Introduction and Doctor Afrinu2019s Background

For the. It's a real privilege. An honor to have Doctor Afrin with us today. And after he received his bachelor's of science and computer science at Clemson University, he earned his MD at the Medical University of South Carolina in 1988, where he also pursued internal medicine residency and hematology oncology, clinical and research fellowships.

And while on faculty at Muskie, he was active in medical education plus informational technology and educational administration. Since 2014 and 2017, he's been furthering his interest in mental disease at the University of Minnesota.

He was developing an independent institute for advancing care, research and education. Marcel disease. He has spoken widely in these areas of focus, and he served on editorial boards for several journals and medical advisory boards for various organizations, including the Marcel I society.

I know you also now have a private practice. Can you tell us how you got into mast cell diseases and researching this and treating patients and really being one of the, I think of as the the front leaders and innovators and getting this information out about how common this this disorder is and changing the face of it.

How Mast Cell Disease Entered His Practice

Well, it's kind of a long story, but, to make the proverbial long story short, I came across a patient a number of years ago who was, represented to me as having a particular diagnosis, which, when I saw her really didn't add up and began looking for what was the correct diagnosis.

To make a very long story short, I eventually, determined that she had, what? At the time, I could only call as an atypical Joe psychosis. And, upon giving her appropriate treatment, she got much better for the first time in many years.

And I then from all that I had learned through the process of trying to figure out what was going on in her and getting her better, I, began to recognize that this condition, which soon became known as Marcel Activation Syndrome, was actually present in a lot of other patients who were chronically, mysteriously, multi, systemically ill.

And the more I began looking for it, in patients who had no clear diagnosis to explain their many troubles, the more I found it. I mean, it certainly is not the explanation for every mysteriously ill patient, but I, began learning fairly quickly that it's actually, not the rare disease that masto psychosis is.

It's a very common disease. But one has to learn how to recognize it. It's a complex and highly variable disease from one patient to the next. So coming to understand, I mean, like every disease, there are patterns to it, but it's, challenging to learn how to see those patterns when the superficial symptoms, are so different from one patient to the next.

But once you can, once you learn how to recognize it, you can diagnose it, because there are tests that can be run. And once it's diagnose, good news that there are many treatments that have been found helpful in various patients.

And even though we don't have any reliable way, to, predict which of these treatments will best help the individual patient, nevertheless, if the doctor and the patient, both of them are sufficiently patient and persistent and methodical in stepping through the trials of these, different treatments one at a time, in my experience, most of these patients, no matter how many years or decades they've been mysteriously unwell, most of them actually can eventually identify some cocktail of national targeted treatments, which gets them significantly better.

And as I began to see how many of these mysteriously ill patients, actually could be, legitimately diagnosed with this and treated and actually improve with a cell targeted treatment, things just kind of naturally fell into place that, it was a good way for me to, focus the, my, my career at that point.

So and that's the short version. Well, you've brought so much hope, both of my own life dealing with nasal activation syndrome. And I know the lives of hundreds of thousands of people who go from specialist to specialist.

And it seems like people can take up to ten years or longer to figure out what's going on. If they're lucky enough to get a good diagnosis. What are some of the.

Core Symptom Patterns and Disease Variability

I know you've done a good amount of research on the types of symptom presentations that can show up, and that's what makes this so challenging at times, because there are these variable presentations, one person looks completely different than another person.

What are some of the symptoms that people can be looking for? And how does this person probably better than focusing on specific symptoms is the, look at the categories of symptoms that mast cell activation syndrome patients present with their, the symptoms are direct conflict.

The symptoms of this disease are direct consequences of the natural effects of the various mediators, that are, naturally produced and released by mast cells, which in truth or present everywhere in the body, the those dominantly at the environmental interfaces and in the walls of, vessels and neurons.

But the biologists have now documented, the mast cell produces more than a thousand, mediators, each of which has a huge range of effects, all throughout the body.

