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Hi everyone, today we're talking about mast cells histamine and Mast Cell Activation Syndrome. So let me go over some of the key things that are involved with these key issues. There's been a lot of questions about mast cells and a Mast Cell Activation Syndrome and some of the things that are involved with it. What I want to do is kind of clarify the confusion. One of the key things that is happening a lot right now is that there are a lot of people that are going on low histamine diets and I've seen in my own practice patients coming in, they're already on a gluten free diet, dairy free diet, they're already off lectins and the autoimmune paleo diet, then they add on top of that they're now on histamine free or low histamine diet, and pretty much their diet is just... their exposure to dietary foods is starting to decrease, and they're starting to have some major problems. Now, the key thing is... the first thing you have to understand is that if you actually do have an issue with histamine, you're going to have symptoms of histamine issues or histamine problem.

So symptoms of a histamine problem are going to be you actually have reactions in your skin urticaria like a red rash itchy area of your skin that develops when you get exposed to the food, when you get exposed to pet dander or something in environment. Nasal congestion is another major one, you can have other issues like... even if it's very severe you can have anaphylaxis. You can have wheezing in respiratory issues, you can have chronic gastrointestinal issues and migraine issues, and those are all part of the whole histamine reaction. If you're not having those types of reactions then you probably don't need to be so worried about histamine. So histamine is a chemical signaling agent that act as a neurotransmitter and as an immune signaling compound. For some people that have histamine reactions you want to try to figure out what's the cause, what's the mechanism and what's really involved. Now, here's your biggest clue, if you're a chronically sick patient and you're tired and fatigued and you look on the internet, you're going to find tons of symptoms on histamine intolerance, and you're going to maybe make the assumption that if you have lots of food sensitivities that you may have histamine intolerance, and you may need to take something like colic DAO as a digestive support... as a supplement to help break down histamine or you need to go on histamine free diet. This is something that you really want to avoid.

If you actually do have signs reactions and urticaria and skin redness and skin inflammation being exposed to foods or a trigger, or if you have chronic symptoms that are just all over the place and it's hard to distinguish them. I mean an anti-histamine should make a big change for you. So one of the key things is just determine if you actually do have any benefits with taking an anti-histamine, and if you do have any benefits taking an anti-histamine then it's a strong clue that you may have this whole histamine mast cell response. Having multiple food sensitivities doesn't mean you have a mast cell histamine response. So let me clarify a few things, let me talk about mast cells and histamines. I need about a good 20 minutes to give you some background information, and then we can take some questions if people have them.

So one of the first things to really understand is that when you're looking at the immune response... let's start with food, and it would apply to food or environmental chemicals. When you have an environmental response to food or to an environmental chemical, one of the key things to understand is that there're different types of immune responses, and these are dictated by different immunoglobulins or different antibodies. So the key thing with food sensitivities, these are not allergies and food sensitivities involve what are called an IgE response... I'm sorry, an IgG response or an IgM response. These are different immunoglobulins and these are delayed food sensitivities.

This delayed food sensitivity response like if you ever had a food sensitivity test done with someone, if you look at the results it'll say something like carrot IgG or wheat IgG or IgM or IgA. So those are delayed food sensitivities and they don't really activate the histamine pathway. The only thing that really activates the histamine pathway when you look at food proteins is an IgE and that is in relation to an immediate reaction. So one of the key things to know if it's a histamine reaction it's actually part of this whole mast cell histamine intolerance issue, is if you get exposed to something and the symptoms are immediate so you get exposed to food like cheese and then you get skin reactions right away, or you have some wheezing that takes place right away. So, that's the key feature.

Histamine responses to foods into environmental compounds are activated through immunoglobulin E IgE and then within two to three minutes or very quickly there's a reaction. Whereas food sensitivities are delayed and they're not really involved with the whole histamine response. Okay? Now when you have an IgE response... IgE is immunoglobulin E, so for different reasons we have different sensitivities, but if you have an allergic reaction or an IgE reaction to foods and environmental chemicals, those antibodies called IgE then activate immune cells called mast cells. Then mast cells release a whole bunch of chemical mediators one of them being histamine, and histamine then gets released into the system and histamine has different effects throughout the body because we have different histamine receptors. So we have histamine receptors throughout our skin that can cause... these are H1 and H4 receptors, they can cause itching and redness and inflammation.

With histamine receptors in our gut which are involved with the motility, smooth muscle contractions of the gut, acid enzyme release. So you can have disruption of your gastrointestinal function with excess histamine response, and then there's histamine receptors in the brain called H3 receptors, and they are involved with neurotransmitter activity. So you can have all types of cognitive responses with it or mood changes or irritability or anger when you have a histamine response, and when people take an anti-histamine they kind of block all four so that's why some people have significant side effects. But if you have excess histamine you may actually notice some benefits when you take an anti-histamine. So when you're looking at... as a person looking at, is histamine an issue for you? Do you need to go on a low histamine diet? You got to ask yourself, are you having immediate reactions? Are you having these IgE allergic reactions, or are they just delayed food sensitivities? If they're delayed food sensitivities you're wasting your time with histamine free diet.

Now, let's go back to the mast cells, the mast cells that we produce... that we have in our body, they are there in a normal state and we'll look at the different degrees of mast cell activity, we don't even notice it, we may get exposed to some kind of antigen or some kind of trigger and our mast cells quickly taken place, we triggered inflammatory response to deal with the antigen or trigger or anti-inflammatory systems come in right away, and we deal with it and we have no reactions. Now, when you go to... so that's like a basic healthy ideal response without muscles work and histamine and IgE reactions in a very healthy individual, healthy response. When you go to the next level, the second level of histamine reactions then you have a person who has like occasional skin reactions, they get an occasional rash, they get sinus congestion and some days are different than other days. They'll many times know what the trigger is, they may know that they're allergic to cats or they may know that they're certain allergic to pollen, if there's high pollen in the air they're going to have some sinus issues and some wheezing issues. So those are people that have some subtle issues with histamine responses.

