Your Microbiome: The Gut-Brain Axis and Longevity Transcript

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Introduction to Dr. Emeran Mayer

– Welcome to another episode of Reversing Inflammaging Summit Body and Mind Longevity Medicine. I'm your host, Dr. Stephen Sideroff. And I've been looking forward to this particular episode for a long time.

It's actually a U C L A colleague, Dr. Emeran Mayer is a gastroenterologist, a neuroscientist and distinguished professor, research professor in the Department of Medicine, Geffen School of Medicine at U C L A.

He's also uh a Oppenheimer Center for Neurobiology of Stress and and resilience director, executive director and founding director of the Goodman Luskin Microbiome Center also at U C L A. Amon is such a pleasure to have you here.

Welcome. – Yeah. Thanks for inviting me Steven and we look forward to this conversation. – Yes, thank you. And by the way, as I mentioned, you know, I've heard you speak before.

So this is this is a piece of the whole puzzle around longevity that that really is very important. Can you just give us a little bit background on how you got interested in the area that of your research?

– Yeah, I mean, I could give you the long version, you know, which I'm still looking back now. I'm kind of amazed how it happened. I mean, from an early interest in mainly in psychology and the social sciences when I was in college. And then just because of my, um, you know, ex excellent G P A people talked me into it.

You have to go to medical school, which I went into without a lot of enthusiasm. But it was always the idea I would ultimately go into psychiatry. So, you know, that continues to interest me and it pursued me when I picked my thesis advisor in, in in medical school. Um I wanted somebody who, where I could work on the interaction between the brain and the body in some ways.

And that was sort of before this became sort of really acceptable to the mainstream medicine. But I did find somebody after a long search was doing research, um fundamental research on brain heart interactions, um sympathetic nervous system, regulating blood flow and coronary blood flow.

From Psychiatry to the Brain-Gut-Microbiome Field

And then after a uh an X turn ship at the mass general, um in gastroenterology, it shifted myself from The clinical specialty of gastroenterology was just more interesting to me than cardiology at the time, this was in the late 70s.

And then, um from that time on, I pursued that original interest in mind body, which went back right to my late teens. I would say, I don't know why. Quite honestly, I don't have any, any symptoms like that. So a lot of people get to that point because they have some problem. I did not.

But I've initially focused on irritable bowel syndrome, which was sort of the, the most likely that people would accept, you know, brain gut interactions.

But then, you know, with a, With the Microbiome Revolution, about 10 plus years ago, I realized this has a much wider impact. This the spring got microbiome interaction than, than IBS symptoms. And so really branched out and was lucky to get, get on either SP I or CO P I on a variety of grants from Autism Spectrum Disorder, too early cognitive decline. And IBD with that system played a role. So then I sort of left I B S behind I that, that to me was a lot more interesting this bigger picture and have sort of been pursuing this ever since and founding this, this usually microbiome center was driven by that same, the main impact, I mean, the main emphasis is on, on brain gut microbiome interactions in that center.

– Yes. So before we dive into that question, I would love for you to give our audience your perspective on the aging process and longevity. – Well, so I, you know, I have to say that I'm not a longevity researcher but with um studying and, and realizing the the deep involvement of the brink of microbiome system system, I call it because it's, it's not an access, it's not a one directional interaction of the brain with the gut or the other way around.

It's these multiple feedback loops that connect, you know, the brain, the immune system, the gut microbiome, what I like to call the God, connect them um with each other. And we know now that one outcome of these interactions, if, if they're not, if they're being perturbed, chronically is low grade inflammation and and obviously, low grade inflammation is a key factor in uh in aging, in many processes in processes, but in aging.

So all these diseases that we see that I think are related to that. Um As Hippocrates said, all diseases start in the gut, I mean, wasn't quite correct but almost um I say all the chronic diseases start in the gut. Um and obviously, these chronic diseases like chronic non alcoholic liver disease and colon cancer and, you know, I B D and early cognitive decline, coronary disease, um they all affect our major, major factors in in longevity. So I would say now there are studies that have looked at a few studies that have looked at the the changes of the brink of microbiome system in aging.

