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Hi everyone. Today we're going to talk about PANDAS and PANS. This topic was picked because people had requested it. And if you do have some recommendations for future talks, please let us know. I should also point out that tomorrow's International PANDAS and PANS day.

Let's review some of the key concepts today, and I'll talk to you about mechanisms of action, and the clinical mechanisms, and the research behind it, and then the clinical strategies that are involved with it. And then talk about some treatment suggestions that may be somewhat helpful, but just go over the facts and mechanisms that are related to improving outcomes, and so forth.

PANDAS is really short for Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infection. And this was initially an observation that was made when various children would get a streptococcus infection, like strep throat or strep pneumonia, and then after that have an onset of acute neurological symptoms. Later on it was discovered that it wasn't just streptococcus, and the term used was PANS, Pediatric Acute-onset Neuropsychiatric Syndrome. Most of the patients that end up suffering from PANDAS or PANS end up with usually what are called motor movement disorders. We'll talk about that a little bit, and also things like OCD and anxiety, and behaviors like that, and reactions like that.

By the way, if you're a parent, and if you have children especially in the pediatric age group, this is something you should be aware of, and know that these mechanisms are very prevalent, and the rates of PANDAS and PANS totally overwhelm the rates of autism ... so it's much, much more common ... and it typically goes overlooked.

The basic clinical presentation is that you have a child that has an infection. Let's say they have a streptococcus infection of some kind, maybe it's upper respiratory, maybe there's strep throat. And then, all of a sudden, anywhere from an acute immediate onset of symptoms while they're having the infection, or to even sometimes up to four months afterwards, they start to develop neurological symptoms, like OCD, anxiety, tics, choreiform movements, sensory sensitivities, and this has never happened before. And then they have this new set of symptoms and clinical expressions that have never happened prior to the infection, so there's a clear timeline of no neurological symptoms, infection, and then somewhere between right during the infection or up to four months afterwards, these symptoms start to develop. And it is probably one of the major causes for a lot of children that are suffering from different types of movement disorders, and so forth.

So what's happening? What's the mechanism of action? Well, the mechanism of action that is understood right now in literature is something called molecular mimicry, also known as cross-reactivity.

Let's talk about the classical PANDAS form first. With classical PANDAS, you have the key antigen that triggered the infection, the streptococcal infection, so someone gets a strep infection. Now, what's happening is that the streptococcus infection is leading to the development of antibodies. Well those antibodies that are produced against streptococcus have the ability to bind to areas of the brain called the basal ganglia, and specifically to what are called dopamine receptors, D1 and D2 dopamine receptors, in the basal ganglia. And those antibody attachments to this area of the brain then lead to an immune response against that area of the brain, and there's an immunological injury to the basal ganglia.

That's the main mechanism of the classical PANDAS. The streptococcal infection takes place, antibodies are formed, the protein structure of the streptococcus bacteria is very similar in its amino acid sequence homology to the D1, D2 proteins in the area of the brain in the basal ganglia. So antibodies that are formed to help deal with the infection can then also attach to different target proteins in the brain and cause an immunological response against them. That's the concept of cross-reactivity or molecular mimicry. It's found with autoimmune diseases and it's found with PANDAS.

Now, one of the key things is that it doesn't have to be streptococcus. Different types of pathogens have the ability to induce cross-reactivity and molecular mimicry and create these inflammatory or autoimmune cross-reactive reactions in the brain. So it doesn't have to be streptococcus, but that was really the classical form.

Why do some children get an infection and get PANDAS and PANS, and why do some children do not? Well obviously, it's not the infection itself that causes this. There has to be the right environment for this immunological response to take place. For example, one of the key ones is permeability of the blood-brain barrier. For example, streptococcus is too large. Its molecular weight is too large to cross a healthy blood-brain barrier. So one of the mechanisms that is reported in literature that may play a role in why some children develop PANDAS is because they have blood-brain barrier permeability. And the slang term for this is leaky brain. Just like people have intestinal barrier permeability called leaky gut, the same thing can happen with the blood-brain barrier.

And we also know that there is some strong relationships between leaky gut and leaky brain. We published a study in the International Molecular Science, where we looked at patients that had inflammatory bowel diseases, and found that they had significant correlation in risk for having blood-brain barrier permeability, by looking at different protein markers. Other researchers have found similar things. but we know that one of the reasons is if, for example, a child has intestinal permeability, maybe from being sensitive to food proteins ... common ones are gluten, dairy, eggs, soy ... they have recently taken antibiotics, they maybe have had even intestinal infections; something breaks down their barriers, and specifically the blood-brain barrier.

And also, having reduced antioxidant reserves, getting exposed to free radicals can break down the barriers, whether it's the gut barrier, the lung barrier, or the blood-brain

barrier. Depletion of glutathione has been shown to lead to these barriers breaking down. Glutathione comes from sulfur, sulfur amino acid foods. So you take the average kid that is only eating mac and cheese every day, and doesn't eat any healthy food, doesn't have any sulfur in their diet, doesn't have any vegetables in their diet, then those things can all lead to reduced glutathione, increased inflammation, barrier issues. So that may be one of the mechanisms that is increasing the risk for some children to develop PANDAS.

Now it's not just barrier compromise. In order for a cross-reactivity to happen, the other thing that we know about in the literature is that there has to be some loss of immune tolerance. Immune tolerance is a term that's used to explain how the nervous system has an appropriate response to self-tissue or not. And there's lots of different cells and mechanisms involved with this. There are cells called regulatory T cells; they can be dysfunctional. There can be abnormal dendritic cells in the brain. The microglia can be overactive. So it seems to be that it's not just the infection that causes this, because most kids that have an infection or streptococcus are not going to end up with PANDAS or PANS. So it's the infection combined with some degree of blood-brain barrier permeability and some degree of immune tolerance loss that then sets up the stage for this cross-reactivity to happen.

