Opening on Folinic Acid and Patient Support

test these children because what you're going to see is this much more prevalent than you think. And when you implement supports and you put in the folinic acid, you are going see changes.

Please do not be scared to use folicic and to build up to the weight-dependent dose. You're not going the see the same responses if you just use five milligrams and think, oh, well, we put it in folonic acid and we don't see any improvement.

It doesn't work. That's not true. Not only do you have to give the right form of folate, you to have the proper dose, and you do it for a period of time.

I think minimum amount of three to six months to really see a difference at full dose. So I just encourage you, please bring it to your practice. Please bring to patients you are doing a service to those families.

Hi, and welcome to the Lime Bites podcast, where we shine a light on the misunderstood science of Lyme and other vector borne diseases, as well as the truths that many still miss.

I'm Dr. Mariah Hinchy, naturopathic physician and fellow of the Medical Academy of Pediatric Special Needs. I specialize in treating chronic Lyme disease, as well as other complex inflammatory conditions.

In this podcast, we break down what's working and what is not. We share the facts that most people miss, challenge outdated thinking, and give both patients and practitioners the tools to heal smarter.

So let's get into it and change the way we heal Lyma. Hi and welcome to another episode of the Lime Bites podcast, Rebuilding Immunity, Reducing Inflammation, and Redefining Recovery.

I'm your host, Dr. Mariah Hinchey, naturopathic physician and fellow of both the Medical Academy of Pediatrics and Special Needs, as well as the International LIME and Associated Diseases Society.

One of the central themes of this podcast and really of my entire approach to healing chronic vector-borne disease is that treating the organism is only one piece of recovery.

Podcast Introduction and Episode Overview

These infections can leave behind profound inflammation, immune dysregulation, autoimmunity, neurological dysfunction, mitochondrial dysfunction gut disruption and changes in the terrain that may continue driving symptoms even while we're addressing the infection itself or after the Infection has gone.

So if we want lasting recovery we have to ask not only what organisms are present but also what have these organisms disrupted and what do we need to restore proper function?

And that's exactly what led to the study we're talking about today. For years, both my guest and I have seen extraordinarily high rates of anxiety, OCD, intrusive thoughts and fears, depression, tics, and other neuropsychiatric symptoms in patients with Lyme and Other Vector-Borne Diseases.

We also know that infections, including vector-borne infections are often a large piece of the picture in children with PANS. That raised an important question.

Could cerebral folate deficiency and specifically autoimmunity against the foliate receptor be another piece the neuroinflammatory puzzle in vector borne disease?

So we decided to look, and what we found was remarkable. 61.8% of the 68 vector-borne disease-positive patients in our study tested positive for folate receptor alpha-autoantibodies, or FRAAs.

And the story gets even more interesting when we look at PANs and at a finding called the soluble foliate receptor. Now, why does this matter clinically?

because of folate transport into the brain is being disrupted by foliate receptor autoimmunity. Treating the infection alone will not address that downstream problem.

And it gives us another actionable piece of the terrain to investigate and to heal. One that may include eliminating mammalian milk exposure and using high dose folic acid or prescription leukovirin to help bypass impaired folite receptor transport.

Now today, we're going to unpack what we found, why we think it matters, and what it could mean for patients struggling with persistent neuropsychiatric symptoms.

Joining me is my friend, colleague and lead author of our study, Dr. Lindsay Wells. Dr Wells is a naturopathic physician and also a fellow of the Medical Academy of Pediatrics and Special Needs.

She specializes in complex pediatric and neuroimmune conditions, including PANS pandas, autism spectrum disorder, and Lyme and other vector-borne diseases.

Welcome back to Lime Bites, Lindsay. I'm so excited to finally sit down and talk to you about our study. Thank you so much for having me. This is very exciting.

So is. So let's start out. Give us, you know, everyone just heard my little version of why we did this study. Let's hear it from you and your own words.

Why Folate Receptor Autoimmunity Matters

Sure. So, our study is something that I'm so excited that we finally have out in the world. It took a lot of time and effort. And I really think it's groundbreaking because it is the first study in this population that really looks at folate receptor autoantibodies and how that could impact children with vector-borne disease, and with that, we hope that maybe it could even help adults with Vector-Borne Disease as well.

And so, you know, this study really, from my point of view, as you mentioned, the children in our practice, they have significant neuropsychiatric symptoms.

One of the main parts of treatment needs to be symptom support. How do we get that child and that family dynamic feeling better as quick as possible? And when we treat the underlying infection with antimicrobials, although the children get better, it takes time, right?

So I felt like there was an urgency to kind of figure out what else we can do to help to support the with their symptoms while continuing to work on the infectious piece underneath.

And it was just evident that there's more going on. Our kids are complex. It's not just the underlying infection that we need to address. I think you mentioned that in your introduction there.