They, which would obviously expect because I mean, the brain changes, um um they got to a lesser degree but um that with aging, the signaling, the baseline of the signaling um changes and but what's come out, you know, of these researchers, the and then there's like always in this field, there's some diverging opinions on this but that somebody who lives who lives a healthy lifestyle with exercise and healthy diet, particularly the microbiome will not change that dramatically.

Well, we have initially thought are these age related changes in the microbiome really to the age related changes in these lifestyles for many people.

And so on the other hand, you could say, you know, can you and there is evidence for that with modifications of these various lifestyle factors that affect the bring up microbiome system. Many studies have shown that you can add 10, 5 to 10 disease free uh years to your life. So I think there's clearly the data that not just that you can find it um in if you do studies, but also that interventions um you know, have a, have a major impact on longevity.

Systems Biology and the Gut Connectome

– Well, so to begin with, that's great news that it's a variable of lifestyle because that's something that everybody has some control over. But let's take a step back and you know, you've talked about the bidirectional interactions between brain gut, the immune system and how they form a system for essentially for homeostasis. Can you explain how that works?

So we have a foundation for our conversation. – Yeah. So the the early concepts you know, that, that, that we had and that it's still prevalent really amongst um you know, physicians and researchers that there's the brain gut axis that, you know, the brain affects things that go on within the gut.

Then there's a lot of people, particularly amongst my colleagues and in gastroenterology to think the opposite way. It's, it's all in the gut that affects, you know, the brain.

But in, in reality, as I mentioned earlier, you know, we are in the midst of a paradigm shift in, in science, in society as well. But in focus on science that we look at at complex systems, not, not identifying, you know, a particular receptor subtype or a particular node in the system. But, and, and that has led to the change in the Norman Clay Church, for example, we don't talk about brain regions where we talk now about the brain connect.

Um I like to talk about the gut connect um because it connects immune cells, nerve cells, endocrine cells and epithelial cells together. Um And, and then, you know, we like we don't talk about microbiota, but we talk about the microbiome with all the genetic information and these systems that all systems, you can understand all these entities as systems, but they're not independent. So they're part of a larger so you can scale it up. And ultimately, you know, there's, there's some people have have shown us that this, this scaling up to different levels was even

beyond the body. I mean, there's networks in our social environment that affect our genome and and it translates it down.

So I've become a huge fan. I mean, if I started my career over again, I would definitely have a major uh emphasis on, on systems biology and, and, and the mathematics that it takes, it's, it's essentially changes the way you do the statistics and you analyze the data. It's – Emeran can you give an example of that, like the systems and how they?

– So for example, you know, when we started with brain imaging, I don't know, 25 years ago, um everybody was talking about and you know, a lot of lay people have seen this in the media that the region lights up.

So like the, you know, the light lights up more in people with, there are more anxious and more stressed. And so in the meantime, that's completely abandoned, you know, that that regional lighting up this regional hyperactivity, it's it's now how, how connected is the Amygdala with all the brain regions or with specific regions within the brain and how these these mathematically expressed connectivity measures, how they related to disease processes.

For example, um It's made it more difficult because you need larger sample sizes. So before, you know, we published papers, a lot of people published papers with 20 individuals was a recent article in nature of science that said that you could basically forget about all these publications because if you try to repeat them in larger samples, none of them will be reproducible. So now we're looking at data sets of 100 thousands of patients and look at these connectivity measures within a system within the brain. Um So, you know, a lay example of this would be if you want to understand um if you want to understand how, how city functions and you focus on, on, on, on one aspect, which could be, yeah, I, I don't know what to pick, you know, I mean, the mayor could, could you explain if the mayor is male or female or if the what age the male has, could you explain the complexity of the city um which, you know, we know you can't. And it's the same, the same way of looking at the interconnectedness of elements.

I find it intriguing, you know, ancient healing traditions have, have understood this empirically and intuitively, you know, Buddhism is essentially the, it's not religion, it's the teaching of interconnectedness and every aspect. Um you know, diabetic theory is kind of a similar, not, not, not as clear cut as, as, as Buddhism, but then it continued all the way onto the Greeks and, and only with, with the renaissance and with the cart, with the true Western um you know, breakthrough of the Western scientific thought.

