Psychoneuroimmunology: The New Psychiatry

Trudy Scott interviews Dr. Kelly Brogan, MD on season 2 of The Anxiety Summit

Based on this review paper, Stress and the brain-gut axis in functional and chronic-inflammatory gastrointestinal diseases: A transdisciplinary challenge, published November 2019, this topic is still very relevant and a testament to the leading-edge subject matter presented by Dr. Brogan in 2014 on season 2 of The Anxiety Summit.

It also ties in perfectly with The Anxiety Summit 5: Gut-Brain Axis theme.

Here is an excerpt from the above paper:

*The broad role of stress in the brain-gut axis is widely acknowledged, with implications for multiple prevalent health conditions that are characterized by chronic gastrointestinal symptoms. These include the functional gastrointestinal disorders (FGID), such as irritable bowel syndrome and functional dyspepsia, as well as inflammatory bowel diseases (IBD) like ulcerative colitis and Crohn’s disease. Although the afferent and efferent pathways linking the gut and the brain are modulated by stress, the fields of neurogastroenterology and psychoneuroendocrinology (PNE) / psychoneuroimmunology (PNI) remain only loosely connected. We aim to contribute to bringing these fields closer together by drawing attention to a fascinating, evolving research area, targeting an audience with a strong interest in the role of stress in health and disease.*
Psychoneuroimmunology, The New Psychiatry

- The role of inflammation in anxiety and depression
- Hormones and where the endocrine system fits in
- Where inflammation comes from
- What a healthy microbiome looks like
- Natural lifestyle interventions to reverse symptoms and favorite nutraceuticals
- Why psychiatrists don’t know about this

“Psychoneuroimmunology, the new psychiatry”...“Cytokines in the blood, or inflammatory messengers, such as CRP, IL-1, IL-6, and TNF-alpha are predictive and linearly related to depression and anxiety, especially in women.”

Dr Kelly Brogan MD, boarded in Psychiatry/ Psychosomatic Medicine/ Reproductive Psychiatry and Integrative Holistic Medicine

The Anxiety Summit
Hosted by Trudy Scott, Food Mood Expert
Season 2 • Nov 3 -16, 2014

Trudy Scott: Hello and welcome to this interview on Season 2 of The Anxiety Summit. This is your host, Trudy Scott here. I’m a certified nutritionist. I’m known as a mood expert and I’m the author of the Antianxiety Food Solution. If you tuned into Season One, you'll remember today's wonderful speaker from that summit – Dr. Kelly Brogan.

She spoke on “Misunderstood and mistreated: re-inventing psychiatry.” We touched on inflammation in the gut and today's topic is going to take a deeper dive into the same fascinating topic. The title is “Psychoneuroimmunology, The New Psychiatry.”

Kelly, welcome. It's a real pleasure having you back.

Kelly Brogan: Thank you for keeping this going. This is very exciting. Thanks for having me.
Trudy Scott: Well, I'm just really pleased to have you here. So, let me read your bio and then we'll get started right away because this is really very fascinating and I know you've got some great information to share. Dr. Brogan is boarded in psychiatry, psychosomatic medicine, reproductive psychiatry, and integrative, holistic medicine and practices functional medicine – a root cause approach to illness – as a manifestation of multiple, inter-related systems. After studying cognitive neuroscience at MIT and receiving her MD from Cornell University, she completed her residency and fellowship at Bellevue NYU. She's one of the nation's only physicians of perinatal psychiatric training who takes a holistic, evidence based approach into the care of patients with a focus on environmental medicine and nutrition.

She is also a mom of two and an active supporter of women's birth experience rights, to birth empowerment, and limiting of unnecessary intervention. She is a medical director for Fearless Parent and an advisory board member for Green Med Info, Pathways to Family Wellness, NYS Perinatal Association, and Fisher Wallace. She practices in New York City and is on the faculty at NYU Bellevue.

So, let's get started with our topic – “Psychoneuroimmunology, The New Psychiatry.” And I would love you to just share what psychoneuroimmunology is.

Kelly Brogan: Absolutely. So, it's probably one of my favorite words and –

Trudy Scott: Me too.

Kelly Brogan: And there's a whole discipline devoted to it, but you wouldn't know that, you know, from the lay press headlines. It's sort of tucked in the archives of Pub Med online, but it's really a robust and burgeoning field. And I think why it's so appealing is because, you know, the limitations of conventional psychiatry, as we discussed last season, are apparent in moderate to minimal response rates, in short and long terms side effects. You know, I think the whole field is ready for a rebirth. And this is from the conventional side of the aisle and certainly from the holistic side of the aisle. We've been pioneering this for some time now. But what psychoneuroimmunology refers to is essentially the inherent inter-connectedness between multiple systems. So, it's about no longer looking at psychiatry as a head up phenomenon, which at best can result in limited outcomes and at worst, can be quite dangerous. And what psychoneuroimmunology implies is
that there is a relationship between neurology – so, between brain science – and the immune system. But it also sort of – and actually, sometimes it's called psychoneuroendocrinology – it also sort of ropes in the gut and the endocrine system with the implication being that you cannot treat one without knowledge about the others. So, I think it's very exciting and really is a term that embodies functional medicine, or naturopathy at its best.

Trudy Scott: Wonderful. And, as you say, it brings in all components – that we're getting to the root cause of the problem. I love it. Now, let's talk about the role of inflammation and how this ties into psychoneuroimmunology and then anxiety and depression.

Kelly Brogan: Okay. So, you know, what psychiatry has been operating under for about the past 50 or so years is termed the monoamine hypothesis, right? And that refers to this notion that there is a chemical imbalance – primarily serotonin, dopamine, and norepinephrine – underlying the pathologies that we are labeling as psychiatric. And frankly, it's a very broad swath, right? So, it ranges from eating disorders to multiple different anxiety syndromes from OCD (obsessive-compulsive disorder) to phobias to generalized anxiety and of course includes depression.

