



Your Functional Medicine Expert®
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[#34: Dr. Jill Interviews Bob Miller on Histamine Intolerance](#)

Text:

Dr. Jill 0:12

Hello everybody! We are back again with one of my very favorite people in the world, Bob Miller, and we're going to talk about histamine today. I'm super excited because I know many of you are listening now or will listen to the recording later; this is a really common, complex topic that affects many, many of our patients and that I think will be relevant to you today. Now, if you know Bob and have seen some of our other videos, first of all, just for background, you can find all of them on my YouTube channel, which is just under my name, Jill Carnahan. If you search on YouTube, you'll find them all there. I just encourage you to subscribe because you get updates when I post new videos like this one. I think this is number four, right, Bob?

Bob Miller 0:52

I do believe [it's] number four, yes.

Dr. Jill 0:54

Awesome. Very good. If you haven't heard me introduce Bob, I'll just give you a brief background. He's been giving some amazing conferences. His company, Nutrigenetic Research, always dives into the pathways, the genomics, and some of the mechanisms behind what we see as physicians in clinical practice. I find him incredibly helpful as an educator. He still consults with both physicians and patients. He's a traditionally trained naturopath who specializes in the field of genetic-specific nutrition.

Dr. Jill 1:28

He earned his degree at the Trinity School of Natural Health and is board certified through the ANMA. In '93, he opened his Tree of Life practice and has served as a traditional naturopath for 27 years. Now, in the past decade or so, he's really gone into this genetic research. If you want to read more about him, his website is Tree of Life Health, tolhealth.com, and the other one for all the research and education is nutrigeneticresearch.org. So there are two sites, but nutrigeneticresearch.org is probably where you'll find most of the events and education. Is that right, Bob?

Bob Miller 2:07

Absolutely, yes.

Dr. Jill 2:08

Okay. Did I miss anything else? [Is there] anywhere else people can find you?

Bob Miller 2:11

Well, that was it.

Dr. Jill 2:12

That's enough, huh? You put on some amazing courses for physicians, so if you're a physician or someone who just wants to learn more, that's one way that I would dive in with the Nutrigenetic Research website and some of the education that Bob has there.

Dr. Jill 2:27

So today we're going to talk about histamine, Bob. I'm sure you have some slides, so let me make sure that is on to share. And if you want to share and dive right in, we are looking forward to this.

Bob Miller 2:37

Okay. We've been talking about histamine probably for the last 10 years, and what I find interesting is that, probably in the last couple of months, I've begun to realize that histamine is probably more of a serious issue than we ever realized. I'm just beginning to realize that. It's not just your itchy eyes and runny nose; there's a whole lot more to histamine. So let's do a screen share and dive right in.

Bob Miller 3:06

I hear that all the time; people say, "Oh, I don't have a histamine problem because I don't have itchy eyes or a runny nose." But that's just not the case. So let's dive into the slides here.

Dr. Jill 3:20

And Bob, just to frame this, just yesterday I was in the clinic with a patient. She's a young woman. She actually has a history of leukemia, but it's all controlled. She's not in any sort of acute illness with the cancer at all, but she had a history of rapid heart rate—tachycardia—in response to foods and different things. She saw a cardiologist; she saw a pulmonologist; she saw many, many specialists, and no one could figure it out. The common thing that we've been working on together and getting some really good traction in her case is histamine. So she went on a very low histamine diet, and we

were looking at other pathways and some of the stuff you're teaching today. But that might be—just for listeners—one way to frame it because you wouldn't typically think of someone who's presenting with an irregular heart rate [as having a] histamine [issue]. Yet in her case, that was the primary issue.

Bob Miller 4:07

Absolutely, okay. Are you seeing my screen?

Dr. Jill 4:09

Looks good, yes.

Bob Miller 4:11

All right. So we're going to dig right into it. Histamine, interestingly, is a signaling molecule. What a miracle we are, Dr. Jill, when you think about how the body was created. We have all these signals that are going on, and we're sitting around not knowing it's all happening, but underneath, [there's] lots of communication going on. Histamine is an example of a chemical messenger that mediates signals or information between various types of cells. There you can see histamine with secreting cells and target cells doing miraculous types of things.

Bob Miller 4:46

Now, histamine is very complex. You can see from this chart that it can cause frequent heartbeats, blood clots, gastric acid, [and] secretion, it causes blood vessels to dilate—that's why so many people might have low blood pressure—bronchial constriction, getting short of breath, it increases the permeability of the capillaries, [and] it causes histamine to be released, swelling, and inflammation. All of those are controlled by histamine. It's part of what causes food sensitivities, but it's also part of tissue healing [and] our psychological and cognitive health, [and] it's involved with our sleep-wake cycles and vascular functions.

