Introduction to Folinic Acid Safety

What is the toxicity seen with using high dose calcium folinate or folinic acid? Like what are the dangers in using it? At this dosage that we're talking about, at the two milligrams per kilogram up to 50 milligrams per day, there really isn't any concerns in regards to toxicity here.

I mean, if your child or you are not going to tolerate it, you're going to feel that effect of the irritability, the agitation, sleep disturbances, And you're going to back it up.

Some people will do research and confuse folinic acid with folic acid. And folic acid is a synthetic form of folate that has been shown in some studies, which have gone back and forth, controversial a little bit, of perhaps an increase in some cancers.

I want to be very clear, folinic acid is not the same as folic acid. And therefore, the concerns of high dose of folic acid, they're not warranted when we're talking about folinic acid here.

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.

Podcast and Guest Introduction

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's not.

We share the facts that most people miss, we challenge outdated thinking, and we give both patients and practitioners the tools to heal smarter. So let's get into it and change the way we heal Lyme.

Welcome back to Lime Bites, Rebuilding Immunity, Reversing Inflammation, and Redefining Recovery. Many children with abrupt neuropsychiatric symptoms or developmental regression are presumed primary psychiatric patients, but often the root cause lies deeper.

In some cases, cerebral folate deficiency driven by folate receptor alpha autoantibodies is the underlying cause. These autoantibodies impair the transport of 5-methyltetrahydrofolate across the coracoid plexus blood-brain barrier, causing folate deficiency in the central nervous system even when blood folate levels are normal.

Meanwhile, emerging research suggests that infections, metabolic stress, and immune activation may trigger or exacerbate the folate receptor alpha autoantibody production and folate transport disruption, further linking this mechanism to chronic infection-driven neuroinflammatory illness.

Today we'll connect these pieces, how the folate receptor alpha autoantibodies and cerebral folate deficiency can manifest clinically, how vector borne and stealth infections may drive or worsen this process, and what it means for diagnosis and treatment in children presenting with neuroimmune symptoms.

Our guest today, Dr.

What Cerebral Folate Deficiency Is

Lindsay Wells, is a Connecticut-licensed naturopathic physician specializing in pediatric neuroimmune disorders, including Pans-Pandas, Lyme and other vector-borne diseases, and emerging metabolic drivers such as cerebral

folate deficiency.

She brings deep clinical experience in integrating infection treatment, immune modulation, and metabolic repair in children who have been underserved by conventional medicine.

If you've ever wondered whether psychiatric symptoms or regression might actually stem from folate transport blockade plus infection triggered immune stress, this conversation will help you see the underlying biology and a path towards recovery.

This is Lyme Bites. Let true healing begin. Welcome, Dr. Wells. Thank you so much for joining us today. Oh, thank you for having me. I'm really honored to be here.

Oh, and I'm so honored to have you. So let's start with some basics. Describe for our listeners what cerebral folate deficiency is and means and what folate receptor autoantibodies are.

yeah so in simple terms cerebral folate deficiency just means not getting enough folate into the brain okay so cerebral means brain folate deficiency means not enough folate so that's just simple terms and so what can happen when we're not getting enough folate into the brain is there can be issues with detoxification, there can be issues with neurotransmitter production, and many other things.

And that's where we kind of, it's an important conversation that we're talking about for our children and adults who may have neuropsychiatric symptoms.

So how somebody gets cerebral folate deficiency, one of the ways is developing these folate receptor autoantibodies. And so essentially these are antibodies that are produced that block the receptors on our blood brain barrier.

to not allow the folate to get in. So we know that the brain is a very tightly regulated system, or at least we hope that it will be, right? And so on the blood-brain barrier, there's going to be receptors, and those receptors are specific for methyl tetrahydrofolate, that bioactive form of folate.

they have to bind into that receptor in order to be brought into the brain. But what happens is these auto antibodies, they can kind of mutate or block the ability of those receptors to function optimally, not allowing the folate in.

Okay. So how does this differ from someone just having like a folate deficiency that's system? Yeah, it's a great question. So you can have normal levels of folate in the body and still have cerebral folate deficiency.

Vice versa is you can be deficient in folate systemically and not have cerebral folate deficiency. And so with systemic folate deficiency, you're going to be thinking of things more like anemia, you know, maybe some immune dysregulation, which could or could not be related to cerebral folate deficiency.

