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LuAnn Heinen:

Emeran Mayer is a world-renowned gastroenterologist and neuroscientist studying how the digestive system and the nervous system interact in health and disease. He's a distinguished research professor in the Departments of Medicine, Physiology and Psychiatry at the David Geffen School of Medicine at UCLA and Executive Director of the G. Oppenheimer Center for Neurobiology of Stress and Resilience, funded by the NIH and philanthropy.

I'm LuAnn Heinen, and this is the Business Group on Health podcast, conversations with experts on the most important health and well-being issues facing employers. My guest is Emeran Mayer, and we'll be talking about the body's largest immune organ, the gut biome and its connection to our physical and mental health.

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Welcome to the podcast, Dr. Mayer.

Emeran Mayer, MD:

Nice to be on it. Thanks for inviting me.

LuAnn Heinen:

I'd like to start with what brought you to this line of study and research, well before gut health was the hot topic it's become?

Emeran Mayer, MD:

Well, it's really been a career-long interest of mine. I've always been interested in mind or brain body interactions all the way back to medical school. I first started studying during my thesis work, the interactions within the brain and the heart. Then during my clinical training, I decided gastroenterology was really my field. I realized that a lot of patients had some aspect of brain-gut disturbance, which at the time was really not something that was in vogue or popular. I've really pursued this for the last 35 years or so.

LuAnn Heinen:

Well, tell us a little bit more about the gut and, in particular, what the gut biome is.

Emeran Mayer, MD:

The gut, contrary to what most people believe, it's not a simple tube optimized for digestion and absorption. It's the most complex organ in our body. It has its own nervous system, about a hundred million nerve cells. It has 80% of all our immune cells in the body. It has the biggest endocrine system producing lots of hormones, satiety hormones, for example, are an important one. All these cell types that are present in the gut that you won't see, even when you do an endoscopy, you won't see them, they're hidden under the surface of the gut, but they are able to interact with these 40 trillion microbial organisms that live inside our gut. They're really living in symbiosis with our gut and with our body because there's connecting pathways between the microbes, the gut, and then from there on, to the brain, to the liver, to all the other organs.

LuAnn Heinen:

I learned in biology quite a while ago that the brain controlled everything. The brain controlled the nervous system. The brain controlled all of our systems. How exactly does the gut relate to our brain, and with a

hundred million nerve cells and 80% of our immune cells and some ability to control hormones through like its own endocrine system, how does it compete with the brain?

Emeran Mayer, MD:

The brain-gut interactions or the brain-gut microbiome interactions, I like to refer to them as a system of interconnected hubs or nodes, so it's not the linear concept that we traditionally have applied to biology that there's one control organ and it controls everything else. It's a bidirectional communication. The microbes and the gut send signals to the brain, the brain processes every signal that comes from the gut, even though we don't perceive most of them consciously. Then it responds to them. Most of the time, the brain doesn't really need to interfere with the functioning of the gut because of that little brain we have in our gut, which runs essentially the digestive functions. But every time there's a stress signal or distress signal coming up from the gut, the brain will get engaged. It will either produce a pain sensation or a sensation of discomfort, but at the same time, it will send back signals via the stress pathways, through the autonomic nervous system, that can change every gut function.

A lot of people are now focusing on the prominent role of the gut, but we shouldn't forget that what happens in the gut is in some ways a mirror image of what happens in the emotional part of our brain. If we are angry, if we are fearful, if you are happy, the brain will send these non-perceived nonconscious signals to the gut and adapts every gut function, including the microbes. So, the microbes know if you are stressed, if you're angry, if you are afraid, or if you're happy, the microbes will know it and will change their function and the gut will know it and the immune system will know it. The best way to explain it is a bidirectional, complex, interacting system with all parts contributing to the end result, which is maintaining health and homeostasis.

LuAnn Heinen:

That is really something. I mean the physical and emotional manifestations of this gut-brain connection are things that probably most of us don't understand.

Emeran Mayer, MD:

Yes, most people don't know about it. It's great that lay public is so interested in gut health now. I think it's a great thing. It's clearly leading to improved nutrition, diet, health-promoting behaviors. Few people understand the complexity of that system and how central it is to our health, in combination with the immune system and the nervous system. It certainly changed my view. When I started studying this, it was always the brain-gut access, this linear concept that the brain controls the gut and the gut send signals to the brain. This is clearly changed for me in terms of a systems biological paradigm shift that you look at this in a very different way. I think if you want to contribute to our health, both maintaining health, but also treating some of these chronic illnesses, I think it's essential that we have this new view of the brain-gut microbiome system.