And when this cross-reactivity happens, these antibodies that are formed against the pathogen then also cause an immunological response in the brain, and for the most part, there's injury to the brain. So these children unfortunately end up with immune-mediated injury to their brain, and then they can develop a whole host of symptoms.

The most common symptoms you'll see with kids that have PANDAS is OCD. Some of them have an inability to control their emotions, so they'll just start laughing all the time or crying all the time. They have a really hard time gating their emotional response. They may have very exaggerated fears for things like the door not being locked. They can have hallucinations. There's even some kids with PANDAS that jump out of cars that are moving. They can mutilate themselves. They can be very, very sensitive to light or sound. They can have rituals associated with OCD, with having to click something on seven times, or have to wash their hands 20 times a day. Those are all the typical symptoms you see with the kids that are suffering from PANDAS or PANS.

They also end up having things like Tourette Syndrome, where they have these motor reactions or verbal responses. Tourette Syndrome isn't just saying profane words. Sometimes there are profane words involved, but there is motor Tourette Syndrome, and sensory, and a mixed. Most will have the mixed. And with the Tourette Syndrome, you may get a spontaneous kind of reaction. It could be motor, like you're jumping around, or it could be a verbal, where you just say something. Another common symptom is tics. Tics are defined as a movement disorder, where a kid may have an unbelievable urge to, for example, rub their eyes, or blink. Or have to clear their throat. Actually, clearing their throat is one of the most common tics. They just feel this urge to have to do it, have to do it, have to do it, and they can suppress it, and then at some

point the urge gets too much and they have to, for example, clear their throat. So those are tics.

Some kids get what's called chorea or choreiform activity, which is like a non-predictable type of movement, almost like they're dancing. Chorea means dance in Latin, so they get these movement disorders of that type that are associated with it.

Why does all this happen? Well, let me try to explain this to you and kind of explain why these symptoms take place, and so forth. So if you remember, the mechanism behind this is that there's an immunological response, probably from cross-reactivity, that destroys an area of the brain called the basal ganglia. So the question to ask is: what does the basal ganglia do? The basal ganglia has lots of different functions, but one of the essential functions of the basal ganglia is to shut down and to dampen input coming into an area of the brain called the thalamus.

The thalamus is an area of the brain called the relay center. And every input that goes to the brain will go through the thalamus, with the exception of smell. Olfactory pathways, smell pathways, do not have to go through the thalamic projections but everything else. So sensory perception, the way you can feel hot, cold sensation; proprioception, where your brain figures out where your muscles are in space, where you can perceive things like vibration; hearing sound; visual pathways, where colors come in. Even cognitive thoughts that reverberate through your brain, different pathways, they're all going through these thalamic projections. So your thalamus is then relaying these inputs coming in from all the receptors in your brain to the different regions in the brain that are involved.

But it's a lot of input. And one of the ways the brain controls and regulates its function is the basal ganglia. The thalamus is right in the middle of the brain, and then the basal ganglia is right around it, and the basal ganglia gates or inhibits these inputs so there is not an exaggerated response. So it kind of calms things down, it shuts down the thalamus so there isn't these exaggerated responses.

There's three different loops in the basal ganglia. One is called the sensory loop, one is called the motor loop, and one is called the limbic or emotional loop. The sensory loop processes information to areas of the brain called the parietal lobe, where we perceive sensation. The motor loop is involved with muscle function, and it coordinates the areas of the brain that are involved with muscle movements. And then the emotional loop relays information to an area of your brain called the limbic system, where we have emotional thoughts. So the basal ganglia is dampening input to the thalamus to control these different loops.

And what you see when the basal ganglia is injured is you can't gate or calm down these loops, so you can have different types of expressions, and based on where the injury is in the basal ganglia, you can have different symptoms. So you can have 1000 different children suffering from PANDAS or PANS, and they'll all have different symptoms. But they're all basal ganglionic symptoms.

So you can have one child, for example, that has injury to their sensory loop of their basal ganglia from the infection, and then they may be extremely sensitive to touch, or the body may hurt. Their body hurts all the time, they have to get distracted and focus on something for their body to not hurt; maybe a video game, or thinking, or calculating, or counting backwards or whatever they need to do, but they may have this exaggerated sensory perception. It could be burning, it could be pain, it could just be numbness, but that's all part of the sensory loop being dysfunctional.

It could also be sensitivity to sensory input coming in from visual pathways, so they really can't handle any bright areas, and they have to wear sunglasses. They prefer lights to be turned down.

They could have part of the sensory loop involved with their hearing pathways, where they're extremely, extremely sensitive to sound, and really cannot tolerate high-pitched sounds or even low pitches. It can vary on the pitch, depending on again, which part of the brain is injured. So we see all these different types of sensory sensitivities when the basal ganglionic sensory loop is involved.

Now, if the basal ganglionic motor loop is involved, that's where you can see things like tics, or there's blinking, clearing their throat, or having to rub their nose. Whatever that may be, this urge to have to constantly repeat the activity, of doing some kind of muscle-coordinated activity, whether it's rubbing or blinking or clearing their throat, those are associated with the motor loop being injured. So you can have children that have basal ganglia injury to this loop and they can, for example, blink their eyes, and do this, and they can do that all day. They can't help it. They're unfortunately frustrated, because they just have this urge happening, and then it becomes very disruptive in classrooms and other settings, and they're really not in control of it. That's the motor loop.

Then we have the emotional loop of this basal ganglia, and if that area is injured, then you can have significant separation anxiety. For example, kids with their parents. If their limbic loop is injured, they can completely overreact with fear in situations that don't call for it. They can have severe panic for minor things that don't justify the degree of anxiety for it. That's the emotional loop.

So at the end of the day, when you look at what's happening with PANDAS and PANS, there's an infection, antibodies are made against the infection. For some susceptible subgroups of children, maybe blood-brain barrier permeability in combination with loss of tolerance, those antibodies attach to the basal ganglia. The basal ganglia has different regions, different loops that are involved with brain functions: a sensory loop, a motor loop, and an emotional loop. And depending on which of those loops are injured, you can get different expressions of symptoms. So that's the basic mechanism of action, pathophysiology, of PANS and PANDAS.