Then you have people that have chronic histamine issues and this is where the next degree of severity comes in, which is like histamine intolerances. Histamine intolerance is mean these people that have these have constant sinus issues, constant wheezing, constant gastrointestinal issues, migraines, vasodilation issues, just kind of weird symptoms and it may have started very slowly and gotten worse over time. So, that's really dealing with the histamine intolerance issue, and then the next severity of it is something called Mast Cell Activation Syndrome, where you have a massive response with mast cells because two things are happening, body is producing excess amounts of mast cells and their response is exaggerated and enhanced, and that's a whole different class. For those people they will have anaphylaxis and they have significant and severe episodes, and they are dealing with chronic immune activation all the time. It's not just an occasional sinus issue and it's not just that they have food sensitivities, they are having constant allergy type responses all the time. So those are kind of the grades of what things are. Okay?

So when you kind of take a look back and you look at... as healthcare professionals as you can look back and look at patients that come in. I see so many patients that are on low histamine diet thinking that it's the thing they need to be doing. When you're in a low histamine diet you're actually getting rid of some really essential foods that are critical, like fermented vegetables or pickled vegetables. Different types of fibers that are critical just to improve your health and microbiome diversity are part of a low histamine diet. So you really have to ask the question do you really need to do that? And once again if you don't have allergy acute immediate histamine related symptoms like wheezing, skin redness issues its less likely. If you've taken anti-histamine and it has no effect on your system, it's less likely that it really is a histamine related issue and low histamine diet is really not a place to spend time on.

Now let's talk about people that actually do have histamine related issues, and what do you do about it and what's going on with them and we can look at the different scales and different severities. Okay, now there's just... something that happens to all of us, all

of us have certain potential risks for different allergies. So some of us may be allergic to cats or pet dander, some of us are allergic to pollen and we have to avoid that, and if we can avoid that we can still function. That's not as big of a deal if it's an occasional thing or a couple things you can figure out and dictate your life around it. However, there are some people that have ongoing chronic histamine reactions and ongoing skin itching and redness and inflammation and IgE issues and migraines and that's a whole different story. So, when you're dealing with those types of reactions there's basically an issue with... there's something causing the trigger production of histamines, or there's an inability to clear histamines or number three, there's an amplified immune response to the whole histamine reaction.

So in a clinical setting if you actually have figured out you do have a histamine issue, that you do actually have histamine intolerance and you do feel better going off being on a low histamine diet, and you do feel better taking anti-histamines like natural ones will be like things like quercetin for example is one of the best ones, or you're taking over the counter anti-histamines they get rid of your symptoms but maybe you don't take them [inaudible 00:12:00] side effects. But you notice that it actually is a histamine based issue, then the clinical setting the questions are, why do you have this chronic ongoing histamine issue? When we look at the reasons of why you're producing too much histamine, one of them is basically you were exposed to something, you could develop IgE reactions to various things for example, we did a talk on mold.

We know that studies have shown that people who are in a damp building with mold for a long period of time, they start to shift from a IgG delayed reaction to a chronic and permanent IgE reaction. So some people can get more toxicities. Mast cells are actually also activated by other immune cells also like eosinophils, parasitic infections activating eosinophils to [inaudible 00:12:54] to activate mast cells, so parasitic infections can do it.

There're studies that show that parakeets from Lyme disease can activate neutrophils and at the turn on mast cells reduces histamine. So you're looking down the path of what could be triggering it if you're dealing with this chronic histamine issue? The treatment isn't histamine or histamine diet, the treatment is to figure out what are the triggers? Now, you can always look in environmental tests that have your doctor want to do those for you, where they look at immunoglobulin E, IgE as an elephant, IgE reactions. They can do those two foods and they can do those two environmental inhalants and then determine if they can find any of those triggers and then that's one thing that if you can find something that's triggering it.

Now, there are less likely things that we talked about, or someone may have different pathogens or infections. We don't know what all of those are in the literature. We know there're some publications of Lyme disease, we know there's some interesting responses with different parasitic infections and some people that really activates the eosinophils to get histamine response. So those are things to look at. And one of the goals I've tried to figure out why some of the histamine intolerances is why they're producing so much of it and trying to find those triggers, and sometimes you can't find

them and sometimes they're not that obvious. If you do have a reaction to triggers like pet dander, or some people have reactions to... let's say pollen` being most common, there is a very effective therapy that has lots of research behind it.

It's a conventional based therapy called LDA, low-dose antigen therapy, where they give very small amounts of an antigen usually in a sublingual drop over a period of time they monitored and these are done by conventionally trained medical physicians' allergist, and you can do low-dose antigen they call it either, they call LDA, low-dose antigen, low-dose allergy, they also call it LDI, low-dose immunotherapy. Those trained physicians that do that, and they can kind of... that's really an effective way for some people to really deal with these IgG responses. Even if they have the exposure to an environmental trigger or to food, like maybe peanuts for example, there's some pretty good outcomes published where people that do low-dose action therapy can calm down that that part of the increased histamine response.

So remember, there's three things to look at when you have an ecosystem response. What are triggers? And then you identify and identify the trigger, you try to remove it if you can and then you can do things like low-dose antigen therapy, and a conventional allergist model to deal with activating that histamine response. The second issue that's involved with having chronic histamine issues is you just may not be clearing it out of your body and there are ways that that can be tested but they're not standardized yet. There's a serum DAO test. There's two enzymes that really are involved with breaking down histamines out of your body. So once you produce histamines, histamines are going to aggravate your... excess system is going to activate H1 receptors and cause skin reactions and they're going to activate one of the H1 through H4 receptors and cause wheezing and neurological symptoms and gastrointestinal issues and vasoconstriction and so forth, but if you can't clear them then that's an issue.