You could think about neural tube defects, right, like when a mother is pregnant with the fetus and not getting enough folate that that could be contributing.

It is different than the MTHFR mutation, which is often a common question I get. So they're separate from each other because it really does come down to those autoantibodies that are occurring at the blood brain barrier.

So if one were to just test for their serum folate levels, that is not at all going to help anyone diagnose cerebral folate deficiency. Not at all. Again, if somebody is deficient in folate, that doesn't mean they have cerebral folate deficiency.

Testing for Folate Receptor Autoantibodies

And then one of the biggest misinterpretations and why I think people get misdiagnosed or don't look further for cerebral folate deficiency is because they run a serum folate in the blood and it's normal.

And they're saying, well, that can't be the problem. That's not true. The only true way to look for cerebral folate deficiency is to look for those autoantibodies.

And that's either through the cerebral spinal fluid by doing a spinal tap or with a specialized test to look for the levels of the autoantibodies. OK, so you just stole my next question.

I was going to ask you, what test would you do? So be a little bit more specific and talk to us about the actual tests that you use in your practice. Yeah, so one of the greatest things for my practice has been the ability to look for cerebral folate deficiency by checking for binding and blocking autoantibodies through a test.

It's called the FRAT test, the folate receptor autoantibody test. It's from a company called Religen. First of all, it looks for the presence. Is it there?

And then it will measure what is the level for the blocking and the binding of the autoantibodies. And so that's what I test for. I honestly, in my practice, do not even look for serum folate because I find that it is not useful and I always kind of ask myself, what am I going to do differently with the results of that test?

And it's not going to change my treatment for cerebral folate deficiency whatsoever. So I really do do that specialized test when I look at the serum in the blood for the autoantibodies.

Now, I have never recommended in my practice anyone to go through, you know, a spinal tap to look for cerebral folate deficiency, even though technically that is considered the gold standard.

Right, but I think one can assume if you have the presence of these blocking or binding antibodies, then you can assume, you know, that that is leading to the cerebral folate deficiency.

Absolutely, and there's research to back that up and to support that using this testing is sufficient to make the conclusion of cerebral folate deficiency to implement treatment to address.

Right. So before we move further, can you describe the difference between a blocking and a binding antibody? Sure. So with the autoantibodies, again, we're talking about the receptors on the blood brain barrier.

So when we have a blocking autoantibody, that's going to actually go into the receptor and block it. So therefore, the methyl tetrahydrofolate, that bioactive form of folate, there's no room for it to go in.

It's actually blocking the ability. Then we have binding autoantibody and that one binds to the receptor somewhere on it and I think of it as like mutating that receptor so it's not no longer functional.

So the again the bioactive form that methyl tetrahydrofolate it can't go into the receptor because the receptor is not the functional structure. And how I describe a receptor to my patients and my practices, I think of it as a lock.

There's going to have a specific key, and that specific key is that methyl tetrahydrofolate. And so if that lock is abnormal in any means, or if it has been mutated or something was put into it, you're not gonna be able to get the key in just right in order to turn to get it into the brain.

And so that's how I describe those blocking and binding autoantibodies. So is it worse to have a binding because the binding is somewhat degrading the receptor versus a blocking is like just blocking it?

Are you ready to revolutionize your approach to diagnosing and healing complex chronic inflammatory illnesses in both adults and children?

Blocking vs Binding Antibodies

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And really we treat them both the same. So it doesn't seem, at least from my practice or my clinical experience, that one is more severe than the other.

You know, we are seeing some different trends that with different conditions, they might be more likely to have blocking or more likely to have binding, or there's even something called a soluble folate receptor.

They might be more likely to have that. And so again, we're just seeing trends and we don't, You know, truly know if it means like severity based on that and you really can also look what's great is not that it's quantitative.

We can see the number for binding and blocking. And so I kind of go based off of those numbers of somebody who it may be more severe. Okay. And so what do you see in your practice, as well as what does the literature say are the drivers of the production of these auto antibodies?

Yeah. Two things that we know. One is that we consider this a non genetic hereditary condition. And so literature is showing that this it's in the family.

So we've looked at children with autism. and have looked at parents and siblings. And what we have found is that there is a correlation of the parents having the folate receptor autoantibodies, or even seeing it in their neurotypical siblings.

So there is some sort of, again, hereditary piece to this, but it isn't a genetic inheritance, essentially. So we call it a non-genetic hereditary condition.

Now, Dr. Fry and some of his colleagues are now working on a multi-generational study on this in particular, looking again at children who have developmental disorders and then looking at parents, grandparents, siblings in a much bigger study so we can get some more information about this.

the other piece that we know that's a contributor is actually dairy. And so dairy also has cow dairy or animal dairy has these folate receptor autoantibodies.

And their structure of that folate receptor autoantibody from animal dairy is 90% similar to what we produce in our body.

Drivers of Autoantibody Production

And so what happens is when we are exposed to dairy, If there is some pre-existing condition or the environment inside of our system is inflamed, an autoimmune type of presentation perhaps, that can cause our own body to make more antibodies, these folate receptor autoantibodies, and therefore contribute to this issue of cerebral folate deficiency.

And I just find it so interesting because when do we introduce dairy into children's diets? When are we told by the pediatrician to implement cow dairy?

The answer is 12 months. And so when is the time that the majority of children are diagnosed with autism? It's between 12 and 18 months. And it's just so interesting to me that it's around that time frame because perhaps Part of the picture, and we do know that this is true in children with autism, is cerebral folate deficiency could be contributing to their overall presentation and perhaps one of the reasons why they're regressing around that time.

Now, is it the only reason? Absolutely not. But it is a contributing factor that needs to be looked at. Yeah. Right. And a genetically susceptible child.

Yes. Okay, so we have a somewhat of a genetic, I'll just keep it simple and say that maybe predisposition, right? Then we have the molecular mimicry with dairy driving an autoimmune process.

And then what role do stealth infections, you know, like Lyme, Babesia, Bartonella, even, you know, perhaps now COVID, or the spike protein at least, like, what do these sort of like immune triggers do to further along this process?

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 Botanicals. 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. Lyme Core Botanicals, herbal medicine you can trust from a doctor who lives this work.

Learn more at Lyme Core Botanicals. That's L-Y-M-E-C-O-R-E dot com. This is just speculation of what I have, you know, of my clinical experience, but all of these infections, right, they're going to contribute to inflammation in the body.

And then with that, it's going to stress out our system. And so what can happen is we can deplete, it can cause depletion of our folate levels. It can deplete some of the co-factors that we need for folate transport, like B12 and B6.

So those are kind of one piece of it, right? And I don't know if it's the chicken or the egg, what comes first, right? But what I see with infections is it contributing to not only systemic inflammation, but the neuroinflammation, which is what is responsible for the manifestation of the neuropsych symptoms.

And again, it's just interesting cerebral folate deficiency, what it has been associated with with mental health conditions, anxiety, treatment resistant depression, OCD types of behaviors, schizophrenia, we found pans and pandas being one.

With that, it's like, are the people who have these underlying infections, who have a predisposition, who then have neuroinflammation and present with psychiatric symptoms, are they the ones that perhaps have cerebral folate deficiency?

Infections, Neuroinflammation, and Symptoms

And is that a driver as to why their neuropsych symptoms are maybe more severe than somebody else who has the same infection who might have more physical symptoms or may not have any symptoms at all?

Right. Yeah. And then taking that inflammation one step further to like imbalancing, you know, the T helper branch of the immune system, pushing TH17, that whole autoimmune process, I would imagine probably fits, you know, pretty closely into this whole, you know, it is an autoimmune process, right?

Right. Absolutely. Okay, so how would you say that the neuroinflammation, because we know that you specialize in vector-borne diseases, as well as autism, as well as Pan's Pandas, so try to help us tease out the difference between the neuroinflammation that you see in your children that maybe have vector-borne disease but not autism or Pan's Pandas, right, versus those children that have maybe one of these other diagnoses where it's the cerebral folate deficiency that is like front and center, like the crux of the problem.

Right. So I'll just take autism because that's, you know, a population where this is very prevalent and one of the big symptoms that I'm looking for that doesn't have to do with underlying infections that could mainly be because of cerebral folate deficiency is going to be speech and communication delays, right?

Or even some regression in speech in that child or potentially epilepsy and seizure activity. Those are kind of the symptoms I want to rule out cerebral folate deficiency for, but it doesn't necessarily mean that there's an underlying infection.

Now cerebral folate deficiency in maybe a child who has a vector-borne disease, what I'm looking for is that neuropsych symptom onset occurring around that time of the infection.