The majority of children that suffer from PANS or PANDAS end up with actually all three of these loops involved, where they have some emotional loop involvement, so they

have an extreme difficulty controlling their emotions, their fear, and their anxiety. They get some OCD involvement with their emotional loop. They get some sensory loop involvement, where they are very sensitive to light or sound. And then they end up with some motor loop involvements, where they have to clear their throat, and so forth. And this is not psychological. This is physiological. This is not that they're trying to have these behaviors. It's the area of their brain that would dampen these movements is now injured. That's the classical pattern of basal ganglia disease and injury. Okay?

Now, how is this diagnosed? Well, the key marker for diagnosis is what's been referred to as the Cunningham panel, but for the most part it's just antibodies to dopamine receptors. It doesn't necessarily have to be a Cunningham panel. That's just a name people have used with a lab that offers it. But for the most part, the path of mechanism is there's antibodies to dopamine receptors, D1 receptors, D2 receptors. There's even literature showing that there's antibodies to GABA receptors, so the areas of the brain that are involved with dampening this thalamic loop through the basal ganglia use dopamine and gamma-Aminobutyric acid, GABA. So antibodies to those receptors is the pathophysiology of these mechanisms.

Those can be measured in blood. So lab tests can be done to measure those markers in blood, and if there's a timeline with history, and those lab markers high, then you can get diagnosed with something like PANS. If someone has high streptococcal markers, like a streptolysin antibody; ASO markers is the marker they use for active and acute streptococcus infection. So if they see what are called ASO titers elevated, and they see the antibodies for, let's say dopamine 1, D1, D2 receptors, with the onset of these acute neurological symptoms, then you have basically diagnosis of potential PANDAS and PANS.

Unfortunately, in the healthcare system, many doctors, physicians, and even neurologists aren't competent in identifying and diagnosing this. And there's still some unnecessary arguments whether the diagnosis and condition is real or not. I think it's been proven that it is very real at this time. But like everything in healthcare, there's outdated physicians, there's healthcare providers and physicians that since they don't know about it, immediately downplay it because of their own incompetence.

The other key thing is that many kids, unfortunately, don't get diagnosed with the condition, and their families may be very, very frustrated. This is why it's important to have these support groups, and these PANDAS and PANS groups out there, to help parents navigate their way through it.

So, what do you do? Well, at some point I think the key thing is to understand that there was injury that happened to the brain, and injury to the brain needs to be managed. And once the infection is gone, then you have to go in there and really apply some applications to it.

The first thing in the clinical setting is: have they started to develop other patterns of neurological autoimmunity? So the fact that they have D1 or D2, dopamine 1 and

dopamine 2 receptors, and GABA receptor antibodies means that their immune system has started to attack their brain. Now, some of these are only these autoimmune responses. By autoimmune, we mean the immune system is attacking the body's own tissue ... auto-immune to the body's own tissue.

Some of these autoimmune reactions only take place during the active infection and when the active infection is gone, these antibodies drop and they're no longer involved. Other times, for other children, the antibodies persist even though the infection is no longer there. That's another key point. Another key point is that for some patients that have PANDAS, once the infection is gone, they don't have this ongoing autoimmune response, the antibodies to the brain are gone. They had the infection; all they have at this point is some degree of brain injury.

For other kids, the antibodies still persist, and at this point, it doesn't have to be streptococcus or any other infection to promote their autoimmune response. Once there's antibodies made to that area of the brain, lack of sleep can flare up their autoimmunity. Anything else that flares their immune system can flare up their autoimmunity.

And this is where we see a lot of difficulty with many parents, because some of these parents ... especially, there is outdated clinical information in a lot of these support groups, where you have parents putting kids on antibiotics over and over and over and over and over again, assuming that there's some type of bacterial infection, and this completely disrupts their microbiome, and disrupts their immune system function, and they can't get out of it. So part of this is the fact that they don't understand that for some children that develop PANDAS or PANS, they may not have the infection anymore, and the reason they're getting symptoms isn't because they have the infection; the reason they're getting symptoms that start to be expressed more, whether it's OCD, or anxiety, or movement disorders, is because they developed antibodies to their brain, and despite the infection being gone, those antibodies or that autoimmune response persists. So it can go either way. That's why it's important to test and see what's there.

In a clinical setting, if you have a child that presents with PANDAS patterns or PANS patterns, if their antibodies are still elevated ... like dopamine 1, dopamine 2, GABA receptor antibodies ... if these antibodies are still elevated, most importantly D1 D2 antibodies, and the infection is no longer there, and there's no patterns of infection with their white blood cell panel, and there's no active infection patterns for specific pathogens, then you know that child has now developed brain autoimmunity, and it doesn't need to be an infection to trigger the responses anymore.

On the other hand, if you see a child has PANDAS symptoms that they've been dealing with, in an acute phase, and you see the antibody is high, and things like ASO titers for streptococcus high, then you know that there's an acute infection that needs to be dealt with. And then you have to see if those antibodies persist down the road. Unfortunately, many children that end up with this pattern, end up having this autoimmunity response

that takes place, and parents and practitioners keep trying to give them antibiotics in treating them, and this disrupts their immune intolerance more. So beware of that.

Also, for some of these kids the injury to the brain is there, and things that cause the blood-brain barrier to break down, like a really unhealthy diet, a really inflammatory diet, will then continue to create that pattern.

I've had many PANDAS patient where there's no chance to get them out of it, because parents are not willing to make some changes. For example, you have a kid that has blood-brain barrier permeability. We can measure that with antibodies, we can measure that with S100B antibodies, they have neurological antibodies, they have leaky gut and these sensitivities to dairy and gluten. The parents just won't get the kid off dairy and gluten because they say their kid has emotional rage when they don't get to eat them, they have to continue feeding them, they have constant inflammation, they're not doing anything for their autoimmunity, they keep doing rounds of antibiotics, and it's like there's no chance. You have to calm down that vicious cycle. So that's one part of it, which I know is hard for some parents, because their kids are suffering and they have some serious rage issues. But some parents figure out how to do it, and some parents don't.

The other key thing is that at some point you have to rehabilitate the brain. There isn't a magic supplement for PANDAS or PANS, just like there isn't a magic supplement for any kind of brain injury. Any strategies that are anti-inflammatory would be ideal for kids suffering from PANDAS and PANS. The most common anti-inflammatory diet that will be best for PANDAS and PANS would be some ketogenic diet. Ketones have an anti-inflammatory effect for brain. Diets that are very high in healthy fats ... olive oil, avocado, fatty fishes ... that would be very good for dampening brain inflammation. Nutraceuticals like turmeric, or cumin, resveratrol, green tea extract have antioxidants, flavonoids, glutathione; those can be helpful to dampen some of the inflammation, but they're not going to fix the condition. They're just going to have anti-inflammatory effect.

And then the brain needs to be activated, so if the basal ganglia is injured, then just like a brain injury, you've got to get activation to the area that's injured, so neurons that are healthy can go around the branched neurons and regain function. Many kids that actually have PANDAS technically grow out of it, and what that really means is they have injury but as their brain continues to develop, they have plasticity or neurons that go over the injured areas, and they get function that comes back.

So when you look at injury to the basal ganglia, there's two main pathways that are really important. One is called the frontal striatal projections; those are areas in the frontal lobe that go to the basal ganglia and activate it. Then there's pathways through the cerebellum called the cerebellum mesencephalic thalamic cortical striatal loop. That's a long neurological term, but it's a pathway where balance and coordination activate in this basal ganglia loop.

Basically movement, exercise, coordinated activities, dance, martial arts, anything that causes focused concentrated movements have phenomenal effects on getting activation to the basal ganglia. Sensory games that really involve focus, concentration can be very helpful. Things called go/no-go exercises can be very helpful. Go/no-go exercises are like red light/green light, Simon Says. Those activate the frontal lobe to really decide to turn on or turn off behavior. They can be very helpful for those activities.

Let me recap, and then we can take some questions.

There's a large group of children that are suffering from PANDAS and PANS that are completely ignored in the healthcare system, and these children end up with things like Tourette Syndrome, tics, OCD, sensory processing disorders. And these children usually have these symptoms develop after some type of infection.

The mechanism for that, that we talked about, is molecular mimicry. The way that this is diagnosed is a very clear timeline from infection to these new neurological symptoms, and there's also evidence of antibodies, especially in the acute stage, to these targeted proteins in the brain for the basal ganglia. The most important ones are called D1, D2 receptors.

For some children, once the infection is gone, those antibodies are no longer there, they don't have the persistent autoimmunity, they just have some brain injury that needs to be rehabilitated. For other children, the infection is gone, but those antibodies persist; we have no idea why that happens. It has to do with their immune system function, but their antibodies to this area of the brain persist, and it doesn't have to be an infection that triggers it. It could be diet, it could be lifestyle, it could be the blood-brain barrier breaking down, anything can then trigger those ongoing flareups where these D1, D2 receptors get activated more and their OCD gets worse, and their movement disorder, like tics or chorea gets worse, and that's more of an autoimmune mechanism.

At the end of the day, we talked about getting into an anti-inflammatory diet and lifestyle, and then doing things to really activate the brain are really essential parts.

With that all being said-

Hi.

... my wonderful wife is here to help me with my questions.

Hi. It's really hot in here.

I know. My air conditioning vent's not working in my office. It's terrible.

So your office is hot and the house is freezing. Sorry.

So, thank you everyone for joining, by the way, and don't forget our website, Dr. K news, drknews.com and please follow us on Facebook. We do these talks regularly.

You get to know what the topics are, and we have a newsletter at drknews.com D-R-K-N-E-W-S dot com.

Hi.

Hi.

So Susan Gwin. Susan's asking: is there a particular screening that would be good for these children once they reach their mid-twenties to see if they are more or less out of the woods?

First of all, there isn't a specific lab test, let's say. You still have antibodies persist, even into adulthood. There's some people that have a neurological autoimmune disease develop at some point in their life, and they have this ongoing autoimmunity for the rest of their life. So that's possible, so you can look at antibodies.

The other key thing I want to mention is that when you look at brain development, there's gray matter and white matter. Gray matter are the neurons themselves, white matter is the myelin, the pathways that go to neurons. Gray matter fully develops usually by age nine. White matter fully develops by age 21, 22, somewhere in the early twenties, and the ability to have recovery is really in that early ages.

If they have any persistent symptoms past age 20, 21, it's very unlikely you're going to make significant change with them. That's why it's so important, once these children are young, to immediately have an aggressive diet and nutrition lifestyle approach, and also to start activating their brain with lots of complex movement tasks like go/no-go, green light/red light, Simon Says, while making sure they have coordinated motor activities like dance, or martial arts, or anything they can really do to coordinate how their muscles turn on and off. Those are going to be critical.

Absolutely staying at home, and eating mac and cheese, and potato chips and just yelling at everyone, and parents not doing anything is going to guarantee permanency of the condition for many kids.

Yeah.

Okay, next question.

Sure. Alex: Would Array 14 from Cyrex be helpful here?

Array 14. Array 14 will screen for antibodies to various pathogen infections. It can be helpful to give a clue of what's going on, but some of those pathogenic markers can be from exposure in the past. Some antibodies persist in the body for up to one to two years. So it can be helpful to give you a clue the pathogens are there. The most important marker would be looking at dopamine, dopamine 2 receptors.

The Cunningham panel is the standard right now for evaluating PANDAS and PANS. I think it's Moleculera Labs that does that panel.

Okay. Carp is asking: when is it time to drop seeking bugs and attacking pathogens, and to go for the autoimmune treatments?

Yeah, this is a good question. So when do you stop chasing pathogens and go for the autoimmune treatment?

Right.

When they're no longer an acute case. Like if they don't have fever, they don't have a temperature. If it's strep, then you can look at their ASO titers.

The problem is some people keep going, "Well these ASO titers are not outside the range, but they're suspicious to me." There's a point you got to stop doing that.

But also, the biggest clue is to really look at the white blood cell count. If you look at a complete blood cell count, a CBC, there's patterns for white blood cells, and then there's different types of white blood cells, neutrophils, eosinophils, basophils, and lymphocytes. If you see someone that's got an active infection, you're going to see in many cases, their white blood cells might be a little bit off. Their lymphocytes would be off, and even more thorough than that, you should probably look at something called the T and B cell profile.

The T and B cell profile will look at patterns for an active infection by looking at what are called helper cells and suppressor cells. When people have active infections, they have what's called a T helper/suppressor ratio that you can measure. If that's abnormal, then you probably still suspect that there's an infection.

If all those are normal and the child has persistent symptoms and antibodies are high, it's really time to focus on autoimmune management, improving their immune tolerance, and really starting to rehabilitate their brain. Especially before you get to age nine for gray matter, and before you get to age early twenties for white matter.

Okay. Merritt: Can teeth grinding while awake be a motor symptom?

Teeth grinding while you're awake, bruxism? Not necessarily. It depends on if there's an urge or there's stress. If there's an urge to do it, that's called a tic. It's happening in only in a timeline fashion, it could be an expression of a motor response, but it's not the most common one. But it can occur.

That's the thing with infections in the brain. Depending on which pathway it hits, you can have a whole varied list of symptoms, and this is why one child is different than another. But if it was just grinding their teeth and no other symptoms, like OCD, or sensory overload symptoms, or severe anxiety, then I probably wouldn't think it'd be a pattern associated with PANS or PANDAS.

Okay. Carla's asking: Would you treat tics the same way you treat stimming? S-T-I-M-M-I-N-G. I don't know what stimming is.

I don't know what that is either.

Okay. Meme is asking: are heavy metals like mercury a cause, or is it just from infection?

It's just from infection.

So listen, mercury, lead, all these different chemicals, they're all bad. But they don't cause molecular mimicry to a specific target area of the brain. That's the key difference. Listen, if you have mercury or lead in your brain, it's going to be all over your brain, it's not going to go to specifically one side of your brain, and it's not going to cause an acute series of symptoms for most people. Unless you get severe, acute mercury poisoning, but then you're going to have a whole list of symptoms, which is pretty rare.

When people like to measure someone's heavy metals through a different test and the levels are high, guess what? That's how it is with every single person that you measure. It's pretty rare to see someone that doesn't have those levels of some degree of mercury or lead in their body, just from the water we drink, the food we eat that has some degree of those things in there. Not to say that it's good, but you can't say it's the cause. So in the typical world of alternative medicine, where people just continue to follow dogma, people sometimes just blame everything on heavy metals, and it's no exception with PANS or PANDAS.

But the actual mechanism of PANS and PANDAS isn't directly related to heavy metals, it's related to molecular mimicry, specific to dopamine receptors in the basal ganglia. And that cannot happen with a chemical; it happens only with a very specific antibody for those target sites.

Okay. So I don't have her name, but ... oh, here it is. Casmin: Is there anything neurologists can do, or are we better off just using diet and supplements?

A neurologist can be a key person to help find the diagnosis, monitor examination findings. If you have a neurologist trained in PANDAS and PANS, and he can document what the exam findings are abnormal and see if they're changing over time, that can be very helpful. If they can run the antibody test, that can be very helpful. So there's definitely a place for the diagnosis.

However, there's no drug that you give these patients, outside of the acute phase of infection. So if they don't have an acute infection and they're kind of in the point where they have a brain injury from the infection, that's where you're going to get really maybe more with a person trained in brain rehabilitation, whether it's a physical therapist or anyone who knows how to rehabilitate the brain to some degree, or just getting the person really active and motivated with different sets of exercises, and then diet, nutrition, and lifestyle to improve brain function and control autoimmunity with whatever kind of practitioner you find that is on your team, would be ideal.

Okay. Carla: why so much focus on strep when anti-DNase B is positive? My son has so many pathogens, could this marker tell you something else?

The focus is on strep because that's the one that was first identified. It doesn't have to be strep. That's why there's PANS versus PANDAS now. And most cases are not strep. So the reason there's an emphasis on strep is just because that was the first mechanism that was identified, and that's when they first saw that cross-reactivity response and reaction. So usually whatever's first gets the most attention, but it doesn't have to be streptococcus. That's my guess why.

Okay. Carla: once the blood-brain barrier is broken, wouldn't Superfood push the immune system too far, causing too much excitatory behavior?

Superfood?

That's what it says. Superfood.

Okay. I don't know what Superfood is, but once the blood-brain barrier is permeable ... and we have different degrees of permeability over our lung barrier, gut barrier, blood-brain barrier at different times, based on multiple variables. The blood-brain barrier gets permeable at times, and it also heals pretty quickly. So we have different degrees of permeability.

Some viruses can get through the intact and healthy blood-brain barrier, but things like streptococcus can't get through unless the blood-brain barrier is breached. But when a virus or pathogen gets into the brain, whether the blood-brain barrier is permeable or not, the blood-brain barrier does open at that point. And even more so, even if it was permeable, because at that point there are cells called astroglial cells, and these astroglial cells open up the blood-brain barrier so T cells can come in and help deal with the infection. And then what T cells will do is they will actually attack tissues that have antibodies stuck to them, which would be the basal ganglia.

So Superfoods, I'm not sure they have any real ... I'm not sure what that means, but if you're referring to Superfoods, like high antioxidant foods, like acai or blueberries or various high flavonoid-based foods, those things have been shown to have anti-inflammatory effects, help heal the blood-brain barrier, help dampen inflammation, help support the immune system. That would be ideal.