We've kind of abandoned this holistic or systems based analysis of understanding. And I find it really intriguing that we're coming back to the science is moving back in that direction and many examples for that how um so as I mentioned that the brain connect on the God connect on you know, still most of my colleagues in G I, they are fascinated by, you know, the like the serotonin containing cells in the gut.

And that's the biggest seat of location for the serotonin. But they don't realize that the serotonin cells are connected to everything else, to certain microbes, to immune cells, to the to the enteric nervous system.

Um you know, with the gut connect um essentially and ultimately, I think we'll explain, we'll be able to explain altered gut function with this cut connect on concept, not with individual cells.

– The the goal of optimal functioning would be to maintain this homeostasis or place of balance between these different uh parts of the body, the brain, the gut and the immune system. What is, what are some of the main things that throw off that homeostasis that cause us that cause imbalance in the system? – Yeah. So I should emphasize, you know, systems obviously have a bandwidth with which they within which they can oscillate.

That's the resilience, obviously a key hallmark of any system. And um some people based on genetic background have a wider bandwidth of resistance and others. And um so just there's two kind of perturbations that affect this, this this brink of microbiome home use static system.

One come one component comes from the outside world. So what we call now the expose um um just really another fancy term for the environmental factors, anything from um from diet toxins, um you know, stressors, um psychosocial stressors, and then you have the uh the other group of, of perturbations which are diet related.

Um So our systems are optimized for a certain diet that our ancestors have, have eaten for, you know, hundreds of thousands of, of years with variations and these variations were within the bandwidth of the system.

What Disrupts Homeostasis and Drives Inflammation

But what has happened in the last 75 years, you know, there has been such a dramatic change in, in lifestyle and, and, and diet um that this is becoming a perturbation for the bring up microbiome system that it cannot deal properly with.

And essentially what whenever the bandwidth is, is overcome. A key response to the system is an engagement of the immune system, which is kind of a, you know, we had the nervous um does the stress response to the nervous system of the brain. But then we have a sort of a more ancient immune system, stress response which, which will cause engagement of um you know, the innate immune system and then the adaptive immune system.

And, and it will lead to this finding that we have today that so many people even on the outside, healthy people have markers for this low grade inflammation.

And – So you're saying that whether it's the outside environment and stressors, what was the word you used to expose expos OEMs or it's some aspects of the diet, they take the body out of this place of balance, that the body is actually it's okay to have some flexibility. Flexibility is good.

But either the diet or the external stressors take the the this uh out further out of balance and it affects the immune system. How else does it impact that the microbiome?

– Okay. So, you know, we know both from studies, animal studies and human studies that, that stress, even acute stress changes the microbiome composition and, and, and function. And there's lots of studies now with diet in animals. Um it's, it's one of the shortcomings of this whole field of microbiome science that we have a lot more animal studies that point to causality and very few human studies, most of the human studies are cross sectional epidemiological observation allele but big numbers, you know, it's like comparing in a population of like the Harvard nursing study, you know, 20 plus 1000 people, we can compare those on a certain diet compared to those on another diet. And then you look at their health status and measurements and but, but in terms of, you know, causality that's harder to derive from um from the human studies. So now the studies coming up that, that actually filled this gap. Um and, But, you know, with, with the microbiome research, it's, it's been an interesting phenomenon.

It's, it's early on, you know, it's 10, it's 10 years essentially. Um and I think we're still at the very beginning of understanding it. And so people have prematurely jumped on the findings from the animal studies and the Human Association studies to talk about causality, you know, is um just, just, just, you know, next week's two papers coming out in nature, communication, nature about association between depression and they got microbiome in large data sets. And, but it certainly does not prove that these, these altered gut microbiome compositions and diversity measures are really play a causal role in, in depression. Could be the other way around.

It could be that if your mind is depressed and the outflow of the autonomic nervous system and you know, hp access to the body are altered that this alters the milieu that the microbes live in.