There's so many different areas that need look at. In my experience, I started my practice really focusing on children with autism. And so I had a strong foundation in folate receptor autoantibodies and cerebral foliate deficiency, impacting symptoms like speech dysfluency and speech and communication issues, autism-like symptoms, and also we were noticing that it was helping anxiety.

And this we then continued to do in our children that have pans and pandas, who have underlying vector-borne disease, And we are seeing improvements in symptoms.

So I really think that was kind of you and I coming together and putting our heads together, and being like, maybe this could be something here. And we need to explore further.

Absolutely. I think not only, to your point, yes, this can speed up the rate in which these patients start to see a reduction in those neuropsychiatric symptoms, But I would even like push it to the other end where like, let's say that you were able to completely eradicate the infection if you haven't dealt with that autoimmune process that is now going on in the body.

Like, you know, yes, maybe it was stirred up by the presence of the infections, but it's now gonna continue until you're able Stop that and we'll get to this, you know in more detail as we go But like one of the main drivers through molecular mimicry like with that animal milk protein so it's like if if you don't uncover this piece of a puzzle with your patient and you Don't address it and turn that autoimmune process off The patient theoretically would just continue to have those symptoms long after the infection is gone Well, I think we saw that in that big Danish study that was done that looked at post-treatment Lyme disease and showed that there was a significant risk for having mental disorders like anxiety, depression, suicidal ideation and even an increased risk of suicide.

And, you know, when I read that study, that really stuck with me, right? Because, I mean, we see it in practice every day, but like the people they were talking about were the the families that we love, the children that love the adults that and we care for.

So absolutely, those adults in that they they treated for vector-borne disease. Likely not long enough, they still treated and still suffering significantly for years afterwards.

And so I completely agree that, yes, it can maybe speed up the progress during treatment, but afterwards as well, if we don't address this, and it's a piece of that person's overall picture, we might not make as much progress as we were hoping to.

Study Rationale and Clinical Overlap

So I think for our listeners, I want to go over some stats because when people think of vector-borne disease, they usually don't think neuropsychiatric symptoms.

And for listeners that don t know this, for a lot of children, vector borne disease presents more with neuropsychiatric symptoms than physical symptoms.

And in some kids, it's like neuro psychiatric symptoms and you know, some pain that gets dismissed is like growing pain, right? So there's a few studies that was done.

One of the studies showed that anxiety was present in 73 and a half percent of the entire study population. Now this population had some vector-borne disease.

OCD was present in 58.8 percent. Autism spectrum disorder in 36. 8 percent, ADHD in 25. So nearly half of whole cohort, 47.1, had a PANS-PANDAS diagnosis.

So this is such a significant clinical overlap in neuropsychiatric disorders amongst the vector borne disease associated cohort of the study, which included all of these different symptoms or diagnoses as well as pans pandas.

So I just think that's so important to highlight for our listeners. Absolutely. And one thing we didn't look at was also, you know, aggression and rage and anger in children.

That tends to be a really big clue as well, that there could be potential, vector-borne disease. So, I agree, most of the time our kids, they are presenting with neuropsych symptoms as one of their main symptoms for vector borne and why we have to look further for it.

So let's take a few steps back in case our listeners aren't familiar with what cerebral folate deficiency is, because I would argue that probably mostly people have never heard of it unless they or their child, you know, was lucky enough to see a medical professional versed in it who has given them this diagnosis.

So, let us go back to basics. Tell our listener what Cerebral Folate Deficiency is. Are you ready to transform the way you diagnose and treat complex chronic inflammatory illness?

Because what if everything you've been taught to treat separately is actually deeply connected? At the Lime Bite Symposium, we're bringing it all together.

Join us November 13th and 14th at the Fort Lauderdale Pompano Beach Resort in Florida. or attend virtually from anywhere for the premier functional medicine conference on complex chronic illness.

This year, we're diving deep into the interconnected drivers of chronic disease, including neuroinflammation, immune dysregulation, COVID spike protein related pathology, mold and mycotoxin illness, breast implant illness pans pandas, and of course, Lyme and other vector borne infections.

Because the reality is, your patients don't have just one of these. They have several. And if you're not trained to recognize how these layers interact, you'll continue to miss the root cause.

If you are a patient still searching for answers, this is the information that your doctor may be missing. This is how we move from symptom management to true healing.

So join us in Pompano Beach or from anywhere in the world. Don't get left behind. Register now at limebites.com. That's L Y M E B Y T E S.com Yeah, so cerebral folate deficiency is essentially just not getting enough folates into the brain.

And so folite is a very important vitamin. It's vitamin B9. We hear a lot about this during conception and when a mother is pregnant, right? You need to have some sort of foliate to help to prevent neural tube disorders and help decrease the potential of neurodevelopmental disorders in the offspring.

And then I feel like that's kind of it. That's all we hear about. And most of the time, unfortunately, women aren't even given the right form of folate during pregnancy.

But folates is actually critical all throughout our lifespan at every different point in time. Folate, we need it for our immune system. We need for neurotransmitter production, RNA, DNA.

amino acid synthesis. But a lot of times what we don't hear about is how we need folate in the brain. And we in standard medicine will just maybe measure folates in serum and the blood and we'll say, oh, there's plenty of folated there, but that's actually not reflective as to what is happening inside of the brains.

The brain is a very tightly regulated system, which is the wonderful thing. It has receptors on the Blood Brain Barrier.

Cerebral Folate Deficiency Explained

These receptors I think of as LOX, and they have specific keys that will bind into them and unlock and then be able to bring that key into the brain essentially.

And so we have receptors on the Brain for folate. What can happen is there can be these autoantibodies that either block the ability to get folated in or they bind to the receptor and kind of disfigure it, so they don't allow it yet again, the key to go in and be drawn in.

This then causes a deficiency of folate. That can present in different studies we know with neurodevelopmental disorders. So we that like autism, that's where the majority of the studies are.

It can cause seizures. We know that it's been associated with treatment resistant depression, anxiety, schizophrenia, acute onset dementia. So there are a lot of consequences to not getting folate in the brain, or not giving enough folates in brain I should say.

And so that's really what our study was looking at for cerebral foliate deficiency, the children with vector-borne disease who are not given enough of folated into the brains.

So I want to make it very clear to our listeners, if we were to do any sort of blood test for folic acid or folate, it would not pick up this deficiency.

So it has absolutely nothing to with the blood levels. They can be completely normal, but that does not reflect what is actually the cerebral foliate level.

Absolutely, that's exactly right. And then not that you would want to put a child through a spinal tap or anything like that, but if you were to do that type of testing, would that accurately measure cerebral folate levels?

Yes, it would. And so, in the cerebral spinal fluid, you would be able to see the levels of folate that you'd be getting into the brain. However, I don't know about you.

I didn't order spinal tabs, and you know, that's not routine here, but that is really the gold standard to be to measure folates and to look for these folic receptor autoantibodies.

But luckily, we now have a specialty blood test. that we are able to order and be able see if the child has the presence of these autoantibodies. And it's a relatively easy test that you do with a simple blood draw.

It's relatively affordable. I would say the biggest disadvantage now, because there's really only one company that does it, is just how long it takes to get your kit and get the results.

But it is well worth the time, the effort, and the weight. So the company is called Religen, right? And you need a physician to order the test for you.

And right now, what is the turnaround time? It's taking about a month to get the kit and anywhere from 90 to 121 days to So now they, I guess there was some changes in the company and now we're getting the results quicker.

They were getting them in about 30 days, which is fantastic, but it does take a bit of time to get the kit. You know, if you have to talk to your physician, they have, you know make an account with the There's a little bit of logistical work beforehand if you're not going to a provider who's already established with the company and running this test.

But luckily, we are seeing the turnaround a bit quicker now, but this is just recent. Previously, it was about 12 weeks to get back the results. And before we get into the actual study, tell our listeners quickly, how does this test help you?

What exactly does it show you and what does that mean? This test, it looks for the presence of these autoantibodies that either block receptors or bind to the receptors and disfigure it.

So there's two findings that it looks for blocking autoantibodies and the binding auto antibodies and so that's essentially what it's measuring. If it comes up positive for either one of those it then changes treatment plan because it helps to guide us with what form a folate that this child needs, which is folinic acid.

And it also helps to tell us, essentially, not necessarily the dose, because we know the those which are weight dependent, but that it needs to be high dose folicic.

It also tells us some dietary information, what you had mentioned before, that that child need to come off of dairy. And what's most interesting, which I'm excited to share in a little bit about one of our findings, is there's an

abnormal finding which is the soluble folate receptor.

And if that comes up, that helps to guide us actually with dosing because it tells us that that child might need even higher dosings than the weight-dependent dose that we previously would have recommended.

So I think it's very valuable information, just the levels in general, if we get essentially that soluble folate receptor finding to help guide treatment.

So sometimes even if it is negative, I will still do a trial of salinic acid, but I find having the actual data is important.

Testing for FRAAs and Soluble Folate Receptor

Let's dive into the actually study. Okay, all right. So highlight for us, like the population, the parameters. Yes. And so we included 68 children who had confirmed vector-borne disease.

All of these children had confirm vector borne disease from iGenex testing. I just wanted to point that out, which I find to be highly sensitive testing and one of the gold standards that we utilize, at least in my practice.

This was, these labs were drawn at their initial console and at the same time we also drew for the folate receptor autoantibodies. And what we found is that 61.8% of these children were positive for foliate receptor antibody.

Just for people who aren't good with percents, that's 42 out of the 68 patients. Yes. Big number. Yes, absolutely. And this actually goes, this is pretty consistent with the findings previously in PANS pandas, which is we found 63.8% were positive for the folate receptor alpha autoantibodies in the Pans and Pandas population.

It is even consistent what we're finding in autism, those studies can range up to about 71 to 75% of the children being positive. So to you, what does the 61.8% prevalence tell you clinically?

Yeah, so clinically what it's telling me is that there is some autoimmune type of process, right, that is happening with these underlying infections or, yeah, or all of these conditions, autism, pans-pandas, vector-borne disease, other mental health conditions like treatment-resistant depression, they're not so separate.

There's something over connecting all of them, right? And so we know it's complicated, but there's some going on with the immune system, mitochondrial dysfunction, gut dysbiosis.

Like, there is something that's connecting them all. And, so, instead of thinking that everything is separate, I think we need to be thinking more mechanistically and what's happening underneath the system that's kind of putting these threads together and part of that could potentially be related to the folate receptor autoantibodies.

And beyond that too, it's like we know vector-borne disease, the prevalence of autoimmunity is so high in this population, number one. And number two, you know, I wholeheartedly believe and arrange my entire approach to treating these infections based off of the resulting immune dysregulation that is a known outcome of these infection.

In fact, what allows them to stay chronically hidden in the body, or not so hidden, in a lot of cases, for years or even decades. Absolutely. So I know one of the things you're most excited about and can't wait to talk about is this soluble folate receptor finding.

Explain a little bit more deeply. You hinted that if it's there, we need even higher doses of folinic acid. But what exactly does it mean technically?

Are you suffering from Lyme disease or another complex chronic illness and aren't sure who to trust when it comes to herbal supplements? Hi, I'm Dr. Mariah Hinchey, founder of LyMe Core Botanicals.

As a naturopathic physician specializing in complex, chronic, infection-driven illnesses like LyME disease, i needed

herbal medicine I could truly trust.

That's why I formulated LyMe Core botanicles. where our herbal tinctures are handcrafted in small batches right here in Connecticut. We use the whole herb, never isolates, to preserve the full spectrum of medicinal compounds.

Every single step from sourcing to extraction is done with precision to ensure maximum purity, potency, and consistency. These are the same herbal formulas I used to heal myself and have used for years to help my patients and family members heal too.

And now I'm making them available to practitioners and patients everywhere. Lymecore Botanicals, herbal medicine you can trust from a doctor who lives this work.

Learn more at LymencoreBotanicles.com With the soluble folate receptor, so essentially what this is, is it's a protein that has a high affinity for binding folates.

So when this present, what it can cause is even more severe foliate deficiency, right? Because it is in our bloodstream, it in the cerebral spinal fluid, and essentially it binding the foli, but it not going anywhere.

Study Results in Vector-Borne Disease

The folite is not being delivered to our tissues and to ourselves. And so when this finding is there, it's an abnormal finding when they're looking for the blocking alpha autoantibody.

Because what they see is when the put the agents in to kind of measure the levels of the auto antibodies, its less than they would have expected for what the added in, to test for, because there's the soluble folate receptor that's just binding up all the folates.

And so it comes up in the blocking category of, and previously we didn't know really much about it and we still don't really know much it. It's kind of interesting.

There's only been one study done in autism that looked at the children who were coming up with the soluble folate receptor. And what they found was that those children were more medically complex.

They were probably more severe. They also tended to respond to higher doses of the therapeutic dose of two milligrams per kilogram, up to 50 milligrams, per day.

And when I contacted the company, Relagym, I was asking about like, what is the percentage that we see of soluble folate receptor of a population that's tested?

Now, keep in mind. The population that's being tested are ones that already have neurodevelopmental disorders. And they were saying about five of the population will come up with the soluble folate receptor.

But what we found in our study was 11.8% were coming up positive for soluable folates. So double. Double. A population already has neuropsychiatric, for the most part, neuropsychiatric symptoms.

Yes. Or you wouldn't even have had this test done. Yes. It really was like, what does this mean? This is actually pretty much, in my opinion, the most interesting finding.

So it was double what we would expect to see. Now, on top of that, out of the 68 tested positive for the soluble folate receptor, seven out eight of them had confirmed Borrelia infection.

The other one had an indeterminate relapsing fever Borrelia, so still had Borrellia species. in their blood. So that was also like, wait a second, is there something going on with the Borrelia species or the Borelia species family that's contributing to the soluble folate receptor or vice versa causing people to be more symptomatic?

And so I don't know what it means. I haven't done more research on it. It's just, it makes you pause to think of like you know, this spirochete, how much it does in the body and how it could potentially be playing a role here as well.

And then if somebody, like a child with autism, is testing for soluble folate receptor, they absolutely should be testing underlying vector-borne disease, but specifically the Borrelia species.