So that will be the depression, kind of those negative talks, even some suicidal ideology being a big one there, or the people who don't respond to psychiatric medications, right?

So, you know, their child has severe anxiety. They've tried some SSRIs or some, you know, depression, and they tried SSRIs or antipsychotics for some OCD, or even ADHD, whether, you know, for executive functioning or, you know, ability for attention and focus, but they're not getting any Movement on using stimulants like that's a huge key to me as we've used psychiatric meds that should potentially work if it's a true mental health condition and yet they don't.

And so, therefore, we need to explore further and it can be based off of this cerebral folate deficiency. And what's really interesting in the research is those who did utilize psychiatric medication, when they implemented folinic acid, there were significant improvements in their mental health symptoms.

And it's thought to help to potentiate the medications that they're already using, right? So it's thought to help those psychiatric medications. Perhaps it's just helping because they were deficient in folate and they needed that in the brain.

But it's just, that's really what I'm kind of looking at here is in vector-borne disease, it's more of like the mental health piece and the psychiatric symptoms when perhaps in autism or developmental delays, it's more of the regressive symptoms, more of the autism-like symptoms, epilepsy and whatnot.

Okay. So, and you can reference both your clinical experience as well as the literature, but how often do you see cerebral folate deficiency in, and we can split it up kind of into the three populations, whether it's vector-borne disease, Pans-Pandas, or autism spectrum disorder.

Kind of like, what are the stats? Yeah, so I've been looking at this in my practice. So Dr. Nancy O'Hara and I published a paper last year, last February, looking at children with pans and pandas and cerebral folate deficiency.

We just looked at the prevalence of it. And what we found was that about 64% of children were diagnosed with cerebral folate deficiency who had pans and pandas.

And that statistic remains the same here at my practice now. When it comes to autism, we're looking at about 70%. And then for vector-borne disease, I'm also looking at my data right now, which was a bigger population than what I had with pans and pandas, and it's looking about over 60%. with cerebral folate deficiency.

And there's some interesting characteristics that I'm seeing in the data, at least with my clinical data.

PANS and PANDAS Overview

One of them with PANS and PANDAS, which was published, is that those children who had PANS and PANDAS with cerebral folate deficiency, their levels for the binding and the blocking were much higher than what we see on average in children with autism.

What that means, not quite sure. It's just interesting that their levels were higher. Now, with the vector borne disease, I'm seeing more soluble folate receptors than I am in my other populations like autism and pans and pandas.

Again, what it means, I'm not quite sure. This is just an observation when looking at the data. So what I guess to answer your question is in all 3 categories and all of diagnoses here, it's like a 60% or higher prevalence, which is significant.

Very significant. So I think we should pause for a sec and just talk about for our listeners that maybe don't know what pans or pandas is. Can you briefly describe those two illnesses for our listeners?

Yeah, so pans and pandas pans is mainly what I see here in my practice, which is pediatric acute onset neuropsychiatric syndrome. This is an umbrella term.

So, what this means is that there's a child that can also help happen adult, but it is technically a pediatric illness. Where there has been some sort of trigger, most likely an infectious trigger, but there we do know there are some other triggers that are not infectious based that can be metabolic based or environmental based, but we'll stick first with the infections.

And they get an infection that then causes inflammation in the body, then neuroinflammation. And how this child presents is with an acute, abrupt onset of neuropsychiatric symptoms.

So this is like an overnight change. And one of the really Key factors is when a parent comes in and says, you know, my child changed on this day, you know, at this time, they know it to the day.

So it really is that abrupt onset. And what it is is with usually we see some OCD or severe separation anxiety, and then other neuropsychiatric symptoms, including, you know, behavioral regressions, like this might be a child who then all of a sudden starts to watch TV shows or plays with toys that are not appropriate for their age, they were much younger.

There could be decline in academic skills. Usually we see that in math or reading. We can see urinary symptoms. The biggest one is enuresis, which is wetting of the bed of a child who was previously dry, but it can present with urinary frequency or urgency.

Ticks is another big one. When your kid didn't have a tick and then all of a sudden they had an infection, they started to tick and then, you know, a tick that might wax and wane that kind of goes away and comes back during times of stress or again infection.

And there can be, you know, I do see some aggression and ADHD type of symptoms, irritability, sleep disturbances. Again, these are all symptoms that really feel like they come out of the blue and they're not characteristic for your child.

And as a parent, you know, something is wrong. Something is different and something is wrong and there is something going on and we need to figure out, you know, the root cause.

And this just isn't mental health issues because it doesn't just happen overnight. Right. Right. And I think that's such an important point for anyone listening, whether you're a practitioner or or a patient, you know, any abrupt

change in anything regarding the brain, whether it's your cognition or your you know, your emotions or anything, you know, primary mental health issues or cognitive issues do not just happen overnight.

So you always have to, you know, look deeper, make sure that it's not infection driven, you know, so big, big red flag to have an abrupt change with anything regarding the brain.

And then pandas is associated with strep. That's the only trigger, right? And so when I said pans before and saying it was an umbrella term, the infection can be strep plus something else.

So like mycoplasma is the second most common infection. We have viruses, COVID, and I do categorize vector-borne disease underneath here, even though technically it's not in the diagnostic criteria.

When to Suspect Cerebral Folate Deficiency

not because it isn't a trigger, but because of more political reasons, more than anything. It used to be under the umbrella in the 2012 research, white paper, excuse me, but it was since removed.

And so, you know, that pants is usually my kids, it might start with strep, but then they have more triggers. And so it then moves into a pants category.

Right. Okay, so are there, so in addition to what you were just describing, so to be clear to our listeners, what Dr. Wells was just describing were the symptoms of PANS.

and or pandas. And as I'm sure you noticed, especially since we have such a, you know, most of our listeners are pretty astute about Lyme and vector borne diseases, you know, there's a huge overlap in symptoms for vector borne diseases too with what's already been said.

So in addition to the symptoms that you've mentioned, what other symptoms would be red flags that would lead you to want to order a frat test or assess for cerebral folate deficiency?

Yeah, again, it's any mental health concern that is coming up with the vector-borne disease or infections in general. So again, it has to be, okay, we've tried psychiatric medications that they've made no change, we run cerebral folate deficiency.

A child is anxious, they have OCD, they have tics, they have ADHD, any speech dysfluency, so maybe our child's starting to stutter all of a sudden. That we see is a symptom of PANS and PANDAS, and we see it in about 54% of children.

It's kind of high, the research showed. I don't see it that high in my practice, but that's something that we would look for for cerebral folate deficiency if there was any seizure.

Like activity, a little bit of zoning out, I would look for that because that can happen with some of my kids with vector borne disease, but it really has to do mainly with the mental health concerns, anxiety, depression, ticks, ADHD.

And what about in adults? Yes. So in adults, brain fog is a big one, as well as memory loss. And so there has been some key studies that have shown with kind of like an acute, abrupt more dementia actually being related to cerebral folate deficiency.

And then when treating appropriately with folinic acid, there was improvement in their dementia and their memory. So that's a bigger one that I see in adults.

I also tend to see if there's like a schizophrenia type presentation that you can see. And again, older teenagers or adults, bipolar, those are more what I see with the cerebral folate deficiency.

Okay. And are there other like nutrient deficiencies or comorbidities that might make a child more vulnerable to developing cerebral folate deficiency or worsen the downstream effects?

You know, that's a good question. Not necessarily that I see. Of course, we want to make sure that they have robust B vitamins, you know, including B12, for instance, which is going to be a cofactor there.

But a lot of times I don't see that just because somebody's B12 deficient then means they have cerebral folate deficiency. But it could mean that the treatment of the folinic acid doesn't work as well as it potentially could if we don't have those cofactors in.

Right. And how important is removing dairy from the diet? You know, what if someone just said, you know, they just want to cut back? I mean, we're talking about strict, at least I, you know, very, very black and white here.

You know, it's like strict 100% avoidance, like no matter what, how important is that?

Adult Presentations and Comorbidities

Or isn't it in part of the treatment for correcting this, because it can be corrected. And I think that's a huge point that we need to talk about. Yes.

Well, I'll answer the first part there of it's extremely important. I always tell my patients, like, I can supplement you with folinic acid or you can take folinic acid until we're blue in the face, right?

But if you're going to continue to consume dairy, the body is going to continue to produce the autoantibodies. And then there was a very interesting research article done where they, I mean it was only one, where they, and it was a very small population, so I want to be clear on this, but they looked at the removal of cow dairy, just cow dairy, and they then tested the autoantibodies.