And so it's with an interesting stage, I think it's I would say if I had to bet my money on it, I think that the, that, that these changes, that the we talked about these perturbations of the system probably play the major role in the observations of the microbiome changes that we see. Rather than saying the main new world is now all the mental disorders can be explained by microbiome changes.

I don't believe that. But – Let me say that I'm glad you said what you would put your, your money on because that's partly what we're interested in is you who comes from this knowledge base, this huge knowledge base in this area, have some opinions about what the connections are and the significance of those connections.

So I'm very much interested in your perspective because, you know, we're learning so much about the interaction

between the microbiome and our emotions as well as the microbiome and how it might impact cognitive functioning. So I would love for you to share what your perspective is on those connections and perhaps the causality or at least what imbalance may seem to be correlated with those impairments, whether it's emotional or mental. – Yeah. So I mean, I should mention, you know, I looked at your book that will be coming out that you were nice enough to send me.

So this PDF and obviously, you couldn't agree more with the concepts that you laid out there in terms of, you know, how perceptions and your way you cope with, with stress, what impact this has.

Microbiome Links to Mood, Cognition, and Chronic Disease

So my, it's been kind of a development. So I am a scientist, I've come up with a hypothesis. I believe them, I try to refine them on an ongoing basis. I believe them as long as they fit the data and the observations and when the, that the science deviates from it, then I'm always willing to, to change it. And so right now what I feel is that without chronic diseases that, you know, have a period often of like with Parkinson's of 12 to 15 years or you don't really develop the full blown neurological syndrome, but you can detect things in the gut, you know, with constipation and biopsies and same thing with cognitive decline, you could probably, um you know, pick up people, we know it today, we don't have an increased risk in the earliest signs of this neural neural inflammation and no degeneration. I think these chronic diseases where you have decades of this abnormal signaling like this immune signaling to the brain.

I think those are the ones where the microbiome plays a significant role, both in terms of Early diagnosis, possibly that you can predict if you do, you know, and microbiome analysis at the age of 40 or 50, that you can predict the risk together with other factors of that person developing Alzheimer's disease, same with Parkinson's um that may potentially play a role also with, with some forms of depression, particularly the forms of depression that people have found evidence for, for inflammation, for this low grade inflammation.

But I think a lot of the other ones like you know, anxiety, attention deficit disorders. I I'm very skeptical even I B S sort of my own, you know, area of long time interest.

The evidence is very mixed that microbes play a positive role in, in, in, in I B S. But a lot of evidence suggests the stress that people with I B S are under changes the microbial ecosystem, you know, and um so I would say I, I see two different types of disorders.

The one that, that have low grade chronic information as a, as a key, key path, a physiological component, I think they are related, we know they're related to diet and diet is always translated through the microbiome into, you know, molecules that affect the immune system.

So I think that's a whole group of disorders where the this microbiome concept and a causative role is, is quite likely the others. I'm, I haven't seen really the proof of it, you know, I think, but then as I said earlier, we're just at the beginning of this field, I mean, there may be dramatic changes all of a sudden that, you know, will suddenly change my opinion on it.

– So yeah, there's always, and with human studies, it's even more difficult to determine what's causative and what's just correlation a lot. And I know that's always an ongoing kind of question and a lot of these areas, hopefully we'll keep getting more and more information that gives us the answers.

But can you just explain how the gut microbiome affects the brain? How, what's the communication process there? – Yeah. So there's multiple communication pathways. So one is sort of one of the main sources for David influence or, and feed our microbiome is clearly our diet, you know, and the ideal diet for the microbes we've deviated from that increasingly over the last 50 75 years. So the complex carbohydrates and fiber that's contained in, in, in plant based foods, for example. So we know a lot about this heart's broken down by microbes into short chain fatty assets that you know, I have have both beneficial effects on the integrity of the gut.

But also the short chain fatty assets are sort of our bodies aspirin because they have anti inflammatory effects on

every level from the interior nervous system um to you know, anywhere in the body and particularly within the brain.

