Mast Cell Activation Syndrome and Long Haul: what you need to know Transcript

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Introduction to Mast Cells and Long COVID

– So welcome to another call them additions. I like to call it an addition of overcoming long covid and chronic fatigue. And today it's uh always a delight. But this one is a special one.

Talk to Dr. Tania Dempsey about mast cell activation and long haul and chronic fatigue. We're going to touch a lot of interesting subjects. Dr. Dempsey has a practice in purchase New York. I believe that's the aim practice?

– Aims center for personalized medicine. – Aims and she works with Dr. Larry Afrin who has been responsible for teaching most of us that there's more to mast cells and rashes. And um I always think that Dr. Dempsey has done a lot to teach the rest of us that it's all connected.

And especially so with that on that note, Dr. Dempsey, how your first long covid patients? When did you start seeing them? And when did you start noticing that there was more afoot than this?

Quote unquote long covid, – You know, pretty early on. Actually, I had a few patients in March of 2020 2020 right? We probably have some patients earlier.

But in March, uh both my parents got that first wave of Covid uh my best friend and then some several patients and you know, we didn't know we didn't have any resources. We did not have any understanding.

We didn't really understand like what, how we were going to get these people through this right. And so some of the patients had a fairly uneventful course and some patients had a very eventful course um requiring um hospitalization, oxygen antibiotics. We were, you know, we were sort of throwing a lot of different things that people and what I noticed is that a lot of my patients because I have a mast cell practice, right? I specialize in focus and vector borne infections and chronic fatigue syndrome. So my my practice is already, you know, patients who have some kind of immune dysfunction.

And so there were these patients early on who had lingering symptoms. You know, they got covid. Well even some of them didn't couldn't get testing. It was crazy time very early on in 2020 we thought they had Covid and some of them would just have, you know, weeks of trouble breathing, shortness of breath fatigue.

The fatigue was always, you know, a big part of this. And so very early on, we knew there was something about this virus that was different, you know. And then, you know, certainly at the, during the second wave um at the end of 2020 and early 21 it became very, very clear that this virus was different and that we were going to see an epidemic of of chronic illness related to it. – And it's funny, patients won't understand this, but I'm almost jealous because, you know, we're in in Marin county and Marin county locked down so hard.

There was nobody on the street that I did not see COVID patients until like January of 2021.

Early Long COVID Cases and Immune Dysfunction

I mean it was like another world. I would be listening every day about the news from New York and the East Coast and and in L. A. But Marin County in amongst our patient population, they just locked down so hard. It was it was it was only you know, in the following year when I started to see the long code with people start showing up.

But then again most of them were from elsewhere. My patients just because they locked down. It didn't. And so your experience is really, it is just so reminder of in a way how different the the experience was in America actually depending where you were being worked right in the beginning it was. – And I would I'll say what I think is interesting is that you know, I mentioned some of my patients had Covid and you know have have had struggles. But I will say that I actually don't have any patients that I know of that were patients of mine who got Covid who

then went on to have long haul syndrome. And I think, but I've certainly seen lots of patients you know consult with me and I think the key was that they were already being treated for for immune dysfunction, mast cell activation syndrome.

So even though some of them had prolonged some prolonged illness, they didn't really turn into long haul thankfully the majority or maybe all um because I believe that we have been doing things to to maybe you know, support them better. And a lot of people out there didn't have that support. – I think that's true.

I mean, again, just from the experience that our patients did not, not many of even the ones who got covid they were they were taking, you know, generally things that modulated their immune response and that prevented this unbridled immune response from getting started and from carrying on again, we don't have enough numbers. But I can say, yeah, our patients did not get long covid. I yeah, that is true. You know, and so the the the what you've seen because I think that what's so important is that I remember right in the beginning there were reports from England. I mean, one of some of the doctors there were saying like, you know, oh this is mast cell activation, you know that they felt that long covid was. And I think it's more complicated than that, but maybe just let's step back for a minute and tell people a little bit what mast cell activation is.

– Yeah I think it's important to start there and sort of evolve into the but but the reality is that mast cells are part of your immune system there, your first line of defense against the environment, right?

Your body lives smell, you know, breathes in lots of things uh swallows lots of things that could actually be dangerous. So your mast cells are in these locations all over your body ready to defend and they're in the respiratory tract.

So if you breathe in a virus there there um if you breathe in a toxin there there there in the G. I. Tract and they're in the skin they're basically in all tissue and all organs. Everyone has them.

And I like the way I like to think about it is if you have normal mast cells okay they can react to things that are foreign. So you get a virus let's say covid you have normal mast cells, your immune system is normal. You get covid and these mast cells see the virus they tell the other immune cells come on help me out here and they all you know kind of you know pitch in and and kind of helped to clear the virus and then after this happens um everything sort of resets the immune system resets.