They found that there was a significant decrease. Then they had the study participants reintroduce the dairy. And what they found is that the autoantibodies went even higher than they were originally.

And so I often get questions about like, is this a forever thing? And it very well could be. It's long term. It's not gonna be, you know, three months and then let's see how the person does.

It's like, this is more of a longer term dietary intervention because the body is essentially producing auto antibodies. And you're contributing to the problem by, you know, consuming dairy.

So it's unfortunate. I do tell people it's more of a longer term elimination. When I'm talking with patients that are familiar with celiac, because it's way more common, or when I'm talking to other medical practitioners, I put it in the…

If you had celiac disease, or you're treating a patient with celiac, the level that you would go to to avoid gluten is the level that you need to go to to avoid dairy when you have these folate receptor autoantibodies.

Yes, that's a perfect comparison. Yeah. Okay, so talk to us more about your treatment approach. So if you have somebody with cerebral folate deficiency and they have the autoantibodies, aside from 100% removing dairy from the diet, what are your next steps?

You're going to add in folinic acid in the form of calcium folinate. And so you do it. It has to be weight-based. So this is what I'm also seeing being a downfall of treatment is that people are not doing it weight-based.

They're just adding in folinic acid, and it's way too low for it to be therapeutic for somebody who has cerebral folate deficiency. So the literature states that it has to be two milligrams per kilogram up to 50 milligrams per day.

And most kids are going to be at that high dose of 50 milligrams per day. So if you are getting a prescription for five

milligrams, Great, you have some flenic acid, but to be therapeutic, you need to be 10 times higher than that.

Or if you're supplementing and you're supplementing with 800 micrograms, again, you need to be over 50 times higher than that to be therapeutic, to really understand if this is something that can help your child's symptoms.

Right.

Dairy Elimination and Treatment Basics

So talk to us about the difference between folinic acid, which can be prescribed as leukovorin, versus using methylfolate, which is more readily available and can be found as a supplement in a much, much higher dose.

Yeah. Methyl tetrahydrofolate is the bioactive form of folate. That's going to be the form that can bind into the receptors and be drawn into the brain.

However, when you have these folate receptor autoantibodies, you're not able to get that methyl tetrahydrofolate. into those receptors as we would like.

So what happens is there's a different carrier transport on the blood-brain barrier that helps to shuttle in folinic acid. And that's called the reduced folate carrier.

So that's going to be what is utilized when you give high doses of folinic acid. So it's completely using essentially a different system that is going to be more from folinic acid rather than methyl tetrahydrofolate.

Also, all the research has really been done on folinic acid in the form of the calcium folinate from leukovorin rather than methyl tetrahydrofolate. And what I find is that at higher doses that we need to be therapeutic, like the 50 milligrams, Really, the folinic acid is much better tolerated compared to methyl tetrahydrofolate because the methyl tetrahydrofolate won't be able to use that carrier transport as well as folinic acid.

So does that answer? So does. So why do we need such high doses? Yes. So that's another great question. I think it's because not all of it is going to be utilized, right?

And so we essentially need to flood the system in order to, I mean, beat out some of those autoantibodies and then also to be able to get enough to be shuttled in through that carrier transport.

Right. So the big piece is that when you're using the high dose folinic acid, you're able to bypass the receptor and use that secondary transport system.

Yes. Okay. So when you've removed dairy, when you've got them on the appropriate dose based off of that individual's body weight, and I know that you do a lot of other things, and let's assume you're addressing the terrain and all of those things that I know that you do, How long does it typically take to see improvements in, whether it's speech or cognition or emotional regulation or just, you know, kind of like the turnaround of these symptoms?

Well, the biggest thing is you can't just jump right to their weight-based dose. You have to build up on that dose because what happens is when you start to flood the system with folinic acid, it's going to start to help with neurotransmitter production.

So all of a sudden, there's going to be a big increase in serotonin, dopamine, BH4. And what that can cause is some irritability, agitation, or sleep disturbances in kids.

So it takes a while to build up on that. full dose which going in I think kind of quickly which is like every week you're increasing up a dose that can take up to six weeks.

Sometimes it's double that for people where I say it's going to take you know 12 weeks or so to get up to the full dose. Then once you're at full dose, you should give the trial at least six months.

You will notice something within that six month period of time if it's going to be helpful or not. Usually, it's pretty quick that you see something, but everyone is a little bit different.

