## Introduction and Guest Welcome

Hey, everybody. Welcome back to another episode and another interview on our sexual dysfunction summit. I'm Dr. Diane Mueller, your co-host. I'm really excited today to bring on this amazing researcher.

So much knowledge and folate in my age of in genetics. Beyond we're going to tie all of that to hormones, to libido and more. So welcome to the summit. Dr.

Carolyn Ledowsky, it's great to have you. Hi Diane, so nice to be here. I can't wait to get stuck into this topic. Yes, yes, yes. Me too. Me too. We already had a really fun conversation offline that's making me so excited about everything that's coming and our time together.

And before we jump into all the juiciness of it, let's start with just like giving everybody a sense of how you got into researching. Research is always so interesting to me as far as how people identify something that they're so passionate about and go so, so, so deep into a topic like you are with genetics and MTHFR and folate.

So can you walk us through the journey of just how you got involved in your work for us? MM Yes, thank you. I will. When I first started out, I had a mentor who was real, a real stickler for understanding blood work.

And so I used to do the Bloods and I do my analysis. And I came across this little thing that kept bugging me. And that was half of the people had high folate in the blood and the other half didn't.

And I thought, That's really weird. Why would you have high folate?

## Discovering MTHFR and Folate Research

And when I rang the lab and asked them why someone would have high folate, they said, Oh, that's a really good thing. They're having a lot of leafy green vegetables.

And I thought, No, they're actually not. These people are sitting in front of me and I know they're not having it. A lot of leafy green vegetables. So I thought, okay, that's not the answer I wanted.

And I kept searching, searching, searching and could not find the answer. Everybody gave me that same answer and I was in a conference in Melbourne about 13 years ago, actually a bit longer now.

And a doctor they said, well, MTHFR is associated with disturbed blood levels of folate. And I went, What? Oh my goodness, that's what I want. So I made a beeline for and said, What is this MTHFR gene?

And she said, Oh, it's a gene that regulates you, folate. And I said, How do I find out more? She said, Just Google. So I then became obsessed with this gene and I read every paper I could possibly read.

I read everything. And I used to sit till 3:00 in the morning and just read, read, read. And my husband thought I was going crazy and I started to experiment with different folate levels.

So when I saw the high folate in the blood, that made me want to check MTHFR So I checked MTHFR and sure enough it was always the polymorphism was always a so then I thought, okay, these people have a family history of anxiety and depression and cardiovascular disease and multiple miscarriage.

And at the time methyl folate wasn't an it was an in Australia. So I used to bring it in and give samples to my patients and see if they had a good reaction.

And sure enough the folate level in the blood came down and they started to feel better. And I thought, hang on,

there's something in this. And that thing got me into the fertility side of things because I kept seeing these women that had had recurrent miscarriage and they were just being told, Go home, there's nothing you can do, keep trying.

It's a numbers game. And I thought, No, it's not. Because when I change the form of folate and increase the dose of folate, we had a really good success.

So I then did a race, my first research degree was an honors, and I looked at women within fertility. I did a case series of women with infertility who had MTHFR And so these women had presented with multiple miscarriage, failed IVF, diagnosed with unexplained infertility.

So we took them all of folate, put them on methyl folate, and we had a 91.3% success rate at a live birth. So then my supervisor said, Oh, okay, you need to go on and do a PhD, which is what I'm currently doing.

And we're doing a pilot study for a randomized clinical trial to test a prenatal multivitamin with folic acid versus methyl folate in women with recurrent miscarriage.

Thank you so much for all of that. I want to first just like mention what you said around that whole thing around. Oh, folate ties must be the dark leafy greens.

And just how often I feel like that comes up in medicine in general. Right around. It's like, oh, it's no big deal. Just ignore that. I'm sure it's just this weird thing somebody's doing.

Or maybe it's good, like your example, and you know how amazing it is to really watch the pattern and really be just that interested in understanding, right?

This isn't making sense. This isn't adding up. I feel like we see that in clinical practice and bloodwork all the time. People coming in with very basic things around like you're just dehydrated is another example of one that all, you know, all here.

