

Histamine, Hormonal Harmony and Health

Guest - Dr Meg Mill

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[00:00:09.440] Dr Anu Arasu

Hi, everybody. I'm Dr Anu, and today I'm joined by Meg Mill. Meg is a doctor of pharmacy. She's also a Functional Medicine Practitioner with over two decades of experience. She's a best-selling author, host of her own podcast, A Little Bit Healthier. And she's also hosting her own summit, All About Histamine. Welcome, Meg.

Dr Meg Mill

Hi. Thank you so much for having me.

Dr Anu Arasu

Thanks for being here. So, Meg, while we've got you, tell us a bit about histamine and hormones, because I believe that there is a link. And not many people know much about, I suppose, either of these subjects, but certainly not together. So we would love to get your input.

Dr Meg Mill

Yes, absolutely. So I'm going to start, actually by going a little back a step and just talking a little bit about histamine and how it's processed and then rolling into how it's going to relate to hormones, so we understand where it's coming from. So we'll do a brief Histamine 101 to get into it and then bring it in. Because I do see this so commonly with so many women that I work with that have hormonal imbalances and histamine issues. It's really unidentified. It's really fascinating. So I'm so excited to get started.

Histamine is something in general, I think, in our bodies that gets a bad rap, sort of like cortisol. Because there are a lot of complications when it comes to histamine, like cortisol, that we see all the negative side-effects, but it does actually have purpose. So when your immune system detects an allergy or an invader, histamine is primarily released from your mast cells or your basophils to increase your blood vessel permeability so that you can actually reach the cells that are being affected more quickly. So there's purpose in immune defense and inflammatory response and actually regulating gastric acid and all of those things that we need.

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But what happens is when we get this overload of histamine, we start having symptoms. And so I like to think of histamine... I like to give an analogy of a bucket with holes in the bottom. So if you're looking at it as a bucket and your body is the bucket and you have holes in the bottom of that bucket that are... And sometimes people can, you could use a bathtub, too. You're filling the bathtub, or you're filling the bucket and you're draining. So you eat something with histamine. You're exposed to an allergen. You have all these things. These are all filling your bucket.

You keep putting things in, but your body's processing it out, too. So we're going to get into the way we process it, but we're processing it out, so it's flowing out of the bucket. Well, the problem happens as a result of one of two imbalances. Either we fill our bucket too fast, too much, or our holes get clogged. And when that starts to happen, we start to get this overload of histamine, and that's when we start getting all of these symptoms. And really, because histamine affects... You know, your mast cells are in almost every cell of your body, so you're really getting these overall body effects.

I think a lot of people think that histamine is just allergies, but we can have anything from anxiety to sleep disturbances to allergies. I see it a lot when we have hormonal migraines. A lot of times we have these underlying histamine issues, and we can get into that. Asthma. Then we can have gut infections, irregular periods, PMS. All these different things can actually be coming from histamine because it's an overall body response.

We'll start by saying what clogs the holes? What makes the bucket stop emptying? And that is the way we're processing histamine. So we have two different enzymes in ways that we break down histamine, and one is diamine oxidase, and we do that through our gut. And the other one is Histamine N-Methyltransferase, and that's going to be in your cells. So there are different things that start to happen that create these enzymes to become compromised so that we can't actually break down the histamine in our body.

So if we're looking first at diamine oxidase, we have things like your genetic factors. So I'm one of those unfortunate people that do have a genetic variant in my DAO enzyme. Now that I know that and can do all the things to get over that and compensate, I can deal with it. But some people have these genetic variants that they don't even know about, that they're not able to process histamine well.

But another one of the main things that we see, and we can get more into this, is GI disorders. So once you get an imbalance in your gut bacteria, it impacts your DAO enzyme, and you can no longer break down histamine very well.

We can also see things like nutrient deficiencies, because we need things like B6, copper, vitamin C to be able to create this DAO enzyme. We need those to support the DAO enzyme. So if you're not getting the nutrient deficiencies, you can have an impaired enzyme, which again, goes back to some of these... We'll talk about some of these cyclical things that happen. You get impaired gut health, you're not absorbing as well. You don't get the nutrients, you don't have the enzyme breakdown as much. So we can get into some of these cycles.

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And then we can fill the bucket up too much where you're just eating too many histamine rich foods. We can also have medications that can impact it. And I'm going to give you the whole dynamic of hormonal imbalances, because that estrogen can play a huge role here. And then we have the Histamine N-Methyltransferase. So that's not in the gut, but that's actually within your cells. Each cell has this. So when we start to have issues with methylation. So you may have heard of it, like the MTHFR genetic variant, different genetic variants.