LuAnn Heinen:

What are some of the physical and emotional manifestations of the gut-brain connection?

Emeran Mayer, MD:

As I mentioned, any emotional reaction in our brain will have a mirror image in the body and particularly in the gut and it's transmitted via these nerve pathways that go through the autonomic nervous system, goes from the brain to the gut, but also cortisol and other hormones that can alter gut activity. When I say gut, it always means microbial activity as well. Stress also, both acute stress and chronic stress, will create a different gut or state of the gut that may either be symptomatic or cramps, bloating, discomfort. It also may even interfere with the normal digestion that the gut normally does. One simple advice when you sit down for a meal is don't do it when you're stressed out, your gut will not be in the right mood, just like you are not, your gut will not be in the right mood to digest this food properly.

LuAnn Heinen:

What about the connection to more serious diseases? Things like development over time of Alzheimer's or Parkinson's.

Emeran Mayer, MD:

Yes, this is a fascinating question because very few people would've thought, before this sort of first popped up in the lay press, that something like Alzheimer's disease or Parkinson's would have anything to do with the gut. There's pretty good epidemiology on this, that Parkinson's, for example, can start in the gut up to 14 years before there's any neurological manifestations and emotional changes. If you could take a biopsy in your intestine at this early stage, people present with nuance had constipation. If you took a biopsy, you will see the same histological changes in the nervous system in the gut that later appear in the central nervous system. Imagine 14 years before anything happens at the brain level, there's already this process going on with degeneration of nerve cells in the gut, resulting in constipation, and then it starts that gradually this process moves up through the vagus nerve that connects us with the brain stem and the brain.

These changes gradually migrate up in this nerve and then manifest at brain stem level, brain level, cortical level, ultimately, producing all these characteristic neurological changes. With Alzheimer's disease, there's also now growing evidence that metabolites being generated by microbes, by an altered gut microbiome, play a role in the neuro inflammation and neurodegeneration in the brain of vulnerable people that have, for example, a family history of Alzheimer's disease or have biochemical, these biomarkers, of Alzheimer's disease. It's kind of amazing that two diseases that have been exclusively thought to be happening at the brain level, that they would start in the gut and where the gut would play a major role in determining the course. This, of course, opens up amazing opportunities for intervention. These are devastating diseases. We certainly don't have cures for them or effective treatments. In the case of Alzheimer's, if we have more than 10-years time to interfere with that development of disease from the gut to the brain, this opens up a huge opportunity for novel therapeutic interventions, either aimed at the microbiome or aimed at the gut.

LuAnn Heinen:

We're going talk about what makes for a healthy gut, but is it true that a largely plant-based diet is associated with lower risk and severity of COVID-19?

Emeran Mayer, MD:

There's epidemiological studies. I'm sure there will be more data coming out on this. It has been shown that starting out in the beginning people with an unhealthy gut microbiome are more likely to develop more severe forms of COVID-19, are more likely to end up in the intensive care unit, more likely to die. There's also evidence that they're more likely to develop long COVID. It's a very complicated problem, obviously, but if you think about it in simple terms, COVID-19 doesn't really happen in the gut primarily, it happens in the lungs, in the respiratory system, but since all the immune cells that ultimately end up in the pulmonary, in the respiratory system, in the lungs, go through the gut, they're altered. So in general, there was an increased responsiveness of immune cells. For example, this term cytokine storm, an increased immune response to the virus in the lungs, because they have been programmed in the gut in response to a poor nutrition, a weak compromised gut microbiome. There's also been data that people in lower socioeconomic parts of the society with a poor diet were disproportionately affected by COVID-19, particularly with the more serious complications. There's clearly a direct link, I would say, between an unhealthy diet, a compromised gut microbiome, an overactive immune system, and the complications of COVID-19.

LuAnn Heinen:

Here's an easy question, no science needed - maybe, maybe not. We hear people talking about their gut decisions. Is there evidence for that?

Emeran Mayer, MD:

When I wrote my first book, this was something that fascinated me, this prevalence of terms that gut feelings or gut reactions in our language. It was pretty interesting while writing the book, I paid a lot of attention to this and there was not a day that I wouldn't hear in the news at least five times that prominent people in sports and politics would use that expression. So diving a little bit deeper, it gets really complicated and hypothetical. What I came up with, sort of one of the explanations, is there's clearly always a reaction at the brain level to an emotional situation, to a stressor, to happy or negative events, but this doesn't just happen at the brain. As we talked about earlier, there's always a gut component to any emotion. What the brain does, there's quite a bit of evidence for that, it stores all these emotional moments somewhere in the brain. I use this expression in

tiny video clips. Every emotional experience that we have gone through from the time we were infants, with a lot of negative emotions, with gut reactions, all this is stored somewhere in the brain, in a super computer, and just like a search engine for Netflix or Google, our brain can access this vast database, helping to make a decision based on these previous emotional moments. That's something I've discussed with other prominent neuroscientists. I think right now, this super-computer model that we have obviously will get more sophisticated in the future, but right now it's a good way to think about this. Making a gut-based decision is a decision that you don't go through a plus and minus list with rational, slow, linear process, which could take you days, but it happens instantaneously because your brain can access, just like when you type in the first letter in a Google source, it can give you the right answer. That's a good model right now to understand that.