So talk to us a little bit more. So you mentioned the link between what you're already noticing in some of your research and study around fertility, around lowering miscarriage rates and methyl folate.

I want to talk about more around the genetics and hormones in more details related to sexual dysfunction. But let's take a step back for a second just to make sure that everybody's on the same page.

I know a lot of people know about MTHFR and it's called the Mother Effer. You know, Gene, I hear a lot of people call it passionately sometimes, but I know there's people listening that have not heard of this.

So I just want to get everybody on the same page. And we're talking about methyl folate and this genetic anomaly. Can you just set the foundation for us?

Yes. So we have a folate pathway that makes our biologically active folate, which is methyl folate. And when we say biologically active folate, it's the folate that the body uses to do everything it needs to do.

Right, particularly methylated DNA, which is incredibly important for the quality of DNA for fertility.

## How MTHFR Affects Folate and Methylation

We also need this methyl folate to make a product called SAMe which is what we call the universal methyl donor in the body. And what that means is it acts like a cofactor and an on off switch for so many important metabolic processes.

So, for example, for us to make phosphatidylcholine for our brain to work well, we need SAMe for our detoxification of our estrogens. We need this SAMe for us to make creatine.

We need SAMe creatine is for our muscles and our brain energy. So there's so many important what we call methyltransferase is that are really important biochemical pathways that the starting ingredient to make those work is methyl folate.

So what MTHFR does, it's the last step in that folate pathway to convert non activated fall lights into methyl folate. And so it's a gene that can be downregulated.

So if someone has a polymorphism or we used to say mutation, we don't say that anymore. But just so it's easy if someone has a mutation, it downregulate c the efficiency of that enzyme.

So if you have two copies of this one gene, you can be downregulated by 70%. So you can imagine then if all these important for your hormones, for your mood, for your DNA, for your immune function, all of these things need it.

If it's downregulated by 70%, that's going to have a big impact. And so where we see the majority of people suffering from this downregulation, it can be particularly mood, anxiety and depression.

Those people that don't particularly cope with stress that seem to react to stress more than others, where we have hormones and particularly toxic estrogens building up in the body.

There's so many different aspects where we might say recurrent miscarriage, family history of cardiovascular disease, family history of varicose veins.

These are all areas where we say, Oh, hang on, is there an MTHFR polymorphism possible? Yeah. Thank you. That helps a lot. And I think it's important to just say how widespread.

Right. We're talking about these widespread impacts, which is probably one of the reasons why it does not get looked at still as much as it perhaps should, because of the inability sometimes to think about that, because so many different things can be impacted.

So let's talk about hormones as we're talking about sexual health and libido on the summit. And you mentioned estrogen, so maybe we can start there. How is empty of our how is this gene involved called and the activation of folate involved in estrogen and estrogen clearance and estrogen metabolism in the body.

So as I said, we we have this MTA chip that makes cell activated folate, methyl folic, and then that gets brought into the cycle that makes semi. Now the way that we break down estrogens, it's primarily through an enzyme called Comt catcall methyltransferase.

And what happens is this Comt gene is incredibly important in getting rid of toxic estrogens. And we know that our four hydroxy estrogens, which are the more dangerous ones that need to be then methylated to not be dangerous, are these contain and support set.

So if this Comt enzyme is lacking activity because the metal folate is low and we don't have enough semi to support it, then estrogen will build up. There are other key genes too that are involved in estrogen metabolism.

## Estrogen Metabolism and Detox Pathways

So phase one detox genes. C, why? P one, b one that is an upregulation. If someone has a polymorphism, it's it's the enzyme works too fast and what happens in phase one is imagine this is a toxin.

It actually its job is to break it apart. And so you end up with this big toxin that needs to be then eradicated by phase two. And so what happens is if Comt is slow and it can't do the job, you've got a lot more of these toxic elements sitting in the blood and you can't get rid of it.

So this is why we need our phase one, phase two detox enzymes to work together. So Comt is really important. See why p1b1 is really important and one of the others is our glucagon addition gene.