And these are all diagnoses that are treated with, quote, unquote, “antidepressants, SSRIs and SSNRIs”. And so through deductive reasoning, you know, the field has essentially made the assumption that if these medications are having an effect, it must be because of what we know about their, quote, unquote, “primary mechanism,” which is that these medications interfere with the trafficking of these specific neurotransmitters, right? So, you know, people in the conventional realm, heading up the NIMH (National Institute of Medical Health), are coming out and making claims essentially supporting the fact that this science has never been validated. And we need to go back to the drawing board because of limited outcomes and potentially, misconception at the root of the practice of psychiatry today. So, there is an effort on the part of those even with conflicts of interest in and out of the pharmaceutical industry.

There is an effort to sort of turn the page. And what many are speaking about is something called the cytokine model, which has been around since 1991 – you know, the first paper hypothesizing about this model. So, it's been a growing literature for some time. And what it refers to is this: essentially it looks at depression or anxiety, for example, as this non-specific sort of fever that tells us actually very little about what's causing the body to react, but tells us that there is an expression of imbalance and that the body is
working to recalibrate. So, there's some sort of stressor or triggers or assault and the compensatory response on the part of the body is what we are seeing as these psychiatric symptoms.

And it's actually more broadly applied. The literature is there for schizophrenia, and bipolar disorder, but there certainly is the most in depression and a growing literature in anxieties, specifically. So, when we think about this model, we have a couple of different tenants that underlie it. When I say “we” I talk about the brilliant people who are doing this research. Not me.

But, you know, we have these biomarkers, right? So, psychiatrists have been desperate for some sort of biological legitimization of what they're doing since the inception of the field. And, you know, we may sort of have what we ask for at this point. At least it's seeming to take shape. And when I talk about biomarkers, what I mean is that there are these inflammatory messengers that circulate and they have names like C-reactive protein (CRP), interleukin-1, interleukin-6, and TNF-alpha.

And in the literature, essentially, you know, there has been validated relationships between symptoms and these blood measures, so that they can be – especially in women – predictive, so that you might have elevations in some of these measures like CRP before the onset of your symptoms. They can be linearly correlated so that the higher these serum levels are, the most symptomatic you are and when they are resolved, your symptoms also resolve. And that they seem to be particularly relevant for some subsets of depression and anxiety, specifically – an interest of mine, which is – postpartum, but also what is called atypical depression. And that is a bit different than what we refer to as melancholic depression, which is sort of what it sounds like. Because atypical depression is characterized by oversleeping, overeating – sort of like, cravings.

Also, there's a difference in feeling - a bit better in the afternoons relative to the mornings. So, we sort of start to draw in the relevance of the cortisol rhythm over the course of the day as a modulator of these inflammatory messengers. And it just helps us to start to think about how some subsets, at least, of what we are calling depression, anxiety, and bipolar disorders specifically, may actually be inflammatory response. And in this way, you know, these diagnoses are just joining the ranks of the rest of chronic disease, right? So, autoimmune disorders, cancer, diabetes, different metabolic syndromes, cardiovascular disease – all of the
cutting edge research in these different pathologies is suggesting that inflammation is the underlying driver.

And some of the researchers like Maze and Raison, who have over the years tried to flush out this theory based on the science, suggest that at some point in our evolution, this inflammatory response was adaptive, right? Because it helped us to slow down, withdraw, avoid others, decrease our activity for recovery. But we've essentially turned an acute response that was adaptive at some point in our evolutionary history into a chronic response that now the brain has to contend with and decide, “Am I going to continue to allow this inflammatory response to exist? Am I going to try and suppress it with cortisol? Am I going to turn cortisol off at some point?”

So, we see this sort of more chronic picture of unremitting symptoms that have a connection to many other physical states, right? So, I haven't seen a patient, probably ever, who doesn't have a single physical complaint. Whether it's headache or body aches or joint aches or gastrointestinal changes like constipation, they always sort of come with this syndromal picture of bodily response. So, okay, so the biomarkers are one.

We also have animal models. I always find the idea of an animal model of depression or anxiety sort of like a funny concept but this is really what is going on in terms of research. And they use things like what are called forced swim tests. So, essentially, the animals stop trying at a certain point and that's considered one of the models of depression. And one of the ways that they induce it is by injection of an endotoxin called lipopolysaccharide. And this is essentially a way to inflame the animal.

And what's interesting is that this – we start to think of, “Okay, so where does this inflammation come from?” And maybe we'll talk about that in a little bit. Lipopolysaccharide is made by a component of gram-negative bacteria in our gut. It's supposed to be retained in our gut, not floating around in our blood stream. So, it's a bit of a look through the key hole as to where this inflammatory response may originate.

But what's interesting is that in some of these rodents, they knock out a gene for a specific cytokine called interleukin-1 and the mice are actually protected against lipopolysaccharide mediated symptoms. So, we know that there is a relationship between the inflammatory insult, but then the messengers, these cytokines – in the expressions of what we are seeing, quote, unquote, “clinically”.
And then the third tenant is that we have some pharmacologic data that supports this model, right? So, we know that in Hepatitis C, 45 percent of patients develop depression with interferon treatment, which is essentially an inflammatory treatment, which is far more than we can consider a routine side effect, right? So, it's suggestive of something important in terms of the mechanism of that medication and also the development of psychiatric symptoms.

And then a number of trials have taken a look at anti-inflammatory agents like Celecoxib or Infliximab – you know, these sort of anti-inflammatory medications – and they have found that when patients have these inflammatory markers present and they are treatment resistant – meaning they haven't been helped by the conventional paradigm – you can resolve their symptoms with these anti-inflammatory medications. And there's even some suggestion – which is somewhat controversial – that antidepressants themselves, when they do have an effect, may have an anti-inflammatory effect. So forget about the whole serotonin business for a minute and think about the fact that maybe when they are having an effect, it may be because they down-regulate something called interleukin-6. So, most of the studies are observational, but it is somewhat provocative. So, that's sort of the bedrock for the conceptualization of these pathologies as primarily inflammatory in nature and as representative of what we're calling an evolutionary mismatch, right?

