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SocGen 108

Gut Gurus

All: Hello and welcome to "Gut Gurus"- a podcast created by Michelle Hao, Audrey Smith, and Millie Kirchberg.

****intro music****

Moderator (Audrey): Have any of you ever indulged in one too many Twinkies and just felt kind of down and off after? Or maybe you started having digestive problems after being prescribed antibiotics? Are you chronically stressed, sleep deprived, and fatigued? Or do you suffer from anxiety and depression? If any of these situations apply to you, then keep listening.

Hello! My name is Audrey and I am the host of "Gut Gurus." We have assembled here today to address the topic of the gut microbiome and its connection to mental health. We will first hear from a person affected by gut dysbiosis, which means an imbalance in the gut microbiome, who will tell us about her experience with mental illness. Then we will turn to a panel of experts to see how a wide variety of perspectives can increase our understanding of the gut-brain link. This will include all of the nuances that this topic involves in the fields of research, Western and Eastern medicine, psychiatry, insurance coverage, pharmaceutical regulation and scientific philosophy. Through this we hope to gain insight into the controversies behind this topic and the ways it influences not only our biology, but our society as well. Then we will reconvene to discuss the best future course of action for this patient and suggest the optimal way to approach this issue in the future, on a micro and macro level.

To begin, we'd like to start by talking with an individual who has been personally impacted by gut dysbiosis and mental health. Let me introduce Jenna Christensen, a 25 year-old marketing manager, who is here to tell her story. Following that we will hear from a researcher, Cynthia Cohen, from UCSF, a primary care physician, Dr.

Nefkens, a psychiatrist, Dr. Deirmenjian, a functional medicine doctor, Dr. Law, and a worker for the FDA, Emma Davis. Take it away Jenna.

Jenna (Millie): Hi, thank you so much for having me. I guess to begin I'll give a bit of background on my story. My health was never the best. My mom had a c-section when she gave birth to me and I wasn't breastfed as a baby. I then went on to develop seasonal allergies and eczema throughout my childhood that still plague me today. Sometimes they would get so dry and itchy that my skin would crack and bleed.

Moderator (Audrey): Ah, yes, 25 years ago there wasn't as much knowledge about the importance of developing a healthy microbiome early in life from a vaginal birth and from breastfeeding. It's now commonly known that when children don't develop a healthy microbiome they are much more likely to develop problems such as seasonal allergies, eczema, and autoimmune disorders.

Jenna (Millie): Exactly. To continue with my personal history, my health continued to steadily decline throughout high school. Part of it was probably because I ate a really unhealthy diet filled with sugary and processed junk food; cheaper, unhealthy food was all my family could really afford. My freshman year of college I was also chronically sleep-deprived, pulling all-nighters at least once a week and really stressed out trying to keep up with the demands of my courses. At this same time I fell sick with strep and was prescribed antibiotics by my student health center. This is when things really started to decline. After taking antibiotics I noticed how my immune system never really seemed to recover because I was constantly sick with colds and I went on to develop chronic sinus infections and was prescribed even more antibiotics. After that, I started to have a hard time with my digestion, experiencing chronic stomach aches. At the same time I went from never having many mental health problems to having anxiety that was soaring through the roof and fluctuating depression. Naturally, I went to my primary care physician for this who then referred me to a gastroenterologist for my stomach problems and a psychiatrist for my mental health problems. The gastroenterologist chalked my stomach problems up to my stress and anxiety and the psychiatrist put me on Zoloft for my anxiety and depression. It seemed to help a bit, but my health still feels off and no Western Medicine doctor has been able to give me any answers.

I’m hoping my story will be able to resonate with others who are going through the same issues.

Moderator (Audrey): Thank you so much for sharing your experiences, Jenna. As I mentioned before, we will now turn to a panel of experts to attempt to untangle your personal history and figure out what is contributing to your gastrointestinal and mental health issues. Hopefully, these 5 professionals will be able to help us gain a better understanding of the gut-brain connection and what we can all do to promote better gut and neurological health in our bodies. First, we will hear from a researcher who will explain the science behind the connection between the microbiome and anxiety and depression.