And it would take forever to go through the details of what each mediator can do. But if you're looking at the broad themes of what this, what the majority of the mast cell mediators do, the first thing this is the universal constant of man cell activation syndrome is chronic multi-system inflammation.

Now, obviously, the specifics of how inflammation can manifest or are going to be different specific symptoms in different organs, different systems, different tissues in the body.

You know, for example, inflammation in the respiratory tract, maybe congestion and coughing and, and shortness of breath, inflammation and the GI tract could be abdominal pain, nausea, diarrhea and and so on and so forth that it's, you know, the the specific symptoms are just quite different from one organ system to the next.

But inflammation, chronic multi-system inflammation is the universal constant. The second broad theme to the, the clinical presentation of this disease are, are, allergic like phenomena.

And I put a plus minus in front of that, so chronic multi-system inflammation plus minus allergic type phenomenon. And the reason I say plus minus is there actually are plenty of mixed patients who don't have a speck of, allergy to them.

And then at the opposite end of that spectrum, there are the, relatively few, thank goodness, poor souls who, if you can even imagine such misery, they are literally suffering 24 by seven anaphylaxis.

And then everybody else, with memcache, is somewhere in between those polar opposite ends of the allergy, spectrum. There's one more broad theme we, very commonly see with this disease.

But this is the hardest of all to recognize because these manifestations emerge the slowest of all, you know, inflammatory phenomena, allergic type phenomena tend to, blossom and flare up fairly quickly.

But it turns out that many of the mast cell mediators are also integrally involved in guiding growth and development

in all tissues in the body. So when you have chronic inappropriate production and release of various and sundry of the growth guiding mediators, I think it's easy to then understand how you can get any of a huge variety of abnormalities in growth and development, and potentially any tissue or organ in the body.

So, for example, sometimes it's insufficient, growth, like, slow or delayed or poor healing from, from a wound. Sometimes it's overgrowth, excessive growth and, some of the most common types of overgrowth we see are cysts and, not not that I'm saying that every cyst in every person is a consequence of mast cell disease.

I'm just saying that cysts in various, organs in the body, are, a very common type of, growth abnormality in these patients. So we see cysts, we see abnormal, scarring.

And, excessive fibrosis and scarring. We see, for example, uterine fibroids develop. We see a whole range of, abnormal, excessive vascular growths. Unfortunately, the vast majority of these, abnormal growths are benign, but on occasion, they can be malignant, and sometimes such a malignancy and obviously can come, fairly quickly to, dominate the clinical picture and really, overshadow all the rest of the stuff that's going on with the mast cell activation.

And it can make it even more difficult to recognize there actually is a problem with mast cell activation in that patient. So chronic multi-system inflammation plus minus assorted allergic type phenomena plus minus abnormalities in growth and development are what we call dystrophin isms.

This is the general clinical picture of this disease. I know it's a nebulous picture, but kind of hard to rationally expect a more tightly focused picture when the disease is the consequence.

Was, a zillion different patterns of inappropriate production and release of so many different, of these very potent mediators that are produced and released by the mast cell when if we even just think about the the number of possible permutations between the locations of these mast cells that are being triggered, the over 1000 mediators that can be released in these various combinations.

And then the over 200 receptors that can be triggered. One of the lessons that was hammered home to me very early in my, coming to understand, the behavior of this disease, with regard to just how differently different Marcelle patients can present with respect to any particular biologic parameter.

You know, the very first patient in whom I came to recognize that what was really at the root of her troubles was a cell activation syndrome. I mean, she had a great many different problems, but the dominant problem that had led her to being referred to me, hematologist oncologist, was, a diagnosis of, something we call poly.

So famy of there, which is a malignancy, in the bone marrow in which there's, gross overproduction of red blood cells. But the very next patient, I mean, literally the next patient whom I came to to recognize that what was underlying her vast spectrum of illness, she had actually been referred to me for completely the opposite hematologic problem.