Right. And I think in general, any child with autism needs to be ruled out for vector-borne disease, but even more so if they have the soluble folate receptor.

So I'm really pumped up about that finding. I don't completely know what it means. I hope eventually we will explore further and have more answers about it.

But it is suspicious, interesting, and somewhat exciting. Absolutely. we've talked about before like how cool would it be to be able to go back to that one study on children with autism spectrum disorder and the soluble Foley receptor and see and then of course it depends like was you know was their physician Lyme literate did they even know to look for Borrelia but like it would be so cool to see like okay were they tested for Borelia was it there.

Absolutely. Okay. If there's any type of auto antibody against the folate receptor there, it is 100% strict avoidance of any product made from any milk of So I want to make that clear.

And that is like, no, not a little bit here, and not little there. Oh, it's just a splash. It's an ingredient. As strict as someone with celiac would have to be to avoid gluten.

That is the strictness of this dairy avoidance. Number one, But then getting into number two, with this soluble folate receptor, can you talk a little bit about the dosing and the difference with high folinic?

Sure. So with hi-dose folic acid, what you want to utilize for cerebral foliate deficiency or having a positive folite receptor autoantibody test is two milligrams per kilogram.

up to 50 milligrams per day. That is what is documented in research. Now there are some of us and some our colleagues are going higher than that, but this is whats documented and researched.

And so you would want to build up that weight dependent dose upto 50mg perday.

Soluble Folate Receptor and Borrelia Link

What we're seeing in the children with soluble folate receptor is that they might need higher doses to respond, or we could get even more therapeutic benefit by going higher.

And really what we are looking at is doubling that dose to up to 100 milligrams of flenic acid per day. Okay, and that's such an important piece to point out because, you know, most of the literature is just talking about that standard dose up to 50 milligrams and a lot of clinicians are stopping there.

Yes, absolutely. All right, so now let's talk about another clinical finding, one that I think is so important to talk, about and that's the relationship with PANS-PANDAS.

So among the FRAA positive vector-borne disease patients, 57.1 had Pans-pandas compared with 30.8% of the FRAA negative vector borne disease patient. So this translates into an odds ratio of three and the association reached statistical significance.

So break this down for our listeners in English and tell us like how do you interpret that and how you use this information when you have a child sitting in front of you that has PANS plus potential evidence of a vector borne infection.

So, I mean, in simple terms, it just meant that those in the study who had vector-borne disease, they were three

times more likely to also have a diagnosis of pans and pandas, okay, who were positive for the folate receptor autoantibodies.

And I think it shows the correlation here of, like, we see a high level of folates receptor antibodies in pans-and-pandas population anyway, again, at 63.8%. In my practice, and I'm sure in your practice as well, these children with pans and pandas, most of them have underlying vector-borne disease, which I think might actually even be at the root of why they're susceptible to pans surprising.

To me, I would say I think it's just confirming what we're seeing clinically, that there's an overlap between children who have vector-borne disease and pans and pandas, and that, there is the potential that if their pans-and-pandas is due to one of the infections being vector borne disease, they're three times more likely to also be positive for the folate receptor autoantibodies.

So, yet again, add it on top of what their little body is already going through. and potentially another avenue or another route for treatment to really get them to feeling more comfortable and getting back to their happy carefree childhood.

So we know that it is through molecular mimicry. I would imagine that's a word that a lot of our listeners haven't heard before. Yeah. So why don't you explain like, so how does this autoimmune process happen because of dairy?

Can you explained that sort of process to people? Sure. What happens is when we consume dairy, some of us will have an immune response to the proteins in that dairy from the milk from different animals.

So when you say mammalian milk, that's cow, buffalo, sheep, goat, camel, donkey. Any animal that produces milk that is not human and you're consuming that milk.

Your body can start to produce antibodies against it because it's having an immune response. Now those proteins, those have a 90% similarity to the folate receptor that we have on our brain.

And so what happens is if our immune system is making these antibodies against the protein in the milk, it will start to get confused because the structure is so similar to that of the full eight receptor on the brain that it then starts to attack that foliate receptor in that brain by either binding or blocking it.

Dairy Avoidance and Molecular Mimicry

that then contributes to what we're talking about, the cerebral folate deficiency. So that's what happens. And what see is when we remove milk and dairy from the diet, that auto antibody levels, they almost go down to baseline.

They decrease significantly. But you had mentioned this is a long-term treatment, as strict as you would have to be. I loved your analogy about the like celiac disease with gluten.

I think it's a wonderful analogy to this because in a very small study, we found that when they reintroduced dairy after three months, guess what happens?

Their folate receptor autoantibodies, they went higher than they were initially. Like there was an even more profound immune response that occurred. So, therefore, it really is a long-term, strict elimination of dairy.

