159: Dr Jill interviews Dr Jill Schofield on the Breast Implant Illness - MCAS, POTS connection

Text:

Dr. Jill Carnahan 0:12
Well, hello, everybody. Welcome to another episode of Dr. Jill Live. I am here with my friend and colleague, another Dr. Jill—Schofield—today. We're actually neighbors. We're both practicing in Colorado. We were just saying when we got on how it's been so neat because we share a lot of the same patients. I know I've heard great things about her. So we shared a lot of the same past as far as the kind of complex chronic illness that we both see. Today, we are going to dive into the specifics of breast implant illness. I know for a lot of my female listeners and maybe men who have a spouse or partner—anyone out there—this has been a big, hot topic. We're going to dive into some of the discussion on the details around that. But before I do, I want to introduce my guest.

Dr. Jill Carnahan 0:56
Dr. Schofield is the founder and director of the Center for Multisystem Disease. She graduated from the University of Colorado School of Medicine with honors in 1995 and completed her internship and residency in internal medicine at Johns Hopkins Hospital in Baltimore from '95 to '98. She worked for many years as a hospitalist and teaching attending at St. Joseph Hospital in Denver before developing an interest in autoimmune disease. She's published a number of original research papers and regularly presents her work at national and international meetings. She's an associate clinical professor at the University of Colorado in the Department of Medicine.

Dr. Jill Carnahan 1:28
She was a recipient of the Dysautonomia Support Network Patient's Choice Game Changer Award—I can totally see how that would go; that's amazing—for her work in the use of immunoglobulin therapy and autoimmune dysautonomia. Her primary areas of interest are the antiphospholipid syndrome and the emerging fields of autoimmune dysautonomia and mast cell activation syndrome. That's what's really special about our talk today because, whether you know it or not, our topic on breast implant illness is kind of going to dovetail. So first of all, just welcome, and thank you so much for taking the time today, Dr. Jill!

Dr. Jill Schofield 2:03
Yes, thanks so much for having me. I have mutual respect for you as well. So I appreciate the compliments, but I look forward to sharing this conversation today about what I think is a really important topic.

Dr. Jill Carnahan 2:18
Yes, me too. I am absolutely delighted to have you here because it's such a relevant thing. Before we dive into that topic, I always love to know—we heard a little bit about your background; you actually trained here in Colorado and went to Johns Hopkins—how did you first get interested in medicine? What was your path to medicine?

Dr. Jill Schofield 2:35
Oh, in medicine. When I was four, my cousin, who was six, said she wanted to be a nurse, and I said, "I want to be a doctor." She became a nurse—she's an ICU nurse today—and I became a doctor. So I never really wavered from that. I loved watching doctor shows from a young age and went straight through the path.

Dr. Jill Carnahan 2:57
That's amazing. So you were six and she was four, or was it the opposite?

Dr. Jill Schofield 3:00
No, I was four when she was six. I was very young when I knew that.

Dr. Jill Carnahan 3:04
That is amazing. And you know what's even more amazing is you've chosen, like I have, a very complex… If any area of medicine is complex and difficult, we're in it, right? And it's interesting. It takes a special person. How did you go from internal medicine… You clearly had some experiences that kind of led you down the [path of] dysautonomia and antiphospholipid…

Dr. Jill Schofield 3:26
Yes, that's a great question. Well, I was going to do oncology. I was in a fellowship for that, and I quickly realized that was not the field for me. I didn't like telling people they were going to die. It felt like cookbook medicine; the diagnosis was already made. It just felt really boring to me and also stressful trying to deliver the

message—a negative message—to people. So I took what was going to be a temporary job as a hospitalist, and I loved it. I did that while my kids were growing up. I was able to work part-time. It was perfect.

Dr. Jill Schofield 4:00
Then, at some point, I ran into a couple of patients in a row with antiphospholipid syndrome and started to learn a lot about that through these few patients; one of them was a nurse, and two of them had POTS. That's when I reached out to Dr. Hughes, the British rheumatologist who first described antiphospholipid syndrome, or Hughes syndrome, and he described the link with POTS.

Dr. Jill Schofield 4:28
So then I went to the university and did two years of multidisciplinary training in autoimmune disease. While I was there, I started a POTS clinic. These patients, as you know, are very complex. Once you start doing POTS and autoimmunity, you quickly start to learn about mast cell activation, although it wasn't so quickly because it was a very new and emerging area. I went to work with Dr. Afrin when he was at the University of Minnesota. I went to work with Dr. Brent Goodman at Mayo [Clinic] in Scottsdale, who's got a practice very similar to mine and is an autonomic specialist.

Dr. Jill Schofield 5:09
I also went to a lot of international meetings. That was when I first learned about breast implant illness from Dr. Yehuda Shoenfeld, who's the guy who described ASIA, or autoimmune/autoinflammatory syndromes induced by adjuvants—of which breast implant illness is probably the most common type of ASIA. So my eyes were always open to that because I went to that lecture very early in that two-year training period that I did. Basically, those patients developed what we now know as long COVID. It's very much the same illness; it's just a different trigger. You and I, and other people who were doing this work before COVID, were seeing all the same patients.