You know one of the ways mast cells defend us is actually they they explode they d granulated they produce these Granules of different chemicals, inflammatory mediators and they explode and that's how they're trying to kill let's say the virus and in a normal person the mast cells will do that and and it also they do other things too.

But those mast cells but they return to normal and they wait for the next offense, right? Something that's going to attack. But in people who have a syndrome, mast cell activation syndrome, they have what we'll call abnormal or aberrant reacting mast cells.

So these mast cells are not just ready to are primed to react to the virus but they may even at baseline be reacting to things that they shouldn't be reacting to.

You know maybe a food, maybe a medication ascent. There's there are all these things that it's getting these signals crossed, essentially reacting releasing these chemicals. These chemicals are inflammatory.

If you have this reaction let's say in your respiratory tract you might have asthma, trouble breathing, wheezing. The mast cells are reacting in the stomach or the G.

I. tract, you might be nauseous, you might have diarrhea or constipation. If they're reacting in the skin you might have hives in the nervous system, you might have um uh numbness, tingling, dizziness, migraines. So the point is that that that some people who have these abnormal mast cells, they are already reactive.

Then they see something like Covid. So they're already primed then they're really primed and now they're seeing

this virus in a way that is just you know a little bit more exaggerated.

The response is more exaggerated.

What Mast Cell Activation Syndrome Is

The response to the rest of the immune system may be more exaggerated. And patients with mass cell activation syndrome will never return back to normal after they're done with Covid they or anything else.

The mast cells will always be abnormal but they'll go back to maybe their baseline hopefully and not a higher baseline. So I think that what's important about national activation syndrome is that it is really a condition that is it's a multi system because it can affect every organ tissue in the body and it's inflammatory.

And again it can present to be problematic for infections like Covid, but it's problematic if you're reacting to the environment abnormally. They are, environment unfortunately is very toxic and you know at some point our bodies have to kind of deal with our environment. But if patients who have this are are constantly fighting, you know, they're they're in this constant state of everything around them in them is poison. And so I hope that kind of explains. – It summed it up just that these mast cells are too easy to be triggered.

You know, I always compare them to like an irritable child. You know, we want your mast cells to be adult. Like and instead you've got a five year old that's been up too late. You know, and it's just yeah, because and and that's what makes it so frustrating because the many of the things that they're reacting to are not inherently bad for us, they just the mass cell becomes confused and everything becomes the enemy and what people I think need to understand is that you've got different types. Maybe you want to speak to this a little bit different types of mast cells in different parts of the body?

Because that's what most doctors think about mass cells just in terms of a rash or an allergy or acute allergy, you know, and and I think that's where people get get disappointed when they go to their physicians and they go walk in and say I have mast cell activation. And the doctor just kind of like, you know, eyes glaze over and goes, well you don't have mass psychosis, which is a cancer and you're not losing. So what are you talking about?

So I mean can you just just how can people talk to their doctors? Maybe I just realized that that's something that that is frustrating. I think sometimes when people listen to these summits, they come away with information because we're so used to talking about it and we forget what it sounded like the first time we heard it from a patient.

So is there any way you could think that people could begin to have this conversation with a doctor who is not on board yet? – Well, do you want me to cover the first question about the mast cells or do you want me to cover? – Okay, I'm sorry.

You've got me there. I don't know the first question but for the first one, – I'm gonna do the first one then I'm gonna do the second one. Okay, Okay, so mast cells again, they're your line of defense for the environment, right? And I didn't mention that mast cells are really what's responsible for allergy. Now, allergy is not mast cell activation syndrome. Allergy is really that you have these mast cells in the respiratory tract let's say. And let's say you have an allergy to pollen and you breathe in the pollen and you're allergic to pollen.

You have these antibodies that are against pollen trying to fight pollen. And those antibodies actually bind to the mast cell. There are these like antennas receptors we call them and it binds to the mast cell and says bad pollen is here and it sends that signal that the mast cells have to explode.

And one of the chemicals that mast cells make is history. So you have a release of histamine. And people who have allergies know that when they have this release of histamine in the respiratory tract they get congested, they get runny itchy eyes and they get they might have asthma or trouble breathing.

They may get a rash if it's in there on their skin. So so masses are involved in that, right? But but in allergy it's really just that it's an allergic response and the rest of the time the mast cells are quote unquote normal, they're not

reacting abnormally to anything else.