DAO diamine oxidase is an enzyme that clears it that can be measured in blood test for some people, but there's little controversy if the results are accurate. There's mixed research with this right now and it's not really commonly available with most labs. So but it is an enzyme that's involved with clearing histamines. And then there's another enzyme involved with occurrence of histamines called histidine methyltransferase, and histidine methyltransferase is used to also clear histamine. So if someone has histamine intolerance and you've looked at triggers, the next place to look at is the possibility that they're not clearing it fast enough. So DAO is an enzyme, you can actually take do supplements that are over the counter, you can order them off Amazon, and you can try DAO supplements and see if that helps you get rid of some of your symptoms.

The other pathway that's really important is this histidine methyltransferase pathway which is dependent upon what are called methyl donors, and methyl donors are one carbon groups and your liver process then gets rid of histamine by adding a carbon group to it and this process is called methylation. And methylation requires nutrition nutritional compounds especially folate and B12, B18. These are compounds trimethylglycine that are involved with this whole methylation response. These days you can just look at nutritional formulations just from methylation. You'll see a bunch of them

on the internet and they have basically the B vitamins and methyl donors that we talked about like trimethylglycine, and B vitamins and folate all in there to help support that pathway. So some people need methylation support. Some people go on multiple medications and deplete their methylation pathways and then they can't clear histamines, and then they have to have additional methylation support to make a change there.

The second part of dealing with chronic histamine intolerances is to find out a way to clear them. So you have the DAO pathway and then you have the methylation pathway, okay? Now, the third part that's really involved with looking at people that are suffering from chronic histamine intolerance issues is what's called amplification of the immune response. So let me explain this. In the field of immunology there's a mechanism called amplification, and amplification means you have an immune response but it's exaggerated. It's too much. It's not an appropriate response. The response is too great for the antigen that's there. These can happen for a couple of reasons with histamine one of them is associated with prostaglandin imbalances or leukotriene imbalances, let me explain that.

When you're looking at mast cells and they get activated by whatever the trigger is, they release histamines and then release cytokines and they release different messenger proteins. But the pathway that's involved with mast cells to deal with an immune trigger is also through this inflammatory process called prostaglandins and leukotrienes. Prostaglandins and leukotrienes are compounds that are also significantly impacted by diet. You could have an amplification of the histamine response if you have an underlying prostaglandin and leukotriene issue and the most common cause of that is really related to your isn't your dietary fat intake. Prostaglandins can either be proinflammatory or anti-inflammatory. If you have a diet that's promoting increased amounts of proinflammatory prostaglandins and leukotrienes, then when you have a histamine reaction, it can be amplified.

So prostaglandins typically shift into a proinflammatory state that can amplify the histamine response if your diet is really too high in things like red meat, animal products, shellfish, and fried foods, and vegetable oils. That has to be counterbalanced with diets really high in fish oils, and flaxseed oils that really have an anti-inflammatory effect. So sometimes we see people that exaggerate histamine response because they're eating a lot of vegetable oil every day, and they're eating a lot of shellfish, or red meats or they're just not getting enough fish oil. They just... some people say I hate fish, I never eat fish. Some people want a low fish diet because of histamine reactions, but fish oils provide an essential source of prostaglandin support. Flaxseed oil is another key essential fatty acid that can help produce the anti-inflammatory prostaglandins.

When we see people that have histamine intolerance reactions, remember we're looking at three things. One is what are the triggers? Two are they clearing it out? And three, what's amplifying it? One of the most significant amplifiers of histamine reactions are these prostaglandin imbalances, these leukotriene imbalances. So you really want to take a look at good versus bad fats, and really get rid of all the fried in vegetable oils

and really increase things like flaxseed and fish oil. That'd be one way to deal with the histamine reaction. The other part of an amplified immune response goes back to what's called immune tolerance, and I've talked about this many times. I developed an online program called the 3D Immune Tolerance Program, and it really involves different parts of the immune system is called dendritic cells and Kupffer cells and Treg cells. Those cells respond to things like vitamin D, antioxidants, [inaudible 00:22:35]. Those are important and part of loss of tolerance that we know about in the immunology pure read literature are actually things like intestinal permeability, leaky gut and even lung barrier permeability, we had a whole talk on lung barrier permeability.

You could have your lung permeable from lack of antioxidants and chronic environmental exposures and now when you eat age cheese, or have a glass of red wine, your histamine response is amplified because your immune response is amplified. Now, when you really look at people that have histamine reactions, and histamine intolerances, there's usually multiple factors that are all adding up that are causing it. They're having maybe all three of those mechanisms involved. So let me repeat them. So number one, one of the key things that causes increased histamine responses is they're getting exposure. So maybe they are having way too much wine and ate cheese than they normally do so their histamine mode is just going up from exposure. And in combination with that they're around different environmental exposures to let's say pollen, that's adding to their histamine activation. So now they have this huge antigen load which is part of one of the triggers press for the trigger part of it.

Two maybe their DAO enzyme is genetically low, or maybe they DAO enzyme that clears that histamines is okay, but their methylation pathway's problem because they're just not getting enough methyl donors in their diet. They're not getting enough B12 and folate. There's a whole list of things that cause methylation bounces, let's say the clearance pathway is low and then let's add on top of that they have some stress, and now they're dysregulating their immune system. Now, they have also some subtle leaky gut from other issues, maybe some subtle leaky gut, maybe their vitamin D deficient. The host of all these factors are then going to amplify the response. So when you're looking at the actual clinical treatment and management of histamine intolerance, it's not a low histamine diet. Low histamine diet is just there so you don't have as many flare ups because you can't clear histamine.