Oh. Stimming equals stimulation. What is stimming? It's the hallmark sign of ASD, actions such as headbanging, standing on the ground twirling over and over.

Wait, those are all just movement disorders.

Okay. So the question was then, sorry: would you treat tics the same way as you treat headbanging? Sorry, I read it wrong.

Yeah. How you treat a movement disorder is going to be based on the level of skill of whoever you're seeing. If you work with very talented person that can rehabilitate the

brain, they can be very focused, and find things that change exam findings and implement those therapies. To be quite honest, most people can't, and there's a small amount of practitioners that know how to work with conditions. I'll give you an example. "Don't call our office, we don't have room for new patients right now. We're just overwhelmed."

So anything you can do to activate movement is your way to go. And actually, there's nothing better than exercise and movement and cognitive tasks that are challenging for a child to rebuild the basal ganglia. That would be your first go-to place more than anything else.

In one sense, you can do specific therapies, different for different types of conditions based on the child's physical examination findings. It's not so much related to what type of movement disorder they have. But for the most part, get them to move, get them to do coordinated activities, get them to be involved with complex motor tasks. And to be honest, most kids that have these patterns, they find it very difficult to do, so they hate it, and they don't want to do it, so you have to kind of deal with that challenge.

The biggest challenges when children have injury to the basal ganglia, the things that will help them, whether it's cleaning up their diet, and the things that will help them, like doing complex motor movements, like playing a sport, or doing dance are the things they will fight to not do. They don't want to do it because it's hard for them to do it, and that's the challenge parents have.

Yeah.

I think as an analysis, sometimes I've seen patients where I've done a very, very thorough neurologic exam, identified exactly what key things will change their exam findings, but the kids won't do them. And there's a big fight with the parents trying to get their kids to do them, and the kids won't do them, and then basically all that entire workup and evaluation had no real effect because they just couldn't change that pattern.

Yeah.

It's unfortunate.

Yeah. It's a struggle. It's a struggle.

It's a struggle. And also the key thing is dopamine receptors are involved with motivation, so the other key thing is when the dopamine receptor function goes down, the children obviously are not trying to be difficult; dopamine is involved with motivation, drive, focus, initiation, so they actually had injury to the area of the brain they need to activate to get out of it. And this is the difficulty of the condition itself, because with low dopamine, with low dopamine activity, it's very, very hard to initiate, to stay motivated, and it's very difficult for parents to get kids to do this because of that pathophysiology.

Okay. Nicole is asking: Is there any overlap in PANDAS symptoms and ADHD symptoms?

No. They're totally different. PANDAS and ADHD are different. PANDAS is very specific to basal ganglionic symptoms and ADHD is very specific to lack of frontal cortex activity. However, I guess you could say there is some slight overlap, which is that when ADHD, since they don't have focused attention and concentration, they can't suppress some of their activities, and they become what's called hyperactive. But they're really not hyperactive, they just don't have control of dampening their urges. That does involve the frontal lobe activating the basal ganglia, but the key thing with ADHD is that their frontal lobe, especially with focused concentration and attention, are impaired.

You can also have children that have both. It's not uncommon to have the autoimmune response also cause inflammation cause injury to the frontal lobe, and now they have ADHD symptoms in combination with basal ganglionic symptoms. So the inflammatory responses that contribute to infection and lead to PANDAS or PANS can also lead to autoimmunity against just basic myelin or myelin basic protein, and other areas in the brain besides the basal ganglia can also be involved.

Okay. Leanne: what about adult strep antibodies and ASO titers? What do you do about that?

What's interesting is we know with children they have this vulnerability to this cross-reactivity in the basal ganglia, and it doesn't seem to be as much of a factor with adults. For some reason, with adults when they get strep infection and other types of pathogens, they're not as prone to cross-reactivity.

The exception to that is adults that have immune dysregulation and already have some autoimmune disease. So remember that in order for this concept of molecular mimicry or cross-reactivity to happen, where antibodies are formed against the pathogen, and then attach to self-tissue proteins, you have to lose something called immune tolerance. And people that have autoimmune disease lost their tolerance. So with adults, you're really only worried about the cross-reactivity typically with those that have lost their tolerance. Your biggest clue is that they already have an autoimmune disease, like Hashimoto's, or RA, and so forth.

We also have an online program on immune tolerance at drknews, where we teach people how to improve their diet, nutrition, and lifestyle and take different strategies to improve their tolerance issues. If you're interested in that, you can check it out at drknews.

Okay. Can you explain how IVIG works? I'm sorry with the initials. I don't know what that means.

Yeah, immunoglobulin therapy, IVIG?

Yeah.

The way this works is they do an IV with IgG antibodies, and the IgG antibodies compete with pathogenic antibodies, so the antibodies that will attack the basal ganglia

are no longer able to attach to the basal ganglia because the IgGs are competing with it, and it decreases the autoimmune response against it.

So IVIG therapy can be a very good strategy in the acute states of infection. But here's the problem. The infections happen, the brain is injured. A year down the road, when someone's trying to do IVIG therapy, it really might have no effect at all. It's best used during acute infection stage.

And I got to say, that's, I think, the biggest issue with the PANS and PANDAS community not understanding. Once the infection happens and there's persistent antibodies, there's no more pathogen to go after. You have to treat other things. IVIG is only best when the pathogen is involved.

Okay. A lot of people are asking about keto for kids. One person is saying, "Since dairy is so inflammatory would you recommend keto dairy-free?"

Yes.

Also, is keto safe for kids as they're developing? That kind of thing.

Yeah. Let's talk about keto. By the way, we did a video on ketogenic diet, I think, two weeks ago.

I don't remember.

It's in our library. It's in our library.

It's in there.

Okay. So yes, you can do keto with kids. Definitely dairy is inflammatory. In our talk, we always recommend doing ketogenic without dairy, so you want to use vegan-type cheeses, like coconut based cheeses, for example. And they're actually really good.

We don't eat cheese, so to us they're really good.

