

Dr. Mariam Hanna

Hello, I'm Dr. Mariam Hanna, and this is The Allergist, a show that separates myth from medicine, deciphering allergies and understanding the immune system. For over a hundred years, immunotherapy has been part of the allergist's arsenal. We can manage allergic rhinitis, but aeroallergen immunotherapy is disease-modifying.

It can change the course of this disease. This is a condition that affects quality of life, sleep, school, daily function, seasonally, and for some, year-round. Immunotherapy offers another path.

Not all immunotherapy, however, is the same. Not all doses are the same, not all regimens are the same, and not all patients are the same. Today, we're walking through that rhinitis consult, the one where patients are looking for that golden ticket.

We'll break down the risks, the benefits, and the safety considerations, because while uncommon, this is a therapy that can kill. To help us navigate this, I'm joined by a true leader in immunotherapy and allergy. I'm pleased to introduce today's guest, a mentor to actually many allergists out there.

Dr. Susan Wasserman is a professor of medicine at McMaster University and director of the Division of Clinical Immunology and Allergy. She leads the Adverse Reactions Clinic at St. Jo's Healthcare Hamilton and the Schroeder Allergy and Immunology Research Institute. A national leader in immunotherapy and food allergy, we'll cover the aeroallergen part today, she's shaped actually multiple guidelines and spearheaded a national immunotherapy manual for trainees.

This is that golden book that many of us continue to use in clinic. She's also president of the Canadian Allergy, Asthma, and Immunology Foundation, also known as CAIF, and the past president of the Canadian Society of Allergy and Clinical Immunology. Dr. Wasserman, thank you so much for joining us, and welcome to the podcast.

Dr. Susan Wasserman

Oh, hi, Mariam, it's a pleasure to be here.

Dr. