Understanding & Recognizing A Biology of Trauma

Matthew Cook, M.D. interviewing **Aimie Apigian, M.D.**

Matthew Cook, M.D.
Well, hi, welcome to the Peptide Summit. Today I wanna introduce you to my friend, Dr. Aimie Apigian and she's an awesome doctor. We actually met through my friend, Dr. Winston Ibrahim who's an entrepreneur and amazing person and we have talked quite a bit about addiction and NAD and some interesting things that Aimie's been involved in. She is gonna talk today about peptides, addiction and neurobiology and ways to help treat trauma in the body. So welcome to the podcast.

Aimie Apigian, M.D.
Thank you, Dr. Cook, it's always good to see you and I love the work that you're doing and so I'm excited to be here.

Matthew Cook, M.D.
Okay, great. Well, where should we start? We have so much to talk about and I think-

Aimie Apigian, M.D.
There's so much.

Matthew Cook, M.D.
It's a lot of overlap. Maybe let's talk about this addiction conversation you, we were just talking before we started. I was super impressed with your background in using NAD, you were one of the early people doing it like me and had used it. What was your experience, your sort of initial experience with addiction, NAD and then how did that bring you kind of to this moment?

Aimie Apigian, M.D.
Yeah, this has been something that's been a game changer for me and NAD has been personally and professionally something that I have now used quite a bit and I still remember that first time

that I tried NAD and it was through an IV and I don't think that it was that big of a dose, I think maybe 500 milligrams and my goodness, like I was, I was a believer at that point, it was a rather fast infusion just 'cause I was short on time, right? We're always running busy and so I'm like, all right, we're gonna do this. I wanna give this a try. So let's get it in and so I remember all of the side effects that I had while I was having the infusion. My chest was really heavy. I thought my heart was gonna beat outta my chest. A lot of stomach cramps, flushing, but I was like, I gotta get through this and what I found afterwards though was whole life was brighter and clear and crisper and I remember driving right after that and just noticing like how much more aware I was and how fast my brain was making decisions and then I get to the detox clinic that I was running and I noticed that when I was typing my notes, I have never been able to type that fast and make such few mistakes and it was like this realization of, oh, this is what it feels like to be super human, right? Like you're doing these things that it's, it's without any additional effort on your part, like it literally is just flowing out of you. So at that point, yes, I leaned into NAD and like, all right, I need to know more about this. I want to figure out how I can apply this to the people that I'm working with and when I've looked at really how trauma and stored trauma in the body has affected the nervous system, what I've really landed on is how much of an energy problem it is and we can talk about the regulation of the nervous system.

We can talk about all of the, the state of the nervous system that runs on high energy until it collapses and goes into overwhelm, but then once it goes into that overwhelm, it really is an energy problem and so I say that, hey, trauma is an energy problem and addiction is just one of those downstream effects of these stored trauma patterns in our nervous system and so when I started to look at using NAD for addictions, which again is just a downstream effect of stored trauma in the body and I saw how much of a difference it was making just by bringing energy into their system and what their bodies were able to do. It's almost like you're giving the body the nutrients and the assistance that it needs to now heal itself and so I found that everything else that we were doing, it just worked so much better when we were bringing NAD into the equation because of its effects on the body on a cellular level and allowing it to have more energy available through its effects in the mitochondria. So NAD is something that no matter what addiction I'm working with and whether that's even behavioral or whether that's a substance, that NAD is a core nutrient in that protocol that we're using.

Matthew Cook, M.D.
That's a good one. What do you mean by stored trauma in the body? How would you, tell me about that.

Aimie Apigian, M.D.
Yeah, so, we know that trauma has an effect on the body, but that's kind of where we've left it and it's been rather a nebulous thing and in looking at how trauma affects the body, we wanna differentiate between stress and trauma. So stress is something that stresses us out. It puts our nervous system into a sympathetic state, which is a high energy state and if we can get through that stress, then our bodies can kind of come back to its prior state of health. It's when things either become a chronic stress or become a trauma and trauma is defined as anything that overwhelms the nervous system and while people will experience that overwhelm on an emotional level, what we know is that that overwhelm is happening on a cellular level. So something is happening on the cellular level that cues the autonomic nervous system to say, hey, this is bigger than what we can sustain, rather than staying in a high energy sympathetic state, we actually need to shut down and we call that the dorsal vagal response and the body shifts into an energy conservation state and so there's just heaviness, there's fatigue, there's a lot of inflammation associated with that, even inflammation in the brain with primed microglia and so it's this whole different state and that overwhelm state, that low energy, energy conservation state, that is the chronic effects of trauma stored in the body and those are the patterns that we see and what happens to the nervous system is just that. Now it's operating on such a kind of like, let's just get through this mode. It doesn't feel like it has enough nutrients. It doesn't feel like it has the right chemistry or even the neurotransmitters and so something has cued it to say, you know what? We just need to shift down, go into a energy conservation state and then that pattern of overwhelm gets wired into our nervous system, so that now with future events or triggers, it doesn't take much to go from, oh my goodness, there's a potential danger and I'm just gonna immediately go into overwhelm and so that's the stored trauma in the body. It actually gets stored in the nervous system and goes into this pattern of overwhelm that happens on a cellular level.

Matthew Cook, M.D.
Okay, that's a good one. That's a good one. So then if I was gonna play ping pong with that, so then if you're stuck in fight or flight, if you're stuck in a, basically the balance of the nervous system gets sort of upset and stuck in a triggered pattern, then the downstream effect of that is,

is we tend not to feel good, our limbic system's not working as well and then one of the side effects that we use in terms of a coping mechanism of dealing with that is substances and that leads to addiction and so then another way of saying that might be that putting co-factors that optimize biochemistry like NAD or peptides suddenly resets the balance of the autonomic nervous system, resets basically neurobiology and so then we're going upstream of addiction to try to get people to feel better so that they're not trapped in that addictive spiral that is downstream.