And do I see families that make progress and children that makes progress just putting in folinic acid and not removing dairy? Yeah, sure. But let me tell you something.

If your child is responding just to folicic without removing the dairy, can you think about what their response would be if you actually removed the diary?

it would be that much more profound. And so, it's important, and it is a critical piece of the treatment plan. It is. and

It's not that hard to do. You know, when you think about it, It might seem overwhelming to begin with, but it it actually not hard.

And when families take this on and they do it together and make a dairy-free household, it really makes supporting that one child, that individual so much easier.

And it sounds very daunting, but as a very dairy free household I promise you that it is absolutely easily achievable and you can still enjoy food to the max.

And I'll leave that point at that. Let's talk more about using folinic acid. let's Talk about leukovorin, let talk about the mechanisms and why it's so important that we are using a folanic acid product and not methylfolate or folic or something else.

Get into like that, that physiology with us. Sure, so I'm just going to start with folic acid. Folic acid is a synthetic form of folate. This is made in the lab, this is, you know, a form that the body really can't utilize and plug into its pathways, okay?

So that form is one that I think should be avoided. I really think it comes down to methyl tetrahydrofolate and folinic and there's a difference here.

The methyl-tetra-hydrafolite, is the most bioactive form. It is what can bind into the receptor and be drawn into But the issue here is that the receptors are not functioning properly, okay?

So we then need to figure out what can we do to get folate into the brain? And what we have found is there are carrier transports on the brains. And there's one called the reduced folic carrier.

This helps to shuttle folinic acid into brain. We don't have studies to really show that methyl tetrahydrofolate can utilize this alternative shuttle transport.

It's phylinic acid and that's where the distinction matters and it's critical because you will not get the same results using methyl tetrahydrofolate than you Even if they're at the same dose, clinically we don't see the improvements.

So you absolutely need to use folinic acid, and we like to the form of calcium foliny for the folicicacid. And that's what the…form of the prescription, leukovorin.

Leukevorin is folonic acid and what is used in the studies to help with cerebral folate deficiency. We also know that the use of folinic acid with the same form, calcium folinate, if not in the form of leukovorin, we can also reproduce a lot of those similar benefits as well.

And then I think it's important to note too, because there aren't a lots of sources that you can just get over the counter of fulonic acid or calcium fulinate.

So if a parent is left trying to use methylfolate and you're going to super high doses of methyl folate, like you can actually have some pretty crazy side effects, right?

Where someone starts over-methylating and they become extremely irritable, anxious, except that you do not see as readily when you are using the high-doses of folinic acid.

Do you experience that same phenomenon? Because I know that I do. Absolutely. So with folinic acid, it's still possible that we can get some irritability and agitation, sometimes sleep disturbances, like difficulty falling asleep.

But it is seen immediately, within that day that you dose, and then when you decrease the dose back down, It resolves. With methyl tetrahydrofolate, those symptoms are amplified much more than they are with folinic acid.

Folinic Acid Treatment and Dosing

And I feel like the symptoms that I see, they last longer. You know, even when you decrease back down the dose or you take it off, like, the child still has a hard time kind of coming back to equilibrium.

So I really encourage, if you're going to use high doses, you really need to be using folicic and not methyl tetrahydrofolate. Okay, so I want to get into how you titrate in a moment, but I wanted you to answer this question for people that are wondering, is there a toxic dose of folinic acid?

And then other than having some agitation, irritability, things that you just mentioned, are there any other potential negative consequences or side effects of using it in high dose fashion?

So, folic acid or folate is benign. It's a water soluble vitamin. So you will just excrete out what you don't need. When we talk about toxicity, there's no known toxicity with that.

There are side effects though, and the side-effects as I previously mentioned are irritability, agitation, and difficulty falling asleep. The reason that's happening is because, think about it, we need folate to make our neurotransmitters.

When somebody has cerebral foliate deficiency, what happens is they're not getting enough folite into the brain, so their neurotrasmiters aren't, you know, the production is not going as quickly or as much as we would like.

You start shuttling folade in, their pathways start moving quicker. They start making more serotonin, more dopamine. what that can happen. If that happens at too high of a rate, too quick, the person can be irritable, agitated, and have difficulty falling asleep.

It's so benign because, again, we just go back down to the next lower dosage or we stop it and the symptoms improve by the day. There's no lasting effects whatsoever because again it's a water-soluble vitamin and we're just excreting it out.

Yeah, with that, like I feel very comfortable using high doses, but you do have to build it up to kind of prevent those negative side effects. Now, are there other side-effects?

In literature, we've seen that there can be some aggression in children with autism. But I, you know, knock on wood have not seen in my practice because the way that you build up on the dose and titrating up, this matters to decrease the potential of having side affects.

And so in studies that have been done on cerebral folate deficiency and FRAA-associated neurodevelopmental conditions, leukovorin has been the form of calcium folinate used.