We don't have any dairy, so if you eat a lot of normal cheese then you might not think it's so good. But you want to do ketogenic with a dairy-free diet. And you want to do lots of vegetables. That's the key thing. You have to have lots of diverse vegetables to really support nutrients, health of the microbiome, while a person's doing a ketogenic diet.

The biggest difficulty with kids is that there's no sugar because when you're doing a ketogenic diet, you can't sugar and sweets, so it's getting them out of that sugar, that sweet-tasting phase of it. But ketosis can be done with kids.

Here's the key thing. There's no nutrient deficiency in a ketogenic diet. If you're doing ketogenic diet with vegetables, a diverse list of vegetables, you're getting every single micronutrient and macronutrient. You're just having a diet that's decreasing insulin surges by having a higher percentage of calories coming from healthy fats. Now if you

do ketogenic diet with bacon, butter, cheese, fried foods, that's not going to be beneficial.

Right. Right. Exactly.

Yeah.

Okay. We've done a bunch of keto stuff. Okay. Are you going to have a program on this?

No.

Maybe like Save Your Brain, or ...

Oh yeah, yeah. No we haven't thought about that. We are creating some programs for next year to help patients navigate their way through some conditions, like we did the Save Your Brain program. Which is not really for PANDAS, it's for adults that are starting to notice some cognitive decline. That's an online program that you can check out at drknews. We're finishing up a GI program to help people navigate their way through unhealthy GI symptoms. But with the Kharrazian Institute, where I teach post-graduate education healthcare professionals, next year we do have a course on childhood developmental disorders, and we're going to be covering a section on PANDAS and PANS with the research, with much more detail. But that's as far as what's in the schedule books. But thank you for asking.

Okay. Do you find the same concept of autoimmunity in PANDAS and not treating the infection similar in Lymes? Meaning don't go after the pathogen but the autoimmunity?

Yes.

You go for the pathogen, just not [inaudible 00:52:11].

So Lyme, once it gets past the acute phase, and the injury's there, and the tick has outsmarted the immune system, it's always hiding, and can always hide faster than it can be eradicated, then you basically have to treat. Many patients that have Lyme end up with autoimmunity, so they have antibodies to their brain, they have antibodies to different target proteins, and with them it's really implementing an autoimmune diet, nutrition, lifestyle to decrease the expression of their disease. And they can function better when they implement those strategies. But there is some overlap and similarities between that.

Okay. Michael's asking: what are your thoughts on Mucuna pruriens seed extract for dopamine? [inaudible 00:52:52].

Yeah, Mucuna pruriens is a natural form of dopamine that can be used. It's not going to have much of an impact with PANDAS or PANS. And it doesn't have much of an impact with Parkinsonian Disease. It does seem to only work best to help mood. If someone's a

little blue and their dopamine level's a little bit low, *Mucuna pruriens* can be very helpful. But at the end of the day, PANDAS and PANS is all about autoimmunity management, inflammation, and then brain rehabilitation. You won't really get much clinical effect with using *Mucuna pruriens*, which is a natural dopamine compound.

Okay. A lot of people are asking about your thoughts on the Wahls and Bredesen programs.

Terry Wahls?

Yeah, I think Terry Wahls. Yeah, I'm pretty sure.

Terry Wahls ... awesome, big fan, love Terry Wahls. Everyone should check out her website. Dale Bredesen?

Dale Bredesen, yeah.

Awesome, fantastic researcher, great stuff, big fan.

And they're good people.

Good people. I have a lot of respect for all their work, and I love what they do. Big fan of both of them.

Okay. Yeah. Kenny: what about restorative supplements like phosphatidylcholine and phosphatidylserine?

Yes. These are different things. When you look at how you can improve brain function, phosphatidylserine, phosphatidylcholine, EPA, like fish oils, they can all be good sources of helping improve more healthy nutrients to the brain. But the condition isn't caused by a brain nutrient deficiency. The condition is caused by an immune attack against targeted proteins in the brain. So even though it can be useful to help support the brain from a nutritional point of view, you still need to do activities that get that basal ganglia to develop.

It's just like someone has a brain injury, they have to do rehabilitation to activate their brain so they can recover. So just like someone who has a brain injury can't walk, they're going to have to try to walk and do things to get those neurons to reconnect again. You can't just do it with phosphatidylcholine or phosphatidylserine. However, taking those things while you're doing therapy may not be such a bad idea, because they do help support the nutritional status of the brain, which would be a beneficial thing as you're trying to improve its connectivity and plasticity.

Okay. One of the Tammys is saying: I hear parents say constantly that EMF causes an open blood-brain barrier. Can they link EMF to this brain damage?

Yes.

What are your thoughts?

Yes. There is some literature that EMF does disrupt brain activity, and there are even some early patterns that it can break down the blood-brain barrier. But again, to what degree and to what degree sensitivity does the person have?

If you actually take someone's food content throughout the day and measure the amount of chemicals in it, even if it's organic, you're going to find: there's some chemicals in here. And you can say, "Well that disrupts your brain, so you shouldn't be eating any food." It's like: well, there's a point where our body has to have some resilience. So when the body's healthy, it should have some resilience against inflammatory foods, it should have some resilience against infections, it should have some resilience against EMFs.

But there are people that have injury to the brain, and they lose that resilience, and EMFs will absolutely flare them up. They need to follow different strategies to reduce EMFs in their home. There's blankets they can get over their bed, like drapes, so they get less EMF activity. They can put things on their computer, they can use different headsets for their phone. But those strategies may have to be incorporated with them, and it's not uncommon for children that have had injury to their brain from PANDAS or PANS mechanisms to become extremely sensitive to EMF. But as their brain becomes healthier, then they have greater resiliency to that, and that will be a good sign to see a child that actually is no longer sensitive to being moved around a computer or in a building with lots of EMF activity. Yeah.

Yeah. Okay. I'm not sure who's asking this. Can strep antibodies and low platelets be related?