Researcher (Michelle): Hi everybody- my name is Cynthia Cohen. I am a psychiatry resident pursuing my PhD at UCSF. I have been researching the gut microbiome-mental health connection for my dissertation so I think I will be able to provide some good scientific background on the topic. Thank you for having me on this panel and thank you to Jenna for being willing to share your story!

It is interesting that you have seen a connection between your gastrointestinal issues and your mental health because the gut-brain axis is quite a hot topic among researchers today. We have done a lot of research trying to identify the mechanism by which the brain and gut communicate with each other. We have figured out that there is indeed a physical connection between these 2 organ systems. The vagus nerve serves as a neuronal pathway between the central nervous system and the brain. The vagus nerve is responsible for a lot of your body’s involuntary responses, including regulating the passage and digestion of food through the intestines. A lot of mice studies have suggested that the vagus nerve serves as some kind of “hot line” that lets the microbiome “talk” to the brain, but we’re not sure exactly how this works yet. Also, this hot line is not unidirectional. The digestive system and the nervous system are connected via bidirectional feedback loops. Psychological stress can cause increased permeability of intestinal membranes, and diets high in fat and sugar have also been shown to cause more porous intestinal lining.

Jenna (Millie): Oh that makes sense! So maybe the way I was eating

earlier in my life and my stressful college years caused my stomach pain and chronic digestive issues?

Researcher (Michelle): That's totally possible. The increased intestinal permeability that comes from stress and a poor diet leads to food antigens and bacterial components like liposaccharide endotoxin (or LPS, which is a component of the bacterial wall) to be released into systemic circulation. Presence of LPS has been linked to depressive symptoms, which provides another piece of the puzzle in terms of how the gut can affect our psychiatric state.

Additionally, many neurotransmitters, including acetylcholine, serotonin, dopamine and gamma aminobutyric acid, are produced in the GI tract. In fact, 95% of your total serotonin, a neurotransmitter responsible for regulating mood and promoting happiness, is produced by the microbiome. A poor diet feeds the "bad bacteria" in your gut, which means less of those good bacteria can produce essential neurotransmitters in the GI tract. This can then cause side-effects of psychiatric disorders like anxiety and depression. Microbiota have also been found to play an important role in regulating the Hypothalamic-Pituitary-Axis, a hormonal axis which controls your stress response and is chronically activated in patients with anxiety and depression. Alternatively, hormones from our brain also regulate neurotransmitter production and the GI tract, and dysregulation of these hormones can also lead to psychosis. So it works both ways.

The problem with speaking definitively about the microbiome-mental health connection is that so far, most of the research that has been done is on animals. For example, the literature shows that mice that have been raised in a completely sterile, pathogen-free environment, and thus have no microbiome, have dysregulation in their neuroendocrine and behavioral responses to stress when compared to control mice. Also, many studies have exposed mice to antibiotics and probiotics to evaluate the effect on their mental health when their microbiome is altered drastically. One study exposed mice to antibiotics for two weeks and found that they had altered neuronal activity and decreased social recognition, pointing towards an altered psychiatric state. Another study gave mice probiotics for 2 weeks and found significant reduction of anxiety-like behaviors, and I know of at least 8 studies that found improvement in depressive symptoms in mice that were given probiotics.

Despite the fact that there is a lot more research with animals than humans, I do know of 4 human studies that have correlated probiotic usage with improvements in anxiety and 5 studies that show reduced depression. Additionally, in human patients with Irritable Bowel Syndrome, probiotics have been shown to improve both physical and the accompanying psychiatric symptoms. There are probably a lot more studies out there that claim correlations between gut composition and mental health too, but those are the ones I am familiar with. To me, the literature points to a strong correlation between microbiome composition and mental health, but unfortunately, it's still not really enough to claim a causational relationship.