The real clinical battle with people that have histamine intolerance issues is find the antigens, deal with support clearance of histamine, and number three figure out how to make sure there're no mechanisms that are causing amplification of the immune response. So in a clinical setting, you may need to treat leaky gut, leaky lungs, you may need to check vitamin D levels, and for the vitamin D levels you may have to do an IgE test, look for any kind of environmental food triggers, they may do some low dose antigen therapy, they may go through a host of strategies just to improve their overall health. Those are the those are the key things and I think the frustration is with many people that are dealing with chronic histamine intolerance issues is they're just trying to find like the one supplement. So they go, "I tried DAO, it didn't work. So what do I do now?" Or they tried one sup one versus another.

Now, if you do have... if you're suffering from histamine intolerance issues and you just can't handle any source of like red wine, or cheese, or fermented foods, and yet it's very clear when you take anti histamines your symptoms improved to some degree, you may need to be on a low diet until you can figure things out. But ultimately, it's improving overall health that it's not just about... it's just not about one thing. Those are the key things I just wanted to cover with you before we take questions here. The last part of this I just want to quickly talk about as we get set up for questions here is something called Mast Cell Activation Syndrome. Mast cell activation stream is like the most aggressive form of histamine reaction, and these are when these mast cells are overly active and there's there is an increased amount of mast cells being produced. Whenever you have Mast Cell Activation Syndrome there're different criteria that are needed for the diagnosis.

Many people have been diagnosed with Mast Cell Activation Syndrome inappropriately and there's also a lot of people that have it that aren't being diagnosed, so let me talk about those for a second. There's three criteria to talk about Mast Cell Activation Syndrome. Number one, there has to be histamine reaction symptoms in two or more organs like the skin, the lungs, the GI tract, cardiovascular system. Someone has to have let's say, urticaria and redness inflammation, and wheezing and asthma, and chronic gastrointestinal motility issues and a combination of all those of two more tissues to even be considered for muscle activation syndrome. Number two, they do lab testing, and within a period of a mast cell immune response they need to get their serum tryptase levels measured, and if the serum tryptase levels are measured, they compare that to baseline and if it's gone up more than 20% and that's the two of the criteria. And then number three, the key way to really confirm the diagnosis that they go on histamine blockers, and they get one leukotriene blockers and immune suppressors, and see if that calms down their symptoms and if it does, then they know that they can be diagnosed with Mast Cell Activation Syndrome.

At that point if someone really does have Mast Cell Activation Syndrome, I mean pharmacology is something that really can make a big difference for them and they may not get much out of just taking quercetin or magnesium or a ginger extract or other things people typically use for histamine responses. So, that's the other thing with mast cell. Now, you have to know that with Mast Cell Activation Syndrome when it is very severe and very serious and people are having breathing issues and even anaphylaxis, they then have to immediately identify is it primary, secondary or idiopathic? So they can do some gene testing and do biopsies in tissues to determine what's there? Is it the KIT gene... you need to set this associate Mast Cell Activation Syndrome, but secondary it could be related to infection like for example [inaudible 00:28:46] can activate neutrophils that then turn on mast cells, or it could be idiopathic meaning they just can't find the cause.

That's the end of the spectrum, the Mast Cell Activation Syndrome. All of the things we talked about by trying to look for antigens, optimizing clearance of histamines and then trying to decrease amplification of the immune response by improving tolerance and looking at partial bans still apply to mast cell, but mast cell activations are so aggressive

that patients that actually do have that severity of the mast cell response typically need pharmacology to function. Okay, let's take questions.

Hi.

Hi.

**Hi. [Sui 00:29:28] asked, "What would be the... what is the..." Oh, it went away. "What would be the relation with multiple chemical sensitivities?"**

So multiple chemical sensitivities are not directly associated with mast cells in immune responses. Chemicals don't cause an IgE reaction. Chemicals can impact your lung barrier and they can cause them to break down, chemicals can dis-regulate your immune system to some degree, but they're not going to be a direct drive of causing histamine responses. So that's one of the key things when you look at... let's say mercury or lead or BPA. They can disrupt the immune system but they're not going to directly cause mast cell activation. So if you have significant reactions to chemicals, that's not a histamine issue. That's more of an immune... what they call chemical tolerance issue. You can check out the 3D Immune Tolerance Program we made, it goes into how to improve your immune tolerance and we have articles written to as well. So you can find that at my website, Dr. K. News. D-R-K-N-E-W-S.com and our immune tolerance program is called the 3D Immune Tolerance Program, and also if you're going to check that out please don't forget to follow us on Facebook so you can get access to all the talks that we do.

**Okay, [Lynn 00:30:58] is asking, but a few other people have asked the same kind of thing. "How can I fix my leaky gut with a diet to help MCAS if fermented foods are a no, no?"**

Well, that's the key question and it's like do you really... well, first of all do you really have Mast Cell Activation Syndrome? Mast Cell Activation Syndrome is serious stuff. There's no guessing you have Mast Cell Activation Syndrome because you're getting anaphylaxis, you're not breathing, you're having severe skin reactions. So if you actually have Mast Cell Activation Syndrome and you have severe load of histamines, then eating fermented foods would cause a severe response for you. Now, if you can't do that then you can... and you really do have intolerance to histamine based foods, so you can't take fermented foods you're worried about fixing a leaky gut, one of the things you can do is you can take what are called short-chain fatty acids, and butyrate is the most common available supplement you can get online. Like if you go to Amazon or something but short-chained fatty acids are really one of the key benefits of fibers in the end product of what fibers do.

When you ingest fermented foods or fibers they help make bacteria... have beneficial bacteria and the beneficial bacteria produces things called short-chained fatty acids. It's these short-chained fatty acids that have been shown to help leaky gut heal, they help build what are called codon proteins and they help activate Treg cells which calm down intestinal inflammation. So when I have patients for example that have small intestinal

bacterial overgrowth, or people that truly can handle histamine based foods or fermented foods, then one way to get around that is just to use butyrate as a supplement, and you have some effect on the same pathways by avoiding the fiber or histamine load.

**Okay. Mariana asks, "Have you seen a connection between MCAS and parasites?"**

Yeah, I mean there are connection between Mast Cell Activation Syndrome and parasites. However, parasites alone may be one of the factors with Mast Cell Activation Syndrome. Mast Cell Activation Syndrome is serious stuff. People throw this diagnosis around like it's just, "Oh, I have a skin reaction. I can have [inaudible 00:33:08] Mast cell activation has three very specific criteria, and by the way when you get diagnosed with Mass Activation Syndrome, they have to rule out tumors, they have to rule out mast cell leukemia, they have to rule out mastomas which really produce mass cells. If you've [inaudible 00:33:29] Mast Cell Activation Syndrome you actually have it and you actually have all the criteria. You just may have histamine intolerances, and whether it's mass cell activations or histamine intolerances, remember there's three things you clinically want to make sure you do. Look for as many triggers as one of them, support clearance of histamines and then three look at things that can amplify the histamine response.

Parasites are a number one, it can be a trigger. Parasites activate in the gut immune cells called eosinophils. Eosinophils send direct messenger protein activation signals to mast cells to cause them to activate and proliferate and to releases histamine. You can have parasites be one part of the antigen load or histamine load with Mast Cell Activation Syndrome or histamine intolerance for sure.

**Okay, Jill is asking and a few other people are saying, what can they Google or what can they do to learn on their own or see studies about how a diet can cause amplification of an immune response?**

Yes, application of immune response is a general term that you're going to have to look under stuff... under the words of oral tolerance, or immune tolerance. So if you go to the National Library of Medicine, all the pure reviewed publications are there. You can just type in the word oral tolerance and find everything you're looking for, oral tolerance and diet, oral tolerance to vitamin. You better have some time in your hands because there're thousands of papers there.

Yeah.

But that's what You'll find information. I summarized all that for you in the 3D Immune Tolerance Program, but you'll have plenty of information to read if you're interested in that topic.

**So Candice is asking, "Would the immune tolerance program be beneficial for someone with significant histamine responses?" Will the immune tolerance program be important for someone who has exaggerated histamine responses?**

Yes.

Yes and no because remember there's three things that cause histamine issues. If your histamine issues are related to chronic antigen load and you just have to find the antigen load or low-dose antigen therapy then it may even get intolerance issue. If you have issues with clearance, maybe it's a methylation issue, maybe you genetically aren't making as much DAO pathway done, maybe you need to take DAO or methyl donors. But if you really do have amplification issue, that's when the 3D Immune Tolerance Program can give you some aspect of support but it may not be the mechanism for you. But one of the things that we don't cover in the 3D Immune Tolerance Program that's important for mast cells that amplifies it, is that prostaglandin imbalance.

So you just have to make sure you do have a diet that's really high in things like fish oils, and flaxseed oil, and not overburdened by a diet that's really high in fried foods or vegetable oils. Because that'll switch your prostaglandins in a way that histamines amplify this leukotriene response and then that could be why you're having problems. So I would say, look at your prostaglandin issues too.

It may or may not be part of the spectrum that can help you if you have histamine tolerance issues, but it's not the only part of it.

**[Elaine 00:36:32]... here Elaine says, "Any thoughts on low IgE on an immunoglobulin test after mold sickness? Other Igs are normal."**

Low IgE.

E like elephant, on immunoglobulin test after [inaudible 00:36:50]

Yeah, if you have any kind of trigger. For example, if you have mold illness or something like that and you do a blood test. In acute stages or when someone's immune system is still intact, you'll see very high immunoglobulins on a blood test for whatever the mold species is, to they're reacting to. But just like anything, the immune system does wear out. And if someone starts to have immune exhaustion and immune fatigue, or immune compromise, and especially when you start to see the total white blood cells can go down a little bit, or even maybe just their B cell called the CD 19 can't go down, then they are just basically getting wiped out. So it's a big indication that the immune system is really compromised. So low IgE just means immune compromised, and it's specific to that immunoglobulin response. So any chronic activation of that pathway can exhaust it.

**Okay, Melissa is asking, "How do, or do hormones factor into histamine levels?"**

Hormones have an impact on immune cells that then modulate amplification. So remember, I actually did a talk once on how hormones impact immune tolerance and that was fun. Because it is an extensive literature you have to do to come up with this talk. But immune cells that... they amplify the immune response to histamines whether it's mast cells, whether it's dendritic cells, whether it's Kupffer cells, whether it's cytotoxic T cells, they all have receptors for hormones and they're all the hormones, their thyroid hormones, estrogen, progesterone, testosterone. So hormones have a very effective, or very strong impact on immune cells and immune function, but it's not direct enough where we can go, "You have Mast Cell Activation Syndrome, so you may have a hormone deficiency issue." It's more like you have chronic mast cell issues or histamine issues, and you got to just get healthier and maybe as you've bounced out an underlying thyroid issue, or you bounce out underlying hormone issue, you're not as reactive to the same histamine response as before but it won't be as direct as hormone imbalance. Now you have Mast Cell Activation Syndrome or something like that.