Aimie Apigian, M.D.
Exactly, we're actually able to address the true root cause that's kind of fueling these downstream effects like an addiction.

Matthew Cook, M.D.
Right, you know, I had always hoped that that was gonna be true and for me and for, even my clinical experience, I feel that that's true now, but, you know, I don't think that this was really broadly known even when we trained and I think when we trained, there was an idea that like, diabetes was a medical condition and addiction was like a weak constitution.

Aimie Apigian, M.D.
Hmm-mm, yeah and even trauma, right? So trauma, addictions, up until now it really all has been seen as you're just a weak person. You are, it's all in your head, it's all in your thoughts and you need to do therapy. You need to go to counseling, you need to talk about things and yet what we know now and what I'm kind of contributing to the field is that, no, you guys, like this is biology and this is all things that are happening on a cellular level and it doesn't really matter what kind of all goes into that sense of overwhelm on a cellular level but by the time it goes into that overwhelm, it always involves nutrients. It always involves mitochondria. It always involves inflammation and so by being able to address that and bring energy and bring solutions and bring tools for these things, then it helps the nervous system have more resources and have more resilience. So we're really talking about building resilience on a cellular level. Whereas many people have still just seen resilience, oh, you know, you just change your mindset, change your thoughts and that's just simply not true.

Matthew Cook, M.D.
So then this is the Peptide Summit. So then if we were gonna try to build resilience at a cellular level, and, you know, we have NAD out there in many forms, injection, IV, subcutaneous injections, patches and stuff like that. What about peptides? What's your experience with addiction and peptides?

Aimie Apigian, M.D.
So again, peptides are something that are so powerful in being able to address these biology aspects that keep a person stuck in this state of their nervous system, where then they're looking and they're needing things to help regulate and not feel the intensity of the dysregulation of their nervous system and so just even mentioning the inflammation, right? Like inflammation is a big piece of a biology of trauma and thankfully we've got some pretty powerful peptides that can address inflammation, even just BPC-157, that's something that can be very specific. So many people use it for different sports injuries, for example, right? I'm using it more for the injuries that are happening to the digestive system or the general inflammation that can happen as a result of substance use or that will continue to fuel substance use and so I'm using it both in the injectable form to address general inflammation but even general inflammation in the whole digestive tract but then also sometimes it's more limited to the stomach and gastritis and some of these things that you wouldn't think about it but that, the pain from that, or the downstream effects that that has on the whole digestive system, that will continue to fuel substance use or an addiction because of the effects that that has on everything else in the body and so having the oral capsules for the BPC-157 allows me to really target the damage that's been done to the stomach lining and to that early digestive tract and bring that back to a place of health so that the body's able to have more of the nutrients and less of those energy draining problems that are happening in the system but then we've got other peptides that address inflammation as well. So, those are exciting tools that I find very innovative and very helpful for addictions.

Matthew Cook, M.D.
It's interesting. The self medication sort of coping aspect of addiction is, is that a lot of times, well, if someone drinks too much and then they start to have neurological inflammation as a side effect of drinking, then one of the coping mechanisms is more drinking and then same with almost all sort of addictions and then also, you know, you get gastritis and all of these other

things, you know, BPC-157 is actually secreted by the stomach. I think just layering in pep, something that's anti-inflammatory as a coping mechanism, that's gonna help you can be so helpful because all of a sudden, if you start to have something that kind of can reset things, suddenly there's, the trigger to self-medicate is not as intens, right?

Aimie Apigian, M.D.
Exactly, and it allows for that pause, right? So you have maybe what would be a normal life trigger, an emotional trigger for you, but now because your inflammation levels are lower, you have that moment of pause to be like, do I really wanna do that? Or do I wanna try something else? It gives you a greater capacity to actually make the different decisions. Whereas if you don't address the inflammation, it is nearly impossible. It is such a strong pull to, I know this works, my brain knows that this works and that it relieves the pain, it brings on this sense of numbness and I, you know, I don't really care and that's a very welcome place when there's all of this other stuff going on in the body and so when there's this unaddressed inflammation, my goodness, it is so hard to break what has become a self-fulfilling feedback cycle.

Matthew Cook, M.D.
What about, we were talking about Cmax and Selank.

Aimie Apigian, M.D.
Yes.

Matthew Cook, M.D.
I've been fans of, what's been your experience with those in general and maybe even specifically across a couple different types of addictions.

Aimie Apigian, M.D.
Yeah, so I have been using some of these peptides that are more like cognitive peptides as well and they have been very helpful and especially even the Cmax, right? Like Cmax is something where in the studies, they notice benefits for symptoms of ADHD. Well, if you look at ADHD, that is really a nervous system that's just dysregulated and it can't focus and there's usually inflammation involved with that. There's usually also some neurotransmitters involved with that and so here we have this peptide that is able to address the true root cause of those symptoms. So it actually elevates the brain derived neurotrophic factor and that, even by itself will help with

the neuroplasticity which is what we need to enhance when we're working with addictions and forming new pathways, forming new habits in the nervous system. But some of the other exciting things about the Cmax were its anxiolytic effects and its antidepressant effects and it also has an effect on the immune system. So all of these effects from the Cmax have been really helpful. There's been another one, the Rg3. So regenerative growth factor three, that's been another kind of cognitive peptide that's been helpful for addressing some of these more brain types of symptoms associated with addictions and again, it's not gonna be enough just by themselves to be like, oh, you have an addiction, go take some Cmax, go take some Rg3 but the more tools that you have, then the more you're able to just bring in that resilience on a cellular level. So that like you're talking about those triggers, those pulls are just not as intense as they would be otherwise and so the Rg3, this was, I was using this more as a nasal spray and it actually helps with increasing the cellular resistance to stress in the nervous system in the brain and it will act on the brain immune cells and kind of reduce the inflammatory cascade that can release, especially with addictions, especially with substance use. There is so much brain inflammation that is associated with that and so these peptides that really help target just bringing down that inflammatory cascade that can happen is so helpful.