Everything is just allergy. But in mast cell activation syndrome, we're talking about mast cells that are other parts of the body that are releasing different types of chemicals. Sometimes it's histamine, but there are thousands of chemicals that mast cells can make.

And every part of the body might have different mast cells making different chemicals and causing a different response inflammation is by far the biggest response.

So inflammation in the, you know, respiratory tract obviously is gonna cause these symptoms. We discussed that look like allergy. Some patients have this allergic like reaction, but they go to the allergist and they're told they don't have an allergy.

So they can't the allergy tests are normal. So that's impossible. They're, you know, they're really not allergic to anything. So they're imagining their symptoms, right? But um but really it's an inflammatory response, it's not in that case, in their case allergy, but it's it's it's a process.

It's still sending a signal to the mast cells. Bad. Something's bad. Let's fight again explode. Degranulated, we say, releasing these different chemicals causing inflammation.

So the symptoms can be different in different parts of the body. And I think that's important to note. And I think that one of the things that's difficult for patient sort of tying it into your second question is that again, if they don't have typical symptoms of what doctors were taught related to mast cells, then they're discounted, right? If you have anxiety, migraines, um, joint pain, you know, all these different symptoms, stomach pains, nausea, right?

That's not on their radar, that's not on the doctor's radar, right. The doctor's not thinking, oh, mast cells could be involved in all those things. They're thinking patient has a stomach problem.

The patient has migraines, the patient has an anxiety problem. So, I'm gonna send them to the psychiatrist and all of a sudden the patient now has this multiple problem list. But it's all they're all related.

They're all related. And so, so how do we get, how do patients talk to this difficult question? Right. I think one of the things that I really encourage patients to do is to is to come armed with information. Right. There's literature, you know, I published God reference published, we've published a lot together.

There are lots of literature, there's enough now that you can print those articles out and and and or send the links to your doctors and let them start to read and start to understand that it's not a made up disease. We have medical data, we have medical, you know, support in the literature credibility that that respects this.

You know, this diagnosis, but it's difficult. You know you can't change every doctor's mind about this, right? But I think that helping them understand, you know, there's one article we published looking at how to diagnose mast cell activation syndrome. And in that article there's a huge um, uh, depends on the all the symptoms, you know, which is just, I mean, hundreds, hundreds of symptoms. You know you could print that out and say look you know look I have this one this one this one maybe this expo is it?

You know I think this is one way I mean I have to think about this more but you know. – It is difficult and I think just armed with the idea that when you walk into uh the average doctors office and it's just knowledge based.

How to Discuss MCAS with Doctors

I mean to be fair it's we're taught you know we're taught a whole bunch of stuff in medical school and unless a new drug comes out that has enough money behind it to teach all the doctors about something new they don't learn you know because you're running on what you already know and um when it comes to something like mast cell activation um no drug company has yet got on the bandwagon. So doctors are still operating under the idea that mast cells either are involved with allergy and in the definition that they're taught in medical school is allergy

involves I.

G. E. This immunoglobulin that is specific that that protects your body to as as as Dutch deputy was saying like you know pollens and extraneous extraneous things from the environment. And if the I.

G. E. Is not elevated or you know or your your blood tests for I. G. E Allergies aren't positive then they discount the idea that mast cells have anything to do with anything.

And that's so just be aware that you're gonna run into that and just smile and I said the good thing is um yeah now doctor Dr. Dempsey and Dr. Afrin and others have articles that that are available and and and readable and they're not that intimidating.

And if you have if you if your doctor has no interest you really have to find another doctor fortunately. But so and when it comes to long haul Covid what has been your experience with treating people with with some of the mast cell interventions. – You know again I think that the MCAS is a piece of that puzzle of long haul Covid there's no doubt in my mind there's some literature now people are starting to look at it.

They're starting to see that massive targeted therapy is helping some patients. I'm the first to say like that. It may not be the only thing that explains long haul covid. There's so much more.

This is such a complex problem. And so I hope that research continues and all these other realms you know. But the part that I know that I can help patients with is to help to modulate their immune response.

So if their mast cells are dysfunctional and they continue to be dysfunctional after Covid. And they don't reset to normal um they're going to be in an inflammatory state.

You know they may just have fatigue as their main symptoms, they may have breathing issues. That's the one that we see very very commonly. They may have G. I. Issues or persistent gi issues um and a host of other neurologic issues etcetera. Every system can be involved of course.

So you know we're using we're taking these patients and we're using mass cell targeted therapy where we are first testing them and one of the things and I think this is something that we will have to publish is first is we're proving that these long haul patients have mast cell activation syndrome. Okay. And I can't say 100% because the testing is difficult and sometimes we can't you know can't get the answers.