So they, you could almost say that this may be the main factor why we have these brain disorders? Because we don't have the same level of built in anti inflammation that counter acts you know the inflammatory signals.

The other ones are metabolites um that are generally not just the short term fatty acids metabolites that are generated from. Um for example, from molecules that our body produces. Just want to mention.

One example, estrogen is a good example, which is conjugated in the liver excreted through the bile into the second half of the small intestine. And then a certain fraction of these are metabolized by certain microbes into a re absorbable form of estrogen. So then it circulates back in the body.

And depending on if you have the right group of microbes that can do this, you will have higher levels of estrogen like you know, post menopausal state or other situations than somebody who doesn't have these microbes. Another source are a dietary components.

So pretty, the best study example is trip to fan which can be metabolized either with the help of microbes. Um So serotonin synthesis is accomplished in specialized endocrine hormonal cells in the gut. But the main signals that stimulates this uh this enzyme that converts strip defender. Serotonin is modulated by the gut microbes through short chain fatty acids and secondary bile assets.

Um And then there's other tryptophan metabolites. Some of them have positive effects, some have negative effects on brain integrity and excited toxicity within the brain. Um So it also shows you the complexity.

So one molecule trip to fan, you know, portion of the majority is absorbed in the small intestine goes into the systemic circulation sticking up in cells in the brain that produce serotonin for brain regulation.

But then a smaller portion is metabolized by the microbes at the end of the small intestine into these other metabolites that have um you know, like serotonin can you run in and uh indoors that have a complex interaction with each other, the ratio of these molecules influenced by chronic stress and by diet.

How the Gut Communicates with the Brain

So that's where it gets complex. That's where you see how the systems work. They don't work with one molecule. You know, you don't just taking serotonin by itself is not sufficient.

That's not how the body works. It works with both Yin and Yang and then, and antagonizing forces to get the ultimate signal. – Yeah. So I'm hearing some very important things here right now, which is that the best way to maintain optimal levels of, say neurotransmitters or hormones is to have the this gut and the microbiome operating at its optimal level, that one of the consequences of it operating in homeostasis and balanced and not off balance is that it's, it helps maintain levels of hormones and neurotransmitters.

And that's very important when we start talking about longevity because one of the factors in longevity is with age, how some of our hormones, neurotransmitters start to decrease. And what I'm hearing you say is healthy, gut is one way to maintain optimal levels. Is that an accurate statement?

– Yeah. No, absolutely. I mean, there's clearly different physiological, you know, demands on the hormonal system. You know, we don't as older males, we don't need the same amount of androgens and the same thing is true about female sex hormones, but we also don't want to drop below the level that's optimal for, for a certain age. And I think that's where the microbiome come and diet comes in. Um much more than, you know, to another area for me of I've gone back and forth in terms of the supplements, you know, is it um with aging, is it a good idea to take all kinds of supplements to try to reverse the natural process of adaptation of the hormones too to a, to a different study state, you know, which you could say is, is the right steady state. I mean, and I haven't totally come to the right conclusion on that quite honestly.

You know, I think if you, I still believe if you are pursuing a healthy lifestyle with a healthy diet, exercise, you know, mindfulness, um, sleep hygiene, that effect is, is much, much bigger on the system than taking high doses of a certain, You know, of a certain chemical. The same thing is true about probiotics.

You know, if you take billions of colony forming units of 15 different strains of microbes, I mean, is, is that really going to do more than pursuing these other avenues, which I think are the key towards healthy longevity, you know.

– So I'm glad you brought up supplements because one question I had for you is um does the body fully utilize these supplements uh when we take them in or, or not?

– Yeah, that's a good question. Um So I mean, there's different kinds of supplements. I mean, some, some are absorbed in the, in the small intestine. Um The small the system has not evolved to sort of take care of a very high dose that, that you take. Um what you ingest with nutrition is, is a kind of a different paradigm you take in a lot of different, a lot of different chemicals and substances in small amounts, but on a regular basis as opposed to, you know, giving like a big boost of, of one chemical at, you know, without paying attention to all the rest.