And I'm not saying that every mast cell patient has hematologic problems. Again, it's highly variable, but I'm a hematologist oncologist. So before I sort of focusing on mast cell disease, patients were referred to me for hematologic and, you know, general hematologic and oncologic problems.

But the second patient had a condition, that five other hematologists before me had absolutely proven was something called pure red cell, a pleasure in which the bone marrow completely gives up making red blood cells.

It's exactly the opposite. And yet both of those patients turned out to have a mast cell activation syndrome at the root of their problems. And with appropriate mast cell targeted therapy, they both got better pretty quickly.

And I soon came to realize that this, possibility of seeing, polar opposites in any particular biologic parameter, this can easily be seen with mast cell disease.

It just depends on the particular pattern, in which the patient, dysfunctional mast cells are producing and releasing these various mediators, many of the mediators the mast cell has will push a particular parameter in the body in one direction, and the mast cell also produces other mediators, which will push that parameter in exactly the opposite direction.

And you know, the net effect you see on that parameter or in any given mast cell patient depends on, what the balances of the pushes that are coming, the pushes on that parameter that are coming from the different mediators that are being put out by the mast cell, bone growth is is a great example.

Many people are familiar with the, condition of weakening of the bones called, osteopenia, or it's more severe form osteoporosis. And actually, I mean, there can be many causes of osteopenia and osteoporosis, but mast cell disease, makes absolutely can drive osteopenia and osteoporosis.

But at the same time, there also are ways by which mast cells, or I should say, improperly behaving mast cells can produce the opposite condition of an excessive thickening of the bones that we call osteo sclerosis.

Testing, Biomarkers, and Diagnostic Challenges

And so not only can you see some mast cell patients present with osteoporosis and other mast cell patients present with osteo sclerosis, but you also can see, the same mast cell patient present with osteoporosis at one point in his or her life, and osteo sclerosis at a different point in that patient's life, because the particular pattern of inappropriate mast cell mediator production at one point in a mast cell, patients life can be a good bit different than the pattern you see at another point in life.

And in fact, there even are occasional patients who, mast cell patients who will present with both osteoporosis and osteo sclerosis at exactly the same point in time, just in different bones in their bodies.

And this comes about because the dysfunctional mast cells in one part of the body, are misbehaving with a different pattern than the dysfunctional mast cells in another part of the patient's body.

Many times, both patients and doctors assume that the pattern of, improper, mast cell mediator, production and release that you see, in any given mast cell patient that it's it's a single pattern, that is, being, there's a single manner in which all of the dysfunctional mast cells in the patient's body are misbehaving, but actually, that's too simplistic a view of the reality of the matter.

We know from the research that mast cells in different parts of the body, but both normal mast cells and abnormal mast cells in different parts of the body, quite often behave in considerably different fashions.

So this just adds to the variability of the disease, from one patient to the next. As you said, the permutations are almost incalculable. And we have to remember, too, that the mast cells in one part of the body don't have the same concentration of particular receptors as in other.

So this is a very simple example. The amount of H2 receptors in the GI tract on the mast cells versus in other tissues. This is going to lead to what you're describing as well, which has made this mystifying for the vast number of practitioners are trying to find their way through, and even patients trying to figure out what's happening for them.

They're going specialist, a specialist, a specialist, but somebody has to zoom out and look at how are all of these symptoms connected, and is there muscle involvement.

So I know you look a lot this symptomology. And I've, I've worked with, several of your patients and senior incredible reports that you send with them.

And I know you do a good bit of testing as well, and there's a lot of debate about the testing and whether, first of all, which testing to use. And second of all, what happens when all the testing is negative, which isn't uncommon, can we talk about the types of testing that you're finding most valuable in your practice?

It's it's a little bit different from one patient to the next. Again, it's a very heterogeneous disease. The mast cell puts out more than a thousand mediators.