But large percentage, you know, we're probably at about 90% have evidence of mass cell dysfunctional mast cells and mast cell activation syndrome now.

Does that explain all their symptoms? Maybe You know and in some cases I think it does in some cases it's so much more complex they have other things going on also maybe affecting the mast cells but also affecting other parts of the immune system.

So but if I prove that they have MCAS I'm going to go through, you know, my protocol of massive targeted therapy trying to figure out what's the right thing to start with whether it's pharmacologic whether it's nutraceutical, whether it's lifestyle whether it's limbic retraining, we can go through all these different things that I do, but it's but I have found that to be incredibly helpful for a lot of patients. So I know it's a piece, you know, I'll say, I don't know if I should bring this up here, but you know, I think that some of these patients have other things.

They've been sick actually probably for a while before they had covid. Many of them say that they were perfectly healthy before they had Covid. And many of them say that, you know, we see athletes, you know, professional athletes, you know, perfectly healthy and then they have Covid, well, when we take a history, there's actually a flavor of stuff that was going on before, but they were highly functional. And so for whatever reasons, they were able to sort of control this immune dysfunction into covid sort of spotted on out of control. So a lot of those patients not only need massive support and to get them through this, but it's looking at the other stuff that they may have been affected with as well, maybe they have a history of Lyme disease.

They didn't know about another infection. And this was just Covid was like the icing on the cake and it just was not bad analogy, but, you know, it's sort of just brought it all out. It wasn't definitely not anything, but you know what I mean. So, – I mean this is what you're bringing up is I think a crucial point that in this series where you addressed several times, but I think it has to be emphasized over and over again is that, you know, you never, not 100%, but so many people who thought they were healthy.

They were, but they had their bodies were working a little bit over time to control an underlying source of inflammation. That and you know, because chronic, we all have it basically, chronic inflammation in my mind is how we all wind up eventually dying.

MCAS Treatment Approaches for Long COVID

– Actually, that's true, that's right. Yeah, accumulation of inflammation over time, over time. – And so we all have it and, but so many people, especially high functioning folks managed to push through it, you know, they don't because it's you know, maybe they're not getting out of bed with the Enthuse he has than they did before, but as soon as they hit the ground they're going, you know, I mean, it's it's subtle and again and again, we see the chronic how that, you know, that mono that you that lasted a little longer when you were a teenager. Your B cells haven't quite for your t cells actually haven't quite kept that in check. And all it takes is an infection to decide, you know, to lose the control. I think that's one of the things, I think I just want to point out to people and what what you the point that you've been making over and over again is that mass cell isn't everything, but because mast cells engage almost all the rest of the immune system, they're a good indication of immune dis regulation, you know? Yeah, you know, they're there, you know, you can have a T cell that doesn't work right, or a B cell that doesn't work right, or even some neutrophils that are a little off. But at the end of the day, the mast cells are the one that kind of coordinate and are your first responders to almost everywhere in the body and that's what makes them have so much noise.

But so one thing I just like to go back is you talked about the neurologic findings and how do you tie in the neurologic changes that people have? You know, the cognitive little brain fog and you know, and when it's mild it's easy to write off too. I'm just getting older, but when it gets a little more noticeable people go, oh, this is an issue. So how do you tie that in with mast cells?

– You know, I've actually given quite a few lectures on this. I've spoken about it, another podcast, but as I mentioned, you know, mast cells are everywhere, literally every tissue in the body, right? Every organ.

So your nervous system is covered with, I think about it. Like if this is a nerve, you know, nervous, like a wire you have mast cells surrounding that nerve the whole way you have all these mast cells in the brain.

And so you can imagine if the mast cells activate and they released this these inflammatory chemicals these these cytokines chemicals mediators. They will send a message to the nervous system there.

So close there there, right there. They send a message to the nerves. They may send a message to there's another immune cell in the in the brain called the astrocyte. They might send a message there or the microglia. They're sending a message there and and those cells are sending messages back to the mast cell which is maybe causing more inflammation.

But it's this sort of vicious cycle of inflammation. The signals are bad signals. They're they're leading to more inflammation. Now, if you have inflammation in the brain, right, it's going to affect your cognitive ability. It's gonna affect, could affect behavior, could affect mood in psychiatric neuropsychiatric symptoms.

In the peripheral nervous system. You know, a lot of neuropathy. Small fiber neuropathy of various kinds. So the nerves are everywhere. I mean the mast cells are everywhere.

The nerves are and the mast cells are sending these aberrant signals to the nerves. The nerves are then releasing their own set of of signals and neurotransmitters inappropriately.