Dr. Jill Schofield 5:58
But I now ask everybody who walks through my door if they ever had breast implants or facial fillers, which are less known to cause the same thing. And I've seen a few cases of that, like Juvederm and Restylane setting off autoimmune and

autoinflammatory disease. I think I also first learned about that from Dr. Yuhuda Shoenfeld, that it can serve as an immune adjuvant as well.

Dr. Jill Carnahan 6:31
So just for those patients or the general public listening, let's frame this because I love where you're going. And you and I are totally following because we know how these things in our environment can impact our immune system. Let's go back to just antiphospholipid syndrome, your doorway into this. And describe [it] in general: What is that? What might patients notice first? And what would be the markers in the blood for that? And then we'll dive deeper into the triggers and the breast implants.

Dr. Jill Schofield 6:55
Yes, that is one of the autoimmune conditions, or at least the autoantibodies that can be produced or found in patients with breast implant illness. It's not really called antiphospholipid syndrome unless you've had a blood clot or severe pregnancy morbidity. But it's basically a systemic autoimmune disease—kind of a cousin of lupus. In fact, about a fifth of patients with lupus have antiphospholipid syndrome. The syndrome was first described in patients with lupus. It was later found that it's actually more common. It occurs more commonly without lupus. This is the so-called primary antiphospholipid syndrome.

Dr. Jill Schofield 7:34
The hallmarks of antiphospholipid syndrome, as I already alluded to, are blood clots, both in the arteries and in the veins. Really, clotting can occur anywhere. It can be a very potent clotting disorder. And then serious pregnancy complications like stillbirth, lateness carriage, preeclampsia, eclampsia, and intrauterine growth restriction. But the patients that have POTS, most often… Well, I guess many of them actually do meet the criteria. The criteria in many of the autoimmune diseases, as you know, are like capturing the tip of the iceberg. But there is actually a code for antiphospholipid antibody positivity. I tend to follow that strictly. I go off the criteria. So most people actually don't meet the criteria for the syndrome.

Dr. Jill Carnahan 8:31
So you could have antiphospholipid antibodies and not the syndrome because you haven't got a clot and not truly lupus because of the skin manifestations.

Dr. Jill Schofield 8:39
Yes. My patients with POTS don't usually have lupus.

Dr. Jill Carnahan 8:31
I would say I agree; I see much more antiphospholipid antibodies without the whole sequela.

Dr. Jill Schofield 8:53
Exactly. And it's important to catch them before. I find that if you know somebody has it, you can often prevent them from having a clot. It's the people who don't know they have the antibodies that are kind of a walking time bomb.

Dr. Jill Carnahan 9:08
Yes. And I love that you mentioned long COVID because we're seeing what we've already seen for years. It's just that there are so many more people who are affected and who are having these kinds of syndromes as that virus was a trigger, just like all these others.

Dr. Jill Schofield 9:23
It just majorly blows up mast cells—and occasionally autoimmunity, but more, I think, mast cells.

Dr. Jill Carnahan 9:29
Also, just for clarity, are you talking about anticardiolipin and antiphospholipid? Or what actual test—

Dr. Jill Schofield 9:35
Well, there are three criteria tests. One is the lupus anticoagulant, which is actually not an antibody test but a clotting test. And then there are anticardiolipin antibodies, beta-2 glycoprotein [antibodies], ANT1 antibodies, and a couple of non-criteria antibodies. I always test for the non-criteria antibodies too, because some patients only have the non-criteria antibodies, and sometimes they have two or three of them. And I know that they're playing a role in their illness because they have features of the illness, including things like livedo reticularis, which is a lacy pattern on the skin that's seen in a significant subset of APS patients. They have

brain nodes. They have refractory migraines. They have cognitive dysfunction. They have white matter changes. They have valvular thickening. They have a low platelet count. There are various features of antiphospholipid syndrome that aren't even included at all in the criteria.

Dr. Jill Schofield 10:37
And POTS—I go to the international APS meetings, and it's not even discussed. It's not even on the radar. I'm sure if you go to the Sjogren's meetings, POTS isn't even on the radar either, and there's a strong link there. I think it's just that the rheumatologists have no training in POTS. They are not interested in adding that to their skill set because there are too many patients who fit into the boxes that meet the criteria for the FDA-approved biologics that they treat, so it doesn't make sense for them to add that on. But it has left a lot of people falling through the cracks who have these conditions. I know that these autoimmune conditions are causative of POTS because if you treat them with IVIG, they get better—the ones who have those antibodies persistently present and features of those autoimmune conditions. But everything is slow. We all know. Evidence is slow in medicine, especially in areas where the mainstream has no interest.

Dr. Jill Carnahan 11:54
I love that you say that because, again, I use medications just like you do, and they're very appropriate. But some of these big blockbuster biologics have all the money behind them, so of course, that's the direction that medicine gets taught. If you have a TNF-alpha blocker, well, let's use this, and let's use the diagnoses. And then the rest of the stuff, like you said, falls through the cracks, because sometimes it's as simple as electrolytes, beta-blockers, or some of these things that are generic or inexpensive.