**Okay. So Sui is also asking, "Why would intolerance is increased over time?" You kind of answered [inaudible 00:39:13]**

Intolerance increases over time just like our metabolism slows down as we get older, and we get bigger ears and bigger noses, and all the other things that happen. Our cell division and our efficiency for cell division changes as we get older, and one of the things that happens to our immune system becomes less efficient. So it's just one of the terrible things about the aging process, our immune system becomes less efficient as we get older just like we lose bone density and everything else.

**Okay, Dana is asking, "How do you increase microbiome diversity if you have histamine intolerance? Many of the ideal fruits and veggies to increase diversity are high in histamines."**

Exactly. That's a really good point.

Thank you Dana.

Thank you Dana. So, that is one of the difficult situations. And this is again, why you really have to make sure if you're going on a low histamine diet, you actually have a histamine problem. Because when you start cutting out some of the most essential foods for the guts especially fermented vegetables, it's going to get in the way of your healing. Also if you keep cutting down foods, the less food diversity you have the less microbiome diversity you have which then perpetuates your amplification process reaction to histamines. So it can be done, you just get a diverse vegetable and even diverse fruit, diet or foods on low histamine that don't cause reactions for you. It's just more work, but it's definitely possible.

Yeah, and you can go to markets you don't normally go to and get-

Yeah.

Yeah.

You go to markets like Asian markets and find vegetables that you normally don't see that you can eat, and that's a good strategy as well.

**Okay. Okay, okay, this is kind of general but is stress a true trigger?**

Yes, stress is a true trigger but it's also the ultimate clinical cop out.

Yes.

What happens when people don't know what's going on clinicians, like if you don't know what to do just blame it on stress. Stress alone cannot cause Mast Cell Activation Syndrome or histamine intolerance, so that's number one. Stress basically adds fuel to the fire wherever the fire is, but it's not directly related to it. I mean dealing with stress is important. However, you still have to find the three things we talked about. What are triggers causing the antigen load? Is there an issue with histamine clearance or something amplifying the immune response? Stress really comes into the third part of which is amplifying the immune response because stress has been shown to do a few things, it just causes Treg cells to dysfunction, which can amplify the response to histamine. It can actually cause barriers to break down the lung barrier and gut barrier, So now you're more reactive to allergens whether it's inhalants or food proteins. So it's a part of it but it's also the ultimate cop out. So you can't ignore it but you don't want to blame everything on it.

**Okay. Monica, "What about probiotics for [inaudible 00:42:27]?"**

Yeah, probiotics are probably one of the least effective ways to actually improve your immune tolerance. Using something like short-chain fatty acid and butyrate would be much, much more effective. What we're learning about probiotics and the literature is that probiotics have varied effects on different hosts, of different hosts being the person taking it. So different probiotic strains work differently for different gut microbiomes, and there's a large variation of them. If you're going to look at immune support, you're better off taking short-chain fatty acids like butyrate or probiotic for immune tolerance any day.

**Oh, okay. Sean, "Can you please explain the CD4 to CD8 ratio and its role in immune resilience or immune balancing?"**

Sure, if you do a comprehensive immune panel called let's say Team B cell profile, they'll have something called the CD4 which are T helper cells and CD8 which are T suppressor cells. There's a ratio between help or many activate your immune system and suppressors, which means calming down your immune system. Ideal CD4/CD8 ratios like around in a functional range ideal ranges like 1.5 to two. If you see it above two especially see it above a lab range that tells us the immune system is actively fighting something, and then if you see the CD4/CD8 ratio really just depleted and low then you probably have some type of immune suppression so it's not able to properly respond to any kind of antigen trigger. You don't typically see major imbalances in

CD4/CD8 ratios with Mast Cell Activation Syndrome and histamine issues. You see them more really involved with active infections directly and autoimmune disease.

**Okay, Peter asks, "Can you talk about histamine as a neurotransmitter and how it can affect the brain?"**

Sure. So histamine is an excitatory neurotransmitter and histamine actually histamine interceptors, H3 receptors are found all throughout the brain. Meaning that they control frontal lobe, occipital lobe, parietal lobe, they control autonomic senders. They have a whole range of effects and one of the key things with histamine is that there isn't one symptom associated with it. So when people for example have issues with histamines they take histamine blocker or they take something to suppress their histamine levels, they can get some cognitive events. They're trying to make drugs that specifically block H1 receptors and not the H3 receptors but it's not... they haven't been successful making that drug completely effective, there's still effects in the brain. So people will have all types of diverse symptoms, some people will actually get crazy and get angry with histamine reactions or anti-histamines. Some people will have cognitive issues they can't think, they can't focus so it kind of goes all over the place.

It's not one specific symptom, however the most common things people have when they have low histamine is they get too much excitation of their brain when their histamine levels are high. So it's almost like they can't focus on something, and then they also end up activating areas of the limbic system which makes him really angry and agitated, irritable. So those are the most common neurotransmitter reaction responses clinically we see with histamine pathways.

**Okay. Joy is saying, "My toddler is gluten dairy free because he has a reaction to those foods. His pediatrician said we could cause him to have a gluten sensitivity by not giving him gluten at a young age. Is that true?"**

There is some truth to that. There is a paper that was published that showed... First of all they showed with celiac disease sibilings, if they expose them to trace amounts of gluten that they actually had less reacted gluten responses and celiac disease expressions when they got older, that some a little bit of priming was important for them to activate that response. Now, for most people giving gluten to kids early that reactions are going to cause a serious amount of problems. I think if your gluten free you're going to get some of those accidental exposures anyways. So you're going to have some immune tolerance priming, but the big statement of just... so I think they're referencing that type of literature, but the general concept of just not eating it so you're going to develop sensitivity to it that's not going to happen. That's not how the immune system works.