Bob Miller 5:27

So the topic today was the good, the bad, and the ugly. We need histamine. In many of our talks before, Dr. Jill, we spoke about too little or too much of anything is a problem. So you can have too little histamine, you can have an adequate amount, or you can have excess. [When histamine is] low, you could have neurological dysfunction, impaired tissue repair because histamine is needed, an altered immune response, reduced gene expression, [and] reduced gastric secretions. When it's adequate, you're going to have good neurological functions, good tissue repair, [and] it will support your immune system, support gene expression, and support digestive and gastric functions. But like

we often say, when it's in excess, we have a problem as well: Neurological dysfunction—actually, what is used to repair the tissue in excess will cause tissue damage rather than healthy immune function—chronic inflammation or allergies, altered gene expression, and food sensitivities.

Bob Miller 6:36

One of the reasons I think I'm getting so excited about histamine is because we've spoken about this in previous [discussions] on your Facebook Live. We believe environmental factors are upregulating the mast cells that are creating these to be excessive, and we'll touch on that a little bit. But I encourage everybody to go back and look at the last webinar we did.

Bob Miller 6:58

Now, many people talk about histamine, but they don't talk about this enzyme, histidine decarboxylase. This uses B6 to take histidine—not histamine—which is an amino acid, and turn it into histamine. Let me pull over one of my charts here. We've talked about mast cells many times, and so many people are having increased mast cell activation. Then the HDC enzyme with B6 takes that amino acid, histidine, [and] makes it into histamine. Just to give a bird's eye view, we're going to be talking about how we need cortisol to reduce histamine, we need diamine oxidase—TOA—to break it down, we need an enzyme called histamine N-methyltransferase, and something that people don't talk about very often is glucuronidation; that is another process that will reduce histamine.

Bob Miller 8:01

We talked about this in previous webinars, so I don't want to cover it now—I'd encourage everyone to go back—but we've talked about how environmental factors are stimulating the mast cells [and] the histamine. Those who may have difficulty with their adrenals not making enough DAO, having a weakness in HNMT, or [having a] weakness in glucuronidation are going to have high histamine. As we spoke about in our last broadcast, histamine actually comes back and stimulates the renin enzyme to create this whole process to stimulate the NOX enzyme again to make more histamine. We'll get into that, but I think that's why we're seeing such a rise in histamine: Environmental factors are actually causing that problem. That's why some people have a negative reaction to B6. One of my coaching clients today, as we talked about it, said, "I feel terrible when I take B6." Practitioners try to keep going for it and give it to them. Well, it was because they had this problem with the histidine turning into histamine.

Bob Miller 9:11

Now, here's what happens: Histamine is primarily synthesized in mast cells in the brain and in the stomach. Here's a little chart that shows your stored histamine and the induced histamine. [To save] time, we're not going to go through all of this detail, but

someone may want to pause this webinar to just look at that chart a little more closely if they want to dig into it. Now, we've spoken about this before: Mast cells are a specialized type of white blood cell; they're a critical part of the immune system, and they protect us from pathogens. Without active mast cells, we'd die of infection; we wouldn't make it. God put that there to protect us. That's our immune system. However, as we've been saying for a couple of years, we believe that environmental factors that we weren't exposed to 50 to 75 years ago are upregulating the mast cells. For example, Dr. Jill, how many people do you see now that you think have mast cell [activation] compared to 10 years ago?

Dr. Jill 10:14

Yes, Bob, I always give the example of eosinophilic esophagitis, which is kind of an allergic type of pathway. Back in medical school, we were taught it was a zebra, which means you don't ever see it—it's rare. We see that all the time now. That's just one example of these types of reactions. Even the epidemic of GERD or gastroesophageal reflux, which is also related, as you saw with the low production of stomach acid, etc., and many, many, many, other things. I would say now that at least 50% of my patients have some form of mast cell activation. That's a huge number.