I don't know enough of your background story, Dr. Cook, to know if you've, how much brain inflammation you've got, this has been something that I've lived with. I've had a number of concussions over the years and never, never knew about this prime microglia and brain inflammation until several years ago and so always just thought like my goodness, I'm weak, right? Like I just need to have more willpower because I saw some of the things that I would do and the brain fog and the depression and the anxiety. Like, I thought that those were all just kind of like my psychology and my thoughts and I needed to work through those some more and once I learned about this brain inflammation piece and I started to use peptides myself to help address that, my goodness, like everything changed and so being able to bring that in for these addictions where there's, I have not seen one person who is actively involved in a substance use and does not have brain inflammation. So that of brings me to the other cog, well, I should, I like to call it a cognitive peptide 'cause that's how I use it. However, it is actually listed more under a pro-sexual peptide which is fun and so melanotan II is one that I use for brain inflammation and it's been powerful and also for gut inflammation. So melanotan II has been one of those like secret little of weapons I can bring in and when someone has a lot of digestive issues, when they've got, even food sensitivities or maybe their gut is so messed up that it's like they have pain with no matter what they eat. That is a good time when I bring in the melanotan II and there's

such a correlation between the gut inflammation and the brain inflammation through that vagus nerve connection that melanotan II actually addresses both and so it is neuroprotective and it actually is acting on the melanocortin receptors in the brain for these anti-inflammatory effects and so being able to bring this in for both the digestive system and the brain inflammation has been huge and of course there's other effects, some good, some not so good, right? It can be associated with a lot of nausea and so people actually use this peptide for a weight loss peptide as well. So.

Matthew Cook, M.D.
I know, it's kinda, it's interesting the diversity is sort of-

Aimie Apigian, M.D.
Yes.

Matthew Cook, M.D.
Of uses and sort of strategies. But it's kinda interesting, you know, hearing you is, you know, traditionally there was an idea, okay. maybe we're just gonna put somebody on Prozac if they're depressed, so it's like, a mono drug as a, to work on one pathway that would have the end result of something for, you know, like increasing a neurotransmitter but then often then the body starts to compensate for that. Whereas, this is sort of a multi strategy concept of trying to optimize biochemistry through a variety of different mechanisms.

Aimie Apigian, M.D.
Absolutely, and that's been one of the most frustrating things for me being in conventional medicine, which is why I eventually left conventional medicine, right? Is because all we've had are medications and those medications are foreign substances and so we're introducing foreign substances into a system that's already all over the place, already struggling with so much havoc and what I inevitably saw was that they may work for a time, they may, not always, right? And especially in the context of an addiction because of the other substances that they have been using, it seems it's harder for medications to actually help them the way that they might help somebody else but even so, if those medications did initially help them, they soon wore off and they were needing higher dosages, higher dosages, higher dosages and now we have them dependent on this other foreign substance that's not actually addressing the true root cause and so what I love about peptides is that I can use them and have the peace of mind that I am

not introducing anything foreign into their body. I am only enhancing signals and communication systems that are already existing in the body, but maybe just have been dampened down by everything else that they've been doing, their lifestyle, their choices, their diet, everything else and it's been dampened down and I'm just enhancing things that are already there and so it's a very natural way for me to address more of the true root cause and help them not to become dependent on another substance that eventually will not work for them either.

Matthew Cook, M.D.
So then on melanotan, so then interestingly, what I found is sometimes you can start very low-

Aimie Apigian, M.D.
Very low, yes.

Matthew Cook, M.D.
And so then that'll be helpful because that low dose will allow you to come up with less nausea. Some people have told me if they take melanotan with BPC, they'll have a little bit less nausea, which is interesting. You have to be careful with that one 'cause the other side effect, it can give you a tan and so then, and interestingly, like a friend of mine who's Jewish and fairly was somewhat light skin, but then got fairly dark, surprisingly dark and then certain ethnicities that are in, can get darker a little bit more so it's important to know. I need more of that, but-

Aimie Apigian, M.D.
My skin color definitely changed with melanotan, definitely, 100% and not only that, but in myself and most of the people that I have used this on as well, they're freckles will get darker and they'll notice skin marks, freckles that were so light before they never even noticed them and then all of a sudden they're seeing them and they're like, I never knew that I had a freckle there and so yes, that is an important thing to note about the melanotan too and, yet being someone who has been so light skinned my whole life, I've got the blue eyes, I've got so many risk factors for skin cancer. I've got, you know, the mini awful, awful sun burns during childhood as well. It actually is one of the additional benefits of the melanotan II that it is protective against sun radiation effects and so for me, even when I'm expecting to travel, I've got a trip coming up to Mexico, for example and I know that I'm gonna be, you know, in more of a southern hemisphere area and more exposed to the sun, I'm dosing myself on melanotan II before my trips so that I have more

of those protective effects and I'm not burning, but I'm more tanning and so helping myself reduce my skin cancer risks.