And of course, there's always different factors going on. transitions, the start of the school year, getting an infection, allergies, stressors at home.

So I like to give it that six month mark, but really you do usually see something once you get to the full dose pretty quickly. Okay. So what are some of the most commonly, I don't want to call them adverse, but you know, like the paradoxal responses that we don't necessarily want to see.

Folinic Acid Dosing and Methylfolate Differences

What are they most typically and how do you differentiate them from, whether it's a detox reaction or I wouldn't necessarily say a Herx, but you know, we can throw that in there, over-methylation, et cetera.

Yeah. And so the most common symptoms that you might see from going up too quickly, too fast, I would say, is agitation and irritability. The second, or I guess the third one I'd say here is sleep disturbances, like a harder time falling asleep.

That tends to be like more of an insomnia type of presentation. In the literature, they do say aggression can be one, but I'm going to knock on wood, I have never seen that being a symptom.

Now, how do I know it's from the folinic acid rather than it being from something else? Is it happens that day that you increase the dosage or you added it in, and then when you don't give it the next day, all the symptoms, like those increased agitation, irritability, sleep disturbances, they've all resolved.

So if it is because of that dose, you will see an improvement by the next day when you don't give it. Oh, it's very quick. You know right away. It's not very confusing.

Okay and then for parents who are listening or even clinicians where let's say you're doing the therapy and it's one of these like miraculous cases right where you have a child start gaining speech right or they're you know they went from from maybe even no words like nonverbal to now having some words and, you know, communicating better and whatnot.

But like we have sort of like this, you know, undesirable behavior going on on the other end. I mean, I just think it's so important for everyone to realize, like, that is still such a great improvement, like that it clearly it's it's working, it's doing something.

And so you try to hold on to the good and not the bad. But if someone is really kind of disrupting everything because of, I don't want to call it a side effect, but for lack of a better word, how do you navigate through that?

Do you go back to the highest tolerable dose without these symptoms coming on? Or how do you walk parents or other clinicians that you teach through this?

So it really depends on the severity, right? So if there's speech, I am hesitant to just automatically go back down because I'll try to say with love, like, let's try to push through for a little bit longer because the system can recalibrate, right, especially with the neurotransmitters.

And we hope that that's going to be the case. But if it really is too disruptive or it's lasting and, you know, over a week, then I will try to decrease the dose back and then see if we continue to maintain that gain that we got from speech and communication, which I often do see that we get to maintain that.

And then we hold there and then try again to increase, but in a longer stretch. So maybe in two weeks or three weeks before going up again. And then, of course, if we decrease and we lose speech, we talk through of maybe trying to just go up a little like half of what we were at at the next increase and just see what we can get that way.

So looking at the bigger picture, because I think it's rare, right, that you ever see a child that doesn't have a multitude of things going on between infections, toxicity, you know, immune dysregulation, etc.

How do you sequence your treatment? Like, is it important to deal with inflammation or immune dysregulation or know, the infections or mold or toxicity or, you know, is fixing the cerebral folate deficiency like at the actual, you know, like at the top of the totem pole here?

Like, is there a sequential order for you? So when I address a case, I really do follow that three-pronged approach, which is going to be implementing antimicrobial support, implementing immunomodulatory support with anti-inflammatories, and then the third being symptom support.

And where I put cerebral folate deficiency and the use of folinic acid is in the symptom support, actually. And because it is such a it can be so long to get on that full dosage, I really kind of have to prioritize it, right?

And so I try to at least get an anti-inflammatory on and some sort of antimicrobial, and then I put on that folinic acid there.

Titration, Side Effects, and Treatment Sequencing

So for the clinicians listening, what can you tell them to help them better recognize when these are true primary psychiatric presentations versus those that are driven by infection or cerebral folate deficiency, et cetera?

Yeah, so I think taking a really good history of the medical history of like the onset of when the symptoms came on. Were they always there? Were they gradual and then intensified?

Or was it more of like an abrupt onset? And then also asking what has been helpful for them? Like if you can, you know, they've tried again multiple supports for mental health conditions with no improvement.

It's not a mental health issue. It's an underlying inflammatory issue that could be driven from the infections or it could be from the cerebral folate deficiency.