Can strep antibodies and low platelets be related? Well, strep antibodies are just telling me that you have antibodies against a specific pathogen, and low platelets is ... If low platelets are there, and white blood cells and red blood cells are normal, and that's unique, it's not necessarily complete immune compromise, or bone marrow issues.

But one of the most common causes for people that have low platelets is actually just a vitamin K deficiency. Vitamin K is essential for producing platelets. Like vitamin D has gotten a lot of attention in the past few years, as finding that many people are really deficient in vitamin D, I think in the next five, 10 years, there's going to be an explosion of vitamin K being popular, people actually have vitamin K deficiency.

So it doesn't hurt to take some vitamin K and see if that improves your platelets. And vitamin K is also really important for immune function as well. That would be my initial thoughts with that question.

Yeah. Okay. Catherine: what causes white matter to degrade?

To degrade? White matter is the sheath around neurons, and white matter is basically very vulnerable and sensitive to any kind of inflammation. When we look at cells and look at tissues, the amount of antioxidants you have against them protect against injury and damage. Well, white matter doesn't have antioxidants or things to protect it, so it's

very, very vulnerable to any kind of infection, any kind of inflammatory response. It's very vulnerable to hypoxia, lack of oxygen going to the brain. It's very vulnerable to free radicals. And one of the findings that you see with MRI findings is just what are called white matter hyperintensities, which is white matter lesions. And they're so frequent now that the radiologists are classifying these as a normal variant of aging, meaning somehow it's okay to have injury to your white matter as you get older, and that's okay.

I don't think that's okay. I don't think you should have any hyperintensities. There's many papers that have been published. One of the papers that has been published is why white matter hyperintensity is not so benign, where they argue the fact that these white matter injuries that are so common in MRIs aren't necessarily okay. They're actually saying that there's an inflammatory response.

So anything inflammatory can damage these white matter areas.

Okay. Because you opened the door for vitamin K ...

Okay.

K1, K2; is vitamin K1 more important than K2? Does it matter?

Again, this is nutritional debate talk.

There's like six questions.

Yeah. I don't have a position on that.

Okay.

I'm undecided.

Okay. That's fair. So TM: testing for that permeability.

Yes.

Basically, how to diagnose leaky BBB? And GI map zonulin?

Yep. The way you check for leaky gut is by, for me, I like to use a panel through Cyrex Laboratories called Array Number two. And they check for zonulin occludin antibodies, actomyosin antibodies. Those are the junction proteins of the gut, and if those are elevated, it lets you know there is breakdown of the intestinal barrier.

Cyrex Laboratories also has a panel called Array 20, and that checks for blood-brain barrier permeability. The classical tests that can be done by any conventional lab is S100B. S100B is found to be associated with breakdown of the blood-brain barrier. However, there's other things that can raise S100B, besides blood-brain barrier permeability, that occur. For example, various benign tumors or malignant tumors can sometimes raise them. But S100B is the typical model.

I'm not a big fan of the Vibrant Zoomer test because they don't do the gold standard ELISA testing. They do micro-array analysis, which is not the gold standard. And I don't like to use that test that some people use. I really think you should always use gold standard testing and never a secondary test. So I stick to Cyrex.

Okay. Helen: if an adult has adult onset Tourette's, do the same protocols apply?

Well in adults the most common cause for basal ganglionic injury with Tourette's and these symptoms is actually a mini-stroke. It's not actually from infection.

So this is really, really important. There is blood vessels called the lenticulo striatal vascular system, and these are little blood vessels that go out throughout the basal ganglia, and they're just ready to burst when there's high blood pressure. So when someone has something like acute onset OCD, acute onset restless leg syndrome, acute onset tics as an adult, it's rarely PANDAS or PANS. It's most likely a silent stroke or a mini-stroke that's causing that, and they should definitely be scanned with an MRI and see if they have what's called microvascular disease. They need to check their blood pressure, make sure that's normal.

So acute basal ganglionic symptoms in adults, you should be thinking stroke, mini-stroke, microvascular disease. And then with kids, basal ganglionic symptoms, you should be thinking PANDAS, PANS.

Okay, one last question.

Ah, pressure. Why don't you say your websites and courses that people can look at while I find a question?

What's that?

The websites people can find information on, and your courses that you take. It's my throwback. You panicked me.

Oh, okay. I already mentioned it but, drknews, D-R-K-N-E-W-S dot com is where we have our newsletter and we have our articles, and then if you follow us on our Facebook page; if you're joining us now, thanks for joining us, and you can follow us there.

I always forget to mention that.

Yeah. It's always good to know.

Okay. Any last questions? Think we got it?

I think we got it.

Well thank you for the suggestion for doing a talk on PANDAS/PANS, and there's a few other suggestions we put on the list from people that have joined us. We really appreciate your joining us, and we're always trying to accommodate topics that people are presenting. Hope you found something useful, and if you can share this information

with any parents that are dealing with PANDAS and PANS, that would be really important for them.

The key thing is to, at some point, quit chasing an infection and really go after improving brain function, and improving mechanisms dealing with dampening the autoimmune response and inflammation. And also realizing that part of the pathophysiology of the disease is that these dopamine receptors are dysfunctional, so it's really going to be hard to motivate and get kids suffering from this to change their diet and to do physical activity, but you got to figure out a way to do that.

Okay, one more thing.

Yep.

So people are saying they have your brain book. Does that help? And people are also saying "It's hard for me to get to the brain book. What do I do?"

Okay. The brain book ... I wrote a book called, Why Isn't My Brain Working? Autobiography.

It is not an autobiography.

But that's a book where I went into the literature of all different ways you can support the brain, but it's really designed for adults. It's not really designed for PANDAS or PANS, so that book won't be very useful. And the online program we have, called Save Your Brain, actually came from readers of that book going, "This thing is thick like a brick, and it seems good, but I don't know how to implement it." And that's what we have here. We have the online Save Your Brain program.

Okay. Well, thank you all for joining us, and hopefully you found something useful, and we'll be back next week. Thank you.

Thank you.