Matthew Cook, M.D.
Right, that's a good one and I like that one a lot and then a lot of people will tell you that they have like better erections in the morning, like when they take melanotan. So then there's this one thing that has this diversity of effects across multiple biological systems and as we bring kind of balance to multiple biological systems, I guess that's as upstream as you can go kind of 'cause you're at the cellular level, which then the side effect of that has you feeling good. We were talking about Selank, that's another one that's kind of a feel good peptide. What's been your experience with that in sort of neurological health and then also in addiction?

Aimie Apigian, M.D.
So I've seen a good effect when I've been mixing Selank with Cmax, they seem to have a synergistic effect on their mood properties with the brain. I don't know if that's been your experience as well, but their effects, and it seems to be affecting, especially low serotonin and low dopamine types of symptoms that we're seeing. I'm not one that usually tests for neurotransmitter levels. I find our methods of testing inaccurate and so I'm mostly going off of symptoms and history for people. Sometimes I will also look at genetics to see who has just genetically in their enzymes and their proteins for those systems are more likely to have lower serotonin and lower dopamine levels but those are the populations that I'm seeing responding better to the Selank and also the Cmax and so if it's something where they have the money to invest in themselves. That's a combination that I like to do.

Matthew Cook, M.D.
Yeah, but it's interesting, you know, the Selank acts on the GABA system and then Cmax increases brain derived neurotrophic factor then and I also, I agree totally with you. I liked using them together and so then a lot of times what I'll have people do is make it in a concentration where they can take 25 units of Cmax and 25 units of Selank and you can put it in the same insulin syringe and so the concentration they end up taking is like 750 micrograms of each and so then that has been kind of my favorite just from a dosing perspective and then interesting, and I think they work better together. I've had a lot of people tell me who couldn't sleep, that it was very helpful for sleep. There are some people that have polymorphisms in their genetic code, which is basically like a little error that make it difficult for them to make brain derived

neurotrophic factor and so I'm, we're starting to do genetic testing to see and to, and it may be that some of those people respond better to Cmax but then, you know, I have a lot of friends now who if they're in that kind of one day out of five or one day out of 10, where things start to spin and things start to go sideways, they'll, and even I will also, like if there's kind of a day that's just kind of like, it's just not going well, I'll take Cmax and Selank and then it will kind of turn things around and I've really seen that and so then I kind of encourage kind of on this part of the conversation, that's a fantastic coping mechanism and so I don't, I feel like that Dos Equis commercial. I don't always take peptides but when I do, it's kinda, it's a little bit like that. I don't know what your experience with that is.

Aimie Apigian, M.D.
Yes, and I was also gonna say, when we talk about the brain derived neurotropic factor, this is where I also bring in Dihexa, and Dihexa is not one that I reach for right away, because oftentimes when people are first coming to me, I need to focus on the inflammation. I need to focus on the big things that are really disturbing the whole system, but once we have that better controlled, better managed, now I'm really bringing in things to fine tune the system and so Dihexa is one of those that fine tunes and is, and according to the studies, I think they've shown it to be seven times more powerful than brain derived neurotrophic factor and so when I'm working with someone and now we're kind of also getting over into some of the trauma recovery side of things where I'm needing to help enhance their neuroplasticity, I'm needing to help their neurons make new branches and make new pathways, then Dihexa is kind of one of the best for that phase. It's been more used in the past for Alzheimer's and improving memory because it's kind of pruning some of the older neurons away but again, like when we're talking about trauma and actually having to change how the nervous system is wired, that involves a lot of pruning, that involves forming new branches, new pathways and kind of replacing some of the damaged ones that either are damaged from substance use or chronic stress or high cortisol, all of these things that can damage some of those neurons but Dihexa is one that then I kind of bring in at the end to really help solidify the work, the personal, emotional development work that people are doing and helping that kind of integrate faster by its effects on the nervous system.

Matthew Cook, M.D.
Tell me about how that works.

Aimie Apigian, M.D.
Yeah, so the Dihexa is one that actually works on both hepatocyte growth factor and it induces the dendritic branching and so again, it does cross the blood brain barrier and has been more used in its effects with Parkinson's and Alzheimer's and so that's where it's been studied most. I think that there's quite a few animal models that show that it actually reverses up to 60% percent of damaged cerebral neurons and so that's been the bulk of the emphasis and focus on that and certainly for all of my older patients, I'm asking them to get on Dihexa just, again, for more prevention, right? Even before they have Alzheimer's or memory loss, I'm wanting to prevent us from getting there but then because of it's effects on kind of removing damaged cerebral neurons and we know that with chronic stress and addictions, that is a big part of that process that happens. We can see that from MRIs. We can see that from brain imaging studies that certain areas of the brain are damaged and so being able to have this peptide comes in and actually works on the dendrites and is doing similar work to the brain derived neurotrophic factor but has been shown to be more potent that in its effect for pruning and cleaning up the neurons.

Matthew Cook, M.D.
How do you dose that?

Aimie Apigian, M.D.
That is a good question and I'm trying to think of the dosage off the top of my head. I use it as a cream.

Matthew Cook, M.D.
Yeah, that's what I was gonna lead to.

Aimie Apigian, M.D.
Yeah, so I have them usually put the cream on their neck or on their temples and so, yeah, I don't remember the dosage off the top of my head.