But the fact is that the great majority of them are not presently testable in any clinical laboratories anywhere. They're testable in research laboratories.

That's how we know they exist. But, most of them are not testable in the clinical laboratories of the minority that we can test for in the clinical laboratory, the majority of those are not particularly specific for the mast cells. So as an example, we can test for the level in, in blood or urine of a mediator called interleukin six.

I'll six it's a very potent inflammatory, mediator. And when we find an elevated level of IL six in the blood of the urine, we we know there's a strong inflammatory state and going on in that patient's body.

And the mast cell does make a good bit of IL six. But so to do a number of other types of cells. And so if we find an elevated level of IL six, in the blood of the urine, it doesn't necessarily mean that the mast cells are at the root of the problem there.

So in the end, even though these cells are putting out more than a thousand different mediators, there really are only about ten or so that we can measure in at least some clinical laboratories.

And and which are fairly specific to the mast cell, but if you think about it, if you're only measuring ten out of more than a thousand, the odds are overwhelming, that the symptoms in any given patient as having is coming.

The symptoms are coming about from inappropriate expression and, mediators. Other than what we're measuring, clearly, what we're measuring in these patients is a terribly poor surrogate for the total of the of the signaling chaos that's going on in this disease between the mast cells and all the other cells, in the body.

But at the moment, these ten or so, this is the best we can do, for detecting, for fairly specifically detecting activation of the mast cells. And so this is what we do.

But it is challenging testing. Many of these tests are available only in a very few, specialized reference laboratories. Scattered around the world. Many of these mediators actually have very, short, lifespans in the blood or the urine at, room temperature, let alone at body temperature.

And so, for many of these mediators, it, one has to pay good attention to keeping the specimens continuously chilled. And that's not just at the time of collection in the collecting laboratory, but, at every point there on, because, again, most of these tests are specialized tests that can only be performed in a few laboratories.

So, many of the specimens have to be packed up and shipped out, to these reference laboratories, and one has to take care to pack the specimens in a way that, they will stay continuously chilled.

It's, I'll be the first to acknowledge it. It's not easy, but once you learn all the nuances of this, I will say, and if you have the opportunity to have a chat with the the laboratory personnel who are involved in collecting and processing the samples, I mean, it's a matter of education.

Just like doctors need to be educated about this. So to the laboratory personnel and and pharmacists and insurance companies and so forth, it's all a matter of education.

But once you can kind of get the pipeline in place, you know, have everybody up to speed, then I would describe it as a straightforward process. Not not easy, but but straightforward.

But it does take some effort upfront in learning these nuances and then making sure everybody else in the chain of handling is aware of these nuances as, as well.

There, there, I mean, again, it's not easy. So I'm aware there are many doctors who are, for one reason or another,

not able to surmount these challenges.

And so they are coming to make a diagnosis of the disease, purely on a clinical basis, basically just best clinical guess. And, you know, I can't say there's anything, you know, absolutely wrong about doing that.

If, if the patient or the doctor are facing limitations in what they can do, in the diagnostic process, then you do the best you can with, the resources you've got available.

But I find that, given that most doctors don't yet have any awareness of the disease and therefore the patients are likely going to have to be convincing their local doctors who have never heard of this disease before, that this really is what's at the root of their troubles.

It's really the laboratory evidence that's going to be speaking loudest by far on the patient's behalf. In convincing their local doctors not only now, but for the rest of their lives that they really do have this disease.

So I think if if it's possible to access the testing, it's probably to the patient's long term benefit to acquire the laboratory evidence that, that bolsters everybody's confidence in the correctness of the diagnosis.

At present, there are two different camps of thought, about what testing is appropriate and reasonable to pursue. In, in looking for the laboratory evidence of this disease, there is one group that focuses, largely on a, a marker of mast cell disease called, triptychs. And, and that's largely the only marker they look at.

There's another group that, feels that, based on the available data, that triptychs is a good marker for the rare mast cell disease that the mast cell cancer.