LuAnn Heinen:

We've often heard about the concept of healing the gut. What does that mean and do we all have healing to do?

Emeran Mayer, MD:

Yes, this is a really interesting question for somebody like myself, who's been a gastroenterologist for all my career. What we really dealt with gut diseases, gut diseases means you can see something, you can take a biopsy, you see abnormalities on a biopsy, and the number of gut diseases was relatively limited. The people that have got diseases like inflammatory bowel disease or irritable bowel syndrome or colon cancer or peptic ulcer, this was a relatively small fraction of the population. Now what's happened, this concept of gut health that's become so popular, there's really no basis in terms of, you know, nobody can do an endoscopy and see if you have that kind of a gut health. So you don't have a disease, but you want to know is my gut healthy. You can't see the leakiness. You can't see the low-grade immune activation. You can't see the imbalance of the microbes. All of this in some ways you could say is hypothetical, that kind of gut health is not based on true scientific observations, it's based on observations in animal models, and there's been a lot of speculation about this concept of the leaky gut and all the complications that it can lead to. But it's not something, if you come into my practice and say, do I have a leaky gut? I could not tell you that for sure. I said, yes, certain circumstances would point in that direction, but I can't make a definitive diagnosis of that. We have now two different realms. We have the realm of traditional gastroenterology. We have the realm of functional medicine physicians. For them it's very easy to make these diagnoses, not based on evidence, but just based on what they feel, based on the symptoms. Then we have the science that's trying to provide evidence to support some of these concepts. That's the environment right now, that patients and people that talk about gut health should be aware.

LuAnn Heinen:

I'm speaking with Dr. Emeran Mayer, and this is the Business Group on Health podcast. We'll be back right after the short break.

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LuAnn Heinen:

If you buy into the idea that it makes sense to try and prevent a leaky gut or an unbalanced gut, what should you do, both in the food front or when it comes to maybe more mindfulness or outside the food front?

Emeran Mayer, MD:

This is a very important question. Based on this kind of linear thinking that in the West, we're sort of grown up with this. To think there's only one thing, it's the healthy diet that we need to adhere to or supplements or whatever targeted at the gut, that that would give us a healthy gut. Coming to this new concept that I talked

about before, this brain-gut microbiome system, you have different targets within that system that you can address, that you can target for improving the health of that system. Starting at the brain, clearly a mindful state, minimizing negative emotions, reducing chronic stress. You don't have to worry about acute stress, which is actually a good thing for us, so it's over in a few seconds or minutes, it's the chronic stress and the worry that's really what you want to avoid. So that's dealing with the brain part. Then you want to deal with the microbiome part. A big influence of that is clearly the diet. Also, the immune system. A diet that is high in plant-based foods, it has two types of ingredients. This diet, if it's a very diet with a minimum of 15 different fruits and vegetables and nuts and seeds per week, then it increases the diversity of your gut microbes. It also provides the gut microbes with fuel to generate anti-inflammatory molecules, like the short-chain fatty acids. This is kind of the aspirin of our microbiome system and of our body really. If your microbiome generates enough of these anti-inflammatory substances from the fibers and complex carbohydrates that are in a plant-based diet, then you will downregulate any inflammatory reactions that might be going on, both at the level of the gut, the immune system, but also at the brain, so they get into your systemic and circulation.

There's many other molecules that are generated from a plant-based diet, have been shown to have beneficial effects on your brain-gut microbiome system. There's many other ingredients in the diet that are not exclusively present in the plant-based diet, such as tryptophan, but overall, if you take the benefits that you get from the fiber, the complex carbohydrates, generation of these anti-inflammatory molecules, and other molecules, which have been referred to as the antioxidants in most plant-based foods - in berries, coffee, Kakow, olive oil, just to name a few. They don't really function as antioxidants in our body, because when you ingest the fruits with these compounds, which are called polyphenols, they are such large compounds that they can't be absorbed in our small intestine intact, so they migrate down into our large bowel and they're broken down by the microbes into smaller absorbable molecules, which then exert the beneficial effect on our organs. The fiber, on the one side, is broken down in anti-inflammatory molecules and the polyphenols, on the other side, being broken down into these health-promoting anti-inflammatory molecules are really the two ingredients of a plant-based diet. You won't get them with any of the extreme diets that have been proposed, that come and go. It's kind of amazing to me that this discussion still goes on, where the evidence is so strong.