And then that's telling the mast cell okay keep doing that and then again you get into this very vicious cycle. So um so the neurological effects because again the whole your whole body is covered is you know nerve the nerves run everywhere, right? Different types of nerves.

The mast cells are all there. And so you can imagine that that could lead to you know, significant neurologic manifestations in patients. So I have to say that's probably the number one thing we see.

And I would I would lump fatigue actually kind of into that neurologic um Symptom because many of those patients have fatigue that they describe as it's a combination of brain fog fatigue. So to me that's – I know I mean you know for so many people I think the best way that they understand that fatigue is how how we all feel on that first or second day of a bug. You know any kind of cold.

It's just like where you know you can tell people what you know off the top of your head but if you have to dig further than the top of your head there's nothing there.

And that's what brain fog is like on a lot of levels. And that's what you said, that's the inflammation and we get there lots of different ways. But when the mast cells are activated.

Yeah it's one of the problems are there particular you know of the anti histamines and mast cell stabilizers and the as you say the nutraceuticals are there particular ones that you have found are more helpful for let's say brain fog fatigue or just people with long covid in general. Or just…? – Such a good question.

And unfortunately the answer is no because there are so many different types of mast cells. Every person has multiple types of mast cells making different chemicals.

And then my mast cells are gonna be different from your mast cells. And so every patient is so different. And because the receptors on their surface the chemicals that they're making are so different.

Unfortunately we're at the point where we were kind of it's a lot of trial and error eventually I think what would what would really change this is if we could do genetic testing on the mast cells and then understand what these mast cells are really making.

And if we could do a test on everyone and and then we can target it directly but that we're not there yet for that. So I think what I do usually is I just start with some of the basics right? And some of the basics are are things that that can make a big difference. And that's why I think it's it's important to start their some patients are gonna require more trials and and get a little bit more aggressive with therapy. Some patients we're gonna hit it you know the first time I think generally speaking um I'll tell you a couple of things before I even talk about drugs or or just general vitamins that are that are for histamine and and mast cell stabilization. Vitamin D.

I want to I want to talk about vitamin D. S. Number one thing that I do and sometimes it makes a huge difference. Mast cells have vitamin D receptors on their surface. If you are vitamin D.

Deficient, that's a signal for the mast cell, something's wrong. You know? So if their vitamin D deficient, the first thing I'm gonna do is try to figure out how to get vitamin D into them as a way to stabilize the mast cell. So so that is like number one and then of course there are other things that I'm doing with the patient's right because there's always a lot of other issues that sometimes come up. But the next would be you know sometimes it's as simple as you know an over the counter and history.

We call them H one blockers. You know there is clarity over the counter, There's Claritin, Zyrtec, Allegra and Zeisel. And those are like the we'll call them the second generation.

The first generation are like more sedating and making more sleepy. That's Benadryl that's over the counter. And and so patients can trial and when I walk them through you know one at a time.

You know small dosage. There are different formulations of each. You know what I find with them. Cast patients

that sometimes they're sensitive not to just the drug but the exit P. Ints the fillers that are made you know when you read a label you grab a Claritin there are few different Claritin's on the market.

You no one will have lactose, one will have um mannitol, one will have magnesium scary. And sometimes patients do well with one brand and one formulation or another.

So we walk through that and we you know we work through try the trial and errors. You know. But generally I think it's not a bad place to start especially if they have respiratory symptoms or more allergic type symptoms for the brain fog. It's very very hit or miss sometimes.

Yes an anti histamine can can help. Sometimes I have to move on to the next line of things. There's a church one blockers I mentioned there's a church two blockers and those are histamine blockers that are mostly in the G.

I. Tract but somewhat elsewhere in the body. And those are drugs like Pepcid Tagamet, the old Zantac which I think is coming back. Those blocks different history histamine receptors and you know might help if a histamine is the issue. It might help you know some of the symptoms too much histamine in the brain from the master. Maybe these will help.

And then you know there are these these other drugs very often I'll use Chromelin. Chromelin is a really interesting drug and I and I say I will say that I have some really great responses. I have a handful of patients who have had amazing responses to Chromelin for brain fog and cognitive issues.

And it's interesting because Chromelin is a drug that is not absorbed. So it's a liquid and it's a prescription, you put it in water and you drink and the teaching and if you look at the pharmacologic you know information it doesn't get absorbed into the body. So it just acts on the mast cells in the G.

I. Tract. And so you know some of my patients when I started giving it to them for let's say G. I. Symptoms related to MCAS They would start to say that their anxiety was better. Right?

And you think well how is that possible? Right. So what's interesting is that mast cells communicate with other mast cells everywhere in the body in addition to communicating with the rest of the immune system. So the mast cells being calmed down in the G.