Right.

And there's plenty of food proteins that have similar... enough structural similarity to gluten with other types of food proteins and grains. This is a little bit of an exaggerated claim based on literature I think he's referring to.

Yeah, or she.

Oh, she.

The kid already has symptoms to it.

Yeah, I mean they have symptoms to gluten do not give them gluten.

**Right. Okay. Do mast cells cause adrenalin do mast cells cause anxiety? Affect anxiety. Sorry, affect anxiety.**

Yes, mast cells can cause anxiety, so here's the thing too. Well we know for sure there's four histamine receptors, H1, H2, H3 and H4. There's more but there's one that discovered so far. Just like with GABA they first found GABA A and they found... now there's like I think 26 different GABA receptors [crosstalk 00:47:59] But when you look at how we all function in our own Gene uniqueness, some of us could have exaggerated H1 reaction. So let's get back to receptors, some of us have genetically H3 receptors that have a greater response when they get... when histamine bind to it.

So some people are going to have... they're going to be prone to... for example if their H1 and H4 histamine receptors are genetically more active, just a little bit histamine load can cause severe skin reaction to them and maybe not for someone else. It may not be the total histamine load but their genetic susceptibility to amplify that H1 or H4 receptor. Same thing with the brain, if you have a genetic susceptibility to having greater H3 histamine three receptor amplification, then you're more prone to things like anxiety if you get a histamine reaction.

**Okay. Mariana, "How do I know if the body is Th1 or Th2 dominant if diagnosed with Hashimoto's MCAS and CIRS?"**

Chronic Inflammatory Respiratory, Mast Cell Activation Syndrome and then Hashimoto's. Okay, so you're dealing with a lot. First thing make sure your diagnosis are correct, that's a lot. If you [crosstalk 00:49:22] well, Th1, Th2 dominance and here's the thing it's sometimes clear and sometimes it's not clear. There's different ways to measure it. One of the ways to measure it is to do a blood test to look at cytokines or proteins that T helper one cells or T helper cells Th2 cells release and then that can give you a clue if one side is common or other but it's really the least effective way. The most effective way is do what's called the cytokines stimulated T-test, and this is where you take in the lab antigen presenting T cells and you expose it to an antigen like typically pokeweed mitogen, and then you see what cytokines are released and that gives you a clue of how they're primed. That is a test that's not commercially available right now.

It's it used to be, but it wasn't very popular people [inaudible 00:50:13] the labs are doing it, stop doing it, but it is used in research studies all the time. If you have Chronic Inflammatory Respiratory Syndrome, Mast Cell Activation Syndrome and autoimmunity

you're going to be all over the place. I don't think you're going to get clear Th1, Th2 response window. So that's the best I can answer your question.

**Okay, so Natalie is saying, "You've covered histamine reactions like skin, breathing. What about tinnitus and hot flashes after consuming histamine rich foods? Many like myself have those as well."**

Sure.

Tinnitus and hot flashes.

So if you have tinnitus from histamine that probably... so histamine is an excitatory neurotransmitter, and if you have degeneration in any area of the brain or injury in the brain, when you increase your excitatory neural transmitter load then those symptoms can come out. So it's just like people that consume MSG, some people consume MSG, monosodium glutamate that's also an excitatory neurotransmitter and then there're different reactions. So people consume MSG and they get dizzy and they get nausea and disoriented and vertigo. Some people consume MSG and they get tinnitus, some people consume MSG and they get severe anxiety or mood swings. Some of them consume MSG and they get bright lights, or visual scotomas or things that happened to them. So wherever their brain is already not efficient or injured, is where symptoms come out. So if you have tinnitus and you've got some degree of injury to your auditory receptors, your organ or your auditory cortex and histamine is activating that. So in a clinical setting when I do an evaluation and hear something like that, that clues me into where areas of neuro degeneration are. So in areas of the brain that have neuro degeneration, their cells are unstable and they activate very, very quickly with any kind of stimulus.

So if you're having reactions with histamine to tinnitus, then that suggests you may have some degenerative change that rose the other symptom, I can't remember.

I'm on the next page. Tinnitus...hot flashes.

Hot flashes can be really to just autonomic centers of the brain as well, where you're controlling your hypothalamic thermoregulation centers. So if I ever heard that in history, I'd just be worried about brain health, brain regeneration, if any of these underlying things are there and maybe digging into that approach a little bit more, but histamine is going to cause a diversity of symptoms because we have histamine receptors all throughout our body, and where you see symptoms where people have histamine loads is a clue to the integrity of those tissues.

**Okay. George is asking, "[inaudible 00:53:04] increasing my anxiety due to the L-glutamine in the ingredients, should I stop taking it for leaky gut?"**

If you have an adverse reaction to any supplements you stopped taking it, but let me explain something. There's a theory if you take on L-glutamine it's going to activate L-glutamate and now L-glutamate excitatory, that is not real. That is internet mumbo

jumbo. L-glutamine is not going to convert to L-glutamate in the brain because that's not how the system works. We have pathways within cells that convert glutamate to glutamine and glutamate back glutamine, that are tightly regulated, has no influence by oral ingestion of glutamine. So beware of the completely inaccurate information that taking L-glutamine is going to cause glutamate excitotoxicity issues and glutamine activity. That's people who read something and look at a biochemistry pathway but really don't understand biochemistry and how [inaudible 00:54:01] enzymes work and how modulation of glutamine and glutamate work. Oral glutamine intake does not immediately cause you to have excess glutamate. Anyways-

**Okay, this a little off topic but interesting. Jacqueline asks, "Why might a child with ADHD be calmer on antihistamines? Could it be excess histamine?"**

Well, histamine is excitatory so why my child with Attention Deficit Disorder.