Dr. Jill Carnahan 12:19
So you're saying that there are a lot of people in this big bucket of antiphospholipid antibodies and likeness. And the smaller bucket is the antiphospholipid syndrome, which includes the clots, and somewhere in there is also lupus. But we're seeing larger groups of people with autoimmunity. And then let's link it too—we talked about breast implant illness and all these outside things. Can you take us through: How would something like an implant or fillers actually trigger the immune system to attack itself? Make that connection for us, for our listeners.

Dr. Jill Schofield 12:49
Yes. Silicone is considered an immune adjuvant. So an adjuvant is a chemical that attaches to an antigen—a piece of an infectious agent or whatnot—and makes the immune system recognize it. So if you get a vaccine and they take a piece of a virus and just put the piece of the virus in your body, nothing will happen. The adjuvant attaches to that piece of the virus and attracts the immune system. So it's kind of a nonspecific stimulator of the immune system. For most people, it's okay. But for people, everything exists on a bell-shaped curve, including how active your immune system is. If you're over here and your immune system is more active, you may be tipped over into developing ASIA, an autoimmune/autoinflammatory syndrome induced by adjuvants.

Dr. Jill Schofield 13:52
In historical times before we had vaccines—which by the way, all have an adjuvant except, I believe, the pneumococcal vaccine—the people who had a less active immune system all died of infections. If you go to the Fairmount Cemetery in Denver, you'll see all these tombstones of one-year-olds and two-year-olds. They were all dying of infections. So now it's these people's turn to get tipped over by adjuvants. And silicone is recognized to be an adjuvant now.

Dr. Jill Schofield 14:30
But it's very interesting if you go through the literature about breast implant illness because, up until it was published by the Netherlands in JAMA Oncology in 2018, I believe [there were] 43 cases of anaplastic large cell lymphoma of the breast. And they found an odds ratio of 421 that somebody who had that [also] had breast implants. So, that provided overwhelming evidence that the immune system was in some way being stimulated by the breast implants because the lymphoma is a tumor of the lymphocytes, which are part of the immune system. And they're actually the cells that make the autoantibodies. Before that, publication after publication after publication—the New England Journal of Medicine, FDA—[and] everybody [else] were saying there's no such thing as breast implant illness. And right after that paper, everything just switched. A light switch went off. And now all these papers are coming out: "Oh, yes, they're associated with" this, this, this, and this. And I think in the early days, in the defense of the people who did the early

work, several problems with breast implant illness in terms of trying to characterize it as a real disease entity [are]: One is that it develops gradually.

Dr. Jill Carnahan 16:04
A latency, right?

Dr. Jill Schofield 16:04
It can occur from very quickly after the implants to as late as 50 years. And that same time span was also seen in the women who developed anaplastic large cell lymphoma—1 to 40 years, I think. So if you get sick 20 years later, how do you know it was the breast implants? You don't. Also, women were not actually meeting criteria for things like lupus or rheumatoid arthritis. Instead, a lot of people have POTS, and a lot of people have mast cell activation syndrome, neither of which was described or really… I should say, MCAS was the first case report in 2007. POTS was described in 1983, but it wasn't recognized broadly by anybody until just the last few years, literally. So both of those conditions can be extremely disabling in and of themselves. So people were just having fatigue, rashes, dry eyes, hair loss, post-exertional malaise, tachycardia, and all these things. But they didn't have a diagnosis, so they said they don't have anything—just hysterical women.

Dr. Jill Schofield 17:26
Two things happened. The first was when the Netherlands published this very well-done study from their national pathology database, showing the link with anaplastic large-cell lymphoma. And then women started connecting on social media. And they were like, "I got mine out, and I feel better." "I got mine out, and I feel better." "I got mine out… " So people started saying, "I want mine out." And then some doctors actually listened to the women. So that, coupled with that publication, really changed everything.

Dr. Jill Schofield 18:01
The greatest thing of all—I don't know if you're aware—[was that] in October of 2021, the FDA restricted the sale of breast implants to surgeons who agreed that they would personally go through a seven-page checklist of all the risks of breast implants with the patient. It could not be delegated to a nurse, an aide, or anybody else; it has to be the doctor to the patient. And everything has to be initialed. The patient has to be given a copy of it.

Dr. Jill Schofield 18:31
So now the breast implant business is just going to go [making a tanking gesture] like that because there was actually a study asking the public before they knew this checklist, "Would you consider getting breast implants?" And 65% of women were like, "Yes, yes, that might be good." And then when they saw this checklist, it went way down to—I don't know what number it is—[something] like 15% or 20%. So there are still people who will do it. But at least they will know if they start to get sick that they better get the implants out. So that was—

Dr. Jill Carnahan 19:02
Informed consent is how it should have been.