I. Tract sending a signal. You know, we also make a lot of neurotransmitters in the G. I. Tract. Maybe that's playing a role. Maybe it's sending signals to the rest to the nervous system or I calm down.

So maybe that's why anxiety gets better or brain fog gets better. But it's interesting that's an interesting drug that I sometimes see like when it works it's it's really really nice um doesn't work for everyone.

Kitada often is the other drug that I'll sometimes find be incredibly helpful. Sometimes you have to start low and slow. Same with Chromelin. It has to be compounded.

It's not commercially available as a pill only as an eye drop. But is a mast cell stabilizer. Chromelin is a mast cell stabilizer. Um And but they just work differently. It's sort of like what is there how is their mast cell going to respond to this drug? How is it going to bind to the drug?

What signal is it going to get and how it's going to calm things down?

Neurologic Symptoms, Brain Fog, and Fatigue

So those would be like first line pharmacologic you know sometimes we use corset in course often is as a natural anti histamine, vitamin C. Is a natural anti histamine corset.

It also stabilizes mast cells. There are lots of other things. I think it's just sort of like what I think the patient is going to respond to. Maybe it's not gonna be right. Maybe again trial and error.

Some patients are more accepting of the of the pharma pharmacologic stuff and some are less accepting maybe want to go a different route. There's a there's a supplement that is an enzyme called di amino oxidase which which is an enzyme that breaks down histamine.

And so some patients find that if histamine is their issue and their histamine bucket is too full. Then they take this enzyme and it helps to break down Histamine and they and they feel better and sometimes that histamine issue is related to food or something in the G. I. Tract and sometimes they take that and it's breaking down histamine in their gut and then it's helping their brain fog.

So it's just incredibly complex, fascinating. We're still learning. I still I still learn every day. I learn something new from my patients. They teach me because we don't know everything we need to know for sure. – Yeah. And I think what I want to emphasize to people is just um you know, not giving up. You know, I mean like you don't wanna, on the other hand, you know, when you first get ill, there's lots of possibilities when you look at, you know, you listen to some it's or read things on on on lists and um you know you everything sounds like you sometimes you know, I always tell people that in the old days one man's, one man's Bartonella, you know, list of symptoms for Bartonella looks just like another man's list from babesia, you know, so you gotta be careful.

You don't fall in love with the diagnosis just because the list of symptoms fit you. But if you're working with the doctor or practitioner and you really have good evidence that histamines or that mast cells are playing a role.

Give yourself some time. Don't give up just because you took you know, one or two anti histamines and they didn't work because you gotta give it time and remember you might need to get them compounded if you just keep getting the same if you get really if you feel really bad after you take these you know or they flare your symptoms getting compounded.

It's rare that the drug itself is making drugs have side effects. But these guys generally don't have many um you know when they're in their pure form I mean you know it's just everybody's different but I have to have faith and keep trying.

But so this is so that's this is like you know that was a great overview of of the mass of of the pharmacological approach to mass selling maybe we have time I might want to do a little bit more on if maybe the non pharmacological mother.

But before I get there I want to I want to have time for you to talk a little bit about. Another subject that I think that you you've done a lot to teach people about is the I don't like to call it E. D. S. I think it's more just you know kind of lacks connective tissue is my way of thinking of it. But you know this is something that we have seen for ever since actually going back to Doctor you know in my world.

Dr. Schumacher was the one who taught us to look for like people with limbs with their with their upper limbs longer than their than their height and just for the hyper flexibility and this was he didn't know why but it was again he just saw this and and and we did too.

I was noticing once he told me to look I have to admit I need a little help. But I noticed that all my patients, I mean they're they're hip flexors, not all of them but the vast majority of people who hadn't done anything in years had hip flexors. Like they were doing yoga.

You know like if they didn't have bad arthritis it was surprisingly at their range of motion. So talk and and that see that and we see that connection so talk a little bit about this thing that people are calling E. D. S. And mast cells how it all connects.

– So you know EDs. Or Ehlers Danlos syndrome. Ehlers Danlos syndrome is a group of connective tissue disorders. Some of them have genetic markers that you can test for.

What we're talking about here though is really what we will call hypermobility syndrome. Sometimes it's known as hyper mobile E. D. S. Because E. Ds. Again it's a huge huge sort of umbrella term with a lot of other disorders that

evolved connective tissue but in our patient population this hyper mobility is really significant. Now. Think about what I've been saying right, mast cells are everywhere. They're an all tissue.

Well they're definitely in connective tissue. And mast cells that are normal right at baseline, they're, you know, they're just hanging out there just waiting.