That's called masto psychosis, but it's not so good a marker for the much more common, the much more prevalent mast cell activation syndrome. So even though we still do check triptans in patients with suspected marks, we also, check, you know, like I said, these other, you know, 9 or 10, other mediators, that we feel also can give a fairly specific indication of, of activation of the mast cells.

So there is that, difference of opinion among different groups of doctors. At present, I imagine that in time, as more research gets done, the, the old I mean, this is the way science works is that you do more research, more studies, and bit by bit, you get closer and closer to the real truth of the matter.

And then our diagnostic, processes at that point probably will be much more precise. I mean, it has to be kept in mind that even though this, in truth, is not a new disease, it is a newly recognized disease.

It's only been about 15 years since the first case reports of this were published.

Treatment Approaches and Patient Response

So there really hasn't been that much time for research to be done in this area. And and in truth, not much research has been done. And I think it's only fair to correct arise all of the research that has been done so far as preliminary.

So everybody has to keep those caveats and mind and in setting their expectations as to, how much about this area of medicine and biology we can reasonably be expected to, to know for sure.

It's very early in this, and I think about it in terms of how long there's been diagnostic criteria for things like type two diabetes or Alzheimer's disease versus, I believe, the ICD ten code for mast cell activation syndrome came into existence around 2016.

That's quite new. But we know we have some markers around histamine heparin, prostaglandin D2. One of the other things I often wonder. And we have a urinary marker for histamine.

But I often wonder, well what if it's not the the vascular mast cells that are involved? Are we going to see any

elevation in these blood markers? In my experience, in most mast cell patients, we do, keep in mind that there are very few mast cells actually circulating in the, blood at any given point.

And actually, most of those mast cells are immature or mast cells. Mast cells don't actually mature and and really blossom in their activity until they exit the bloodstream.

And penetrate into various tissues all throughout the body. So, but, but if we, again, if we attend with due diligence to the nuances of, of testing these sensitive mediators, usually we're able to find, a reasonable amount of laboratory evidence to support the diagnosis in a patient whose symptoms are consistent with chronic, inappropriate activation of the mast cells and by symptoms that are consistent with chronic activation.

Again, I'm talking about this general picture of chronic multi-system inflammation plus minus allergic phenomena plus minus just trophies of not and not just the chronic picture, but of course many mast cell patients.

Actually, the large majority of mast cell patients, in addition to their chronic symptoms, they also have, from time to time, these acute flares of various, symptoms.

You know, it's not absolutely necessary. You know, not not every mast salvation has such flares, but most do, you know, the the the ultimate, acute flare, of course, is life threatening.

Anaphylaxis. But the preliminary published research today suggests that only about 7% of kind of patients, have anaphylaxis or anaphylactic Toid, behaviors.

So obviously the large majority of mast cell patients don't have that, they fortunately do not have that pretty scary event in their history. They may well have acute flares of other symptoms, but but fortunately not the anaphylaxis axis.

Yeah. So we have this multi systemic meaning it has to be in at least two or more systems. So people can have they may have skin symptoms and GI symptoms or they may have for example heart palpitation.

They may have some various nervous system type symptoms. And they have what seems to be quite ubiquitous, the post nasal drip and the throat clearing and these kinds of areas.

But we're not going to have just basic allergies. We're going to have a few different things going on for this person. Then there's testing available that hopefully if the samples can be handled correctly, which is tricky and requires being chilled through the entire process.

Hopefully of these, about ten different types of testing mediators, we can get an increase. Although we're not sure about the odds of ten within a thousand possibilities.

And then we have the the third part, which is that there's going to be a positive response at some point to a mast cell stabilizing medication or an antihistamine, some kind of agent.

The possibilities there are quite varied. Yeah. And this brings us to the, another difference between these two camps of thought about diagnose a similar disease.