So you get genes and these are genes that not only help us break down estrogens, but they're incredibly important for most chemicals in our body. In actual fact, it's probably more important than glue to thyroid.

When we have these glucagon, a data for changing glucagon addition is jammed up by a lot of environmental things. But if glucagon addition is downregulated, you're going to see someone holding on to more estrogens.

And what happens when that happens? Well, you get a whole range of things polycystic ovaries, fibrous cystic breasts, endometriosis, cancer, breast cancer, prostate cancer in men.

So we do. And unfortunately, environmentally, there are so many estrogenic things that we really need those pathways to be working well. And then the last one is glucose, because glutathione alone helps us get rid of some of these dangerous bright byproducts that the other enzymes are actually creating.

So there's a lot of different genes that are involved, predominantly the liver and detox and clearance genes that are supporting us. And this Comt gene that we talked about and that's so important is also incredibly important in dopamine and the way that we break dopamine down and we clear dopamine.

And so it's was clear what you had said around the methyl donors needed for the Comt. What about the phase one? And phase two processes? Are those requiring the methyl donors as well?

Well, all detox needs that seemed to be working optimally because the processes MTI makes methyl folate. Methyl folate goes into the methylene cycle, which then goes into our sister thiamin beta synthase pathway, which is our detox pathway.

And so it all leads in the one in that direction of supporting detoxification. So that's why a lot of people will read that. mTOR chapter means we don't detox as well, and that's because we haven't got the good input into that detox pathway.

Perfect. And then what are the topic of epigenetic expression so people can get these genetic polymorphisms measured, right? We can actually test for these things.

And then what do you advise people and what have you seen in your research around okay, we have these polymorphisms. Have they been expressed? Do we need to be concerned that just because somebody tests and they are positive for them that they are expressed and it needs to be treated appropriately?

What do you think about that? That's such a good question, Diane. And my analogy that I like to use, which I think explains it really well, is imagine your driving down a freeway and you have a lot of potholes in your lane.

It doesn't really matter how old the car or how new the car is, it's going to be damaged because you're going to take a wheel off, right? The axle, something's going to happen and it's going to be damaged.

And if you've got rain and hail and snow, you know that pothole is going to get bigger and bigger and bigger. And that's what I liken the genetics to.

Everybody has potholes. Some of them are big potholes. So for example, if you're homozygous chipper and you have a 70% down regulation, I consider that a big pothole.

I also consider your B12 genes to be big potholes because if they are poorly, if you've got those genes, you have a susceptibility for that pothole to get bigger and bigger and bigger.

Every time there's an environmental influence. And so, yes, you hear people say that the genes are not as important, but it's all about the environment.

And to some degree that is true. But who in who nowadays doesn't have an environmental influence? Just the very presence of COVID was one of the biggest environmental influences on our genetics that we've ever had in in the

history of this planet, because we were all hit with a viral load that a lot of people had a predisposition to having high inflammation or, you know, like particularly those interleukin six and inflammatory genes.

And we just didn't have the ability to control it. So how I see that is if I come and I plug that culturally in your lane, it doesn't matter how old your car is, your turtle alone quite well.

As long as you put petrol in it and you look after it. So I like to think of your genetics.

## Genetics, Epigenetics, and Environmental Triggers

Some really don't matter until you've got an environmental insult, but some will always matter because they're so fundamental to your biochemistry. Even the slightest bit of stress can set you off kilter.

So we need to look at the ones that we go, Yeah, look, that's interesting to know it's not really a quote right now. Will you consider that if and when anything happens?

But hey, now you've got two or three we really need to plug up because we believe that you will improve significantly going forward. I love that. I love that analogy and it's so true. Right.

And none of us get out of this world toxin free. It's just not possible. And I think probably what some of our listeners are wondering now is from a standpoint of if they have this particular polymorphism, whether it's hetero or homozygous, if they had this at all, do they wind up are there any certain like environmental toxins that are particularly important to avoid?

Or do you more look at this like a lot of us do clinically around like almost the bucket example of like, okay, well, you just want to make sure that you are largely avoiding as many as possible and lowering the amount of exposure as much as possible or define it to be more specific than that.