We're talking about patients who have dysfunctional mast cells at baseline that are releasing these chemicals very often um to very little stimulus. And if they're these mast cells are reacting at the level of the connective tissue, you can imagine that this inflammatory cascade is now damaging the connective tissue on some level. And um and maybe and so in the majority we're talking about it's the hypermobility. We might see, well, let's just be clear. There are mass cell patients who don't have any connective tissue issues, right?

But there is this association that we're starting to see that many patients have some level of connective tissue disorder. And I will say that I certainly have patients that are on the opposite end of the spectrum, they are stiff, stiff tight beyond what you would expect. And I think that's actually on the same spectrum of connective tissue. I think in them, the mast cell mediators are causing a different um inflammatory response.

And so maybe it's scar tissue, maybe it's something else and it's it's actually contracting versus in some of these patients it's it's sort of making it more lax stretching it out. And so now they're more, you know, limber more hyper mobile. So the association is there.

And you know, I'll add that third piece, The trifecta.

Hypermobility, Dysautonomia, and the MCAS Connection

The other association we see very often is pots or disorder know me or postural or the static tachycardia syndrome. These three seem to go together for some patients. Again, every patient is different.

And so maybe some patients will just have MCAS and some patients will really just have hypermobility. You know, I'm sure their patients out there, we're not seeing them, right? Because you know, I'm attracting a certain patient population, but I'm sure in the general population there are people who are hyper mobile. You know, maybe there are ballerinas who ballet dancers who are um flexible but are healthy and don't have any issue.

But what we're starting to see is that many of these patients who are hyper mobile go on to present with other things that look like more of a chronic inflammatory syndrome which is MCAS. So we're starting to see these connections and that that third piece I mentioned is this dysautonomia which is really like a dysfunction of the nervous system, the autonomic nervous system, you know, your autonomic nervous system is automatic.

You don't think about your heart beating, you don't think about, you don't tell your stomach to digest food, everything's sort of automatic, right? You don't tell yourself to breathe, just breathe automatically and you have mast cells in the nervous system as I said.

And I'm not saying that mast cell activation syndrome is the only cause of this, but it's one potential cause mast cell's get dysfunctional, the level of the nervous system at this part of the nervous system leads to inflammation.

Now this nervous system is reacting inappropriately. And then, you know, you may wind up with a problem like something called gastro paralysis where where the digestion is really slow, the signals are not getting there, that, you know, that the food needs to go down, right? So patients feel full, they feel uncomfortable.

It may present as as pots or postural or the static tachycardia syndrome where they change positions and their heart rate goes up to compensate for the inability to sort of regulate their their blood pressure and they're sort of their their place in space. So these are the things that their patients who have pots, they may not have hypermobility or mast activation syndrome, but more and more we're seeing that many of them do, even if they didn't realize it, we start to see, you know, there's a there's a pots community of of practitioners and patients and so, you know, for a long time they were sort of focusing on this condition, right? But then, but then as those of us

on the outside started to see these patients but also see that they had diagnosed them with the MCAS they started to realize, wait a second, there's this connection, maybe the mast cell is the root of these various conditions.

There's certainly other things at play. There are certainly things that the mast cells are reacting to that's probably spurring them on. Right. I like to I think this is an important point.

It can't just be mast cell activation syndrome though. I I have a hard time thinking that dysfunctional mast cells are constantly dysfunctional and causing this array of of symptoms.

I think it's that those mast cells are dysfunctional and there's a mold exposure. There's an infection, there's some other trigger that really gets them going and then keeps them going until you take away that trigger.

I think that's really the way I'm starting to understand this. – I just yeah, I mean that's one of the reasons that I'm excited to meet you is because I, you know, you agree with my bias, but more importantly, is that you've helped many people about that, that, you know, that mast cells are, you know, you can have, they can have a tendency to be activated, but without a constant irritant in majority of people, that's not going to go anywhere. You know, it's just like this lacks connective tissue if you don't have something that's causing a lot of inflammation, it often doesn't cause a lot of problems, You know, many, you know, it's minor, but when you add inflammation, then suddenly people start getting things like their dislocating their shoulders when they, you know, where they're, they're having problems with their necks that they didn't have without the inflammation coming on, but people don't realize that because you know, we see the body as, as pieces as things that aren't connected and that's the beauty of your work as I know how much you've done to, to, to try to teach doctors how to think that this is a system, you know, it's, you've been, you've been working hard at that, you know, and I, I really, I really appreciate that because it's um, and the fact that you have have actually no written the papers and taken the time.