The first camp that, focuses largely on trip takes, testing, they actually have a requirement, in their diagnostic criteria, their proposal for diagnostic criteria for this disease that patients, that you have to demonstrate a response in at least some of the symptoms to some also targeted, treatment, whereas the other group, that looks at a larger range of mediators, it doesn't take quite such a strict approach and says that, yes, a response to treatment may contribute toward a diagnosis, but it's not necessary.

And that, kind of looseness was, consciously put in those criteria because it was recognized that the disease is so variable in its behavior from one patient to the next that it's, quite likely that at least some mast cell patients are just not going to respond to the first 1 or 2, or maybe even 3 or 4, treatments that are almost randomly selected, to be

tried in the patient can keep in mind we do have a lot of treatments that have been found helpful in various mast cell patients, but no, ways yet.

No methods yet for reliably predicting which treatments are going to help any particular symptoms and any particular mast cell patient. And so I think we can imagine a scenario where, if mast cell disease is suspected in a given patient, and the doctor then goes to empirically try to treat that patient and then applies one treatment, sees no benefit, tries a second treatment, sees no benefit.

I mean, how many of those doctors would then be willing to continue suspecting that it's likely mast cell disease going on here and move on to trying a third or fourth drug, even if they really can't think of any other diagnoses that better account for what's going on with the patient.

So that's why this second group, says that. Yeah, response to therapy can be helpful. But just because a patient has not responded to the first, few, treatments you've empirically tried doesn't even begin to say that it's definite that the patient does not have MCUs in a highly, highly variable disease.

And it's, behavior from patient A patient, a patient, not just in terms of which symptoms you're going to see, but also in terms of which treatments are going to be helpful in any given patient.

And I think that's why it's so important that we keep coming back to these all of these possible permutations between the mast cell locations, the over 200 receptors, the over 1000 mediators.

Because each of these, there's no one all medication that's going to hit all of the receptors address all the mediators. So we've got antihistamines. We've got some local train emitters.

These types of things. It comes back to the importance of the research. You know, there give you another example of the variability. I, I long ago lost count of the number of mast cell patients where when I apply drug X to them, I see one sort of response.

But then there's another large number of patients in whom I apply drug X at the same dose. And even if they superficially appear to have the same symptoms, drug X actually does nothing in those other patients.

Now, there obviously has to be some biologic reason why there's the difference between those groups. But unfortunately, the state of the science, the state of the research in this area at this point is so immature that we are nowhere close to understanding why there are these differences.

You know, I, I'm actually fairly confident and optimistic that as the decades roll on and the we're talking about decades, not years, but as the decades roll on.

Yes, we will make, scientific progress. We will come to much better understand why a given drug has such and such an effect in one patient and different effects in another patient.

And as we come to better understand those mechanisms, then we will get to a point where we can start reliably predicting which drugs ought to work in a given type of mast cell disease.

And a given type of mast cell patient. And that'll allow us to transition away from the current kind of, trial and error, much more smartly predict, which drugs, ought to be helpful in the individual patient.

Based on a better understanding of the science and, and more sophisticated testing that will inevitably follow from, a better understanding of the science.

So we'll get better with this. But it's going to take decades. And in the meantime, don't despair, because, I mean, think of where we stand today, just 15 years from when this was first recognized.

At least we know that it exists, which is a whole lot better situation than we were in before we knew it existed. I

mean, it's not that these patients didn't exist before we knew about the diagnosis.

They were always there. It's just they went from virtually cradle to grave, never being properly diagnosed because we didn't even know the disease existed.

And if you can't make the right diagnosis, the odds of finding effective treatments are pretty slim. So these patients were just chronically ill their entire lot.

But now, even though the state of the science is very immature, we know the disease exists. We already know that, there are a lot of different treatments that have helped various man cell patients.

We also know that most mast cell patients, again, if they and their doctors are sufficiently patient and persistent and methodical and stepping through the trials of these different treatments, most of these patients actually will, get to the goal of feeling significantly better than the pretreatment baseline the majority of the time.