Moderator (Audrey): Thank you Cynthia for your thorough insight into this problem. Your knowledge on the topic really legitimizes the issue that Jenna and countless other individuals affected by gut dysbiosis and mental illness are going through. We are now going to hear from Dr. Julie Nefkens, an internal medicine doctor from Kaiser Permanente Martinez. Dr. Nefkens, as the first person who patients come to with their health problems, could you tell us a bit about your thoughts on the connection between the gut microbiome and mental health?

Primary Care Doc (Tasia): Hi, thank you for having me here today. I have been a physician for 30 years so have seen quite a few patients in my time suffering from both gastrointestinal and mental health problems. I know that Jenna brought up antibiotics in her story and I will say, antibiotics have been a big problem in the healthcare industry in recent years. People always beg me to prescribe them antibiotics, but nobody seems to realize what a big problem antibiotic resistance is and how much antibiotics can wipe out both the good and bad bacteria in your body. Some studies show it can take as much as 2-5 years to replenish your gut bacteria after a round of antibiotics. While I don't have a clear answer about how the gut microbiome and mental health relate to each other since all of the new research being done is still very correlational and therefore hasn't been implemented into hospital protocol, I will say that the vast majority of patients I see with gut problems also have mental health problems. I also think there has been an increase in recent years in cases of gut problems and mental health problems. I wish I had received better training in this area of study, however most of the research is still very new so there's a lot we don't totally know

as of right now. I am really hopeful that in the coming years and as research uncovers more answers that we will be better trained in how to provide the best care possible to our patients who suffer from this problem. That being said, the gut-brain connection is definitely popping up a lot more in my practice. My patients experiencing gut problems often ask for my input on probiotics, however I find it hard advising them when I myself am so confused by the probiotic trend. I can't even walk into a supermarket anymore without being so overwhelmed with all of the probiotic choices and how commercialized gut health has all become. It's very trendy right now. I will say that I believe diet is very important for our overall health, and I do think it could impact mental health. I always encourage my patients to eat a diet with whole, non-processed foods that incorporates as many colorful fruits and vegetables on their plates as possible. The fewer ingredients and more natural something is, the better. I know Jenna had mentioned she was pulling all nighters, and chronic sleep deprivation and stress have actually been proven to increase inflammation in the body, which can contribute to gut and mental health problems. I always remind patients to be mindful of that and incorporate relaxation techniques into their daily lives.

Moderator (Audrey): Thank you so much, Dr. Nefkens, for that insightful answer. It's so great having all of these different perspectives from various experts in their field. We will now be inviting Dr. John Deirmenjian to speak, a psychiatrist who owns a private practice in Beverly Hills.

Psychiatrist (Jack): Hi, I'm very intrigued by what has been said so far and am happy to add in my input. I will say that Jenna's story resonated with me because I see patients in my practice all the time who are experiencing the same types of problems. I would say that anxiety and depression are the two most common reasons people come to me seeking treatment and that there has definitely been an increase in rates of mental health problems in recent decades. I think there could be a lot of reasons for that increase, but the exceedingly stressful way of living in modern society is definitely taking a toll on peoples' mental health. It's becoming a genuine problem where my patients are becoming so anxious and depressed that they have to go on work leave. Just yesterday I was reading an article that said for every $1 the US government puts into mental healthcare, they get a return of $4 with increased worker productivity and fewer mental health leaves of absence. The problem is that mental health is

chronically underfunded, which is a huge problem for a psychiatrist like me because there are all of these people who need my help but don't have insurance coverage. Another issue with medical insurance is that it is separated into mental health coverage and all other kinds of coverage because our society views these 2 aspects of our health as separate. This means that when patients like Jenna go in to see their PCP, they won't be treated holistically for both their mental and physical problems. When a patient comes to me with physical and mental problems that are probably interrelated, I can only help them with their psychiatric issues. And I agree with Dr. Nefkens that many patients I see have both mental health and gastrointestinal problems. I know this because I always check their medical chart for this, given the interactions medications can have with the GI system. I believe the GI problems are often brought on by anxiety, given that anxiety decreases the function of the parasympathetic nervous system which is in charge of regulating digestion. At this point I can't say I know of any link between the gut microbiome specifically and mental health. It's not something psychiatrists are particularly trained in, but after hearing what the panel experts have said today, I think maybe we should be.