I think patients have to understand how much extra work that is and how much dedication that takes to actually do that, you know, so, but to tying this tying this up, you know, there there is, like you said, there's so many pieces, you know, you've seen like, you know, the mast cell and the chronic infections. So do you have any thoughts for the future for long, covid and anything that you'd like to see, you know, like where the researchers should go and any kind of like a prayer for the future.

– I'm an optimist. So I would like to think we're going to figure this out. I think that, you know, doing large trials of mast cell targeted therapy in them and like publishing on that right would be amazing. At least would understand.

I mean, what I'm talking about is somewhat anecdotal, right? But I'm a big believer in evidence based medicine. So I want to be able to prove what we're doing. You know?

I think these patients have to be tested. So hopefully that's for the future. I really love to really understand the role of residual viral particles in the body, whether that's what's spurring on the mast cell, probably not live virus, but viral particles. I really like to understand better the um the underlying issues that these patients, like who are these patients who are the patients who wind up with long covid?

And there may this may be a very diverse group and I certainly have a diverse group of MCAS patients, right? Every single patient is different. But I love for be able, I love for researchers to try to figure out how can we can we predict is there anything we can use to, you know, so that preventatively, you know, if we knew who were the highest risk, we know who the highest risk is for maybe getting covid and winding up in the hospital. But I don't think we really know why people are getting long covid. Like, what is it about them?

Again, I think it's immune dysfunction and other things, we have a similar idea about that, but but if we can measure that and we and people knew, you know, that they may be at higher risk. Are there things that we can use preventatively.

You know, again, we're doing this work, some of it anecdotally right.

Future Research and Lessons from Long COVID

Some of it based on stuff that we know, but it would be nice to be able to help people to understand some of these patients unfortunately had very mild covid by the way, the vast majority of long covid patients had mild symptoms in their in their sort of description, right? Most of them were not hospitalized, but they but their immune system didn't stop and continue this inflammatory system.

So to be able to understand that and being able to to predict, I think would be very, very helpful and then and then prevent prevent, prevent, you know, – That is, you know, I said the since I'm an optimist, I like to think that this is in a way, you know, I said the blessing if there is one of of Covid is that it's opened up the eyes of the medical community to this post viral. So it doesn't have to be virus, but they're hung up on it. We'll call it post viral syndromes that have been that have been a problem forever but have been ignored until recently because because the symptoms that are that are provoked are ones that are easily ignored because their blood counts are normal. You know, that is that is the problem.

You know, I'm with you, I'm a great believer in evidence based medicine is just as I'm the people who heard these podcast who heard these summits will here, I'd like to call it evidence bought medicine because without the money it's hard to collect the evidence, you know, and that's what so so my prayer is is to have a way to actually harvest the information that primary care doctors or consultant doctors like we are get, you know, I mean like if just imagine if, I mean if we actually could collect our data and you know, and and have have scientists really and and researchers look at it. I mean it would be very hard because again that I'm going off here, but just people understand what makes medical science so difficult and make it a science is because science likes experiments with single variables and you cannot do that with people. So we're kind of left with with stuff that that still sounds like anecdotes. You just gotta, I mean you just got a lot of them, you know, and and you know, and and it's it's tough but to collect clean data often means to clean out the human piece, you know, and that's why they study mice because it's easy, they're all the same.

So anyway, just for people to understand that, that's why medical research and things that really we care about, which is human health is so confusing and that's why when you look at the stupid studies, which I call the stupid study.

So the epidemiologic ones that look at like, you know, population studies and that's why one population study tells you, you know, eat me, the next one says be vegetarian.

The other one says drink coffee. The other one says don't drink coffee because they're asking the wrong questions and they're getting garbage because there are some people who should eat meat. There are some people who would be better vegetarians. There's some people who coffee is wonderful for.

There are other people who it is, we're different and until we get that through medicine and figure out a way that really smart people can help us do experiments while we still can hold the variability. That's the human condition.

We're kind of, I'm sorry tirade about it's, it's, I love that I want so much to have data. I want to be able to know how to help my patients. But at this point in time, a lot of it is just what seems to work and yeah, so anyway, but prayers to all of us that through the massive amount of money that's being thrown at this, that there's going to be enough really good intentions smart people are gonna get enough money and we're gonna learn stuff and I hope some of it comes your way.

I know you haven't probably thought about applying for it because it seems overwhelming. But you know what you and Larry are doing. And plus with the group that the groups that you work with, that would be a really wonderful service if you could gather some of this because this is a piece, as you say, you know, it's not the whole story but the mast cell activation, long covid chronic fatigue, right?

Chronic line. They're all woven together and thank you for helping us unleash. We've at least some of the therapies. – Thank you. – It's my pleasure. A pleasure. Dr. Dempsey.

– Yeah, same here. Thank you for having me.