Matthew Cook, M.D.
But, so then this is a useful one for people who are listening who might be a little phobic of needles because the Dihexa comes as a cream and so then you turn and do a number of clicks and then you can rub it on your wrist. You can rub it on your neck. The idea, if you're rubbing it

here and it gets absorbed, it might go to the carotid artery and go to the brain but then the arteries are right underneath, arteries and veins are right underneath your skin, on your wrist. The, you know, I have found also that another group of people who will do real well with Dihexa is some of my neurologically Lyme and mold patients.

Aimie Apigian, M.D.
Yes, hmm-mm, hmm-mm, yes, and that there are so many of those people who identify with kind of this cellular overwhelm and what has happened in their biology and so what I see on the trauma side of things is that there are many people who have this pattern of going into overwhelm, who either were, because of that more prone to Lyme and mold, because they kind of were a better host and recipient for that but then certainly once they have those exposures and they've had those reactions to it, those are hard cycles, harder cycles to break and so much of that is part of this overall kind of biology of trauma that happens that keeps people stuck then also in their anxiety and depression and overwhelm that we associate with stored trauma as well. So a huge, huge, huge part of all of this is that Lyme and mold and those effects and contributions on the nervous system.

Matthew Cook, M.D.
And, yeah, so many people who I think really struggle with addiction have four or five under underlying functional medicine things, I think of Epstein-Barr, Lyme, mold and then all of those things create neurological inflammation and then, like alcohol is a temporary coping mechanism that makes you feel better but then over time worse and then those people have a harder time 'cause they're under the gun because they've got the addiction now and they've got whatever that baseline illness was.

Aimie Apigian, M.D.
Yes, and sometimes it's hard to know what came first, right? Because by the time that they're coming to see us, it really is just this cycle that they feed off of each other and so, you know, what came first? Did the Epstein bar virus come first and then that contributed to this? Or did this kind of start because they had some other dysregulation in their nervous system? They found that that really helped them feel better but then that weakened other areas of their biology that made them a more open recipient to those kinds of things, lowered their immune system so that they couldn't mount the response and actually fell into kind of chronic conditions and symptoms from those infections.

Matthew Cook, M.D.
I had a, I just got a memory. I was at my parents' house and it was 1990 or 1991. So I was studying anatomy and somebody came up to the door and knocked on the door and started like talking and they were kind of drunk, but they were making up stories and so then I would say something and they would just make up a, kept making up and wherever you went, then he would make something up and then you realize it was all sort of made up but it was kind of so hilariously funny that I ended up getting, sort of indulging it and so I talked to him for, you know, 15 minutes 'cause I'd never seen anything quite like that and then I noticed also that he was walking, but he was walking with this kind of wide-based gate, you know? And so that was fairly unusual too and so then I went to my professor and I was like, hey, you know, this thing happened to us yesterday. This person came to the house and I explained everything and then basically he explained to me what Wernicke-Korsakoff psychosis is and so then it's, there's parts of the brain basically that get destroyed by that long term alcohol poisoning and so then if you think of the time course over time, progressive neurological inflammation ends up leading to cell death that then suddenly those parts of the brain come offline and so then, and then in parallel to that, that leads you to start to feel less safe and so then as you've start to feel less safe, why do you feel less safe? Because the autonomic nervous system is one of those areas that I think that starts to get imbalanced and so then people don't feel good from their limbic system. So it's kinda progressively sort of, but everything we're talking about has the potential to sort of turn the direction on all of those things and lift us up.

Aimie Apigian, M.D.
Yes, and what a great example with that Wernicke-Korsakoff encephalopathy because what happens is that that is, that area of the brain is very sensitive to thymine. So B1 and so it's that deficiency that really causes that degree of damage, but what happens is, and this is important for people to know because if you go in and you see somebody with those types of symptoms and you give them a ton of thymine, you're actually gonna make it worse. So even though that is the downstream effect and that's now the problem, there is still the right way and the right dosage and the right sequence to bring in things, like you have to have enough sugar, you have to be feeding the brain everything that it needs or else you can make things worse and so when we're talking about stored trauma in the body and oh my goodness, yeah, we've got all of this inflammation, we've got all of this digestive issues. We've got some mitochondrial compromise, let's throw NAD at it and it's like, whoa, whoa, whoa, whoa, whoa. If you throw NAD into a system

that is low in selenium, that is low in CoQ10, that is low in some of these B vitamins, you may actually be trying to rev the engines without the nutrients that it has to be able to operate at that level and you may cause aa bigger crash. So some people talk about a Herxheimer reaction, right? And I've even had some of that with the melanotan where it almost like is boosting up some of that mitochondrial activity and if there's other deficiencies, if there's other aspects going on that we have not yet addressed or we're not addressing at the same time, it can be too much and that can be, you know, we mentioned the nausea, but I have seen some people kind of experience like a fatigue crash if we start at what would be a regular dose for someone else, but for their system, that's just too much and so there's, you know, the body is an amazing thing. The body is an amazing thing and should be treated gently and with very personalized approach based on everything else, based on all of the stuff that's going on in your biology and not just selecting one thing and saying, well, here's one thing, let me just address that. I feel like that's, you know, it's similar, even though it's better, it's similar to just finding that one pill or that one drug that will just solve that one problem and it's like, no, our body is a system and so things can go wrong and if we just focus on one thing for one part of our system and are neglecting like the bigger picture and acting synergistically to bring everything into a place of health and wholeness.