Moderator (Audrey): That's really interesting stuff, Dr. Derimenjian. I think it's pretty clear that the gut microbiome is affecting not only our bodies, but also altering our communities and societal productivity. Next, we would like to introduce Dr. Law, who is a Traditional Chinese Medicine practitioner, to speak on how holistic Eastern medicine approaches can address some of the uncertainties Dr. Deirmenjian brought up.

Functional Medicine Doctor (Michelle): Hello everyone, thank you for having me. So, first of all, I'd like to go over some Traditional Chinese Medicine basics, since we TCM practitioners view the human body system with an entirely different lens. TCM focuses on the production of "chi," a bodily substance best understood as energy, and optimized flow of qi in the body's numerous qi channels. TCM also constructs the human body as an interconnected system of 12 organs with specific entry and exit points, with each organ representing a specific emotion or sensation. TCM practitioners believe disruptions in channels or qi deficiencies affect the organs representative of certain feelings, which in turn cause deviant emotions and psychiatric disorders.

Jenna (Millie): Oh wow! It's super interesting that you say TCM doctors think of the body as 12 interconnected systems. Throughout my life, whenever I was having my health problems I was referred to separate doctors for each organ system that was dysfunctional. For example, I would be referred to a gastrointestinal doctor for my GI problems and a psychiatrist for my anxiety but I always felt like these issues were interrelated.

Functional Medicine (Michelle): They certainly can be! In the context of TCM, we think gut dysbiosis and subsequent mood disorders like depression and anxiety go hand in hand. In fact, they are commonly diagnosed as "Gu syndrome." Gu syndrome can be traced back thousands of years, and was referred to as "Gu magic" in ancient Chinese historical texts. However, for present-day TCM doctors, it is better understood as a complex parasitic infection. In order to fight Gu syndrome infections, TCM doctors look to restore patients' original gut microbiome profiles over time using diet as herbal therapy. It is essential to remove 'bad foods' and replace them with 'good foods,' which means cutting out foods containing refined sugars, dairy products and gluten because they are more likely to trigger inflammation. 'Good foods' include fermented foods packed with probiotic properties which promote gut flora growth, including Furu, which is fermented tofu, and Douchi, or fermented soybeans. Other qi-promoting foods like ginger, bone broth, cinnamon, black pepper and dates can also be beneficial. These foods possess the amino acid L-glutamine, which is found in Western probiotics to strengthen the intestinal linings of the gut system.

Similarly, a lot of contemporaneous Western procedures and findings actually reflect long-accepted TCM practices. For instance, the first Western fecal transplant was performed in 1958 by Dr. Ben Eiseman to treat C Diff infections, but Ge Hong of China actually began performing fecal transplants 1600 years ago to treat patients in need of improved qi production. So, this suggests that Eastern medicine practices are very effective despite the fact they are not widely accepted by the eurocentric principles of Western science. I often see patients who are frustrated by receiving numerous ineffective and dissimilar treatments from various Western specialty doctors, and feel that they are at their wit's end, and have no choice but to seek alternative treatment from TCM providers. So you know, I do feel as if Western medical practices unfairly discredit Eastern practices because they cannot be explained by eurocentric methods of science, despite having been used and proven effective by ancient civilizations for thousands of years. Unfortunately, one of the big barriers to effectively providing this kind of care to patients is the fact that most Eastern medicine practices are not covered by insurance.

Moderator (Audrey): Thank you very much Dr. Law for your unique perspective on treating gut dysbiosis from outside the bounds of Western medicine. Maybe Jenna will have some luck in getting healthier if she sees a TCM doctor. Next up we have Emma Davis from the FDA. As Cynthia Cohen said, probiotics seem like a very promising treatment for improving gut health, and consequently, mental health. Also, like Dr. Nefkens said, overprescription of antibiotics seems to be a key contributing factor to gut dysbiosis. Now we have Ms. Davis here to give us some legal perspective on the regulation of probiotics and antibiotics.