Dr. Jill Carnahan (pre-recording) 19:06
Hey, everybody. I just stopped by to let you know that my new book, *Unexpected: Finding Resilience through Functional Medicine, Science, and Faith*, is now available for order wherever you purchase books. In this book, I share my own journey of overcoming a life-threatening illness and the tools, tips, tricks, hope, and resilience I found along the way. This book includes practical advice for things like cancer and Crohn's disease and other autoimmune conditions, infections like Lyme or Epstein-Barr, and mold- and biotoxin-related illnesses. What I really hope is that as you read this book, you find transformational wisdom for health and healing. If you want to get your own copy, stop by ReadUnexpected.com. There, you can also collect your free bonuses. So grab your copy today and begin your own transformational journey through functional medicine and finding resilience.

Dr. Jill Schofield 20:02
Yes, because surgeons—you can't really expect them to know about the risk. But I mean, kind of you should. I don't know. I have a little bit of mixed feelings about that. But now they know.

Dr. Jill Carnahan 20:17
Yes, because you and I see all this sequela.

Dr. Jill Schofield 20:20
We see the people who had the implants 20 years ago. And actually, most of the people I see have already had theirs out. They figured it out on their own. They

already had theirs out. And the longer you go between the time you had them in and the time you get them out, the less likely you [are to] benefit, or to the lesser degree you benefit from getting them out. And that's part of the tricky part—you can't guarantee somebody that if they get them out, they're going to be better. But most people are like, "If there's any chance I'll feel better, I'm getting them out."

Dr. Jill Carnahan 20:59
Yes, the same. So you talk about silicone. Obviously, [it's] an adjuvant. Tell us about saline with the silicone because there's still—

Dr. Jill Schofield 21:06
Oh, right. Yes. People thought the saline implants would be safe, but actually, the shell is made of silicone. They turned out to be just as risky.

Dr. Jill Carnahan 21:19
Now, I'm not aware of this, and you probably are way more [aware] than I am, but are there ways to test... because it's almost like the immune system can pick up little pieces of silicone and take them and put them into the lymphatic system. Is there any way to actually test for silicone in the body or antibodies to it?

Dr. Jill Schofield 21:37
Well, there is this reactivity test that I actually have not ordered yet. I have a couple of colleagues who've ordered it. We don't really know how it lines up. It's an out-of-pocket test, so if the patient gets it, it shows, I think, silicates. So we [inaudible] silicone. We all need to go back to chemistry with this stuff. There was one patient who had breast implants, and theirs came back strongly positive. So they took that as a good sign that they should probably get those out. But those tests have not been rigorously studied. If it comes back negative, it probably doesn't rule out that you have—

Dr. Jill Carnahan 20:20
We don't know for sure. Exactly.

Dr. Jill Schofield 22:20
The other thing is that the immune-mediated against silicone is one hypothesis or one mechanism. That probably is true, how it develops. But the other leading one

that's probably less common but still pretty common is that a biofilm forms around the implant made of bacteria, mold, and whatnot, and the immune system reacts to that.

Dr. Jill Carnahan 22:48
A foreign body reaction.

Dr. Jill Schofield 22:50
Yes. And maybe the infection itself is contributing to the illness as well—either/or. And it's probably a heterogeneous group of patients. And then there's a smaller group of patients who actually have an allergic reaction to some component. There are a lot of chemicals and heavy metals in breast implants, too. That's another thing that the FDA mandated—the patient has to be given a card with a list of the entire components that are included in that implant. And it's like, "Ooh!"

Dr. Jill Carnahan 23:23
Yes. It's kind of like dental stuff, too. There are so many different things.

Dr. Jill Schofield 23:27
That's true. That's actually true.

Dr. Jill Carnahan 23:28
Or even [inaudible]. Like, all these things, right?

Dr. Jill Schofield 23:32
Any foreign body.

Dr. Jill Carnahan 23:33
Yes, because I'm sure you see this too. We're talking breast implants. It's such a big deal. Women need to know about this, and if they're suffering, to at least think: Could that be a possibility? But the truth is, even a hip implant, a dental implant, or anything foreign in our body could be similar in triggering an immune response.

Dr. Jill Schofield 23:50
Yes, people get cheek implants, butt implants—that are also made of silicone—chin implants, and penile implants. Those are all the same.

Dr. Jill Carnahan 24:03
Right, similar. So say a woman comes in and they've had breast implants for 10–15 years and they have some autoimmune markers and stuff. What kind of discussion do you have with them about "could this be a possibility"? And how do you navigate helping them decide what to do about it? Take us through a person who might come in and say, "I think some of the symptoms are related." And what would guide you in guiding them?

Dr. Jill Schofield 24:27
Well, I always recommend they get the implants out because there's a really good chance that that's a player in the illness. And, you know, you can't guarantee that it's going to help. But like I said, I have only one person in my practice who comes to mind who has not had hers out, and she is that exact person that you're talking about. I think she actually has an antiphospholipid antibody and symptoms. Triggers trump drugs. If you've got something in your body that's driving the process and you try to treat it, the treatment doesn't usually work that well.