Bob Miller 10:47

Absolutely. When I teach doctors, I'll have them raise their hands [and say], "How many of you are seeing significantly more mast cell activations now, compared to 10–20 years ago?" All the hands go up, and everybody's like, "Yes, what's going on here?" So degranulation from the mast cells is what causes that, and it can be triggered—as we said—by environmental and genetic factors. So the histamine responses depend on the receptor. There are receptor sites that receive the message. The H1 receptor is involved in inflammation and allergies; it is involved with the respiratory tract and vascular permeability. H2 is found in the brain, the heart, the stomach, and various white blood cells that defend against pathogens. Again, this can stimulate gastric acid secretion, mucous secretion in the airways, and vascular permeability. But it also leads to the relaxation of the airways and cells found in blood vessels. H3 [is] only found in the brain [and is involved with] energy levels, sleep-wake cycles, cognitive functions, and inflammation. And then H4 [is] found in the immune cells, along with the nervous system and intestinal and lung cells. This can increase the intracellular calcium of some immune cells for immune responses. That might be a topic all of its own some time, to talk about how EMF is increasing calcium.

Bob Miller 12:18

Now, there's an interesting enzyme called diamine oxidase, sometimes called DAO, and this is what inactivates histamine, [which is] primarily expressed in the GI tract. So that's one of the ways that we break it down. Now, I'm sure you know many people have

been told, "All you need to support your gut—eat these fermented foods and you'll feel better." For some people, that'll work, but as you know, Dr. Jill, some people feel worse, and the reason is they don't have enough DAO to break it down. We've had this conversation many times. Whenever you say that something is always good for everybody, be cautious because everyone is unique. So if someone tells you you're going to feel a whole lot better if you eat sauerkraut, drink kombucha, and do miso and you feel bad, that's because you may not have enough of this DAO.

Bob Miller 13:16

If we have time, we'll talk a little bit about how progesterone supports DAO and other factors that break it down. I don't have specific research, but I've heard that long-term use of histamine blockers can reduce your DAO.

Bob Miller 13:31

Histamine-N-methyltransferase is the major metabolizing enzyme in the brain. Then there's MAO-B, which breaks down that N-methylhistamine from HNMT. Let's just look at this graphically. Here you can see the DAO enzyme that breaks it down. Here's the HNMT and then the MAO. Any disruption along here will cause your inability to break down histamine. I primarily work with genetics, and we look at the HNMT enzymes. That's important, but people forget that genetics is just a part of it. SAME, S-adenosyl-L-methionine, is the cofactor. So if you have perfect genomics on your HNMT and you don't have SAME, this is like a brand-new car without gasoline. So, are genetics important? Sure, they are, but it's just a piece of it. That's why I call it the "3D chess game played underwater." Then, if we create mast cells, mast cells suppress HNMT, and then you can also have an overproduction of histamine. So, is looking at the SNPs important? Sure, but is it just part of it? Absolutely. We just can't put all the emphasis on the SNPs.

Dr. Jill 14:51

Bob, I just want to comment on that to make sure that our listeners are understanding [this]. The methylation process is part of the process that breaks down histamine, and SAME is one of those universal methyl donors. It's interesting because SAME has a lot of uses. It was a universal methyl donor. In the studies against SSRIs, almost all the drugs in that category [tested] at 1200 mg, SAME outperformed all of them. So I frequently use it as an antidepressant now. If you're listening, don't go out and buy SAME without talking to your doctor, especially if you're on medications. But it's pretty powerful for mood, and that makes sense in this realm of histamine as well because histamine is about alertness and cognitive function.

Dr. Jill 15:29

And just like we said in the beginning, Bob, I love how you frame that—the good, the bad, and the ugly. You want some histamine. If you have no histamine, if you're like me, I go comatose with Benadryl, which is an antihistamine; I literally am on the ground, I can't think, can't process, can't do anything. So that shows me what the lack of histamine does. It's this barometer—we want some, [but] not too much.

Bob Miller 15:48

Absolutely. I often talk about Goldilocks and the Three Bears—not too hot, not too cold. That's where we need to find that balance. Now, this is an interesting paper that was printed in 2013. DAO activity was found to be greatest during the luteal phase in healthy women. [It] may be regulated by progesterone. That's why progesterone can be so important.

Dr. Jill 16:12

Sorry, Bob. Our audio got on there. We're good; keep going.

Bob Miller 16:16

Okay. So here's histamine and immune response. Again, it's part of wound healing and tissue repair. So when we get cut or something, we need to dilate those blood vessels, and we need it to be part of the tissue repair; however, excess histamine may inhibit the wound repair. Back to that same thing: We need some—just right—and not too much. So histamine can be released due to inflammatory mediator signaling molecules, and histamine can stimulate inflammation and various inflammatory cytokines.

Bob Miller 16:54

By the way, we're really digging into cytokines, and I'm beginning to think that many of the things we're talking about, including histamine, might be upregulating interleukin-6, which again, you know the pro and con to it. But that's one of the areas that we're really excited about—interleukin-6. If we have time, we'll touch on that just briefly.

