbiome, you could say it stores memories of breastfeeding for example at the earliest parts of life. It stores memories of traumatic stress of antibiotic exposure. All these things are stored somewhere in some ways. We don't know exactly how that is. And again, I just come back to this concept. Imagine trillions of organisms that function in a network that you could call a massive artificial intelligence system with memory. So I think at the moment that's kind of speculation, because we don't really have a way yet to retrieve that. But I think that's a very plausible hypothesis. We have multiple systems in our bodies and brains for cellular memory. There's systems in the brain. But I think the way the brain-gut microbiome system is organized, definitely some of these memories are generated and stored at the gut level.

Kirkland Newman:

Which is fascinating. And so we have to try and moderate our stress and use mindfulness and stress reduction techniques because stress increases gut permeability and decreases the diversity of the gut microbiota. Is that correct?

Emeran Mayer:

Yeah, and it's this interesting phenomenon that the gut has these influences. One is from the brain. One is from the diet, which links us to the external world because we incorporate all kinds of things from the external world. And then the third one is our musculoskeletal and cardiovascular system where exercise influences. It's an integration of physical activity, mental activity, but also of all these things that we incorporate from our external environment. And it's for the only system in the body that has that ability of this integration. I'm a gastroenterologist by training so people might say I'm biased to make the gut microbiome the center of my attention, but that's not the way that my brain works. I always look for alternatives and other explanations. But I've come to this conclusion that it is the central homeostatic system within our bodies, this

brain-gut microbiome system. That's why it's great that this current attention is focused so much on something that's been neglected almost completely until recently.

Emeran Mayer:

So I think a lot more will come out of this with the advances in our ability to characterise microbial function and unravel the mysteries at the brain level, what the brain does with these chemicals that come from the microbes. I think it's going to become even more important for the future. What we can do at the moment is stick with the simple things that we know. It's the exercise, the healthy mind, and the healthy diet. So that's sort of what we have to live with for now. But I would expect that very dramatic increases in our knowledge of the system will happen in the next 10, 20 years.

Kirkland Newman:

And I guess also reduce exposure to toxins and pharmaceutical drugs and toxic heavy metals, molds, all these things that can also disrupt the gut microbiota. Do you think that in, say 10 years, psychiatry will be revolutionised and psychiatrists will take into account this all important gut-brain connection and may actually test for imbalances in the gut? I mean, say the scientific advances come to where you think they're going to come. Is that foreseeable for you?

Emeran Mayer:

It's definitely foreseeable. I think psychiatry has been slow. Even though one of the leading investigators in this field, John Cryan in Ireland, has been one of the pioneers in animal models. But interesting to me is psychiatry has been fairly slow in the uptake of this and this field of nutritional psychiatry is not mainstream yet. But just things like, we talked about this earlier, the fact that similar indole metabolites for example that are produced by microbes have now been identified as being involved in different brain disorders. I think that the underlying vulnerability to develop depression, anxiety, Alzheimer's has a microbial component to it, I think that's sort of what psychiatry really has to incorporate into their disease models. It's the training of psychiatrists. With the history of Freud, who actually looked at the intestinal development phase, he was in some ways closer to that than today's psychiatry; a link between the body and organs and neuroses. But I think there's almost no way around it.

Kirkland Newman:

I agree. And one final thing before I let you go. One of the fascinating things for me is mitochondria and the role of mitochondrial function in mental health issues, whether it's depression or neurodegenerative diseases. And what fascinated me was to know that the mitochondria originally were bacteria. And for instance, things like antibiotics. So some of the same things that damage our gut microbiome also damage our mitochondria. And our gut essentially has a very symbiotic relationship with the mitochondria and that the health of our mitochondria also determines the health of our gut. Do you study that or do you have thoughts about that?

Emeran Mayer:

I don't study it. We have an institute at UCLA that looks at mitochondrial function. But I've always also been intrigued by this idea that these mitochondria are cousins of the microbes living in our gut and probably share many genetic features with them and are susceptible to the same influences. That whole area, I think that's another dimension. I've not seen that being explored in a way that you would think "it should be obvious that we have to look at this". It's not one of these topics that has reached a threshold that people think this is a major revolutionary thinking about the body. But just from what you said, I think it's obvious.

Kirkland Newman:

Yeah. That there's some correlations there.

Kirkland Newman:

Well, Dr. Emeran Mayer, you've been amazing. Thank you so much for your time. I really appreciate it.

Emeran Mayer:

You're welcome. I really enjoyed being on the show and thanks for asking me to.

Kirkland Newman:

Thank you so much and I can't wait for your new book on the gut and the immune system to come out in 2021. What is the name of that?

Emeran Mayer:

It's The Gut-Immune Connection. It's available for pre-order. So for people that can't wait, I would recommend to pre-order it now. It will go into the same areas that we discussed throughout this conversation and obviously expand it in greater detail.

Kirkland Newman:

Fantastic. So The Gut-Immune Connection. Dr. Emeran Mayer, we'll put all that in the show notes. But thank you so much for your time and can't wait for your next book.

Kirkland Newman:

Thank you so much for listening to the MindHealth360 Show. I hope that we've helped you realize that mental health symptoms have root causes that can and need to be addressed in order to sustainably heal and have given you some ideas about steps you, your loved ones, or clients may take to start their healing journey. Please share this interview with anyone you think may find it helpful and don't forget to subscribe to keep up to date with our latest interviews on integrative mental health. If you want further information, please go to www.mindhealth360.com or find us on social media. This information is for educational purposes only and is not intended to diagnose or treat any disease or to replace medical advice. Please always consult your healthcare practitioner before discontinuing any medication or implementing any changes in your diet, lifestyle, or supplement program.