You need SAM-E as a methyl donor for this process. So when we have some of these genetic variances or just are lacking things like B6, B12, folate. That can impair this function, too. So we can start to see some impairment there. And then we also can see the liver... So once we start to have issues, we know our hormones are broken down in the liver. So many things are happening in the liver. So when we start to see liver impairment or over... We can have excess toxins, excess alcohol consumption, things like that can also affect these things as well as medications. So we start to see some of these processes happen where we get clogs.

So now to the question. I know I gave you a lot of background information there, but I wanted to just give you why this is happening. So when I talk about some of this, the kind of the history.

Dr Anu Arasu

Yeah, we're getting a picture of the kind of people that this may be really relevant for. So, thanks for that.

Dr Meg Mill

Yeah, absolutely. I'm going to just do Immune System 101 here, too, because this plays into this estrogen issue. So we see when we're talking about hormones and histamine, the most common hormone that we're thinking of is estrogen. And people with estrogen dominance. Higher levels of estrogen. And so when we're stepping back again to... Histamine is part of our immune system. We have an innate and adaptive immune system.

So your innate immune system is the one that's reactive. That's your first line. The adaptive immune system is detecting certain allergens. But it's in the background. But your mast cells are part of your innate immune system. And so they're going to react when we have things that come in. For invaders, when we need them. The problem happens when we get this overreaction.

So estrogen can actually make your mast cells, which is part of our immune system, more reactive. So our mast cells are what are going to release the histamines. So when we have the estrogen, making the mast cells more reactive, because mast cells actually have estrogen receptors on their surface.

So when estrogen is binding to the receptors, it can actually release... They trigger the release of histamine. And therefore, you can get a higher level... Higher levels of estrogen can increase the histamine release from these cells. So we start to see, oh, if you have increased estrogen, you can get increased histamine.

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Now, it becomes this cyclical problem because histamine can also influence the hypothalamus. So when we're looking at our hormonal axis, we have the HPG-axis, which starts with the hypothalamus. So we know that the hypothalamus is a key region in the brain that's going to stimulate our hormones. And so when we have this, histamine can stimulate the release of gonadotropin-releasing hormones, which can therefore stimulate the pituitary gland to secrete more LH and FSH.

And in response, the ovaries are going to produce more... Release more estrogen. So, as you can see, it starts to become a problem for a lot of people because you start to have estrogen dominance, which is creating more histamine release, and then histamines are creating more estrogen. And so we need to break that cycle.

And to actually make matters a little bit worse... A little bit more complicated anyway. Estrogen can also inhibit the activity of diamine oxidase. So we talked about... That's why I wanted to go into the diamine oxidase. We talked about diamine oxidase as what's helping you break down your histamines when you're eating these foods.

But when you have high levels of estrogen, you can get that inhibited, too. So we can also see where we're not breaking down histamines in our gut as well. So when we're having estrogen dominance, we also will often have low progesterone. So we're having more estrogen and less progesterone.

And so that can also play a role. The lower levels of progesterone, because progesterone is believed to help stabilize mast cells. So when we have this high level of estrogen that's overacting and we don't have the progesterone that's helping to balance, we can kind of get out of control sometimes.

Dr Anu Arasu

Wow. It's such a clear picture on how we can just start to really spiral downwards, because these factors inter-play. What is the typical patient that you would see who is affected by histamine and hormone imbalances? What kind of age range? What kind of symptoms?

Dr Meg Mill

I see a lot of people have hormonal migraines. So when I see people that are getting those hormonal migraines, I think we look at hormones for sure first, but I'm always thinking about histamine because of this dynamic. So a lot of times, once we start to see this patient that comes in and is having these regular hormonal migraines. And you can often see them over a lifetime, so you can see that maybe when they started their period, they've had these monthly migraines.

I think when we're looking at that picture, it's so normalized. It's just like, "Oh, that's just what happens." As we see with so many, when you're having the cramps, when you're having the breast tenderness, when you're having the migraines, it's like, "Oh, that's just part of your period. Oh, that's just part of your cycle." And it's like, "Oh, wait, no."

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As you're talking about probably in this whole summit, we don't need to have any of those symptoms. We can bring them back. So that's one thing I do see and I think you're not thinking of... Because migraines are an actual symptom of histamine issues. So I see that commonly.

Another thing where you can start to see in perimenopause, because we're starting to get this hormonal imbalance. So you naturally are becoming estrogen dominant sometimes because your progesterone is going down first, before we see that decline in estrogen. So as we see some of those hormonal imbalances start to take place, we can sometimes see these... That's why some of the symptoms, I feel like, come out stronger during perimenopause, where you haven't maybe had them before, and now you're getting that shift in hormones, and now they're starting to show more and more.