FDA (Millie's roommate): Hi there, thanks for having me here! I am Emma Davis from the Antimicrobial Drugs Advisory committee of the FDA. My line of work mostly involves the regulation of antibiotics, which, as we know, is currently a pretty controversial topic in the United States. Jenna is not alone in her experience with being over-prescribed antibiotics and noticing adverse affects on her health. The CDC, which the FDA works closely with, estimates that 30% of antibiotic prescriptions are unnecessary. They are commonly over-prescribed in outpatient settings for viral respiratory

infections, like in Jenna's case. As a consequence, antibiotic-resistant bugs are becoming more and more common. Every year about 2 million people develop infections that are antibiotic-resistant and about 20,000 of those people die. In 2015, the FDA approved new drugs to fight these antibiotic-resistant pathogens that are leading to thousands of deaths every year, but one can't help but feel like it is a never ending battle against pathogens that constantly mutate to evade our drugs. We are fully aware of the damage overprescription of antibiotics has done to American citizens and have been working hard to remedy the issue. For example, in 2015, we partnered with the CDC to better regulate and distribute antibiotics. We created a campaign to better educate people on antibiotic usage via brochures, web pages, etc. We have also been urging doctors to prescribe only for legitimate illnesses and better educate their patients on the side effects.

Jenna (Millie): That's good! I wish my doctor would have been a lot more careful when prescribing me antibiotics. I was prescribed them too many times when I probably didn't need them. And I got no warning on the impacts that could have on my microbiome! I also feel like my digestive system wouldn't have been so messed up if I took probiotics at the same time as my antibiotics. Do you guys regulate those?

FDA (Millie's roommate) : Good question. As for FDA regulation of probiotics, sometimes we regulate those, but most often we do not. This is because probiotics are usually sold as dietary supplements or food rather than drugs or a treatment for a disease/disorder. Dietary supplements don't require FDA approval and their labels can say anything they want as long as they aren't health claims. One might say that there are potential issues with this because little regulatory oversight of probiotics might lead to production of low quality or even harmful probiotics, even though they have demonstrated their therapeutic qualities for people with gastrointestinal and other disorders.

Moderator (Audrey): Thank you to each and every one of our panel experts! So, it seems we have a lot of compelling ideas on how to best help Jenna solve her health problems.

Let's start by discussing diet and its impact on gut and mental health. Based on research from our experts in both Eastern and

Western medicine, it seems like one of the most powerful interventions for improved gut health is maintaining a good diet. Cutting out processed foods high in fat and refined sugar like you know, french fries, sodas and battered foods, and instead introducing foods with probiotic content like sauerkraut, fermented soybeans, and fermented tofu, is incredibly important. Is that something you would be willing to do, Jenna?

Jenna (Millie): Yeah! So you mean I should just cut out American food and stick to foods from other diets, right? It sounds like Japanese and Mediterranean diets are way better.

Moderator (Audrey): Well, you are right in that those traditional diets you mentioned have healthful probiotic foods that help a lot with gut dysbiosis. But, we want to be careful in stereotyping or discrediting certain diets, as this can reinforce popular or fad diet movements. As we begin to view food as medicine in managing long-term and preventative care of our gut, we must also be aware of how social forces can influence those views on certain foods. While naturally probiotic foods are beneficial, the food industry has popularized superfood diets and probiotic supplements without real scientific evidence for efficacy.

Jenna (Millie): Oh, I've actually seen a lot of those probiotic supplements at Whole Foods recently. My friends have been telling me to buy them, but I'm suspicious because they aren't regulated by the FDA like Ms. Davis said.