Bob Miller 17:16

So, [going back to histamine], it promotes wakefulness, regulates other neurotransmitters, is part of our eating behavior, satiation, it may decrease the drive for consumption of food, may have a role in the perception of taste, hormone regulation—this was a new one to me as we researched it—seizure regulation, learning, and memory, and coordinates communication between the immune system and the brain. However, aberrant histamine in various nervous systems may have a role in neurodegenerative conditions. For example, low histamine [may have a role in] Alzheimer's [while] high histamine [may have a role in] Parkinson's,

schizophrenia—which all takes us back to balance—addiction, anxiety, and related psychological conditions. Now, one of the things I ponder [is]: Just turn on the news for 10 minutes, and it's pretty clear that a lot of people are becoming very unglued; I have to wonder if these environmental factors that we've been talking about are not just globally raising our histamine levels. I'm just pondering that.

Bob Miller 18:23

Now, here's a study from 2008 that [found that] mast cell-deficient mice had greater anxiety-like behavior. So again, back to mast cells: They're not bad, [but] they need to be balanced. Inhibition of mast cells in the brain was found to increase anxiety-like behavior. Isn't that fascinating? We tend to vilify these mast cells, but the right amount of them is very important.

Dr. Jill 18:49

Bob, I want to comment. With the viral pandemic, we can't stop hearing about that, but viruses are shown in the literature to cause induction of histamine release through interferon. When you get sick with a virus, whether it's a cold, the flu, COVID [or] whatever, you don't feel well—you feel malaise, fatigue, sometimes fluey or a fever—all these things are instigated by interferons in the body and that can cause the release of histamine. I loved your commentary on the environment and what we're seeing—people kind of becoming unglued—because again, this is at play, and the hidden infections, whether they're overt like COVID or other hidden infections that people are suffering from, are playing with our mast cells and our histamine regulation.

Bob Miller 19:31

Absolutely. Now, I found this absolutely fascinating: Insufficient histidine was found to decrease histamine in the brain and induce anxiety-like behaviors, and then the monoamine neurotransmitters were found to be unchanged. So again, we go back to histidine—by the way, we'll list the histidine foods—we need histidine but in excess can create too much histamine and inflammation. So here's another one: Excess histamine may have a role in inflammation and neuroinflammation, again, with psychological and neurological functions. So that balance [is important]. If anybody wants to take one thing away from this whole talk, [it is this]: We need balance in just about everything.

Bob Miller 20:18

Lower concentrations of blood histamine have been found in Alzheimer's. Individuals with an APOE4 allele appeared to have significantly decreased levels of blood histamine. Now interestingly, it's been found to induce wakefulness within a variety of animal models such as acetylcholine, serotonin, and norepinephrine. They're responsible for an estimated 50% of the histamine in the brain. Mast cells also appear to have a role in sleep-wake cycle regulation via histamine release, but [it's] no

surprise; it's complex. So that's why antihistamines can sometimes cause drowsiness, as you just pointed out.

Bob Miller 21:02

Now, interestingly, histamine levels in cerebrospinal fluid have been found to be decreased in individuals with narcolepsy. Isn't that fascinating? But again, it goes back to: Histamine may have a role in promoting wakefulness.

Dr. Jill 21:17

Bob, you and I are on the same wavelength. As you're talking, I was just checking in on the research to see if modafinil could cause an increase in histamine. Modafinil is a drug used for sleep-wake cycles, excessive daytime sleepiness, and narcolepsy. We don't know exactly how it works, but we think it releases dopamine, so it's dopaminergic. However, it also releases histamine. It's no surprise because this is a drug that has been used [for] excessive daytime sleepiness or narcolepsy.

Bob Miller 21:47

Wow, fascinating. Now, look at this study on histamine-N-methyltransferase. Histamine is primarily broken down by HNMT in the brain. HNMT has also been shown to have a critical role in normal sleeping patterns and aggressive behaviors. It's the same pattern [that's] evolving all the time: It can be helpful or harmful. Just as a clinical observation, when we do our health coaching here, we see folks that couldn't find help elsewhere, and many, many times they have lots of homozygous variants in their HNMT genes. And they're sensitive to heat, they're itchy, their brains are racing, if they take a hot shower they get red, mosquito bites [cause a] massive reaction, [and] histamine foods [like] a glass of wine, [for example], can send them off into all kinds of anxiety.