So, our systems are not quite built – or at least yet evolved – to live and function optimally in the current environment. And I find that a very compelling explanation for what we are seeing as an epidemic rise in mental illness country and in the world.

**Trudy Scott:** Excellent. I've got a few follow-up questions, if I may.

**Kelly Brogan:** Absolutely.

**Trudy Scott:** I found it interesting that you talk about the anti-inflammatory medications. And I know we're going to talk more about some natural ways that we can lower inflammation, but just seeing that mechanism I think is very interesting. But a follow on question was the biomarkers. So, you mentioned CRP, C-reactive protein, interleukin-1 and 6, and TNF-alpha. Are the latter – the interleukin-1 and 6 and the TNF-alpha – readily available for testing? And are we seeing correlations between those as being predictive and then also, higher levels causing worse symptoms, as well as the CRP?
**Kelly Brogan:** That's a great question. So, in clinical practice – we talk about functional medicine as having a 17-year lag between what appears in the literature and what gets to you doctors' office, right? And to some extent, with the measurement of cytokines, this has been somewhat difficult to translate because as far as I know, sort of normative range and assessment in the outpatient setting through LabCorp or Quest for these type of bio-reference/ these types of labs, isn't something that most clinicians are ready to do. And what they're noticing in the literature is that these cytokines like interleukin-1 and 6 and TNF-alpha, they're looking at like, qualitative changes over time. But I don't think it's reasonable to expect that – and this is true for almost every lab value – that we have a well-quantified reference range for what is optimal, right?

Because what is optimal is probably a very dynamic variable. It could be optimal for a certain condition under one set of circumstances and not so much under another. What has been better quantified and is a slightly different, very non-specific but pretty well validated indicator is high sensitivity CRPs – the C-reactive protein. In psychiatry, we have a good body of literature that helps us understand what might be a reasonable cutoff, which is three. But, you know, it's highly non-specific.

So, you could have one CRP on a Monday that you don't have the following Friday. So, it's an acute phase reaction. It's something that is part of the body's response mechanism, meaning that we don't want to, you know, overly rely on it. It should inform the treatment generally. So, you know, I will check things like C-reactive protein and homocysteine to get a general picture.

I'll take a look at white blood cell patterns to get a general picture of responsivity. But I also know that, I can have a patient come to me with a C-reactive protein in the high 90s and within two months, it could be below one based on pretty simple interventions. So, in many ways, it's just for trending that I find it relevant because I make very similar considerations around inflammatory response for almost all of my patients. So, I'm not using it the way researchers are using it to identify a subset of patients who are treatment resistant who may be, you know, eligible for another type of pharmacologic interventions. Because that's really how it's being used in the literature.

**Trudy Scott:** Okay. Great. And you mentioned the reasonable cutoff of three, but we really want it to be below one. That's ideal.
Kelly Brogan: Yes. Yes, that's ideal. And it's doable.

Trudy Scott: Oh, yes. I've seen it. People get on a gluten-free diet and their CRP comes way down.

Kelly Brogan: Exactly. In a matter of weeks.

Trudy Scott: Yeah. And we're going to talk about some of those interventions in a second. So, it's really exciting that there is this bio-marker because we keep hearing that there are no tests for mental health disorders, and now, we've got this marker that we could use. So, very exciting.

Kelly Brogan: Yes.

Trudy Scott: And then going back to the LPS – lipopolysaccharide – that's an endotoxin that they introduced into these animals, but this is something that us as humans can be exposed to as well, which could be a contributing factor for some of the inflammation that we might see.

Kelly Brogan: Right. Exactly. And we often are in the setting of what has been dubbed “intestinal permeability” which has been largely legitimized by Alessio Fasano, who is one of the primary researchers elucidating the role of gluten and specifically, its activation of something called zonulin in the promotion of intestinal permeability. But we also have other chief suspects, right? Like, one of the ones I'm very interested in is glyphosate, which is the active ingredient in Round Up.

Also, Bt toxin. So, in genetically modified foods, we have mechanistic reason to believe that they contribute to and synergize with things like gluten in the promotion of intestinal permeability. Another one that I warn a lot of my patients about and that's actually well documented is intestinal permeability that can arise from NSAID exposure. So, you think you're just popping an Advil or a Motrin for your menstrual cramps and, in fact, one of the unintended consequences may be that you're promoting your own intestinal permeability so that the luminal contents – so, whatever's going on in your gut – now has access to your bloodstream and to your immune and inflammatory cascades in ways that it might not have otherwise.

Trudy Scott: Excellent. Do we want to continue with other factors that can cause this inflammation? You've mentioned the NSAIDs and the gluten and the genetically modified foods. Do we want to talk
about sugar and antibiotics right now and then we'll go on to psychoneuroendocrinology, with the connection to the hormones?

Kelly Brogan:

Let's do it. Yes. It's really funny. I was on the train last night and I saw an ad for a new Coca-Cola, right, and it's got a green label and it's called Coca-Cola Life. And it's sweetened with cane sugar and stevia.

I thought – you can't make this stuff up. So, obviously, there is some awareness of the potential problems of sugar and we try to get around it with all the synthetic stuff – with Aspartame and all of the sort of like “me too” chemical agents that now, of course, are raising signals of harm that are too loud to ignore just trying to replicate that sweet taste. So, I think that there's a growing awareness that there may be more to sugar than just cavities, right? And in my practice, it's one of the chief concerns I have. You know, I treat women – reproductive age – most of whom suffer from anxiety, if not all of whom do.