And another fortunate thing is that as best as anybody has been able to tell so far from, again, the the very preliminary research, most of these patients seem to have a relatively normal life span, which means, they're going to live, they're likely going to have the time that's going to be needed by them and their doctors to explore these different treatment options, to find the particular cocktail of mast cell targeted treatments.

That's actually going to be optimal for the individual patient. It usually is a pretty unique cocktail for the individual patient that, that optimally serves that patient.

And sometimes that might be a combination of H1, H2 antihistamines and Crumlin sodium, maybe a tot of we've got singulair. What are some of the other agents that you use most frequently?

It's it's all over the map. They have, non-steroidal anti-inflammatory drugs, even just plain old simple aspirin, can be very helpful in some in some patients.

Current Practice, Book, and Closing Remarks

We need to be a little bit careful with the non-steroidal anti-inflammatory drugs. The end Said's because in some mast cell patients, those drugs actually turn out to be triggers, for flaring up their, their main cell activation.

But then sets can be helpful. Low doses of benzodiazepines can be helpful. The various other anti-inflammatory is, like a tart, often flavonoids, like quercetin and luteal and, cannabidiol.

You know, CBD, and an analog called palm oil ethanol amide sometimes can be helpful, which is the most people know that it's key for low dose naltrexone.

LDN sometimes, can be helpful. I actually was seeing a patient and follow up just yesterday. Who, was reporting in to me after her first, a few weeks on, LDN.

And it was remarkable. How much improvement, she was gaining, variety of symptoms. Including just just, energy. I mean, you know, chronic fatigue is, is one of the most common symptoms, with this disease.

And I'm not saying that LDN is what, fixes, chronic fatigue in, in the majority of Mansell patients. We know it isn't. But, we don't have any particular drug that, is a fix for chronic fatigue in the majority of patients.

It's different in different patient. But still in her, in this particular patient, it was remarkable how much, low doses of naltrexone were, were helping her.

So, you know, sometimes we, we wind up, applying Crumlin not to just one place in the body. We apply to multiple places in the body. And, sometimes we wind up using, drugs from a class called the tyrosine kinase inhibitors.

Unfortunately, in the US at present, they typically are very expensive drugs. But in many other places around the world, they're relatively inexpensive.

And sometimes some of those drugs, certainly not all them, but some of them can be helpful. Honestly, we could spend days talking about all of the treatments that have been found helpful in this disease.

Well, one, I know you have an incredibly busy schedule, and I want to thank you so much for taking time out to talk with us. Both personally, but for the people watching the summit, I want to express a gratitude for what you've done and how you've brought so much awareness, so much hope and possibilities for people.

I want to tell people about your book, Never Bet Against Orcam, which is a game changer, and it has really changed the face of what we know about this.

And this is one of my first introductions and, made a huge difference in my own life, in my practice. And do you still take patients? I know I send people your way.

You're one of the maverick diagnostician in this area. And for people who maybe have more than mass cell activation syndrome, I always encourage that they get a full diagnostic workup with you if they can get in.

Well, I don't know that I agree with the word maverick. That kind of means off the reservation. I actually try to be fairly rigorous in my diagnostic approach.

Rigorous is the goal. I try to adhere, very strictly to the peer reviewed, published diagnostic criteria, for this, disease. But, yes, I am still taking, new patients.

The wait time, you know, it's a few months, but it's not ridiculous. I also see patients by, at least here in the US. I see them by telemedicine. I actually see patients abroad by telemedicine, too.

But those patients do need to actually come see me in person for the initial, consult. But if, if anybody wants to consider, formally consulting with me, they just need to contact my office to inquire about their policies and appointment availability and that sort of stuff.

And I believe your website is aimed center PMCs. So aim center PMCs. The, the aim center for personalized medicine, practice and purchase, New York. Thank you again so much.

Appreciate your time and and all of your wisdom and your research. Right. My pleasure.