Bob Miller 22:43

Plasma histamine levels have been shown to display elevations in the evening, and the varying histamine levels may be due to the regulation of the circadian rhythm in mast cells. One of the areas we want to be looking at soon is the circadian rhythm and the clock genes. It's fascinating. Now, in the stomach, it's released as a response to food consumption. HDC expression—that's the histidine decarboxylase—appears to be regulated by the hormone gastrin.

Bob Miller 23:16

Now, it also has a role in intestinal motility and the ability of your digestive tract to perform critical functions. How many people are having digestive issues? It's rampant. So if you've got poor gut health, you very well might have low DAO. It's found in the villi of the epithelial cells of the small intestine, which is critical for the absorption of

digested nutrients. When the villi are damaged, malnutrition can ensue. Since DAO activity decreases as intestinal mucosa is damaged, DAO activity might be an indicator of any intestinal mucosal damage. And again, clinically observing, when people have difficulty with gluten and histamine, these are many of the people who get autoimmune diseases like Hashimoto's because of their leaky gut. I'm sure you've observed that as well, Dr. Jill.

Dr. Jill 24:13

Yes, absolutely. We use DAO enzymes frequently, and some people really, really benefit. I would say the majority of them have had either inflammatory bowel disease, significant SIBO, or SIFO, which is the bacterial or fungal overgrowth in the small bowel and causes damage to the microvilli, or something like giardia or some parasitic infection or celiac disease.

Bob Miller 24:37

Absolutely! Now, let's talk about excess. It contributes to chronic inflammation. During acute injuries, inflammation is the body's way of initiating repair. However, stating the obvious, unresolved or chronic inflammation can disrupt that homeostasis and may contribute to many conditions. And histamine has the potential to contribute to this chronic inflammation and prevent the body's ability to heal. Now, I'm going to mention this towards the end, but in case somebody doesn't watch the whole podcast here, we spoke about this in our last Facebook Live where histamine—this blows me away—comes back and stimulates renin, [which] stimulates angiotensin I and II, which then can stimulate interleukin-6, and aldosterone stimulates this enzyme [pointing to NOX] that makes more mast cells, and around and around we go.

Dr. Jill 25:35

Yes. And, Bob, I see a small percentage of patients that are literally stuck in this cycle, and they might be bedridden. I've seen young people [in their] 20s and 30s [or] even younger, and I've seen cases of complete alopecia, which is hair loss [or] baldness at 14 or 26. That's also histamine-related in some cases. These are things you may not think about. You think histamine: "Oh, stuffy nose or congestion." This can be completely incapacitating and cause disability in patients.

Bob Miller 26:05

Absolutely, and that's why I'm looking at it more closely. So here are [some] non-specific [signs of histamine], something you were just mentioning: Congestion, difficulty breathing, allergies—the obvious—eczema, flushing, itchiness, swelling, rash, flatulence, bloating, abdominal pain, diarrhea/constipation, nausea, leaky gut, food sensitivities; and I'd put on there the inflammatory bowel diseases as well; and then headache and dizziness.

Bob Miller 26:34

Now, what are some of the sources of excess histamine? High-histamine foods; mold exposure—you and I are both on that same page—a serious problem; allergies; certain medications. And then these are the genes we're going to talk about: The histamine receptors, the histidine decarboxylase, the histamine-N-methyltransferase, the ABP1 that makes the DAO, and the MAO-B. So in my opinion, knowing how these genes are doing is a pretty critical factor in understanding what you have to attack.

Bob Miller 27:08

This is just a couple of slides. This is what they look like. Here are the histamine receptors: 1, 2, 3, and 4. I think most people know this, but when there's a '1,' that means one parent gave them a genetic mutation, and if we see a '2,' both parents did. So here's HDC, and this is the one that I'm really fascinated with. I am seeing [this] when people have mutations in HDC, and mutations are an upregulation, meaning it aggressively takes histidine and turns it into histamine.

Bob Miller 27:42

Just as a side note, this is my own personal health challenge: I was having a flare of digestive issues and threw everything but the kitchen sink at them—this is just in the last couple of months. I found that this was being upregulated, so I did reduce some of the histidine foods [and] took some of the things that calmed down histidine, and within days [the problem was] resolved. Totally amazing! That's not for everybody; that was for me. That's why we can't say, "The pill for the ill."

Bob Miller 28:14

Now, here's the histamine-N-methyltransferase. Every once in a while, I'll see people who [have] 2s all the way down through there and who just cannot clear histamine. Of course, as we said, we need SAME. Again, you could have perfect HNMT—no mutations at all—[but] if you don't have any SAME, it's the new car without gasoline.