So it's a little bit like Chinese medicine, you know, where they mix different things together and, and lower doses was western medicine goes for the one um you know, big hit. So we don't really notice for sure.

A good example with that is definitely not the case is um this whole story about antioxidants, you know, still, still prevalent if if you look at the media and online recommendations. So there's a, there's a group of several molecules that certain vitamins, but there's a lot of what's called these polyphenols, they speak molecules that are contained in, in, in plants. Um virtually in all plants, the plants use these molecules and make these molecules to defend themselves against disease.

So it's, it's kind of interesting and, and when we ingest these molecules, they cannot be absorbed in the small intestine, they go down and we need the microbes to break them down into smaller components. And it's believed that a very small portion based on science, very small portion of this orally ingested antioxidants um that there's some portion really acts as antioxidants because they're converted into something totally different in by, by the microbes that then, you know, acts on our body and our brain. And there's been a recent publication, you know, it's the kind of studies you would like to see a three year study with um flavin. Also, it's, it's, it's one form a common form of, of polyphenols given in a capsule form over three years.

Um and look at its impact on the brain, on the hippocampus, on, on cognitive function and on cardiovascular function. And, and it did show that, you know, over these three years when people consume this, this high amount of that particular molecule, that it had a benefit.

And what's important here is it had a benefit in people that did not consume an adequate amount in their natural diet. In the normal diet. It had no benefits in people that were, you know, consuming a diet high in, in these flannel containing ingredient components.

So I would say with, with, with our, you know, extremely unique diet today, this what's called the standard American diet or sad by its acronym.

Hormones, Supplements, and the Limits of Probiotics

It, may well be that certain supplements that you take such as these flavanols, I've actually started taking them myself, you know, but I was convinced by the evidence that I saw that that may be beneficial, you know, but I, I think for the majority of people that continue their unhealthy lifestyle or their unhealthy diet, it's, it doesn't make a difference, you know, it's just, um that's kind of another thing that because he has his interactions of these different lifestyle factors, each contributing, You know, we don't know, between five say and 15% to the variants of the overall outcome.

Each individual intervention is not, not the determining factor. It's the combination of them that produces the

longevity. – Yeah. So again, it's, it says that usually the natural way of, of producing changes, the best is the best way.

But what I also also heard you suggest, I think there is that when you take supplements, if you have deficits, it can help correct that or contribute to a better result.

But if you're already doing well, a supplement may not make that even better. Is that correct? – That's sort of current thinking, you know, so say, say that, you know, sort of a political way, the people that would need to supplement the most are the ones in, in the lower socioeconomic parts of our society because they are on unhealthy diet much more than, than people living in the west side of Los Angeles or New York. And so they would need it the most, but they probably would not be able to afford it.

You know, they can't even afford a healthy diet. So that's why they eat at mcdonald's. And so it's yeah, I mean, if, if you really want to make a big impact with supplementation, I think it would, it would require sort of a public health effort to get it to the people that needed the most, you know, to, um, or teach individuals in this segment of our society teaching about the health benefits and the danger of an unhealthy diet.

And provide both the diet but also potentially the supplements on a regular basis. – So, yes, so it all, it also suggests we need, need to do a better job at informing the public on all of these subjects.

One of the things that's come up in a couple of our other conversations on this summit has been like, for example, the impact of mouthwash on the oral by biodome uh and also antibiotics as well. Can you say something about that? – Yeah. So this, you know, I said earlier, so the the increase in many of these chronic non transmittable diseases, the epidemic and these diseases. Um so diet is one thing but also the um the excessive and inappropriate use of antibiotics from early on in life.

Both um starting with the pregnant mother, you know, animal studies have shown that um even the one dose of antibiotic to a pregnant mouse mother could affect the microbiome of of the offspring, but then also will be, you know, during delivery in the in the delivery room.

Um you know, the prophylactics for staph infection or often antibiotics are given. And then the first few years of life were often, you know, the pediatricians are pressured by over concerned mothers that their child is suffering from the respiratory tract infection, he or she needs an antibiotic.