Well, where do you start with toxicity? I think when you talking about hormones, the two biggest environmental influences are definitely mold exposure and eight and estrogenic environmental impact.

So credit card receipts, plastic bottles, plastic containers, plastic clean, right. All these things that we have plastic. And I think this is why we're seeing such a huge increase in male prostate cancer, because there is exposed to estrogens as as much as women are.

And they still have the same genes that women have, yet they're not considered to be have a estrogenic problem, which doesn't make any sense. And I think the mold is huge for us.

I mean, we've just had two years of rain. We had an El Nino, whatever it was, and we just had rain after rain. Houses were getting flooded. And when I say flooded to their roofline three times in two years, and these people are going back and living in them now, what people don't understand is that mold exposure and micro toxins from these molds actually completely wreck your hormones.

And so they because predominantly what they're doing is jamming up the glucagon addition pathway, which does not allow us to clear these toxic hormones.

And so we're seeing thyroid disorders. We're seeing polycystic ovaries, we're seeing estrogen dominance, we're seeing cancers. And so I would really express that if anyone is living in a mold house, they absolutely have to do something about it because there is no sure way to ruin your hormones and live and be exposed to a moldy house.

Yeah. Thank you for saying that. It resonates so much with that. I have two different branches of my practice and one is libido and the other is lime and mold.

Oh, they gave. Yeah. So people will say to me like, how are you doing this? Like, how are these things related? And like actually and it's basically like exactly what you just said around like they're branded different.

I do different, slightly different work, but essentially it's largely exactly what you said around like the sexual health and the hormonal imbalances and all that dysfunction so commonly is rooted in environmental toxicity and I see that too, like mold being one of the top, top, top, top toxins.

So I'm so glad you said that. I want to also talk about treatment. So obviously people are coming out and they're you know, the big thing with this is a lot of people are using methyl folate.

So what do you think about, you know, the uses of methyl folate? What about, you know, other supplements such as Sami or creatine, like you mentioned?

And my other question with that is I've read somewhere Yemen where I found this, but that B too and I think it was due to a cofactor of the MTA of our enzyme can actually help with that.

That's conversion. So do you find that that with your research could also be a useful nutrient in in these scenarios. Now and that is a multimillion dollar question.

And I think I think part of the part of the analysis needs to be we always do the genetic test. We do an organic acids test, we do a blood test, and then we do a really thorough case history.

Because what you're trying to evaluate when you're looking at treatments is what are the pieces of the puzzle that need to be put down first? Where do you start?

And a lot of the problems that we found with, particularly when people were first introducing methyl folate, they thought empty of metal folate. Great. I need lots of it.

Let's dove in and they were having serious, significant reactions. And there were some people that used to ring it. So they were having, you know, that was suicidal.

And what we've got to be really careful and methyl folate is usually one of the last things that we introduce because methionine synthase is this key enzyme that takes the metal folate and puts it into that semi cycle.

## Mold, Estrogenic Toxins, and Hormone Disruption

Now if you've got a block and it could be your B12 is low, you've got exposure to yeast, you've got locally design, you've got heavy metals, you've got inflammation, you've got high nitric oxide.

I mean, there's so many things that could actually sit that all low zinc, you know, if you've got any of those things happening, then that methyl folate can't actually be taken up and people will react to it.

And so I always say to the practitioners that I teach, if that happens, you don't just take Fellini and go, Oh, well, that's great, let's have Kalinic, because they don't react to methyl folate.

That's not the answer. The answer is you have to answer the question, why did they react to the methyl folate? And you have to find out what was it that was causing that reaction.

You've got to unpack it and then come back and try it later on once you've done your job. And and this is the thing you can't it's you you shouldn't get into the habit of saying, I have this snake, therefore I need this supplement because everybody's completely different.

And yes, in some instances that might be the case and you might feel better and you might feel the best you've ever felt. But in a lot of cases, that's not the way it works.

You need to do it on an individual basis and say, okay, this person has exposure to mold. I'm definitely not going to give them methyl folate or this person has serious adverse reactions to anything I give them.