Yeah, ADHD be calmer on anti-histamines.

Well, he could be calmer on anti-histamines possibly but it may not be related to histamine mode. So, that's the key thing. It's anti-histamine and histamine is excitatory neural transmitter. Most people that take an anti-histamine do have some degree of sedation and their brain calms down and have less function. So it's with... many kids that have Attention Deficit Disorder they really have areas of the brain that [inaudible 00:54:50] other areas that then lead to hyperactivity. So taking an anti-histamine may just be relating to directly impacting those brain receptors, but not really due to histamine load. When you're really worried about histamine being a physiological problem, is when you're having direct symptoms associated with things like skin irritation, skin redness, sinus congestion, wheezing. Those are bigger clues to really think about histamine issues. Now if he had those symptoms as well as [inaudible 00:55:24] blocker and his brain function improved, then I would say yep histamine overload issue. And then again look for triggers, look for things that cleared out, look for things that amplify that histamine response, go down that pathway but I'm not sure if that's certain in your specific case.

**Okay. [Viera 00:55:44] is asking, "can allergies ever be cured?"**

Can allergies ever be cured? So there is some research that low dose antigen therapy in published literature has corrected allergies, actual allergies, IgE responses. So you might want to look that up and if you're interested in the science just go to National Library of Medicine Pubmed.gov, just type in low dose insulin therapy and there's lots of literature there. So for some people it works very well. Some people have no effect, I think the best thing to do is to improve your immune tolerance and then do low dose antigen therapy, just like if someone was doing fertility treatment you want to get them as healthy as possible before they get fertility treatments so they have the best chance of getting pregnant. But yeah there are ways that allergies can be actually resolved.

Okay. Elizabeth asks-

By the way you can't treat allergy with leaky gut. Leaky gut deals with food sensitivity not necessarily with true allergy.

You cannot.

Cannot.

**Okay, thank you. Elizabeth asks, "Is it possible to have just an overexcited limbic system after lots of stress on your body and have reactions to any type of food, drug, anything put in your body like anything?"**

Yes. So you could have... so there's an area of the brain called the limbic system and limbic system is where you have your fear, anxiety, stress response. It's the area of the brain that actually changes the structure and morphology with people that have Post Traumatic Stress Syndrome for example. That their actual receptor sites activate for a longer period of time, they call that longer potentiation then the receptors become more sensitive to different triggers. So when people actually develop what we call PTSD, there're actual changes in their brain receptors and their brain structures. And at that point anything that can bind and activate them like histamine which is an excitatory neural transmitter can make things worse. So, if you have a PTSD brain and now you have histamine intolerance issues, that's a pretty bad combination. You can definitely to be very aggressive in trying to get your histamine load down in that scenario, because we have receptors that are so reactive to that increase load.

**Okay. Mariana asks, "Is there a connection between high total cortisol, low testosterone and MCAS?"**

There's no specific correlation of any hormone pattern to MCAS, we just know hormones have an impact on the immune system. So, that hormone pattern... any hormone pattern isn't going to be specific to histamines mast cells, Mast Cell Activation Syndrome.

**Okay. Peggy asks, "Do you ever use NeuroQuant to help clinically or study for research?"**

NeuroQuant is just the way that people are using imaging to look into cell volumes of the brain if you're familiar with it, to determine like early neuro degeneration and so forth. NeuroQuant has a lot of promise in helping us understand imaging better when we compare it with people the same age group. It's being already investigated in lots of research studies, so I think it's a useful tool. It's also something more... it's still a new form of assessment. There's lots of debate on the interpretation of NeuroQuant. So I think NeuroQuant is great, it has a lot of potential, it's just going to get... this just needs time to mature, so we can actually determine what's overstating a response with volume and size compared to someone's age group, and what's actually accurate and... but it's a very great technology to have.

**Okay, Didi's asking, "Is there such a thing as a rebound and amplification of histamine intolerance when coming off anti-histamines?"**

When you come off anti-histamines you can have different kind of rebound phenomenon where things get worse because your immune system is already active in other areas, and as you go off you sent it to trigger it and promote it. Rebound phenomenon is also... happens when people go on elimination diet for a period of time. They introduce a food and they get a severe reaction to it, just because their immune system has had a chance to really rub up and react against it when that happens. So yes it is possible, if it happens you're just going to get through it and then know that's part of the response.

**Okay. Chrissy asks, "What is the difference between glutamate, glutamine and glutamic acid? [inaudible 01:00:20] very clearly please."**

Okay. The difference between glutamate-

Glutamate-

Glutamic acid-

And glutamine.

Glutamine.

Yeah, here we go.

Well, they're all structurally different. They all kind of sound similar. They all have an H3 group. They're all very similar that way. Glutamine is a supplement in the food compound that's helped with energy sources in the gut. Glutamine is an amino acid, helps with the energy fuel in the gut, helps support the gut when people are trying to do leaky gut protocol [inaudible 01:01:05] all the time. Glutamate is an excitatory neurotransmitter and there's a pathway between glutamate called glutamic acid, and there's an enzyme called glutamic acid decarboxylase which converts it to glutamate. So they're all different, glutamic acid and glutamate are just a conversion apart. So they are part of a pathway that involves an enzyme called glutamic acid decarboxylase, but at the end of the day they're all different.

Okay.

They just sound the same.

Okay.

Okay, well thank you for joining us today and thank you for all your questions. I hope you found some information useful and please check out our website Dr. K. News, D-R-K-N-E-W-S.com. Join us on our Facebook page and thanks again, I appreciate it.