Dr. Jill Carnahan 25:10
Exactly. It's like mold. I had mold-related illness. If someone's in a house with mold, they will not—

Dr. Jill Schofield 25:13
Exactly. They need to get out of the house. The same concept. So, yes, the VAT—I always recommend it. There's never a reason why I wouldn't recommend it. Some people are very talented at reconstruction. I have on a slide—I don't know how to show it on here—of a reconstruction by Dr. Eva Nagy in Australia, who's a colleague and an oncoplastic breast surgeon interested in breast implant illness. Her autologous reconstruction after explantation looks like the person has implants—like a B-cup.

Dr. Jill Schofield 26:05
I had one patient who was like, "God!" The patients always feel really guilty that they got the breast implants. "It's my fault that I got this illness." No, no, no. It's just our culture. Someone almost talked me into getting them about 15 years ago. I almost went down that road myself. It's just tempting. So this one patient had kind of a

misshapen chest, like, a misshapen sternum and whatnot. She still just felt really bad that she had the implants. I don't know what the skill set of other surgeons besides Dr. Nagy is in [terms of] being able to use autologous fat—autologous meaning the patient's own fat—and certain flaps that they do and lifts that are not using any foreign substances to create a decent outcome that makes the person not completely flatchested. I don't know. I don't know what percent of people are going for the huge look versus [those who] don't want to be super flat-chested. I have no idea. But at least those techniques exist and are probably emerging. And I'm sure they're going to emerge really fast now that the implant business is [inaudible]. It has to be immediately bottoming out with that FDA ruling.

Dr. Jill Carnahan 27:45
I remember hearing that, but I did not read the whole part about the [inaudible].

Dr. Jill Schofield 27:49
Yes. They've literally restricted the sale to surgeons who signed an agreement that they would go through that document. Now, whether that's happening or not, I don't know. But there they could be held liable if they didn't do it because they were sold the implants under the premise that that would occur.

Dr. Jill Carnahan 28:15
So let's talk just a little bit about how this presents. We've talked about mast cell [activation syndrome] and dysautonomia. And you and I know well what this looks like. But for someone out there who is like: "What does it look like? Might I have that?"—because it's so common… I also want to mention, was it 2018 when the first paper came out for mast cell activation?—because we've kind of known—

Dr. Jill Schofield 28:33
Oh, no, the first case report was in 2007. The two publications about how we should diagnose it came from one group in 2010 and another group in 2011. And those two groups are still—

Dr. Jill Carnahan 28:45
Yes, I've seen that. Totally.

Dr. Jill Schofield 28:47

Yes, group one and group two. Group two! [raises hand]

Dr. Jill Carnahan 28:52
I know, exactly. Lawrence Afrin and Theo Theoharides and some of the leaders. You published some work in the mast cell—

Dr. Jill Schofield 28:58
Yes. I was the co-author of the Global Consensus-2 criteria. Dr. Afrin was the first author. He's really the leader of the Consensus-2 group. Dr. Theo Theoharides is kind of a straddler, to be honest.

Dr. Jill Carnahan 29:16
So we'll link if you're listening. We will link that article here so that if you want to know more...

Dr. Jill Schofield 29:21
Yes, I love that article. I give it to all my patients because it goes through the politics of where MCAS stands in the medical community today, the difference between the consensus-1 and the consensus-2 criteria, and what we as the consensus-2 people feel are the problems with the consensus-1 criteria, which are really capturing the tip of the iceberg of patients with mast cell. They don't embrace the link with POTS. They don't embrace the link with Ehlers-Danlos. It's like, "Really?"

Dr. Jill Carnahan 29:52
Yes. So we'll link that up because, I agree, it's one of my favorite papers. And I thought you were an author of that. So thanks for bringing that to the world.

Dr. Jill Schofield 29:59
There are a lot of authors on there for a reason.

Dr. Jill Carnahan 30:03
I know. You guys have worked so hard. So let's describe it for the listeners. Like, I think I've heard about this: What is mast cell activation? Give us just a little overview of that and how it links to dysautonomia.

Dr. Jill Schofield 30:13
Well, let me first explain that there are two arms of the immune system. There's what we call the innate immune system, which is the first responder, where the mast cells reside, and a few other cells. They're very nonspecific in how they respond, but they're very quick to the scene. And the mast cells are the first responders. Then there's the sophisticated or acquired arm of the immune system, where the lymphocytes reside. The lymphocytes are the cells that take their time. They get triggered or stimulated by the innate immune system. They're making a very specific antibody against the specific pathogen, virus, or bacteria. And if the antibody happens to not only recognize that pathogen but also something in your own body, which we call molecular mimicry, then that is actually an autoimmune disease.

Dr. Jill Schofield 31:10
So actually, most autoimmune diseases are diagnosed by autoantibodies, like lupus. You have an ANA; you have double-stranded DNA, etc. Even doctors call everything in this arena autoimmune. But really, these disorders over here of the innate immune system, of which mast activation syndrome is one, we really call auto-inflammatory. And that's where Asia—autoimmune/autoinflammatory syndromes induced by adjuvants—[comes in]. And the people with breast implant illness, honestly, usually have both issues.