So it's hard and it can be overwhelming because there's so many things that we need to look at as a clinician, right, to help our complex patients. but I do find that it's really helpful to get like a broad picture of them and then continue to work on that underlying root cause because I also believe the majority of mental health, it's a secondary.

symptom of what's going on underneath, which is in my practice, it usually has to do with underlying infections. And that's what I specialize in, and that's what I look for.

But cerebral folate deficiency is another piece there to consider. But really, any person coming in with mental health concerns should be digging deeper as to why, because it is likely a secondary symptom to something else happening.

So for our non-clinicians, for patients listening to this podcast, what message do you have for them or for the parents who have been told there's nothing wrong with their child, even though their symptoms are screaming the opposite?

Yeah, I just want to say to all the parents, you know your child best and you continue to work towards finding them relief and finding answers because you can find a clinician that's going to listen to you and work with you.

And just know, trust yourself. keep moving forward and your child is really, really lucky to have you to fight for them. And if you're being told again that it's a mental health condition and you follow their guidance of putting in the supports that they're recommending and it's not helping, there's your answer.

So another big red flag, when your child or you do not respond to the typical medications, treatments, interventions that should address and help to resolve that issue, you're not on the right track and you need to keep going until

you find the true root cause.

Yes. And just try to also just to be that what can help is kind of go back in the history and kind of really look and be a detective, which most of my moms are the best detectives that I know.

But like go back in the history and just look at the timeline and it's going to be right there in front of your face. Okay, so looking ahead, as far as research goes, what gives you the most hope for a better understanding and reversing of cerebral folate deficiency driven by these folate receptor autoantibodies?

You know, I'm really excited about all of the media coverage in regards to Luca Vorin and how this is, you know, at the making headlines and, you know, causing a lot of talk, even if it can be controversial.

Like we've known this for many, many years. Dr. Fry has been at Dr. Quatro has been in the field for a lot of years. We have a lot of papers to support this.

I am very excited that, you know, people are hearing about it, talking about it, because this then means more children are going to get helped. And, you know, parents, you are their biggest advocate.

So keep asking about lukewarm, keep exploring, you know, finding ways if you can't get lukewarm to, you know, try to find the flenic acid at higher dose for your child.

And it really is a pretty benign intervention to to implement and that can have significant gains. And so like I said, I'm very happy. I'm excited about the opportunity for more people to be treated for cerebral folate deficiency.

I'm excited for some of the continued work that is happening with research in regards to cerebral folate deficiency.

Research Outlook and Safety Reassurance

So I think it's all good. It is. You just brought up a good point too. What is the toxicity seen with using high dose calcium folinate or folinic acid?

What are the dangers in using it? At this dosage that we're talking about at the two milligrams per kilogram up to 50 milligrams per day, there really isn't any concerns in regards to toxicity here.

I mean, if your child or you are not going to tolerate it, you're going to feel that effect of the irritability, the agitation, sleep disturbances. And you're going to back it up.

Some people will do research and confuse folic acid with folic acid. And folic acid is a synthetic form of folate that has been shown in some studies, which have gone back and forth, controversial a little bit, of perhaps an increase in some cancers.

I want to be very clear, folic acid is not the same as folic acid. And therefore, the concerns of high dose of folic acid are not they're not warranted when we're talking about flenic acid here.

Thank you for that distinction. And I think it's really important for all of our listeners to hear that. And thank you so much for being here with us.

Any parting words of wisdom you'd like to leave our listeners with before we wrap up? You know, just that you're doing a great job and to keep going, your child's lucky to have you and really consider cerebral folate deficiency.

And even if you get a negative result, at least you, you know, checks that off because sometimes ruling something out is just as effective as ruling something in.

But this also can be kind of what you're missing when we're talking about the symptoms that your child or you might be experiencing. And it really is, like I said, an easier kind of benign intervention that can have a great success and

to get you to where you want to be.

So I hope everyone found this helpful. I'm sure they did. And thank you so much for being here with us, Lindsay. I really appreciate it. Thank you for having me.

Of course. All right. And to our listeners, if you want to hear more from Dr. Wells, if you want to hear her formal presentation on cerebral folate deficiency, you can join us at the Line Bites Symposium, which is November 14th and 15th on Pompano Beach in Fort Lauderdale, Florida.

And if you cannot come in person, you can join us virtually from anywhere. So once again, thank you for joining us and we hope this brought you one step closer to true healing.

If this helped you, share it with someone who needs to hear it too because together we all heal stronger. We'll see you next time. Bye-bye. 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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