Dr. Jill 28:39

Bob, I just want to mention that I love that you shared your personal little bit because people love to hear it and it's so practical. If you had known me, [I had] severe eczema as a child, [and] severe asthma as a child. And then all of a sudden I realized [that] bone broth, fermented foods, kombucha, dried jerkies, and smoked salmon—all these things made me rashy. So it's no wonder. We don't know exactly which genes I have, but it's the same thing.

Dr. Jill 29:03

I never had heard of the low histamine diet. By nature, I gravitated toward that over the years because I knew those foods weren't good. And then one day, maybe five or ten years ago, I realized, "Oh, they all have histamine." If you're listening, you just joined in, and you're thinking you need to eat bone broth, fermented kombucha, sauerkraut, and kimchi—these are great foods for the gut—but guess what? They have a load of histamine, and if you are intolerant to histamine, you will not do well on these foods.

Bob Miller 29:31

I'll never forget the expression on some people's faces when they were saying, "I started eating healthy, and I did things that are supposed to be good for me, and I'm feeling worse." You can just see the expression on their face when it's like, "Oh my!—I was doing all these things that helped and they hurt."

Bob Miller 29:48

Again, like you said, bone broth, [is an example of that]. Bone broth is also high in glutamine. If you've got high glutamate, the last thing you want to do is take more glutamine. Interestingly, my first health coaching client this morning—the same thing. [She was] extremely anxious and was doing l-glutamine for the gut, taking GABA, and drinking bone broth. You could just see the expression on her and her husband's faces when I said, "Well, I think you're going to feel a lot better when you stop doing that." They were like, "Oh, my goodness!" I usually say to them, "I hate when that happens—when you think you're doing something well and you're actually hurting yourself."

Dr. Jill 30:28

I know. People listening, you have heard hundreds of different people, different platforms talk about this and that—it gets confusing. Anyone who's listening here: You're obviously invested in your own health. You might be a physician who wants to know more, so I totally love that. But you really need someone who knows what they're doing to help guide [you]. Like I said, I love talking to colleagues like Bob because I always learn more. Sometimes navigating it yourself can be very confusing.

Bob Miller 30:55

Absolutely. ABP1, particularly this first one right here that ends in 793, [has] mutations on this one [that are] heterozygous, meaning one parent, [which] will reduce the DAO. I've never seen anyone that has a 2 on here who didn't have a serious histamine problem; all the histamine foods were a disaster for them. These are the people who need to reduce their histamine foods and also make DEO enzymes their lifetime friends because they just don't make enough. Many of these people are just sabotaging themselves unknowingly, thinking their gut is upset [and think], "Well, I'll do more of

these fermented foods," and they're feeling worse and worse. Now, don't go away from this saying I'm against fermented foods. They have all kinds of tremendous benefits if you have adequate DAO. And I'm going to mention that copper is a cofactor. Many times we see people with genetic mutations in their copper transports, so they don't make enough DAO despite what's happening.

Bob Miller 32:00

Now, this was an interesting study: During a small clinical analysis, 10 out of the 14 participants with symptoms triggered by histamine-rich foods were found to have reduced DAO activity. It's not a great surprise, but it's nice to see it published in a peer-reviewed study. Here's what it looks like in a healthy individual. Here's histamine intoxication. Here's histamine intolerance. So this could be from an external histamine [source] or not enough of the DAO enzyme.

Bob Miller 32:37

Now, this is [a list of] the histamine-rich foods: Wine, champagne, beer, sauerkraut, vinegar—anything fermented. By the way, that can include fresh fruits that have been sitting in the refrigerator for a couple of days. Pickles, mayonnaise, olives, cured meats, soured foods, dried fruits, most citrus, aged cheese—this one surprises people—nuts. I just had a client a couple of months ago that ate nuts all day, thinking they were good for him. He stopped the nuts and felt better. We tend to think avocados are great for that ketogenic diet, however, if you've got a histamine intolerance, it can work against you. Eggplant, spinach, tomatoes [also]. If I have a slice of tomato, I'm sneezing for the next 10 minutes.

Dr. Jill 33:28

Wow. I wanted to explain two really quick things. In the vegetable category, that looks like nightshades [in your slide], there are eggplants and tomatoes. This is interesting because I don't do well with histamine, so I cannot eat eggplant, avocado, or tomato, but I can eat peppers, so it's not a nightshade issue; it's actually more of a histamine issue. That might help you if you're struggling. If you can have red or green peppers but not eggplant or tomato, that's not a nightshade issue; that's more of a histamine issue.