Dr. Jill Schofield 31:45
Mast cells are the most primitive cells of the immune system. They've actually been around for 500 million years in multicellular organisms, which just kind of blows my mind. But they are hardwired to recognize foreign invaders like bacteria and viruses. They align themselves, or they're present in the highest numbers, in the parts of the body that interface with the environment where they have the best chance of finding a foreign invader because they're like sentinels; they're the first responders. So they're present in the nasorespiratory tract, the GI tract, the skin, and the genitourinary tract in the highest numbers. But they're present throughout the body. And they also love the nerves. They use nerves as a highway to communicate to the rest of the body that we're under attack. So we see a lot of neuropsychiatric issues in mast cells.

Dr. Jill Schofield 32:35

But the kind of hallmark symptoms that are not present in every patient but would clue most people in to start thinking about mast cells would be things like hives, environmental allergies, anaphylaxis, asthma, eczema, and flushing—those kinds of conditions. Those are mostly what are included in the consensus-1 criteria. But then, really, it is a multi-system disorder because there are mast cells throughout the body.

Dr. Jill Schofield 33:08
So we see a tremendous number, as I already said, of neuropsychiatric issues, most commonly anxiety and depression. Women come in and they're like, "I had anxiety for as long as I can remember"—like, three, two, one. I hear that all the time. They have insomnia, depression, ADHD, ADD, autism spectrum—I'm seeing all kinds of people, and autism spectrum has been linked, actually, with mastocytosis too, with a 13-fold increased risk, which is fascinating—PTSD, OCD, ODD, and even bipolar disorder.

Dr. Jill Schofield 33:45
Everybody who's ever walked through my door with bipolar disorder—usually it's kind of poorly characterized—always has mast cell [activation syndrome]. And I'm not saying everybody with those disorders has mast cell [activation syndrome]; I'm just saying everybody who comes to my practice, which is a unique set of patients who often also have POTS and things like that.

Dr. Jill Carnahan 34:04
I would agree with you.

Dr. Jill Schofield 34:05
Yes. And then POTS—not just psychiatric but neuro too. So POTS is number one; autonomic nervous system disorders and other autonomic disorders are a very, very common link with mast cell activation. And it was published, I think last year or maybe the year before, [about] the link between mast cell activation and small fiber neuropathy. The autonomic nerves are a type of small fiber nerve, so there's a really strong link there. I just use this phrase very loosely, but I think mast cell [activation syndrome] is the most common cause of POTS. I use the causation loosely because causation is very hard to prove. But if you see enough patients, you

know without meeting the Consensus-1 people's insurmountable level of proof that they demand.

Dr. Jill Schofield 35:04
If you're a doctor in the trenches, you know a lot of patients. And that's good because mast cell [activation syndrome] is often very treatable with simple drugs. And sometimes not even drugs, just removing the triggers, like changing the diet and getting rid of the fillers and medications and things like that. So what else? Bladder trouble, like urinary infection symptoms without an infection. Or, some people are diagnosed with interstitial cystitis, headaches, seizure-like episodes, any kind of skin manifestation, and frequent nasorespiratory issues like recurrent sinusitis, or chronic nasal congestion.

Dr. Jill Schofield 35:54
There are a huge number of symptoms that patients can develop. And everyone with mast cell activation has their own unique case. So everybody has a different combination of those problems, and they respond to different medications in the way in which their illness manifests. And [how they] might flare looks different from person to person. So that's part of the challenge of mast cell activation; even though it's very treatable, the patient really has to take ownership. They have to put on their detective caps and try to figure out all this stuff. I'm an educator, and you're an educator, and then the patient has to go and—

Dr. Jill Carnahan 36:36
That's the primary [step]—for them to start to connect with it. So let's talk about it that way because we clearly know breast implants are a huge piece of this puzzle for women. But there are so many things that can be triggers. What are some of the common… You mentioned fillers, medications, and different foods.

Dr. Jill Schofield 36:49
Oh, for mast cell [activation syndrome]?

Dr. Jill Carnahan 36:50
Yes. Let's go through the categories. It can be so many different things. What are some of the common ones?

Dr. Jill Schofield 36:57
Well, mold, as you know, is a major trigger, but [so are] all of the chemicals in our environment, which include personal care and cleaning products. That's low-hanging fruit. It's like: Get rid of the plastics; get rid of the coated pans; use the cleaner Seventh Generation Free & Clear instead of Tide and Cascade.

Dr. Jill Carnahan 37:18
And no plugins, please.

Dr. Jill Schofield 37:21
Yes. For most people with mast cell activation syndrome, another piece of it, another clue to it, is that they're sensitive to chemicals. So if you say, "Did any detergents ever bother your skin, or sunscreen, toothpaste, or any scented products?" probably 90%, maybe 95%, will say yes. So there is a small subset of people for whom those things don't seem to bother them. But I'm still like, "Just at least get rid of the plastics and do the simple things." And then there are other people who are so sensitive that they have to go make their own shampoo and things like that. They figure that out themselves. So then, [with] all the chemicals in the "food"—diet is huge—some people can just change to a non-processed anti-inflammatory diet. Oftentimes, that includes going gluten-free and/or dairy-free and seeing what effect high histamine foods have because, for some people, all of those things matter tremendously, and that's all they have to do.