And so we end up with a situation where during the time where we, with this spring of microbiome system is shaped. Um So the most important formative time we bombarded with, with antibiotics, which impaired the normal development from before birth too, after birth. And um so that's, and I'm not sure if that practice has really changed despite, you know, lots of publications on this topic, I mean, there's also, you know, the whole vaginal versus C section delivery conversation which, you know, has a major effect on this development during the first year.

But then it it normalizes after a year, but during the first year, a lot of the interaction between the microbes and the immune system happens. So all this increase in these autoimmune diseases and allergies, you know, like many of these allergies did not exist when I was a medical student that we now deal with and patients talk about that's another impact of these, these changes were made within the medical system.

So even even before this, this child gets to pursue his or her own lifestyle with potential negative effects, it's already handicapped compared to some other individual growing up in a, in a, in a different society. – So are you suggesting that the impairment of the gut microbiome is responsible for these allergies or how to what's the relationship with the growing uh prevalence of allergies?

– So it's the interaction of, so there's kind of a learning phase for the immune system. So each of these systems you know, like the, the gut microbiome, the immune system and our brain have these different periods of training in when somebody is growing up in the life um cycle.

So the first, um you know, I mean, the first couple of years the microbiome is influenced significantly. It's shaped,

it's basic, then the immune system is compromised because the interaction of many benign microbes with immune cells within eight immune cells um teaches the immune system what's good and bad for them.

You know that there are organisms like like h pylori um or I mean, there's a, there's a range of these are called the old friends hypothesis. So these organisms that had have lived with us with humans um for thousands of years and still live. If you go to um to indigenous people, like on the Amazon or in the Orinoco River, they have all these organisms still.

I mean, parasites are also part of this and what, what these organisms, they don't kill anybody, they don't kill the infected um individuals, but they train the immune cells to differentiate between if they're really bad.

Um pathogen comes along to attack that one but not, not the cells or the the immune cells of, you know, of the host that, that are, that are not dangerous. So this whole teaching of differential between good and bad happens during that time period. And you know, when, if you interfere with this in the West, we've done this in many ways, sterile delivery rooms. Um as I mentioned earlier, the just the C section delivery, so they're not exposed to the moms microbiome then um living in city apartments instead of on farms or in, you know, people with, in settings with lots of green spaces and exposure to animals.

Antibiotics, Early Life, and Allergy Risk

Um So all this has contributed and I mean, the system is resilient. So not everybody develops these allergies but in combination with genetic risk factors, you know, that's definitely one of the major reasons and, and it will continue to increase, I, I mean, with more and more people moving into urban environments and away from, you know, from these green spaces, uh this, this will continue to increase pets to a certain degree, can attenuate this if they're present from early on um dogs more than cats. Um But yeah, when, when you go down the whole developmental, like what we have the way we have interacted with our brain gut microbiome system from um pregnancy all the way to old age, what kind of um you know, in senior citizen homes, the lower quality of food with less fiber and, and um like all these things add up to that, we have more of these diseases and in the west were actually very good and um increasing longevity and you know, but with an enormous investment of trillions of dollars of medications and surgeries and medical interventions.

So it's um so – Well, this is a fascinating conversation, Emeran and, and I'm really enjoying it. Uh I'm also struck by what you just said, which is that there's an actual biological learning process that takes place that trains different systems as well because it correlates with some of the things that I've written about, about how our early developmental process affects, how we adapt as adults. And here you're saying that there's a similar biological process that takes place inside of us.

So I find that fascinating. But last couple of questions, if someone has been taking antibiotics or maybe it's a result of what happened during birth, how does one normalize or restore a healthy microbiome? Is there a way of actually regaining a healthy natural bio?

– So, I mean, the thing is, you know, we still don't have a good answer of what is a healthy microbiome? Is it the one that has always come back to this, these indigenous people on the upper Orinoco? Because I was fortunate to visit them and some, some time point in my early career during college.

And so they supposedly have the greatest diversity of anybody in the world on the planet of the microbiome. And you know, I wasn't interested at the time at, at my age, at the time as a medical student before being a medical student.