And, you know, I had a patient in here last week who came in and she was on two medications. She had just gotten out of the hospital. She had been on a laundry list of medications over the past 12 years and she was still having 6 panic attacks a day. I didn't start her on a single supplement. She was already actually trying to exercise – I didn't have to bark up that tree – so really, all that she did in the intervening window between her first consultation and the follow-up appointment a month later was dietary modification.

She came in at her follow-up and she said, “For the first time in my adult life, I have not had a panic attack in 30 days.” I had her blood work back at that point and she had a hemoglobin A1C of 5.9, a fasting blood sugar of 101 – this is like a healthy, young attractive woman, right? This is not like your picture of a diabetic. And so I know all that we had done in that month – it is not magic. All that we did was stabilize her blood sugar and her, quote, unquote, “psychiatric symptoms” disappeared.

So, for me, you know, this is one of many, many, many, many instances in my practice of where the stabilization of blood sugar is the primary intervention, you know, toward resolution of what we are calling anxiety specifically. But also, like sort of the dark underbelly of anxiety – which is like, brain fog, lethargy, sort of like this general sense of malaise, insomnia – and it's all part of that sort of roller coaster of displacing blood sugar instability. So, in addition to being essentially an endocrine disruptor, right – so,
tugging on your insulin and therefore, your cortisol, pulling from your progesterone, interfering with thyroid function – it also is, frankly, inflammatory. So, I remember one of the first times I saw a paper like this – it must have been a decade or so ago – of the acute immunosuppressive effects of sugar. And we know that it's an agent that can influence these cascades that we just spent some time talking about.

So, it's sort of a two-fer or maybe a three-fer, sort of donating to the healing process to eliminate it. But, of course, my angle on that is – and most people who are interested in dysglycemia – is to also simultaneously make more natural fats available for burning. So, I'm very interested in that as a source of inflammation.

I'm also interested in the role of stress response – and some people actually start with this – and certainly there are many therapists and healers who really work on the level of the stress response alone and get the same outcomes that I do with somewhat more complex – or at least demanding – interventions. But we know that the acute stress response recruits cortisol, which is a natural immunosuppressive in the initial response.

But then over time, your brain – which is essentially responsible for recruiting cortisol – says, “You know, this is not adaptive for physiology” and starts to diminish the signals. So, what some people talk about as adrenal fatigue and adrenal burn out – really focusing on the gland – I and some others are interested in looking more at the role of the brain as the master commander of that. So, where the gland is actually somewhat secondary to the decisions, essentially, that the brain is making this chronic stress picture.

And that's really where the role of cultivation of mindfulness, of what I sort of refer to as “personal non-resistance”. This sort of idea of engaging the stress in your life very differently and sort of leaning away from it rather than getting tossed up in the fray is a very powerful tool.

And in fact, you know, research out of the Herbert Benson Institute over four decades has demonstrated that you can have changes in inflammatory and insulin signaling gene responses over 20 minutes of total “novice level meditation,” quote, unquote, which is really a subject listening to a guided visualization in their earbuds. So, this is not master meditators, although, over time, the more you do it, the more robust benefits you get. And so there's been a really interesting body of literature that supports the anti-inflammatory effects of control of relaxation response. So, I think that those are
big ones. And then the primary tie in to maybe what we'll talk about in a bit is – so what is the role of dysbiosis?

So, what is the role of suboptimal gut, microbiota ecosystems in the inflammatory response? And the other two categories I just mentioned directly impact sort of the health of your microbiome. But certainly, so do infections and medications, and there's even things like birth control. So, there's a long list of considerations that we need to start making if we are going to finally acknowledge that the seed of our health is not even just in our gut, but it's specifically in our microbiome. And so that's really been one of the most exciting points of entry for me and where I've really come to focus a lot of my attention, I guess.

_{Trudy Scott:_} Great. And we're going to get on to that one in a second. I just want to go back to two things that you had said. I just think it's wonderful that you can see such amazing results by stabilizing blood sugar. Isn't that so powerful?

_{Kelly Brogan:_} I'm not sure I would believe it if I didn't see it with my own eyes, frankly, given my training and where I'm coming from. And seeing it replicated over and over. And, also, seeing it personally. You know, I was absolutely that girl who ate Snickers and Twizzlers every day and drank six cups of coffee and ran around on carbs and dairy all through my training. And I was hungry all the time.

I was exhausted all the time. And I had practically an arrhythmia, 60 percent of the time with my heart racing through my chest. So I know from personal experience that this is something modifiable – that it's not just the way you are, it's not your personality, and it's certainly not your psychiatric diagnosis that you can take to the grave.

_{Trudy Scott:_} Right. Exactly. And then I'd love you to just give clarification, for those who may not know, HBA1C – what do we want it to be and just explain what it is for folks who may not know.

_{Kelly Brogan:_} Right. So, it's a red blood cell measure of glycated hemoglobin. And essentially, what it demonstrates is the degree of damage of sugar – but also other sorts of advanced glycation end products, like charring your meat and that sort of thing and your baking – over baking sweet things like breads and stuff like that in an oven, even. So there are other sources, but it's primarily from the total quantification of sugar load in your diet and how much it is disrupting cellular function. So, there's actually some debate as to
whether or not it's a very reliable source because the turnover of red blood cells can be different from patient to patient and so you can get false elevations.

When you triangulate it with fasting insulin, fasting glucose and even something called fructose, I mean, you can start to get a picture of how relevant this is for patients. I like to see it definitely below 5.2 – meaning ideally, you know, in the high 4's range. But absolutely not above 5.6. David Perlmutter has collated literature suggesting that above 5.6, you're at statistically significant increased risk of Alzheimer’s. So, we certainly know that there are deleterious effects at the brain level at that point, and that's what's given rise to this notion of diabetes type three, or sort of diabetes of the brain.