Therefore, I've got to start very gently with a pre tox or someone has depression, but it's not serotonin based, it's dopamine based. So yes, I'll give them a lot of methyl folate and a C low tyrosine and they're going to feel great.

So it really is about and I know that some people want to hear that it's individual, but it really is because everybody's different and everybody's got a different environmental influence.

And some people will react to wi fi because of the mold exposure. And so that's going to be a much more important conversation. And you're going to go with completely different supplements that if someone doesn't and end to answer that question about environmental, it's getting harder and harder for us to be clean and our water supply, everything we eat, you know, the pesticides you'll get phosphates, the glyphosate, I mean, where does it end?

And I think we can only do what we can do and be as clean as we possibly can and avoid, like particularly those estrogenic things for as far as hormones go, carry a water bottle with you, you know, make sure you don't take a credit card receipt, say, no, I don't want the receipt.

And if you're working in a supermarket with gloves and don't have, you know, allow those things to touch you, because all these and and all your personal care products, I was so alarmed when I heard this thing that said a woman, when she gets dressed for work and by the time she gets up and walks out of the house, she's been exposed to 300 toxic chemicals.

So thinking about absolutely everything that you put on on around your body and making sure you're changing them to more natural ingredients and cooking from scratch as much as you possibly can.

You know, I try not to buy things in packets because again you're going to have folic acid in Australia. In the US you have fortification of foods with folic acid.

Can we just say one thing on folic acid? Yeah. Sorry, I've been talking nonstop, but I thought it was important at this point when I said packets, we I am of the belief with my research that we have we have reached a limit of how much folic acid we should be having.

And the research says that the enzyme that deals with folic acid, that makes it into methyl folate, it really only copes with 200 micrograms a day. Now, the research we've just done says every single woman in pregnancy who is taking a folic acid based prenatal is exceeding the output toxicity level deemed safe by the Institute of Medicine in the United States.

So we've got to be wary that we are having too much folic acid and we're actually inhibiting the way that this important methyl folate is working. And it is going to affect our hormones, it is going to affect our mental health, it is going to affect our children's health.

So packets try and get rid of packets and try and avoid folic acid in foods. And when you're taking a supplement, don't take it with folic acid. Take it with methyl or firmenich.

## Treatment Strategies and Supplement Caution

Yeah. Thank you. It's really, really exciting research we're doing like we talked about and I can't wait to see what comes out with that. And another thing I just wanted to add real quick about what you're saying around the 300 different types of chemicals that oftentimes women are exposed to before they leave the house is another thing that I've seen is even in natural product lines, when we analyze them, they'll be some things in a natural product line that are actually really clean.

And then the same product line, unfortunately, could have some products that are not clean at all. So that's also a component that I think can be maddening sometimes.

And there's a really great app out there called Gattaca. I don't know. You see, it's why UK. And you go have a look. It's very cool. I would love your opinion on it when you look, but it's very cool.

You can put on your your phone and start scanning products and like the barcode and then I'll list all the chemicals and it rates, you know, according to where they're pulling their research, the severity.

But it's very interesting to see. And then I think. Yeah, it's really user friendly and that's how I've been telling people like just go through your home stuff one at a time as you're replacing stuff, just start learning because some of it's just some sometimes if it says natural, it may or may not be more or less toxic, then, you know, then you think so it's just it's just good to do our due diligence.

And is there anything else when it comes to genes and hormones and treatments in this conversation that you think is like absolutely important that we've got to say today?

Well, I mean, I was thinking when you were talking, you know, one of the things we haven't actually said is that we've talked about toxic estrogen, but why is that important?

And I think a really important thing to to mention is that when your estrogen when you have toxic levels of estrogen and they're not being cleared, it is actually reducing the good levels of your estrogen and it's actually causing a reduction in testosterone.

So you're talking about libido, you're talking about sexual function. This is really critical because you're actually getting a displacement of your good estrogen, your your DHEA.

And that's that's the other thing we haven't talked about is South-Asian form of DHEA is really incredibly important. So these sulfur pathways and making sure that the so fashion in phase two is working.