So talk a little bit about, I mean, it, uh, don't even want to use the word similarities because it's actually the same thing. But just, you know, for our listeners, talk about the difference between calcium folinate and leukovorin.

Yes. So with lukewarm, this is a prescription of folinic acid, calcium folinate, but there are additives to it. And so there can be addatives like lactose, which doesn't really make sense, right, when we're trying to avoid dairy and take dairy out of the diet.

There can also be corn, soy. Food dyes, some of our children can have underlying sensitivities to, or can agitate them. So sometimes, you know, there are kids who go on leukovorin from the pharmacy.

There's these additives in it and they start to have side effects, these agitation irritability, but it's not actually from a calcium folinate. It's actually, from that addatives into the prescription.

So some parents will then go as far as compounding leukovorin, which is just essentially straight calcium folinate, and maybe they add in a more natural flavor for the child to tolerate the taste.

But in reality, that's the difference. Leucovorin has additives from being made in the lab and from the pharmacy

when calcium fulonate is the form of folic acid that we need that helps utilize that extra shuttle pathway, the folate receptor there.

Right. I mean, and you can't really put a trademark on something that exists in nature. So, leukovirin has these other things in it and then that allows them to patent it basically and have it be a drug.

Yes. Okay, so talk to us about the titration. How do you approach this? Do you kind of have like a one-size-fits-all approach or do have a way of knowing how you want to titrate a particular child?

You know, I usually go pretty slow. Like if a child is up to the full dose of 50 milligrams per day, I usually start around five milligrams or 7.5 milligrams and continue to increase in those increments every week.

And I'm usually a pretty good success. So it usually takes about six to between six and 10 weeks to get a child up to their full dose.

Titration, Cofactors, and Clinical Use

Usually I find that this is kind of the sweet spot with weekly increments to decrease the potential of side effects. But, you know, there are kids who are more sensitive than others and we have to go a little slower, meaning every two week incremented, we go up.

And that's okay. I really do start lower between like 5 milligrams and 7.5 milligrams. And now I know you and I practice very similarly. We are naturopathic physicians after all, and we look at the total person and the totally terrain and gut and other nutritional aspects and nutrient deficiencies and things.

So with that being said, are there other co-factors or nutrients that really are a must that either need to be given or need be evaluated when you're using folinic acid?

Yes, so once I get a child up to the full dose of folinic acid, I will add in B12 just to help as a cofactor. It's something that I put in after they get up full-dose, not necessarily before.

And I utilize the standard dose B-12 that would for any child. I don't change that dose to B 12 just because they're on 50 milligrams of Folinac acid.

I do tend to use the form of adenosylcobalamin or hydroxycobilamin rather than a methylcabalamine in, I mean, all of my children in my practice, to be honest.

So I will add that in. I also do recommend, again, the dietary piece of things with removal of the dairy, but also looking to decrease folic acid that's fortified in foods.

And I find that to important as part of treatment plan. But really that, you know, kind of how I address this. you know, put in like a full B complex or anything like that.

So based on what we've found, what would make you think about testing for FRAAs in the entire population of kids that you have in your practice? Well, you know, what we also did find in the study was that we couldn't really tell based on symptoms which child would be positive for the folate receptor autoantibodies and which would child be negative.

So where does that leave us? That leaves us with we need to test all of the children. that come in. And I think this provides extremely valuable information, but on top of that, it changes treatment plan.

You know, like if a child's coming back positive, we address with folinic acid. If they come back with the abnormal finding of the soluble folate receptor, guess what, we go higher and we make sure we rule out Borrelia species in that child.

I encourage all families that come to my practice at least that we dive deeper and look for the folate receptor autoantibodies. Again, my population is a specific population similar to yours, but essentially every child in my practices is getting screened for this.

So, I mean, you know, your specializing in autism spectrum disorder. You're specialising in pans-pandas. Your specialised in paediatric vector-borne diseases.

Just those three populations alone. So the lowest incidence was vector borne disease at 61. And the highest is autism-spectrum disorder in this, what was it, 75? The highest that we found was 75%. And all of them, as we talked about, have some sort of auto-immunity underneath.

Right. It's estimated that one in two children have an autoimmune disease. So then besides these like little niches that we have of populations, is it all children should be looked at for this?

I mean, maybe. I means, okay, so look at how many children having chronic disease at this point, right? And so, yeah. Why not? It is so inexpensive and so non-invasive, why wouldn't we be doing this for our kids?

I mean, I'll just digress for a moment to the whole, like, why aren't we using appropriate screening with specialty tests on all children at their annual physical for at least Babesia, Bartonella, and Borrelia?

Right? I think it's so much more expensive than the frat test, but still. So before I forget, I want to point out, so you see mostly pediatrics, and I've been finding positive frat tests on my adult population with vector-borne disease as well.