This is something that over about two months, you'll see a change. So, if you want to track more immediate changes like over the past two to three weeks, let's say, then you'll probably want to use fasting insulin, glucose, and fructose as an alternative. So, with hemoglobin A1C, you'd see a change within about two months. I think one of my favorite studies was about aboriginal Australians who had sort of integrated into the mainstream and they all had type two diabetes and they were taken out of civilization, essentially, put back in the bush and they were hunting and gathering. And within six weeks, all of them reversed their type two diabetes. In six weeks.

_Trudy Scott:_ Wow.

_Kelly Brogan:_ So, it was pretty compelling, right? I love naturalistic data like that. I think it's so much more exciting than a randomized control trial. But I think that's just a powerful indicator of how fluctuant this can be. And yeah, I think it's something that I take pretty seriously.

_Trudy Scott:_ Wonderful. And then the HBA1C is reflective of the previous three months, correct?

_Kelly Brogan:_ About, yeah. Two to three months.

_Trudy Scott:_ Okay. Great. And then glucose – you mentioned that hers was 101. We want it under 100.

_Kelly Brogan:_ Yeah. I even like to have it under 90 because of some data suggesting that even a point over 89 – start to correlate with insulin resistance. And, you know, Cate Shanahan is a family physician I
really admire and she wrote a great book called *Deep Nutrition* that was very impactful for me. And she sort of collected a lot of the data that suggests that over 90 is concerning. The reference range on your lab slip, yeah, it's going to be 100 – sometimes even 110 – but your insulin signaling mechanism is already largely compromised at that point when you have fasting sugars in that range upon waking.

*Trudy Scott:* Okay. Great. And who wrote that book? Can you just repeat that?

*Kelly Brogan:* Oh, Cate Shanahan.

*Trudy Scott:* Okay.

*Kelly Brogan:* Yeah. She's great.

*Trudy Scott:* Excellent. And then insulin – what do you like to see for insulin?

*Kelly Brogan:* Below six. I like to see it below six. But this is a complex – for my patient population, it's a complex issue because you also don't want it too low because it has many roles, of course – but the role of insulin in conversion of storage for the thyroid to active form. And certainly its role in amino acid passage into the brain so it's a needle you want to thread. Like anything, you want some inflammatory signaling.

You want some cortisol. You want some insulin. But you want to sort of hit that Goldilocks' spot. And so I like to see it between two and six.

*Trudy Scott:* Okay. Great. And then any cutoff for fructosamine?

*Kelly Brogan:* That I normally use mostly for trending. But, below 200 would be nice. And often, I'm just looking at like, decrement. So, I'll see a patient come in with 350 or something and then they'll come back the next time and if they have a 280, I'm pretty excited. So, for me, it's not a hard line. I'm not sure if other people use hard lines on that.

*Trudy Scott:* Okay. Great. And then going back to your comment about the new Coca-Cola. The other whole issue with the cane sugar is that we've got this Round Up that's sprayed on the sugar before harvest. So, we're getting that exposure as well.

*Kelly Brogan:* Exactly. And just – look at the bottle and you think you're getting your serving of vegetable for the day or something like – trying to
suggest that it's some sort of a health food. In many ways, I sort of love it because it's bowing down to this demand that is bubbling up to the service on the part of consumers for some acknowledgment of what these corporations have done to our health over the years. So, you know, they're not trying to make us well or healthy. They're trying to get you to buy their product.

But at least there's an acknowledgment that this is of interest to people, you know, which I think is, in many ways, is kind of nice. It's kind of validating.

**Trudy Scott:** Yeah. And then I do want to just comment on your mindfulness recommendation because that is so powerful. You just mentioned controlling blood sugar, eating real food, and mindfulness and how powerful is that? I just think it's so wonderful. And then I'm glad you mentioned novice because some people think that's a big deal and if someone can just listen to a guided imagery tape and get some amazing results like that, how wonderful is that for a starting point if someone is feeling overwhelmed by the thought of getting into meditation.

**Kelly Brogan:** Absolutely. And I can relate to that, you know. I am not and wasn't ever a new age-y, hippie person. I'm certainly not.

And so then if I put myself in the position of a lot of these patients and I have somebody tell me to meditate, I would just say, “That's not for me. I don't do that” or “I don't have time for that” and what do I need? Like, a picture of Buddha and a cushion? That's ridiculous, right? So, if that is unappealing, then forget all that.

And what you can engage is really simple. And I give my patients sort of a long list of choices from books that come with CDs – to apps on their phone to online websites with streaming MP3s or even to HeartMath, right? And emWave which is like a little biofeedback gadget for those who like – I find it very cool – those who sort of like to see in real time quantification of their progress, which essentially is just this. It uses these lights to tell you how to breathe and it measures your heart rate variability so that you can see that your breathing is actually improving your electronic resonance. It's pretty cool. So, there are many different ways to engage it and the most passive is just plugging in some earphones and listening to a 5 minute – but ideally, 20 minute – guided visualization.

And it seems, according to the data, that just even walking the walk without even really engaging you with any level of expertise,
has beneficial effects. So, there's really no reason not to get started. And I ask patients to just start with just five minutes because most of my patients are moms and they're professionals and I feel like five minutes is about all we mentally feel we can potentially spare. So, let's just start with that and then work up to the 20. And that's all that's required. It's so simple, really.

Trudy Scott: It is. And I'm glad you mentioned giving people a choice because for some, it just feels like, "I can't do that." But I'll do the same. I'll say, "Well, there's this HeartMath tool that you can do on your computer. If you're on your computer anyway during the day, maybe that's something you could do. Pick five minutes out of your day to do that."

There's actually a wonderful HeartMath program – I'm sure you're familiar with it – where you can actually see this picture painting in the colors as you are slowing down your breathing. And I've had a lot of my clients really enjoy that. So, I think it's a matter of finding what's going to work for you and then actually making the time. And five minutes is a great start.

Kelly Brogan: Yeah. It's better than nothing.