But in retrospect, when you look at at their diet and their exposure to natural to soil and they're born on the ground on a banana leaf. And um so they do all the things that nurture this healthy microbiome.

But then you could say they have a healthy microbiome for their environment. You know, ours has adapted and the microbes can adapt rapidly really within 24 hours to go from a meat eater to a vegetarian diet habit.

You, you know, microbes can adapt to this quickly because they have 100 million genes. So they're much better at this than, than we as humans are with our human genes.

So the big question is um should we aim for having got microbiome like the Yanomami Indians who live in a totally different environment and um or um should we, you know, define our healthy microbiome is taking the healthiest people that live in the U S?

And make this make that the ideal, you know. So I think this question has not totally been settled. – What would you, what would you advise somebody who either feels like there's something off with their microbiome or have just gone through surgery or whatever and have had antibiotics? What would be your recommendation?

– So my recommendation would be as, as always go on this, what I would almost call the healthy default diet, you know, which is that I um which in a large variety of, of plant based foods, both fruits, fruits and vegetables um as well as a large variety of fermented foods. So, as evidence that both of these types of foods have an influence on um microbial diversity and on this inflammatory response.

So if you do this for a while, um you're probably doing the most, you know, the most effective based on science that we know today, I mean, you know, people have also recommended or are doing, taking a probiotic. My guess is if I, um you know, if, if I develop gi symptoms from a course of antibiotics, I would probably take a probiotic in addition to these naturally fermented foods.

But the evidence is mixed. I mean, some studies have shown that if you take a probiotic in that situation, it takes longer for your own gut microbes to come back.

So your probiotic suppresses the reestablishment of your healthy. So I think it it's so depends. I would definitely go with the, with the diet intervention first. And if that doesn't work, then I might, you know, take a probiotic. – Thank you.

Very good. So, we're running out of time. I had one last question and I wanted to know if you could share what interests you the most with your own work right now.

Restoring the Microbiome and Current Research

– Well, I mean, I would, I can't wait for the first credible um you know, results from human studies that, that, that demonstrate that some of these hypothesis that we currently have based on these correlation, alleged theological studies is actually uh positive.

And because that would open up a whole range of um of, of interventions that you can then, you know, um target at, at the gut microbiome. Um Another way, another thing that's very interesting is, you know, we have moved away from analyzing and putting a lot of weight on the individual microbes were interested really what they produce, what, what genes they express and what molecules they they produce and to understand how that interaction of thousands of these molecules affects us, the host, you know, body in health and disease.

That's another, I think going to be a very exciting breakthrough to be able to say that. Um in the meantime, you know, I'm excited about studies that we have ongoing where we look for example, at, at these polyphenols, What effect do they have on, on brain structure and, and function? And how does that relate to cognitive performance? But that's just a small aspect of it.

I think the big pictures will take 10, 20 years, I'm sure still and but it will fundamentally change medicine. I think there's one, one, the virtue of a major paradigm shift, I think in, in, in medicine. – This is also fascinating and I really appreciate your perspective and sharing this very valuable and important information.

Emeran, I know you've got some best selling books out. Can you give the names of, of those books as well as how people can reach you? – Yeah, so I published two books and the first one, the mind got connection where I essentially laid out the basic communication systems between the, you know, the mind, the brain and, and they got

in its microbes.

And the second one, the got immune connection, which is kind of almost like a sequel to it brings in the immune system as a sort of the main trance traction mechanism to to our health.

And both of these books are available on, on Amazon. Go to my website Emeranmayer.com and you can sign up for our newsletter and other materials which addresses, you know, topics related to, to this on a weekly basis. So I would encourage anybody who's interested to, to go to this to this possibilities.

– Very good. And then if you have something you want to offer, we will in the notes from this lecture, we will include that so that people can reach out to you for that. – Okay. I'll definitely provide you with that.

– All right, beautiful, beautiful. So Emeran, it's such a pleasure. Thank you so much again and I'm looking forward to the next time we communicate when you'll have some additional information to share with the audience.

Thank you. – Thanks, Steven for inviting me on this, on this, on this show, it's really been always enjoy it to be able to share this information, you know, it's – Great.