And I've not crunched the numbers or done the stats or anything, but these tend to be in adults that have more neuropsychiatric issues. And it's a big piece of the puzzle there.

So even though this episode has really been about pediatrics, I just want to point out that it is not limited to the pediatric population and we are seeing this same disease process in adult as well.

and addressing it is just as important.

Who to Test and Family Screening

And we see this, like in children with autism, there's been multi-generational studies that Dr. Fry has done that has found that the first-degree relatives, the parents and the siblings of the children who are positive for the folate receptor alpha-auto-antibodies were also positive.

So if you're a parent listening and your child is positive, it's important that you then get checked. Because maybe you don't have big symptoms that your children has, but maybe there's underlying anxiety.

Maybe there is some depression. maybe There's some other autoimmune condition or process that's happening for you. And this could also be a part of that.

Thanks for bringing that up because it is important. If you are seeing it in your childhood, It's very possible that You're also going to see it yourself as well.

Absolutely. All right, so we're coming to the end, but I want to bring this up too, because I know we've talked before on other episodes about treating a woman who is about to conceive or through the pregnancy with high-dose folinic acid too.

And then that actually changing outcomes with a women who has had a child who was on the spectrum. Can you quickly comment about that? Sure. So what we found is that If a family has a child with autism and then we looked at their parents, if their parent were positive, either the mother or the father or both, what we found is that if we treated the mothers preconception with 3.75 milligrams of folic acid, that the offspring from that pregnancy did not

have the folate receptor autoantibodies and they were healthy and did have a neurodevelopmental disorder.

Now this was a very, very small study. I want to just preface with that. But I think it's important. This is a finding. So again, any family that has a child who has neurodevelopmental disorders, the parents need to be screened.

Because if you're planning to grow your family, this could be a wonderful preventative intervention to put in that's so simple. Yeah. It's simple, so cheap, it is so easy.

Yes. Okay. So before we close, is there anything you feel like we didn't cover or talk about that you want to share with our audience right now or want us to discuss?

Sure. You know, the big thing is having a conversation with your provider about testing because this can change treatment plan. Again, in the research, we see the use of leukoborin, calcium folonate, However, this can be a barrier for some people to get the prescription.

And if that is the case, there are now different companies that have calcium folinate available at higher dosing. So my hope is that there less barriers for you to gets tested and then also to implement the treatment because it can make a significant difference for your child or for yourself or your whole entire family.

I just encourage you that if you're told no, They can't get the prescription that you explore further. You look further, maybe find another provider or do some research on your own because there are options available out there.

Absolutely. And if there's a clinician listening today and they only have one takeaway from this interview, what would you hope they take away and utilize when they have their next Lyme, PANS, autism spectrum disorder, patient in front of them.

Test. Please test. Make an account with Religen. Go on fratnow.com. Order the kits into your office. test these children because what you're going to see is this is much more prevalent than you think and when you implement support and you put in the folinic acid you are going to see changes.

And please do not be scared to use folinic acid and to build up to the weight-dependent dose. You're not going see the same responses if you just use five milligrams and think, oh, well, we put in folicic and we don't see any improvement.

It doesn't work. That's not true. Not only do you have to give the right form of folate, you And you have to do it for a period of time.

Closing Remarks and How to Connect

I think minimum amount of times is three to six months to really see a difference at full dose. So I just encourage you, please bring it to your practice.

Please bring to patients you are doing a service to those families. Thank you. tell our listeners how they can find you. So if they want to become a patient, how would they do that?

If they wants to learn more about the other big things that you're doing in the world, How can they connect with you? Sure. I am accepting new pediatric patients and I keep my practice to the peds.

And so you can go on my website at lindsaywellsnd.com. All my information about my office is there. And, you know, I also have some information at phalenicacidatemphasis.

com. Our research is all there, as well as a lot of other research. You can follow me on Instagram at Lindsay Wells ND. I love to post all things about pansympandas, vector-borne disease, and about our research findings.

Awesome. And we'll put all of that information in the show notes as well. All right. Well, thank you, everyone.

Thank you Dr. Wells for joining us for another episode of the Lime Bites podcast.

If you found today's conversation helpful, please subscribe, leave a review, and share this episode with someone you love. Together we can change the conversation around Lyme disease and other complex chronic illnesses and what true healing really looks like.

And if you're looking to dive even deeper into these topics with world-renowned experts, be sure to join us at the Lime Bites Symposium, November 13th and 14th.

Dr. Wells will be speaking there in even more depth about our study and clinical pearls to treating all of this. So until next time, remember together, we all heal stronger.

We'll see you later. If this episode gave you an answer, brought you new insight, or made you think differently, subscribe to the Lime Bites podcast and share with someone who's ready to take control of their healing journey.

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