Trudy Scott: Yes. Definitely. Okay. So, now we need to get onto the microbiome. And I actually had the pleasure of interviewing Dr. Ted Dinan for the summit. And as you know, he's the Irish researcher who's coined this term “psychobiotics” –

Kelly Brogan: Psychobiotics, yeah.

Trudy Scott: – together with a colleague. And I know you talk about from the gut to the brain and back again, so let's talk about the gut and what a healthy microbiome looks like.

Kelly Brogan: Yes. It's funny – I wrote a little blog article about his paper and I just found it so exciting. And when he read it – he just happened to read it and contacted me – I felt like I had just gotten an email from George Clooney or something. I was so excited.

Trudy Scott: He's a wonderful man.

Kelly Brogan: Really.

It's just very exciting, you know, that there is beginning to be some acknowledgment in the purview of literature for our co-evolution with the microbial world. And, you know, for the role of things
traditional foods – like, fermented vegetables, for example – why might have cultures done that for so many centuries? What is that about? And was there some ancient wisdom there? And have those practices influenced what our microbes are expecting to see.

So, this is a very, very big topic and it's so big because there is an explosion of literature, really. But the reason I'm so interested in it is for the reason that I mentioned, right? So, we want to ask, “What is driving inflammation? How does it get kicked off?” And to my mind, since the completion of the human genome project in 2002, we've had to figure out where is it that all of our physiologic processes are happening. Because it's certainly not at the one gene equals one protein level, right?

So, that gave birth to the sort of science of epigenetics, but part of this epigenetic puzzle is how much of our epigenetic signaling is carried out at the gut microbe level? So the responsibilities of our gut bacteria – and I'm sure this was discussed – it's a list that is growing every day. So, ranging from: bacteria produce amino acids, they aid in digestion of things, including gluten, that we are largely incapable of digesting. They produce fatty acids like specific saturated fats that have anti-inflammatory effects like butyrate, even at the brain level. In many ways they dictate our immune response because of the gut associated lymphoid tissues.

Seventy percent of our immune system is housed in our gut. It is our greatest interface with the environment. So, when you look at it through that lens, you can really start to see how it is that food can have such an impact, right? And what's important to acknowledge is that the literature has elucidated that there is this bi-directional relationship between the gut and the brain so that what goes on in the gut actually can – primarily through the vagus nerve, but there are also other mechanisms at the blood/brain barrier – translate inflammatory signaling in the gut to the brain. And then brain takes over at that point and the microglia – so, these immune systems in the brain which frankly, we didn't even really know how to role even 10 years ago – start to change the way that, for example, tryptophan is broken down – starts to make different kinds of compound that put you into a vigilant state – you know, a health protective state.

So, it’s very compelling. And the question that I have been very interested in because of the population I treat – which is mostly women who are preparing for pregnancy, pregnant, or post-partum – and you know, I feel passionately about impacting the next generation – is, “so how do we build a healthy microbiome?”
Where does it start? And it appears to really start in utero. One of the many, many, misconceptions we've made in medicine and science is that we used to think that the womb was a sterile place. And now we are learning that there is transfer from the mom's gut through, we think, endonic cells into the fetus, into the baby, in utero.

And the placenta itself even has a now relatively quantified microbiome. So, all of these different areas of the body carry their own signature strain. It's very interesting. So, that is followed up by the relevance of a vaginal birth and even a vaginal home birth, specifically, because of research in 2011 that has suggested that babies born vaginally in the hospital versus born at home vaginally have an elevated risk of colonization with C. difficile — clostridium difficile. And that is followed up by a very tailored conversation between mom and baby around immune factors and gut bacteria in what's called enteromammary circulation.

So, it's gut to breast circulation and distribution of microbes. And also, interestingly, of 200 plus what are called oligosaccharides — so these special types of sugars that don't break down, but are specifically designed, almost, to feed bacteria like bifidobacteria in the infant gut. So, it's this beautiful orchestration of events that seed our infant gut and that's pretty much what we carry with us and what determines our stress signaling pattern into adulthood. And then you use vaccines, you take antibiotics, you take steroids, you take birth control, you eat sugar and processed fats — you live a chronically stressful life. You're exposed to metals and then you end up in my office.

But the most amazing thing —we've already touched on this — is that you would think you’d be sort of pretty screwed at that point, right? Like, it's been three decades of essentially assaulting what took about two years to create with this mother/baby dyad and the truth is, you can still rectify it. You can still fix it and heal it and it can be done in as little as two to six months. I find that really powerful, you know, because I have children; I don't treat them, but I would imagine that would be an important window to intervene and that it would be tough for me to treat the patients that I do who are in their 30s, 40s, 50s, and 60s. But it's amazingly still plastic.

And I think that the greatest way to move the needle — and we have data that within 72 hours of a dietary change, your microbiome shifts. And we don't really yet unfortunately know — and it may even be too late to quantify — what an optimal healthy microbiome
looks like. And that's a bummer because it would have been nice, at some point in history, if our awareness of the microbiome coincided with our ability through the type of technology that we have now to identify a proteomic analysis of bacterial genes. It would have been nice to be able to quantify it then. But, of course, now we have subjects.

If I were to do what is being touted in the lay press as the next miracle cure for inflammatory bowel disease: a fecal transplant – if I were to do a fecal transplant – which is essentially taking a donation of stool into my gut – I don't even know who I would use as a donor. I don't know a person alive who I think has what I would consider a healthy microbiome. And unfortunately, it's because of the trans-generational passage, right? So, I am my mom's microbiome, who is her mom's microbiome, and my children sort of inherit that. So we're in a bit of a pickle there but we do have some interesting data that has looked at hunter/gatherer tribes – specifically the Hazda in Tanzania – and has tried to quantify differences between their microbiome and urban dwelling Italians.