Matthew Cook, M.D.
You know, that's an interesting one because I'm sure you've seen this, but you know, back when, you know, Dr. who I think was the godfather or at least one of the godfathers of using NAD for addiction and so I found out about that and so then and was super interested in it and so then we started using his protocols and so we were using, you know, a thousand milligrams of NAD, you know, and interestingly, there's a cohort of people with alcohol and I think this is people that are drinking like a bottle of vodka a day and there's a cohort of those people, it's just the greatest thing in the world for them and then they can take that and then yet there's also a cohort of people who have, particularly on the chronic infection side of things, and this is this kind of dual diagnosis thing where they can't take that much and so then now that's a super interesting thing, A, from an addiction side, a lot of the people who were really sick, they couldn't, they can't take one drink and so then they're kind of managing their way through that and they may get into that pickle, but A, I found that one to be super interesting and then B, you know, we were talking about peptides. I have really seen the immune peptides be very helpful on addiction. Maybe almost like the most helpful thing that I've personally seen on addiction. I don't know, what's your experience been with that?

Aimie Apigian, M.D.
I am right there with you, Dr. Cook, like inflammation is so much a part of any addiction process. So it's been a piece that I have to address early on if we're gonna make any progress.

Matthew Cook, M.D.
Yeah-

Aimie Apigian, M.D.
Otherwise they still continue to feel like they're just white knuckling it, right? Like they may be sober, they may be , but they are white knuckling it and it's like, yeah, that's not sustainable.

Matthew Cook, M.D.
Right, right.

Aimie Apigian, M.D.
It's only gonna last for so long.

Matthew Cook, M.D.
And I even would, you know, meet people who were sort of famous in anti-addiction or in addiction circles, you know what I mean? And then I would meet them and I would just be overwhelmed by the sense of like, oh my God, this is like totally white knuckling it and then I would be like, oh, and a lot of those people, I got them to do NAD and they're like, oh, that just solved it and so then it's like there's a percentage of people where that's just gonna solve it. However, I think there's a much bigger percentage that need more support and so then the ones that we, you know, we've seen thymus and often one to be very helpful and I think that's in particularly people with immune things like, things like Lyme, the chronic viral stuff and mold and I think that that's a big one. We've seen a lot of benefit with thymus and beta four. We're seeing people taking thymus and beta four for some of the fragments of thymus and beta four and so then, I don't know what your thoughts are on that, but I've really been a fan of the immune peptides. I think they're probably the most important thing to me.

Aimie Apigian, M.D.
Yeah, and they're ones that I personally use myself as well. I will say that I love thymosin beta four, especially in this context of addictions and stored trauma in the body because of its effects

on neurons and restoring them after any kind of a head injury and what we know is how big of a role head injuries cause in inflammation and then mood and addictions and these don't even have to be concussions necessarily, but just injuries and so thymus and beta four is one of those that if I have someone with any kind of a history of a head injury or any time that they would've had kind of that priming of microglia, then the thymus and beta four is one of my favorite ones because not only of its effects on the immune system, but then also specifically it's repairing abilities to the nervous system itself and those neurons.

Matthew Cook, M.D.
Talk about priming of microglia.

Aimie Apigian, M.D.
Yeah, so we have these microglial cells that surround neurons. So neurons are just the fancy word for the nerve cells that make up a nerve and you have these, I call them like gardeners. They are the protectors and they are the cells around the neurons and they are responsible for cleaning things up and protecting them and protecting them means also that when there is some kind of bacteria or something that should not be there, it's going to release inflammation in order to kill that off and protect the nerve cells but what happens is that with certain events and those events can include a head injury, can include anytime where there low oxygen to the brain. So this could have even been at birth if like the cord was wrapped around the neck. That could even be a reason for priming of microglia, periods of time where there would've been low blood flow, all of these and even high stress.

So we now know that high amounts of psychological stress can all also cause priming of microglia but what this priming means is that we have had them be triggered to now become rather than kind of just protector and guardians, now they are like these monsters and they are constantly on the lookout for anything that might be danger. Their threshold for releasing this cascade of inflammation is much lower and so now what happens is that they release the same amount of inflammation in response to things like inadequate sleep or alcohol or a food sensitivity that causes some inflammation in the digestive system or even lower amounts of stress, whether at work or home or travel. So now all of a sudden it's responding to all these other different types of triggers and releasing this huge cascade of inflammation that will cause the brain fog, that will cause some like short-term memory that will make you absent minded. That will make you a little uncoordinated. It depends on where exactly in the brain this priming has

happened but that's what primed microglia refers to and what we want to do is we want to address that by keeping them in a resting state, rather than in an activated state, there is only one way that you can actually reverse priming and that is with fasting but otherwise, you're looking at managing it and managing it is in the form of everything that we can do to keep those cells in a resting state and so that is partly what the, for me, like what the melanotan II and the thymus and beta four help do in the brain is keep those microglial cells that are always ready for a fight and keep them just, you know, everything's good, everything's cool. We don't need inflammation right now.

Matthew Cook, M.D.
That's a good one, and then I would just piggyback on that. One thing that I've seen is thymosin beta four initially can be super helpful, over time if people take it and particularly sometimes when people will take it in higher dosing and then I've seen it a little bit in addiction with people who take it in higher dosing. So there's some people who were taking like very high dosing once a week, like five or 10 milligrams and then people were taking like 1.5 milligrams a day and I will see people at those dosing sometimes have some anxiety or paranoia a little bit, but then with lower dosing, I won't see that and so then, so then that becomes something where with this whole diversity of everything that we're talking about, we've got, you know, Cmax and Selank, we can improve certain biomarkers. We have immune peptides and we have NAD, we have sort of this whole diversity of different things that are gonna manage inflammation. Have you seen that anxiety with people before?