Moderator (Audrey): You're right Jenna, those points are absolutely valid. Your medical doctor should be the one to prescribe prebiotics and probiotics in conjunction with any antibiotic prescriptions, since antibiotics can play a huge role in wiping out your gut microbiome. You had mentioned your experiences with taking multiple rounds of antibiotics, and that brings up one of the institutional problems within the American medical system. Based on our panel's expertise, we believe there must be a change in medical school curriculum that focuses on maintaining microbiome health and changing prescription habits and norms. Doctors must be educated on the effects of overprescription, as the drastic impact on individual patients' psychiatric health is often overlooked and questioned. This should also reflect broader changes in societal attitudes, with the general public understanding that antibiotics can have effects

outside of the commonly known issue of antibiotic resistance. This lends to a bigger paradigm shift towards preventative health over targeted symptom treatment.

Dr. Nefkens (Tasia): I got my medical degree many years ago, and I can definitely say that my education did not emphasize linking the gut microbiome with things like psychiatric illness. When I think about it I find this a bit ridiculous that we didn't put more emphasis on studying microbiome composition because, I mean, the number of bacterial cells outnumber our own cells 10 to 1! That fundamentally shifts the way we think about who we are and how we are made up. Our bodies are only 10% us! So, when we think about our gut health, it becomes much more plausible that changes in our microbiome could drastically alter other bodily functions such as our mental health. Unfortunately, without change in curriculum, I don't see how future doctors will be able to take this kind of thinking and apply it to patient care. There would need to be a fundamental shift to treating patients more holistically.

Jenna (Millie): I definitely agree. When I met with my doctors, I felt like they were trying to cure me one symptom at a time. They were not at all connecting the dots to ensure they were preventing any offshoot effects of my antibiotic use. I wish my insurance covered TCM providers, because I would definitely have liked to see how Eastern medicine might have prevented this. I feel like if I had seen an Eastern medicine doctor sooner I would have learned to prioritize my health more and reduced my stress, instead of following you know, like the work, work, work attitude everyone here has. I almost felt like we glorify stress and overworking instead of recognizing it as a lifestyle imbalance that has all these downstream effects.

Moderator (Audrey): Well, I definitely see how that can be super frustrating. It seems that any potential solutions might require blending approaches from both Eastern and Western medicine, and such a change must be made on a structural level. Like Dr. Law mentioned, the validity of a treatment requires publishings in scientific journals in Western medicine , which mandates compliance with culturally-specific ways of practicing science. More comprehensive and effective treatment plans can be made by taking into consideration that there is a time and place for both Eastern

and Western medical practices. Eastern medicine is best suited for prevention of illness and holistic care, while Western practices are best suited for solving immediate medical afflictions, like open wounds and trauma-related or invasive surgical procedures. As a result, in terms of illnesses like gut dysbiosis and subsequent psychiatric disorder, preventative measures using diet or probiotics, which are more reflective of Eastern approaches, should be integrated in standard medical practice. Realistically speaking, however, differences in health insurance coverage hinder this collaborative viewpoint.

At the same time, we can see recent improvement in inclusion of Eastern medical practices, as therapies like acupuncture and cupping have become increasingly common in hospitals and sports medicine clinics. This may be the first of many steps in incorporating Eastern medicine into the mainstream Western medicine framework to create optimal solutions for complex healthcare problems.

Jenna (Millie): Yeah, I could definitely see how these changes could help improve our collective health as a society.

Moderator (Audrey): Indeed! Well, that seems to be all the time we have for today's segment. Thank you so much Jenna, for sharing your experiences. We hope that the discussion we had today with the help of our panel of experts was illuminating.

Jenna (Millie): Yes, thank you so much everyone for having me! I learned a lot today, and I definitely plan on changing my own personal lifestyle choices to help combat my symptoms. I also really hope to see some of the bigger structural changes we talked about today being implemented one day. Thanks again, and have a wonderful day everyone!

****outro music****

Moderator (Audrey): Special thanks to the people we interviewed to gain insight into our topic: Dr. Jonathan Law O.M.D., Dr. John Deirmenjian M.D., Dr. Janeen Smith M.D, Dr. Julie Nefkens M.D., and Dr. Wade Smith M.D.PhD.