Dr Anu Arasu

Right, and, I mean, there can be many other links, can't there? Because I sometimes see that people in perimenopause become so much more sensitive to alcohol and things like this. What kind of triggers do you think people should be looking out for?

Dr Meg Mill

As far as histamine? Yeah, we see it a lot. When we're thinking about histamine again, we're thinking about the filling of the bucket versus being able to process. So we've talked about the processing and what we need to do there, but then we also need to think about things that are filling the bucket. So you want to look at diet, first of all. So some of the things that you can look at is what does your diet look like? And we want to make sure..

There are a lot of foods that actually are high in histamine. And I think what's really tricky about the foods are that they are not always unhealthy foods. So it's sometimes easier... It's easier to look at sugar. It's easier to look at inflammatory foods, which we want to do. But sometimes we're looking at strawberries and tomatoes and bananas and avocados and things that people are really purposely eating because they're healthy, but they can actually be high in histamine or stimulating histamine release.

And so we want to look at what our diet is and figure out... On my website, it's just megmill.com. I actually have a form that you can... A guide that you can actually list what has histamine, and not. Because there are a lot of confusing lists that aren't true.

If you google it, you're going to get a lot of conflicting information, and sometimes those lists aren't accurate. So I've spent a ton of research really getting the list because there are foods that are high in histamine. There are foods that are histamine-liberating. There are foods that limit the inhibition of DAO. So, like inhibiting that DAO enzyme. There's all sorts of different foods that have different components that play into it.

Another thing when we're talking about food is leftovers. And this can be really hard for people who meal-prep because histamine grows in food. So if you're cooking food and then you're actually

prepping for the week because you have a busy week, that's great. But if you have a histamine issue, you could be triggering yourself. And so looking at some of those things.

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Then we look at mast cell activation syndrome. So sometimes people have oversensitive mast cells. We're seeing this so much more since the pandemic that people are really presenting with mast cell issues. And so it's more and more common. Think of it, if you're someone who just has all of these different symptoms, that you go to your doctor and you say, "Okay, I feel this way and I feel that way". And you get your labs back and they say, "Oh, you're fine. It's fine."

And I had someone tell me, yesterday actually. "I know what fine feels like, and that's not how I feel". Because she was told that by her primary care doctor. And it was like she's saying, "I know what fine feels like, and I'm not that." Really listen to... You have your intuition. You know, there's something off, and that's where...

It's some of these multi-system things that you're having different... Maybe you're having some allergy symptoms, maybe you're having some skin symptoms, some GI symptoms, some headaches, some anxiety, brain fog, fatigue. Well, you may have activated mast cells where you're releasing these chemicals more than other people. And we need to really, in that case, look at why.

Do you have an underlying gut infection? Have you been exposed to certain toxins? Do you have mold exposure? What is going on? And we need to really dig into why some of those things are going on. And then we were talking, just really looking at hormone balance, because when we start to.... Have you ever been evaluated? Have you ever done an in-depth hormone evaluation and seen where your hormones are? Really getting the balance that you need in order to get everything back into place? Because hormones are all about balance. And once you get the balance, you can often see a lot of these symptoms start to go away.

Dr Anu Arasu

On that subject, what would you say to people to look out for with mast cell activation? Because I think this is kind of the key as to why we're doing conferences like this. To raise awareness about all of these seemingly unrelated symptoms and what some of the underlying causes might be. What would you say about mast cell activation? How does that present?

Dr Meg Mill

So mast cell activation is going to be when those mast cells go back to the immune system, just become oversensitized. So in a normal reaction, you're going to have... Let's say you're exposed to the allergy or the toxin. You're going to have the histamine response. It's gonna go, and then it's going to turn off, and then you're going to turn on when you need to, and you're going to turn off.

Well, what happens is these mast cells start to become activated. And so little things, they're either constantly activated or the littlest thing can trigger it. So you start to become sensitive to things that most people aren't sensitive to. I was actually shopping and I walked through... One of the things that just makes me think of it is, I walked through the perfume section of the store, and I'm the kind of person, because I am more sensitive, that I feel like I have to hold my breath.

Because I'll start getting a headache from the smell of the perfume, rather than feeling like, "Oh, all this smells so nice that everyone's sharing this."

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It's like those who are sensitive... Do you react to smell? Do you react to sound? Do you react to... Do you make a line on your skin and it stays red? You can see, do you have sensitive skin? Do you have gut issues? And are you having all of these? We're looking at sensitivities, and they can vary for people. Some people with mast activation syndrome can be highly sensitive where they can't take anything. You can't even take supplements. You react to everything. It can be very extreme, or you can have just some levels of sensitivities.