Dr. Jill 33:56

One other little note is that amines are parts of proteins, especially in meats, and when they get processed, they get converted into histamine. How that happens is when they're aged, smoked, or [when] they sit in your fridge as leftovers... So that's why one night your fresh steak dinner or your fresh seafood dinner is wonderful but left over two days later it makes you react. This is also why if you get flash-frozen fresh fish from Alaska, you're going to be fine, but if those fish were not frozen quickly at the site where they were caught, you might react to them. Or if you go to Whole Foods [and go

to] the fish counter and the fish have been sitting there for a couple of days, you can have an issue. So for you, if you have histamine issues, fresh meats are really important—fresh proteins.

Bob Miller 34:42

Absolutely. I've heard that many times. I had a meal and I was fine; I had it later and I had a reaction. Then you asked them: "Was it sitting in the refrigerator?" You could see their eyes like, "Oh!" All right.

Bob Miller 34:56

All right. This is [a list of] the top 10 histidine-rich foods. Interestingly, [there are] things like pork chops, beef, chicken, tuna, tofu, navy beans, milk, nuts and seeds, grains, and eggs. These do not contain histamine, but they [do] contain histidine. So if your HDC is upregulated, you can see here on the right: Here's histidine, here's the histidine decarboxylase, and [here's] histamine [as a result].

Bob Miller 35:27

Now, evidence-based nutritional support. A low-histamine diet may be beneficial for individuals with those sensitivities. One of the things we've been really digging into is lycopene. Lycopene is in tomatoes, so if you cut the tomatoes, you could be low in lycopene. We've known about this because we've dug into it. Lycopene is a really important antioxidant. Lycopene consumption has been inversely associated with all-cause mortality, and many low-histamine diets may be eliminating or reducing lycopene consumption. I often get asked this question if we give someone lycopene... They'll say: "Well that comes from tomatoes; I shouldn't take that." No, that's just a molecule that's taken out and does not have histamine properties to it. So we've become big fans of lycopene.

Bob Miller 36:21

Here's a study: A low-histamine diet for six to twelve months was found to result in a 100% increase in DAO activity in participants who previously had reduced DAO activity. And then their histamine intolerance disappeared because they allowed their body to catch up.

Bob Miller 36:44

Grilling and frying foods was found to increase the histamine content of various foods, while boiling the foods was found to have no impact or decreased histamine content of the selected foods. So here's another study: During a clinical analysis in healthy women, dietary fatty acids and micronutrients were positively associated with DAO—long-chain

fatty acids and monosaturated fatty acids. Plus phosphorus, calcium, zinc, magnesium, iron, and B12 all supported the DAO activity.

Bob Miller 37:21

Now, as we mentioned earlier, this is a copper-dependent enzyme, and 2 mg for four weeks was found to increase SOD—because superoxide dismutase, of course, is also copper-dependent—and DAO activity in male participants. Just an interesting clinical observation: Many people of Irish descent have a lot of mutations on their copper transporters. [It's] pure speculation, but I have to wonder if that coppery red hair might be the copper coming out rather than being utilized. [It's] Just one of Bob Miller's musings. So we should probably study that sometime.

Dr. Jill 37:56

I love it, and I want to comment because zinc and copper are antagonistic. So I often use zinc in young women who have excess estrogen and copper to bring down the copper. That's actually [very] common. However, as we age, if women are no longer menstruating, and of course, men who don't typically have a monthly issue with blood unless they have colon issues, often could be deficient in copper. So this is worth checking if you're a clinician, and if you're a patient, asking your doctor to check copper and zinc could be really, really important.

Bob Miller 38:25

Sure, and one of the things we've found sometimes is that plasma levels of copper can be good but the red blood cell [count] is low. So I'm a big fan of looking at the red blood cell [count].

Dr. Jill 38:37

I am too, and just a clinical comment, you can ask your doctor to check RBC zinc [and] RBC copper. I do that frequently with my patients.

Bob Miller 38:44

Excellent. Now, DAO was found significantly to reduce histamine-related symptoms in participants with histamine intolerance. That's kind of like, 'Duh!' But they did a study to prove it. Here's another study: DAO supplementation was found to reduce the severity of headaches when it was related to histamine intolerance. Now, quercetin is an anti-inflammatory flavonoid that actually inhibits HDC. That's possibly one of the reasons why quercetin can bring down histamine. Perhaps there are others. Also, EGCG—what's found in green tea—is shown to inhibit HDC in research parameters and may have anti-inflammatory properties.