Dr. Jill Carnahan 38:34
It's funny because over 20 years ago I had Crohn's [disease], breast cancer, and all that. And I had atopic allergies, asthma, eczema, and things like that. And I didn't have any idea about histamine and foods, but all the things that were high in histamine—fermented cheeses, aged meats and cheeses, smoked salmon, bone broth, and kombucha—bothered me. [inaudible]—like, all the fermented products and things. People are like, "What's… " Years ago, I didn't even know that the connection was to histamine. I was like, "These foods are all bothering me." I took them out. Later I was like, "Oh, it's the whole list of histamine foods. Of course."

Dr. Jill Schofield 39:14
Yes. Well, your case is interesting because Crohn's is an auto-inflammatory syndrome. You see the link with all these other spondyloarthropathies,

inflammatory bowel disease—they're all over here—they overlap a lot with mast cell [activation syndrome] and other things. And you just feel like the root problem is in the mast cells. And there's a higher risk of cancer in mast cells. There are all these growth dystrophisms because the mast cells regulate tissue growth. So if I were to put your case together, I would think your root problem was mast cell [activation syndrome].

Dr. Jill Carnahan 39:51
I agree.

Dr. Jill Schofield 39:52
Have you come to that conclusion?

Dr. Jill Carnahan 39:55
Absolutely, 100%.

Dr. Jill Schofield 39:57
Yes, and then you've got the mold exposure.

Dr. Jill Carnahan 39:59
Exactly. Throw all that on there. So obviously, there are some great treatments and stuff. We don't have to go through all that. But what I really want to talk about is IVIG. You're someone who has used that very successfully. I have seen the same. Tell us, first of all: What is it?—for those listening. Also, why might that be a treatment for some of the complex cases? And where have you found it to be most useful?

Dr. Jill Schofield 40:20
Yes. Well, first, it's basically immunoglobulin, which is the antibody part of our blood, the liquid part of our blood. So it's derived from blood donors. You can actually be a plasma donor. I understand they pay quite a lot of money—I don't know how much. And when they make a batch of IVIG, it's pulled from something like 6,000 to 10,000 donors. The reason for that is that the original use for IVIG, which has been around for more than 30 years, maybe 40 years now, was for patients who had immune deficiency. They had low antibody levels, and they were getting recurrent infections. So it makes sense that you would pool antibodies from

all these people who've been exposed to different infections and have antibodies together to most of the things you would want to cover.

Dr. Jill Schofield 41:12
Actually, it doesn't make any intuitive sense that you would use it for an autoimmune disease. You've already got too much immunity, so why would you give more? And it wasn't really anybody's idea; it was just fortuitously found. There was one boy who had an immune deficiency, and he also had ITP, which is autoimmune destruction of the platelets. So they noticed when they gave this kid his IVIG for his immune deficiency that his platelet count would go up. So then they got a couple of other kids, and that was how they figured it out.

Dr. Jill Schofield 41:49
There are about 10 different proposed hypotheses for the way in which IVIG might work for autoimmune diseases, which are extremely complex immunologies. But it honestly works. You can find a paper showing it works for pretty much any autoimmune disease—not auto inflammatory, but autoimmune. So the patients for whom I use it are a very small subset of the patients that I see—patients with refractory dysautonomia, usually POTS. First, even if I know they have antibodies, even if they have 10 antibodies, I still treat their POTS with the typical POTS treatments, or what I call the band-aid treatments, like salt, vasoconstrictors, beta-blockers, volume expansion, and Florina.

Dr. Jill Schofield 42:48
And then I treat what is almost always present [which] is mast cell [activation syndrome] because I don't think I have anybody in my practice with autoimmune dysautonomia who doesn't have at least some degree of mast cell [activation syndrome]. And oftentimes, they have a lot of mast cell [activation syndrome]. So some people get better just by treating their POTS and their mast cell [activation syndrome], even though they have the antibodies. But the people who don't, you know you're missing that piece. So that's a small subset of my practice that I treat with IVIG. And when I put together my data—some years ago, I don't remember, 2018, I think I published this data, because I've been doing this for years already—almost 85% of those patients respond, and they respond dramatically. Their functional ability increases by 50%, which is a lot. If 100% is normal, 0% is dead, and 30% is bedbound, they increased by an average of 52%. Really, the people

who respond respond dramatically. It's a game-changer drug. And for some reason, 15% of the people don't respond.

Dr. Jill Carnahan 44:01
I have seen the same thing.

Dr. Jill Schofield 44:02
And I guess that's true with everything in medicine, right?

Dr. Jill Carnahan 44:05
But I couldn't agree more. I'm such a fan of those really tough cases. Two questions: Are you using the higher [dose], like the autoimmune 2 grams per kilo dose, typically on those patients?