But you want to look at some of these multisystem things. Are you having symptoms in different systems? Are you having brain fog and anxiety and fatigue? But then you also have the allergy symptoms, you have some gut symptoms. And what's tricky is it can be some of them and not all of them, but I say it's someone who feels like they are sensitive and you're going to get checked. You're making that effort.

You know something's off generally, and you can't get the answer because it's very hard to diagnose. There's not easy testing to do. So you're saying your labs are clear, but you still have some of these symptoms. You might have headaches, you might have hormone symptoms, bad PMS. All of those things can also play a role. Does that clarify? I know that it's a complicated syndrome.

Dr Anu Arasu

That really clarifies it, and I think many people can feel very isolated when they start to become sensitive and be restricted in what they can actually do without knowing why. And with the hormone picture, how does that play out? Does it change periods? Does it change any physical symptoms? What do you tend to see on that front?

Dr Meg Mill

We start to see a lot of... We're talking about that estrogen. So we're seeing a lot of the estrogen-dominance symptoms. And like I'm saying, the hormonal migraines and things like that. So I would say it would have more of the estrogen-dominant picture generally. Everyone's so different. So I would say that would be a generality, but you're seeing more of that. Heavy periods, cramping, moodiness.

I actually hear people say, and you probably do too, that I have one good week of the month. They often say, I have one good week of the month, and then it starts all over. And then my symptoms start back up, and then I have PMS, and then I have my period, and then I have another.

So you feel like you're just on that roller-coaster where you're riding the wave of your hormones rather than feeling the same through the month. And I think women's hormones fluctuate. Everyone can have that to a slight degree, but we don't want you living by the feeling that your hormones are controlling your life.

[00:21:23] Dr Anu Arasu

And what would you say to someone that is suspecting they've got something going on that's causing their symptoms? What kind of work-ups should they have? Where should they start?

Dr Meg Mill

So I think the first thing that I would do... A lot of this comes back to gut health when we're talking about the DAO enzymes and really, the histamine. There's a couple of different things here that we would want to talk about the fact that an imbalance in the gut and the gut bacteria can cause an altered DAO enzyme, which is what you need to break down histamine.

Another component comes in that you actually have histamine-producing bacteria that can become overgrown in your gut. So I've had people who actually have had no GI symptoms at all. And I said, "We need to run a stool test." And we're like, "I'm not sure why I'm not having these symptoms."

You're having clear histamine issues. And they have come back where they have these histamine-producing bacteria. And when we're able to eliminate those, a lot of the histamine issues go away. So people that have suffered for years and years and years of histamine issues over decades, we just needed to really do some gut healing and really bring that back into balance and the symptoms just clear up. So I would say really, to go that one thing is really focusing on your gut and your gut health.

That's interesting, too, because it's all of these things that are interconnected. So even when we're talking about gut health and we're talking about hormones and we're looking at things like constipation or high levels of beta-glucuronidase that are actually making estrogen become reabsorbed back into the body.

So in addition to looking at the histamine-producing bacteria, in addition to the DOA enzyme-compromise, we also can get estrogen reabsorption because maybe you're not moving your bowels enough or you have a high level of beta-glucurondase, which is cleaving estrogen and having it back in your system, and then that could be activating you. So that's another thing to even pay attention to.

Then we can start to get things like leaky gut, where you're getting tears in your gut lining. You're getting intestinal permeability, and then you're activating your immune system. So this is all an immune response. So that comes into play. So a lot of times when I'm working with histamine, that's the first place that I will go is working on gut healing. And really with someone, and in a focus with someone who understands the histamine aspect of the gut, too. It's tricky, because when we're talking about...

A lot of people will say, when you're looking at the basics of gut healing, "Take a probiotic, eat fermented foods." Well, those fermented foods are high in histamine. They're just going to bother you. So they're not going to be your friend until everything is healed. So we don't want to put those on. But you hear that. You read it. It's out there.

Even probiotics. While probiotics can be good, there are certain probiotics that can actually have problems for people with histamine. So you need a good probiotic that's not histamine-producing.

That's not going to aggravate those bacteria. So we need to really look at that in a picture that we know will be health-promoting for you.

[00:24:53] Dr Anu Arasu

So this is an example of where testing can really help clarify the picture, because if someone is just following generic advice, they may actually be compounding their histamine and hormone issues.