LuAnn Heinen:

Absolutely. What does a gut expert, for example yourself, eat in a day? Just a few staples, what are some staples in your pantry? I'm going to guess chia seeds.

Emeran Mayer, MD:

Definitely chia seeds. They are very high in fiber and polyphenols. I should say it started out really during the book writing of the *Mind-Gut Connection*. We experienced in the family, this was also during the lockdown, with different ways of creating the gut healthiest food. We started with a breakfast bowl, including whole grain cereal, but it really turned into, I would say, a bowl packed with fiber-containing and polyphenol-containing nuts and seeds, naturally fermented products. We've been eating this every day.

LuAnn Heinen:

Okay, so falling into a food habit is okay for a healthy gut. It doesn't have to be endless variety.

Emeran Mayer, MD:

Yes, I think it's very important to have it. You can vary the components. This current bowl that we create has about between 10 and 15 components, which vary, depending on the seasons, because the kind of berries we add to it are based on the season. Salads are a good example. We actually count the vegetables and the seeds and berries that go into the salads and it can be between 15 and 20 per salad, which comes later in the day for an early dinner. We've also implemented a time restricted eating schedule. I wouldn't call this first polyphenol fiber bowl a breakfast because we delayed this until 11 or 12, so we have our 16 hours in the 24-hour rhythm where we leave the gut empty.

LuAnn Heinen:

Great discipline. What qualifies as a naturally fermented food?

Emeran Mayer, MD:

This is also a good question. Fermentation doesn't generate microbial organisms that necessarily meet the criteria for probiotic. There has to be a demonstrated health benefit. If you eat something, take something, from the outside, there has to be a demonstrated health benefit for us. For many of these things like sauerkraut, kimchi, kombucha, those studies have not been done, so the demonstration has not happened. There are indirect studies that if people are on a varied diet of naturally fermented foods, that this has a positive effect on the diversity of their gut microbiome, a greater effect, surprisingly, than a fiber-rich diet. Something that taste preferences play a role, not everybody likes kimchi, but there's enough things that you can incorporate in any diet or taste preference that will allow you to have at least three of those fermented food products.

LuAnn Heinen:

What about yogurt and sourdough bread?

Emeran Mayer, MD:

It's definitely included. There are different forms of fermented dairy products and kefir to different kinds of yogurts, there are plant-based yogurts. We have done one study where we found that one particular mix of microbial strains in a commercially available yogurt has an effect on brain circuits related to the stress system. There are other studies that do support a health benefit. It's been controversial. With probiotic supplements, I would say to summarize, a kind of controversial area. Definitely science has demonstrated beneficial effects in children and infants with certain health problems, decrease in the risk of asthma and allergies. There are a few companies that are willing to invest the money to do randomized controlled, big studies, to test if certain probiotic strains with or without an added fiber component to, called symbiotics. If they have a positive effect, for example, in irritable bowel syndrome or inflammatory bowel disease or after a course of antibiotics, but the evidence in the adult is not as strong as you would like to see so far.

LuAnn Heinen:

Let's pivot and chat a little bit about things that relate to the employer world. For companies with onsite cafes and vending machines, what kinds of food can they make available to their employees?

Emeran Mayer, MD:

Yes, this is a very important topic. Definitely the accessibility and availability and promotion of healthy drinks, which are essentially drinks without sugar and also without artificial sweeteners. They also have a negative effect on gut microbial function and on gut health. In terms of drinks or in terms of any kind of food, really the removal, as much as possible, of sugar containing items is one of the most important ones. Foods that are minimally processed, I mean all of our foods are processed, obviously yogurt is a processed food. You want something that's minimally processed. That includes also raw vegetables. Then in terms of this flood of bars that has made it into cafeterias, these energy bars, I would say bars that are high in fiber and possibly the polyphenols, I would rank the highest. Not everybody needs to boost their protein intake, if they're on a balanced diet. The employers, I think, have a huge opportunity to offer healthy food items, and then there's obviously the various behavioral measures that would incentivize giving an award. If you have ordered the healthiest food for a week, decreasing the premium that you pay for your health insurance. There are many ways to motivate people to stick with a healthy diet. This has clearly been one of the most difficult challenges for implementing a healthy diet from the employer side is to keep people motivated. Once they understand when employer incentivizes certain food, I think it's easier to be motivated to buy it and to stick with it.