And what's interesting is that they found that there were significant differences, including the fact that the Hazda had no bifidobacter. So, in the holistic and functional medicine community, we think bifidobacter is one of the most important beneficial strains. So, they had no bifidobacter – they also had some strains that we think of as being pathogenic, and there were significant differences between the women and the men. And there was a theory in the Hazda paper that that's because the women eat more tubers and honey than the men. And I think that's really compelling, because it's certainly what I see in my practice is that there is a role for non-grain carbohydrates – specifically starchy vegetables and tubers – for women, that may not be as relevant for men.

So we're doing the best we can with the information we have and more of it is coming down the pike and hopefully, it will be before, as a population, we have diminished what is called the core microbiomes – so, what should be the most optimal expression of our microbiome – before we can quantify it. So, onward.

*Trudy Scott:* Fascinating. Really fascinating. And there's also a lot of research in this area looking at traditional diets and how that can affect the microbiome. And I think I saw a study looking at rural Africans and found that those eating – was this the rural Africans? Was this the Hazda that you're talking about, eating this –
Kelly Brogan: No. You're mentioning another one, which is looking more at sort of like neo-agricultural Africans.

Trudy Scott: Yes.

Kelly Brogan: And they also had differences from – the hunter/gatherers – differences from us. So, differences in diversity, differences in dominant phyla – so it's compelling. I think that's the most interesting because it's not just about what they're eating but it's their soil, right? It's their cultural habits around how they eat. Hopefully, it's not the way I eat half the time, which is a nine-minute lunch break between patients.

So, they're relaxing when they're eating in a different way, different ceremony. So, yeah, it's compelling. Also there's been papers looking at the role of lipopolysaccharides – so, what we mentioned earlier – being diminished by traditional diets relative to a western diet. So, what more information do you need to convince you that cleaning up your diet might be the first step to your mental health? I don't know.

Trudy Scott: Wonderful. And then you mentioned the aboriginals. I bet if they looked at their microbiome – before and after – they would see a big difference once they were back in the bush.

Kelly Brogan: I bet. Absolutely no question. Because there's a lot of compelling suggestion that insulin signaling – and many metabolic parameters – originate in the gut. And that's potentially why things like antimicrobial herbs like Berberine have an impact on insulin signaling – and even comparable to something like Metformin. And it's really because of changes and improvements at the gut level.

And it's really compelling. It's where it's at. The gut is absolutely where it's at.

Trudy Scott: Really interesting. And I did not know that the placenta had a microbiome so that's very interesting. And I know this is your area -looking at women pre-pregnancy and post-pregnancy and it's fascinating.

Kelly Brogan: Yeah. What's weird about it is that it seems to be primarily dominated by a maternal oral flora. So, I don't know. That argues the potential importance of getting, you know, your oral hygiene in check before pregnancy. But, yeah, it's compelling.
Trudy Scott: It is. And then you just mentioned all these exposures of things that we get and you mentioned metals. And I just saw a study that came out this month looking at a yogurt containing bacteria as being successfully protecting children and pregnant women against the effects of heavy metal exposure. They're thinking that might be a factor. So that's another compelling study.

Kelly Brogan: Yeah. I think that's compelling. That study was funded by the Gates' Foundation so I have my suspicions about their agenda, but yes, it is compelling. I mean, there's almost nothing that these bacteria can't do.

It's really incredible. And also, yeah, detoxification of Perchlorate, for example – they really seem to carry most of the weight in terms of our physiologic processes. So, it's best we learn to cooperate with them and stop thinking about germs and microbes as being the enemy that we have to sort of like, blast out of existence when they get unruly. We have to work with them in a totally different mindset.

Trudy Scott: Hm-hmm. Excellent. So, let's talk about diet and some of your favorite nutraceuticals?

Kelly Brogan: Yes. So, the brief overview is that I use Whole30 in my practice. I license their material, the Hartwig material – and it's really just common sense eating. It's in this really pretty package in terms of the PDF, but it's really just common sense eating. So, it's a very primary focus put on the sourcing.

So, I ask my patients to do a month of 100 percent organic, which essentially means, using specific delivery service, or cooking all their food at home for one month. And I ask that they limit their diet to pastured meat, eggs, fish, nuts and seeds, and then fruits and vegetables. And that is it. So, we're not eating dairy, we're not eating legumes, soy, peanuts, and we're not eating, of course, vegetable oils and sugar. I actually don't control for fruit very much.

It's not a big part of what I cut down on unless I'm going for specifically ketogenic diet – a very, very low carb diet – if I have a patient with epilepsy or, you know, acute mania or something along those lines or very resistant blood sugar problems. Then we might do something more ketogenic and control for starchy vegetables and fruit. But usually, in the first month, I take out white potatoes but I leave in sweet. And that's because white potatoes are a type of resistant starch that can either be a great
thing as a pre-biotic that feeds bacteria, but until your bacteria are sort of more aligned optimally, you sort of want to limit these pre-biotics and those types of starchy foods or bacteria. And that's it.

And I ask patients to be very aggressive about fat intake – so, things like coconut oil and ghee and egg yolks – multiple a day. Animal foods. And, you know, avocados, nuts and seeds of course, but really more of the former. And that's how we try to control for the blood sugar picture. And then later, you know, in months two-three sort of a thing, I incorporate more and more starches.

So, I'm a moderate carb kind of gal and even, according to Paul Jannin in The Perfect Health Diet, is potentially even using white rice – cooled, white rice – as a resistant starch. And there are going to be some people for whom white rice or rice itself is a cross-reactant to gluten sensitivity, but many for whom it's not. And so that type of personalization that comes later. And it's really powerful.

I was a vegetarian for a while. I certainly am not in the business of converting ethical vegetarians and vegans into meat eaters. But for those who are interested in promoting health and a diet that does that, I think that this is a pretty good template. The outcomes in terms of what would otherwise be chronic and irreversible conditions, across many different practitioners in this country – including yourself – is we all could tell stories of what a version of this approach can do.