So if you've got something out of balance, particularly toxic estrogen, it is going to affect all your other hormones. And often people will say, oh, yes, but my estrogen is high in my blood.

And we go, Well, that's not what we want. That's saying that there's possibly some toxic estrogen. And when you do the metabolites, you see the metabolites out and they've got a low testosterone or low to hydroxy estrogen, which is what we want.

So doing Dutch tests and doing particularly if you want to look at sexual function, I think one of the biggest genes to look out for men for libido where not so much libido but sexual function and erection is the nitric oxide synthase.

So I don't know if anyone's spoken about that yet, but nitric oxide synthase is an enzyme that helps you make what we call endothelial or nitric oxide, and that's what helps an erection.

So that's and that's the exact mechanism of Viagra. It actually helps endothelial nitric oxide. Now why wouldn't you have good endothelial nitric nitric oxide?

Well, it may be that you've got inflammation that is shut that enzyme down or maybe you have polymorphisms in that gene that are not working as well as they should.

So although Viagra is helping you do what you need to do, it's not actually addressing the root cause. And you could find by doing your genetics and by getting inflammation under control, you can actually get that erection issue under control.

So there's so many aspects of this that can be due to genes, but it can also be due to environmental influences. Yeah, I'm glad you brought that up because we did.

We do have another interview on here. We talk about how erection, erectile dysfunction, sometimes an early sign of cardiovascular disease. So we talked about that.

But true cardiovascular standpoint and OS, but not from the genetic component. So I think that's a really important addition to add to that conversation is like there could be that genetic reason why that whole endothelial

dysfunction is really happening to begin with.

And, you know, and inflammatory causes from toxins and those sorts of things not being detoxed correctly is playing a role. So I think we could go on and on and on and on here because I think one of the biggest things, too, with these this genetic component of things really is the web, right?

We're in a big web of interconnectivity. And truly, the only way to get to the root is by testing by by figuring out where somebody's imbalances are. And like you said, doing proper testing to get those estrogen metabolites to look at some of those more unique and and specific markers versus just like a total estrogen is is very, very important.

## Sex Hormones, Libido, and Nitric Oxide

So I want to make sure that we mention your giveaway. So you are giving away a guide about how genes impact hormones. So you guys make sure you you go around on the opt in on the the speaker information on on Carolyn's page to get that particular downloadable guide, because it's going to give you a lot more information, I think, help you synthesize some of what we talked about here today.

What else do you want to leave people with? I want to make sure to they know how to get a hold of you and that sort of thing as well. Yes, our website is MTHFRsupport.com.au We see patients all around the world because we're predominantly 100% online which was great through COVID here we we actually had a really good I think made people think, oh, I need to do something.

But I would say that if you have a long standing condition that just has not been helped by going to see multiple practitioners. It might be time to look at your genetics and see if there's something that we would call a big pothole that's probably standing in your way.

Because what it means essentially is you'll probably ban dating really well. And I think people with significant potholes, they do Band-Aid and they self-medicate without realizing they're self-medicating.

But they might go and, for example, go and live on a farm away from all the stress and the environmental influences, because that's the only way they can survive.

And that's great, but that's not really the way we want to live. And so I think if there's long standing issues, don't be afraid of the genetics, the genetic reports that we do, which is we do, the smart DNA advanced pathways test.

And it's there are no disease snips in there. I mean, there are none. So we're not talking about the bracket gene. We're not talking about something that's really going to be scary.

We're just talking about genes that affect your metabolism, how you make B12, how you make folate, how you detox, which are biochemical snips. So I know a lot of people say, oh, I don't want to do that, but they don't need to be scared because it's actually very enlightening.

And when you've got the right other tests, as you say around it, it can be the most exciting thing you've ever done. Yeah, thank you for that. I really appreciate you orienting and living, leaving us with hope and not fear around this is exciting.

We're going to get so much information. So thank you so much for being here, y'all. That will have everything to get a hold of of Carolyn in her speaker bio to work with her, her team keep up to date on her research.

I definitely know I will be. And thank you again for a great interview and for your time. Thanks, Diane. It's a pleasure. We'll see you all in the next interview.