Dr. Jill Schofield 44:14
Oh, no, I start with 1. I have a published protocol on POTS because POTS patients don't tend to tolerate IVIG as well. If you give it to people with ITP, they tolerate it fine. Most neurologists are used to giving a 2-gram per kilogram per month dose because they're treating patients with myasthenia gravis or Guillain-Barré on a ventilator, so they just want to slam them. If you give a POTS patient that dose, you will give them such severe aseptic meningitis that they will never take that drug again.

Dr. Jill Carnahan 44:48
Because the mast cells will initially react when you give it, right? So you're actually like [inaudible] the mast cells.

Dr. Jill Schofield 44:54
Yes. So I start with 1 gram per kilogram per month. You're referring to a high dose. So the low dose is for immune deficiency patients—those original patients with low antibodies. Then the high dose is for autoimmune disease, which ranges from 1 gram per kilogram per month to 2 grams per kilogram per month since these patients don't tolerate it well. I personally think the reason they don't tolerate it well is that they all have some degree of mast cell activation, and IVIG seems to activate mast cells. So I start with 1 gram per kilogram per month. I also divide that dose weekly. I divide the monthly dose weekly, so they get a quarter of a gram per

kilogram weekly. Then I try to get them eventually to get the whole dose once a month, one gram per kilogram, once a month. And not everybody gets to that. And then I'll notch people… If people don't get to 80 to 100, I'll go, "Let's go up to 1.15 grams per kilogram… 1.3."

Dr. Jill Schofield 45:57
I would say the average dose that people settle on—you always want to give the lowest most effective dose because it's a burdensome drug, so lung infusion, the higher the dose, [inaudible] side effects; it's extremely costly—is 1.3 grams per kilogram per month. So the neurologists start at 2, and they go down, and I start at 1, and I go up. I'm treating a chronic condition, so I'm in a marathon, not a sprint. They're used to the sprint and they don't recognize that this is different. Or maybe they recognize it, but they're just used to giving that. And I think they don't recognize that POTS patients are different in how they tolerate it. They just don't tolerate it. And if you're on a ventilator anyway, nobody's going to have any side effects.

Dr. Jill Carnahan 46:47
No. And like you, I treat these patients too and work with IVIG. I see all of this—the real reactive… So you have a published protocol. We will link that too. I would love to link those up for people who want to know.

Dr. Jill Schofield 46:58
Oh, yes, I can send that to you.

Dr. Jill Carnahan 47:00
Perfect. Amazing.

Dr. Jill Schofield 47:01
For use in this disautonomia.

Dr. Jill Carnahan 47:05
So in our last few minutes, the only other thing I really want to cover is… We've talked about breast implant illness, how it connects to POTS, mast cell [activation syndrome], and autoimmunity, and why women probably should have them explanted if possible. The woman who's had the explant surgery—and you

mentioned what I see too, [that] there's some percentage, and I'd love to know what you see in the clinic, that gets better—gets better pretty quickly. And then there are a lot of women who struggle, and they need the detoxes. What would you do after explant surgery to help that woman regain her—

Dr. Jill Schofield 47:33
Well, I guess I treat them the same as all the other people. If they have POTS, I treat their POTS. If they have mast cell [activation syndrome], I treat their mast cell [activation syndrome]. If they don't get better by treating POTS and mast cell [activation syndrome], then if they have autoimmunity, I would offer them IVIG. I don't use IVIG unless people are really sick. I define that as the inability to go to work or school because it's just too burdensome. If somebody's got a functional ability of like 70%, it doesn't make sense to spend $200,000 a year and have them hooked up to an IV all day. And the drug itself can cause side effects and everything else. I also use hydroxychloroquine, or Plaquenil, for people with autoantibodies who aren't sick enough to justify IVIG. There are no studies yet in this context, but this is just an emerging area, so we're all learning from each other.

Dr. Jill Carnahan 48:50
We are, aren't we? We need to be on the front line because there are so many patients who need people like you who are looking at this and looking deeper. Well, you have given us such a gift with your knowledge already! And thank you for being at the forefront in these tough cases and also publishing because we need the data sets for [what] physicians can do. Where can people find out more about you, find your papers, and find your work?

Dr. Jill Schofield 49:13
Oh, I have all my papers on my website, which is www.CenterForMultiSystemDisease.com. I have all of my papers [inaudible].

Dr. Jill Carnahan 49:22
Perfect. We will link to that so that anyone who needs to download those...

Dr. Jill Schofield 49:27
Yes. So then I won't send you that. That includes the Global Consensus-2 criteria. The MCAS paper is on there. That can really, really be helpful to get a starting point

with MCAS and the politics. A lot of patients get told, "Oh, you can't have MCAS because your tryptase is normal." And if you read that paper, you'll understand that that's not true.

Dr. Jill Carnahan 49:54
Yes. Thanks for bringing hope and healing to so many. Thanks for the work that you continue to do. And thanks again for today, for your time, your effort, and all of your incredible wisdom. It's so great to connect. And I just want to say that I really appreciate all that you are doing for these patients.

Dr. Jill Schofield 50:10
Thanks so much for having me.

Dr. Jill Schofield 50:11
You're welcome.