So, it's only after that that I start to think about supplementation and usually, by the time I have at least blood work, if not, salivary results or stool results back or fatty acid testing. And I think about the replacement in terms of building blocks. So, minerals like zinc and magnesium and then other micronutrients – iodine, selenium, and inositol. I think about amino acids like theanine and NAC/n-acetyl-cysteine. I'm very big into fatty acids – not as much fish oil. If I use fish oil, it would be for a very short term, high-dose trial – like, two months of three to six grams of a high EPA fish oil.

But I don't think of it as a wellness supplement for everyone because I'm also interested in how we can skew our bodies own mechanisms by taking these super therapeutic nutrients forever. So, you know, meaning that you can suppress your omega six. I also use a lot of evening primrose oil for that reason, cod liver oil – things like butyrate. Of course, curcumin is probably my most favorite of all supplements. I'm very compelled by the data that's
coming out in the psychiatric realm, including placebo control trials, comparator trials to medications, looking at the effects of curcumin. It just, you know, we keep learning about more and more and more, but of course, the effects of turmeric itself – so the actual food – are probably even more robust. In fact, I know them to be.

When we use supplements this way, we're taking sometimes a bit of a pharmaceutical mind to it – isolating the ingredient and dosing it specifically. But I do find that curcumin is another acute intervention I use. And then of course there's gut support – so probiotics and enzymes, betaine hydrochloric acid. Botanicals like rhodiola, ashwagandha – often used to help with cortisol response and then sometimes hormone balancing. So, I use a lot of maca, T3 in my practice and vitamin C for that purpose. Sometimes licorice root.

So, it's a very long list and that's why I think you can totally overwhelm patients with “Here's your 85 supplements to meet every single evidence based problem I suspect you might be having.” But I think it makes a lot more sense to clear the slate. So, exercise, meditation, diet for a month, then we can actually see what's going on. And then we can use these agents strategically and hopefully, in a relatively short terms manner – like, two to nine months maybe – to take it home. So, that's the overview.

**Trudy Scott:** Wonderful. This has been fantastic. And I just love that you say, “Get to the basics, clean the slate, and then add in where you need to.” So, this is wonderful. And to see the amazing results that you see is just fabulous.

We appreciate psychiatrists like you. It's really great. And it's been so wonderful having you on the summit again. Thank you for all this great information. We do have a gift from you and it's at KellyBroganMD.com and we'll make sure that that link is on the page and on the blog for those top seven therapeutic foods. And any final words of wisdom?

**Kelly Brogan:** No, except for that I just realized I didn't say anything about B Vitamins which is very upsetting.

**Trudy Scott:** Oh.

*[Laughter]*
Kelly Brogan: Because it's probably like my most powerful intervention. So, just a shout out for B-12 before we close. I could talk about this all day, Trudy, so this is such an exciting topic and I really appreciate your including me and getting the word out about this to a broader community. Because, you know, it's those of us in the trenches who really see the power of this model of health and are most passionate about it. So, we all need to spread the word together. I think it's wonderful.

Trudy Scott: Great. Well, thanks again, Kelly. It's been fantastic. And thank you, everyone, for joining us on another great interview on The Anxiety Summit. This is Trudy Scott signing off.

Here is the speaker blog: http://www.everywomanover29.com/blog/anxiety-summit-psychoneuroimmunology-new-psychiatry/

Dr. Kelly Brogan MD, Holistic women’s health psychiatry

Dr. Brogan is boarded in Psychiatry/Psychosomatic Medicine/Reproductive Psychiatry and Integrative Holistic Medicine, and practices Functional Medicine, a root-cause approach to illness as a manifestation of multiple-interrelated systems. After studying Cognitive Neuroscience at M.I.T., and receiving her M.D. from Cornell University, she completed her residency and fellowship at Bellevue/NYU. She is one of the nation’s only physicians with perinatal psychiatric training who takes a holistic evidence-based approach in the care of patients with a focus on environmental medicine and nutrition. She is also a mom of two, and an active supporter of women’s birth experience, rights to birth empowerment, and limiting of unnecessary interventions. She is the Medical Director for Fearless Parent, and an advisory board member for GreenMedInfo.com, Pathways to Family Wellness, NYS Perinatal Association, and Fisher Wallace. She practices in NYC and is on faculty at NYU/Bellevue.

An update to this in November 2019: She is now also the author of the NY Times Bestselling book, A Mind of Your Own, Own Your Self, the children’s book, A Time For Rain, co-editor of the landmark textbook, Integrative Therapies for Depression. Her newest book is Own Your Self: The Surprising Path beyond Depression, Anxiety, and Fatigue to Reclaiming Your Authenticity, Vitality, and Freedom.
Trudy Scott, CN, host of the Anxiety Summit, Food Mood expert and author of *The Antianxiety Food Solution*

Food Mood Expert Trudy Scott is a certified nutritionist who educates anxious individuals about nutritional solutions for anxiety. She is known for her expertise in the use of targeted individual amino acids, nutritional solutions for the social anxiety condition called pyroluria, and the harmful effects of benzodiazepines.

Trudy is the author of *The Antianxiety Food Solution: How the Foods You Eat Can Help You Calm Your Anxious Mind, Improve Your Mood and End Cravings* and host of The Anxiety Summit, an online educational platform for both consumers and health professionals, and dubbed “a bouquet of hope”. Trudy also educates health professionals via the Anxiety Nutrition Institute, sharing research and practical how-to steps.

Trudy is passionate about sharing the powerful food mood connection because she experienced the results first-hand, finding complete resolution of her anxiety and panic attacks.

The information provided in The Anxiety Summit via the interviews, the blog posts, the website, the audio files and transcripts, the comments and all other means is for informational and educational purposes only and is not intended as a substitute for advice from your physician or other health care professional. You should consult with a healthcare professional before starting any diet, exercise, or supplementation program, before taking or stopping any medication, or if you have or suspect you may have a health problem.