Dr Meg Mill

Yeah, without understanding that they are... And it's all good advice, but you have to look at the person and what they're going through. And really it's unique for each person. So sometimes that overall, like, okay, fermented foods can be good, but they're not good for you right now for sure, if you're having histamine issues.

Dr Anu Arasu

Yeah. So what kind of easy first steps can people take?

Dr Meg Mill

So I would say the first thing that you can do is just look at your diet. So we're going to look at our diet and see, are you eating foods that are high in histamine? You find that list. Like I said, I have a resource you can go print out and see if you're eating these foods. Sometimes even other foods, like proteins, can bother some people with histamine issues because histamine is made from amino acids. And so sometimes people can have issues even with meats, different meats. And caffeine can bother you sometimes. So looking at your diet.

And then looking at also making sure that you're eating fresh food. Like I said, leftovers can be a problem for people with histamine. And then what I actually have a lot of people do is just actually do a symptom diary. So, not tracking your food every day and maybe not pulling all the foods out right away, because some of these foods, like we said, are healthy. But look at your symptoms and look at your diet and see, okay, every time I eat tomatoes, am I getting some of my symptoms that are bothering me? Every time I eat this food?

I've just worked with so many hundreds of people that it's really amazing what foods come up. It's different for everyone. But when people start to realize, "Oh, my gosh, that food was bothering me and I didn't even realize it and I would have never even suspected it." And then they pull it out and see some of these symptoms clear up. It's really enlightening.

So that's a very easy way to start. That's simple, you can do that. Really, then make sure that you're getting the right nutrients. That you're getting, things like vitamin C, you're getting B6. Things that are going to help really make these enzymes and help you promote... And really eating a balanced, nutritious diet. So that's another thing.

We didn't really even get into... There also is a cortisol component with all of this, too, but working on stress management and bringing down cortisol levels. Because that's another place that we can see some of this mast cell activation and things like that happen. So just even putting lifestyle

things in that you can maybe do some breathwork or some meditation and bring your body back into that parasympathetic. I love vagal nerve toning and different breath work specifically. Really just reducing that overall body stress is really important.

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So we do a lot of... I work a lot with people on that because I think that we're all living in the sympathetic nervous system too much of the time. So we need to bring that down and then really look at environmental stressors. So when we are talking about mast cells, we're talking about toxins and molds and heavy metals and chemicals and allergens around you. And so how can you bring your overall exposure and overall load down in order to calm your immune system and calm your mast cells and bring down those histamine loads.

Dr Anu Arasu

And I think you've given us such an outline there of how you address it long term. Do you find that these things can get better or worse with time? I mean, can they get better if someone goes through menopause, for example?

Dr Meg Mill

Yes. So with hormones, it can. I think with histamine intolerance, it's often a multi-pronged approach. It just depends on, is that your only reason? So I definitely think hormonally, going through menopause, yes. Especially if you have that progesterone drop through perimenopause, your estrogen is dominant. Once your estrogen levels go down. And that's what we actually hormonally often see when we're talking about migraines. I'm bringing that up because there's that common trend.

We often see hormonal migraines decrease after menopause because our estrogen is lower. We're not getting those symptoms anymore. But it just depends, too, on what's in that whole bucket that we're talking about. If it's a hormonal balance and that's it. Then yes, a hormone change can make a difference. If you have more than that going on, sometimes we need to look at the other factors and really look at it as a multi-pronged approach to get everything back into balance.

And then you can definitely... I would say definitely, you can live without symptoms and really get to the root of this. It just takes some investigation. And so it's looking at hormones, looking at gut health, maybe looking at genetics, looking at your toxin exposure. Putting all of those pieces together, and then reregulating your nervous system often and getting some of those things back in balance. And once we do that, we just see the symptoms clear up. And it's really amazing.

Dr Anu Arasu

That's amazing. Meg, where can people find out more about your work?

[00:30:21] Dr Meg Mill

Yes. Well, thank you. My website is <u>megmill.com</u>. It's just m-e-g-m-i-l-l.com. I have, like you mentioned, the podcast called <u>A Little Bit Healthier</u>. So come over and join me over there. I'm actually also hosting a summit on histamine and mast cell activation syndrome in June.

So come on over to my website and we'll have more information about the summit. We're going to do a 7-day deep-dive. And so if you think, like, hey, this might be something that I have. I'd love to share. You're going to get a lot of information, everything you want to know in that summit. And then I'm over on Instagram odrmegmill. It's just D-R-M-E-G-M-I-L-L. So thank you so much for having me today. I love sharing this information.

Dr Anu Arasu

Thanks, Meg. I think you've pointed so many of us to a whole pathway that a lot of us may not have thought about. Thank you.

Dr Meg Mill

Thank you so much.