Bob Miller 39:32

Now, additionally, we just couldn't find the research on it, but testosterone and iodine also inhibit HDC. So particularly now in boys as testosterone levels are dropping and estrogen levels are going up, could this be why college professors tell me that the young boys coming in are so fragile? They get upset quickly, they need their safe spaces, and it's not necessarily their fault, but if their testosterone is going down and their histamine is going up, [it's understandable]. And of course, testosterone also supports COMT, which clears dopamine, so we could theoretically be seeing higher histamine and higher dopamine create some of these emotional issues that are now so popular.

Bob Miller 40:20

I'm going to wrap it up here by showing the Holme cycle. Again, we talked about this in our last webinar, so I'd encourage people to go back if they want the whole details on this. But just the bottom line: Here it illustrates how histamine comes down, stimulates renin, stimulates angiotensin I and II, and that stimulates interleukin-6, aldosterone, NOX, more superoxide, more mast cells, and more histamine. And then if we have glutamate, that will inhibit ACE2. Here you can see: Mast cells, histamine, dopamine, and testosterone stimulate the renin enzymes.

Bob Miller 41:04

Many times, when people have high [levels of] aldosterone, they'll have higher blood pressure and edema because aldosterone causes them to hold on to sodium and excrete potassium. I oftentimes ask people: "Do you, at nighttime when you take your socks off, see an indentation?" I'm seeing that in people in their late 20s and early 30s. They're getting edema because of the aldosterone. And as we support ACE2, that will reduce the aldosterone, we've seen many people drop water weight very quickly, and then the edema goes away. And then, of course, we all know that ACE2 is used by COVID. That might be one of the mechanisms that allows COVID to be part of that cytokine storm.

Dr. Jill 41:53

Yes, Bob. I know I mentioned this before, but when I had the mold illness, I had severe 3+ pitting edema. My ankles looked like elephants, and this was for a couple of years. Because the mast cells and the mycotoxins stimulate that cytokine, I probably had elevated IL-6 as well. I never measured aldosterone and renin at the time, but I'm assuming this was a big part of that pathway.

Bob Miller 42:15

More than likely, yes. So here, I just wanted to show how the mast cells give off the cytokines [and] the IL-13. That's a whole other subject—IL-13 and histamine. So here's the study that shows the role of histamine receptors in the release of renin. We always make sure everything we say has papers behind it. Histamine has been shown to stimulate the release of renin in multiple analyses. To me, I thought that was an incredible clinical pearl—that histamine will stimulate renin.

Bob Miller 42:51

And then this is a paper that not too many people talked about. It looks like we're just about out of time. But this also talks about how we create this cycle that just keeps feeding itself and that's what is named the Holme cycle. That's what this paper was focusing on. This should be a greeting for just about everybody because I think it's what's going on. And then finally, just a quick hormone relationship: The estrogen will stimulate the mast cells, the mast cells will stimulate the histamine, the histamine will stimulate the estrogen, and around we go. That's why making sure we're not in estrogen dominance is so important. It looks like we ended on time.

Bob Miller 43:31

If anyone wants [to know about] our clinic, there's the information, [it's for] health professionals only. DNAsupplementation.com is where we have the online certification course. There's the contact and some of the nutrition that we make. Again, it's for health professionals. So sorry if you're not a health professional—we can't help you out there. So there you go. There's our 45-minute presentation on histamine.

Bob Miller 43:58

Bob, you are right on the dot, and first of all, as always, I always learn new things. I know if you're listening here, you have learned some new things as well. I just saw questions coming in. I'm going to go back and answer those. Maybe Bob will pop in as well, but I loved your interaction today. If you listen to this recording, post questions. We'll pop back in there again. Visit the YouTube channel.

Dr. Jill 44:20

And just a little plug: If you want to know what I dressed up as for Halloween this year, you can check my Instagram [account], @drjillcarnahan; there's a photo there so you can see it. I just literally ran out of the office, changed clothes, and I'm no longer in costume, but if you want to see what my costume was, you can pop into Instagram and check it out.

Bob Miller 44:37

Bob, thank you so much. We're going to do this again, so you guys stay tuned because we're going to have a whole other series coming up, probably in November or

December. Just stay tuned here for the dates. And Bob, we are so grateful for you. Thank you for your time, your expertise, and all that you do for the world and for practitioners. I know you and I are unified, and if we can teach practitioners, we can help more patients, so this is a great way that we can do it. Thank you again for joining us.

Bob Miller 45:02

Well, my pleasure. Like always, it's a lot of fun. I always look forward to it. And thank you for the opportunity for the platform for helping people understand this.

Dr. Jill 45:09

You are welcome. Have a great afternoon!