Aimie Apigian, M.D.
Yes, and how I've dealt with that is that I usually, depending on a person and the severity, you know, of their inflammation, then I usually will do a daily dosing for a week and then back off and only do it once every three weeks, once every four weeks and so that's how I've managed that. I don't know if that's been similar to kind of your protocols that you've developed, but that's something where, again, initially, yeah, we gotta get the information down and so it's daily dosing, not high dosing, but daily dosing for a week and then I back off and kind of let there be these intermittent periods where there's nothing and then I'm reintroducing the signal and that seems to avoid most of that.

Matthew Cook, M.D.
Yeah, so that's a good one 'cause that's like here we are two people doing kind of a similar thing and like, we have not talked about this, but I do the same thing and so then that's a cool, that's awesome. That's awesome for me to hear because, and then it's also the opposite of what was a traditional approach to just getting on one drug for a long time, because it's like going to the gym, there's gonna be muscle confusion if we cycle through a variety of different things, cycling, speaking of cycling through a variety of different things, another, if you said all in, if I had to pick my number two after immune peptides for addiction, I think I would go with mitochondrial peptides. Have you had much experience with that?

Aimie Apigian, M.D.
I have and I am still treading very softly with those because probably the majority of people that I see don't just have an addiction. They also have some of these other diseases, some of these other chronic conditions and so it's been something where when I introduce a mitochondrial, a pure mitochondrial peptide, I see that I have a higher percentage of people who I'm kind of like taking their metabolism to the max and they're just not quite ready for that and so I have been using them, MOTS-c is one that I've been probably using more of lately and I'm just, I'm finding that I'm needing to do lower dosages than what someone else would do who is maybe using it for other purposes. So I'm loving what I'm starting to see and just needing, realizing that, hmm, let me titrate some of the dosages to see how we can get the most benefit from this without tanking their mitochondria, 'cause they're not ready for that. They've had so much damage in their body that they're not ready for just this, all right, and let's rev up the metabolism.

Matthew Cook, M.D.
Hmm-mm, yeah, I like the MOTS-c, there's a couple other, humanin and one called FGL that are mitochondrial peptides that can be helpful. Humanin is pretty easy, it's the least intense of the three and I find that to be, you know, fairly helpful. You know, it's interesting when you think about all inflammatory conditions and particularly chronic viral things can sort of steal energy from the mitochondria and so then that lead, and that ultimately leads, what do we call chronic viral infections? Chronic fatigue syndrome because be basically we're kind of stealing from the mitochondria at some level, energy efficiency goes down and so then, you know, in parallel to that, kind of having a strategy of kind of optimizing mitochondrial function, I think is potentially like the heart and soul of addiction from a certain perspective.

Aimie Apigian, M.D.
Yeah, I have my certification course for providers in the biology of trauma and I have a whole module just on energy and what I call the freeze response and so we hit the mitochondria pretty hard in the energy module and this is all the stuff that we go over, right? Like what are all the different things in a person's lifetime that will slowly start to just compromise the mitochondria and its ability to perform and make energy and do all these other things, right? As well.

Matthew Cook, M.D.
Okay, so drop some knowledge on me. So if I want my mitochondria to get going, what would be the top, your favorite mitochondrial support strategies?

Aimie Apigian, M.D.
My top ones are going to be addressing the oxidative stress, bringing down that burden and so even just depending on where a person's at, but even just simple things like vitamin E and vitamin A and some of, you know, these antioxidants, I use C60 for antioxidant as well. So that would be one category and then of course for me, another category would be actually the building blocks for what the mitochondria needs. So I have a whole list of things that, you know, you are obviously very well familiar with but a CoQ10 and the PQQ and the selenium and all of these nutrients in the building blocks and then with that, then I bring in the NAD and that's kind of like all of the main things. Saying that, like, that's just to address the actual kind of acute way of bringing in energy to the system because then we've gotta address, all right and what has been compromising it? What are the viral infections that we've had? Are we dealing with Lyme? Are we dealing with mold? Are we dealing with toxins? Are we dealing with heavy metals? Do we have a high copper to zinc ratio? Do we have some methylation imbalances? Like, what are the things that have brought in these compromises? What are the things that have brought in oxidative stress? 'Cause now we gotta go find those so that we're not just, again, kinda dealing with the downstream effects, but not really truly dealing with the true root causes.

Matthew Cook, M.D.
Right, right. So then that ties sort of everything back together-

Aimie Apigian, M.D.
Everything.

Matthew Cook, M.D.
And it requires sort of a full court press.

Aimie Apigian, M.D.
Yes.

Matthew Cook, M.D.
That's a basketball analogy for you people out there, of a total approach to everything because basically what happens in addiction and is everything's sort of, everything's broken. I feel like this should be a song, before we go, maybe just to chat a little bit about the trauma because I've been so interested in this, you know, I spent a lot of time, a big chunk of my life doing emergency surgeries and you know, trauma, from kind of a high level, what are your thoughts about trauma and how do you like to put it together?

Aimie Apigian, M.D.
Hmm, and are we talking physical trauma? Are we talking emotional trauma? Are we talking just life trauma?

Matthew Cook, M.D.
You can talk about anything you want.