LuAnn Heinen:

Yes, education is still an opportunity.

Emeran Mayer, MD:

Absolutely.

LuAnn Heinen:

You take an integrative approach to health and incorporate mind and body. What's your call to action for employers?

Emeran Mayer, MD:

Well, it's not just the cafeteria. The lifestyle choices, like all these things that we've been talking about, if you do any of these improvements to your gut health or your diet for a week or a month, and then fall back to your old habits, it's of no use. Similarly, if you stick to your old habits and are on an unhealthy diet, are stressed out, or burned out, taking supplements will not do it, will not help you. I think employers should target to educate their employees about this concept, the interconnectedness within the brain-gut microbiome system. There's a good example with what happened during the pandemic, burnout of health care workers on the front lines. Both the nurses and the physicians that had to deal with this in intensive care units being faced with death and severe disease on a daily basis for months, for years. It's something that has to be addressed.

LuAnn Heinen:

That is chronic stress, as you spoke about.

Emeran Mayer, MD:

Yes, and that chronic stress has the same negative effect on gut health and the gut microbiome as what I call chronic dietary stress, which is the standard American diet - low in fiber, low in polyphenols. The standard American diet has the lowest amount of polyphenols, lowest amount of fiber of most westernized countries in the world. I think if employees understand that connection that there's now several ways to help patients or individuals with these behavioral techniques. There's several apps from digital therapeutics like online CBT, which is very easy to do. There's also online mindfulness. These things are becoming popular, but I think for an employer to incentivize these or provide them to the employees is a great opportunity. The last one is exercise. Moderate exercise definitely has a beneficial effect on gut and microbial health and on brain health, as opposed to extreme exercise, which is a stress for the body, like ultra-marathons and pushing yourself to the limits, which has the opposite effect. It's, again, perceived as a stressor by the body. This daily, moderate, regular exercise, aerobic and weight bearing exercise, is another key component to this. It's easy to talk about this in theory, and here on this interview. Many health care workers, like in LA, they commute, they probably have to get up at five in the morning, they have to commute in traffic to get to their workplace. Same in the evening when they're done. How much time is there to implement these things? Again, this is something which maybe should be offered during the workday that some of these activities are allowed, if there's time allowed during the day.

LuAnn Heinen:

Absolutely. You think it has to factor into scheduling and break times and available nap areas and lots of things. Final question, Dr. Mayer. What don't we know yet about the gut microbiome that you'd love to understand in your lifetime? What are the frontiers?

Emeran Mayer, MD:

What we don't know about the gut microbiome is probably something like 90% of what there is to know about it. I think we're just scratching at the surface of this field. This will ultimately revolutionize the way we practice medicine, the way we eat, the way we test early on for disease, like the first traces of Alzheimer's disease, Parkinson's disease, based on microbiome testing. We have a long way to go. The good thing is there's an exponential growth of the science. What I would like to see would be extremely satisfying to see diagnostic tests, early diagnostic tests in asymptomatic individuals, that they have a high risk of developing Parkinson's in about 10 or 14 years, and then having an intervention, which right now would be dietary, but having an intervention that can either slow or prevent this progression to the full neurological disease.

I think there's a good chance to see this happening in Parkinson's and Alzheimer's. I would also like to see, another disease we haven't talked about is autism spectrum, a devastating disease, obviously for parents, increasing in its prevalence over the last 60 years, continue to increase. The mind-gut microbiome system seems to be playing a key part. I think if we solve this problem, it will be a tremendous success and forward thinking. I think testing, early testing characterization, not what we do now, just measuring what microbes you have in your stool, that's not going to give you the answer. You have to really be able to measure the molecules that your microbes produce and which you can detect in your blood with a simple test, with a drop

of blood. I think these are the things that I'm optimistic to be able to see in the next 10 years of coming to fruition.

LuAnn Heinen:

Well, thank you so much. That's hopeful. That's exciting. I really appreciate your time today, Dr. Emeran Mayer.

Emeran Mayer, MD:

Yes, thanks LuAnn. It was a pleasure talking to you and hopefully the information is useful to your audience.

LuAnn Heinen:

I've been speaking with Emeran Mayer, a gastroenterologist and neuroscientist with an integrative view of brain and body and chronic disease. He's the author of nearly 400 scientific articles and two recent books of popular interest, *The Mind-Gut Connection* and *The Gut-Immune Connection*. His website is <https://emeranmayer.com/>. Check it out for videos, podcasts, and gut-healthy recipes.

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