Aimie Apigian, M.D.
Sure, okay. So when I look at trauma, I really like to start with as early on in the developmental process as I can, because that's where the nervous system is forming and so by the time that we're leaving, even early childhood, we already have the formation of our nervous system and now we're just kind of piling on life experiences and so it's been fascinating for me to really lean into neuro-development and even pre-verbal neuro-development, what are the things that a baby needs in order to have their nervous system start to be developing in a way that will lend itself to feeling safe and secure and there's so much work around movement and some of this neurodevelopmental reorganization that can happen later on in life if we don't get the right movement that we need. So one of the things that is foundational to this is even how much tummy time does a baby get and we don't think of, you know, tummy time and trauma and yet when we look at, hey, this trauma is all about the nervous system and how much capacity for stress it has before that stress becomes too much and it breaks us and it overwhelms us and so

when we look at what is the capacity of our nervous system, we do, we have to go back to how does the nervous system even develop and form in a way that allows it to have this capacity to hold stress and to not break and so there's been so many social changes that have happened over the decades, Dr. Cook, that have lended itself to more and more people being more prone to trauma than ever before, simply because of our early childhood experiences and now we have baby carriers. Now we have cell phones. Now we have all this kind of stuff that actually directly disrupts the healthy neurodevelopmental process that is designed to instill, to wire into our nervous system a sense of security, a sense of safety and especially over this last, you know, a couple years with a pandemic and everything, it's been so obvious that most people having nervous system that is wired for fear, that is why wired for insecurity and that's where trauma starts. It's this felt sense in the body.

It's not in our thoughts, right? Like our logic will only reach so far. It's actually the felt sense in our body, the gut intuition, all of these things that we need to start to realize is our autonomic nervous system and our autonomic nervous system is what drives our health, is what drives our decisions on a subconscious level that we are not even aware of and so all of life experiences become important in the sense of how it is affecting our nervous system and is it fueling our sense of insecurity or is it fueling a sense of security? Because out of that will either come inflammation and disease and chronic conditions and addictions and relationship problems and fear or we are fueling a biology of health and wholeness where we feel generally secure in the world, where we feel like, hey, I can, I can solve problems. I have creativity. I can stay grounded and I don't lose myself and with that, then you have this biology that is balanced. You have your hormones balanced, you have your immune system balanced where it's fighting off infections and yet not overreacting. Over here in kinda like the biology of trauma, there's a lot of autoimmune things that develop and so there's just such a clear distinction that happens with a nervous system that has a basic sense of insecurity, which is trauma, these are trauma patterns and a nervous system that is wired for security and safety and does not have those trauma patterns wired into it.

Matthew Cook, M.D.
And I think they're, I don't know what the numbers are gonna end up being, but I bet you that 10 or 20 or maybe 30% of people that get COVID will probably qualify based on certain diagnostic criteria for PTSD.

Aimie Apigian, M.D.
Yes.

Matthew Cook, M.D.
Because it's such a, it has the potential to be such a life and death type of situation and so then, it's an exciting moment for us to begin to realize, oh, okay, we have an ability to begin to, you know, potentially reset that and the sooner we intervene to rebalance the nervous system after a big and stressful immune event and so then, that's a good one too, because then you go, oh, okay. Probably immune peptides, probably thymus and peptides are gonna be pretty helpful for those people because that's a two for one.

Aimie Apigian, M.D.
Yep, hmm-mm. Yeah, and this is where we can see clearly how addressing the immune system is going to affect the nervous system. It's going to help bring a person back from this biology of trauma and the cycle of trauma that's all developed into this biology of health and wholeness and that it's going to affect their thoughts. It's going to affect their mood. It's gonna actually help improve any PTSD symptoms and yet we're looking at their immune system. It's like, how cool is that?

Matthew Cook, M.D.
Yeah, I had a cool treatment yesterday of one of my really good friends was here and so then the, for some reason, I don't know why, but we decided, he was kinda like, you never know what you're gonna talk about and so then there was all of this topic of childhood, a lot of childhood trauma and the trauma of the womb came up and so then you just reminded me of that and so I was trying to figure out, you know, my take on it and we, and so then I did a stellate ganglion block, which turns the fight or flight nervous system off and a vagus nerve kinda brought him into kind of like a super calm state and so then we were lying. He was lying there and I was just kind of talking to him and kind of guiding him through a meditation and so then we went and we saw him in the womb. So I did this meditation of him being in the womb and then we saw, we made this, I said, imagine that you chose to go there and then because you knew that you were gonna be exposed to that trauma and all of that stuff and then we went back and then into the future and then we saw him as like a wise old man who'd solved everything and was sitting under like a tree and he had a visualization of like a 5,000 year old tree. So he was sitting under

that tree and he'd come to complete peace with everything and total balance and so then we did this meditation that the trauma of infancy in childhood and being in the womb was chosen so that it could eventually take him to this place to total peace and balance and that now he was just in the middle of it and so then we went back and forth and then he got all of these interesting realizations and so it was just like, kind of amazing and you realize that, so then I told him, I said, you know, this is, I go, this is just a trauma rebranding exercise and, you know, in a way that's probably, I was listening to you. I feel like we have probably very similar approaches and think about things in very similar ways. So I'm excited and honored to kind of hear your perspectives.

Aimie Apigian, M.D.
Likewise, and it's always nice to have colleagues that I can relate to. I think that for both of us, so much of our journey has been like, we're the oddball, right? We're different than many of the other doctors and so it's been so nice to connect with like-minded colleagues who are doing amazing work like you are Dr. Cook.

Matthew Cook, M.D.
Oh, thanks, you are too and, you know, I think this is just gonna be like the normal practice of medicine because-

Aimie Apigian, M.D.
I sure hope so, I see that happening, hmm-mm.

Matthew Cook, M.D.
Yeah, so, well, I'm delighted to talk to you and I look forward, well, I'm gonna plan on doing another podcast with you again soon to hear what you're up to.

Aimie Apigian, M.D.
Sounds good, thank you.

Matthew Cook, M.D.
Okay, have a great day.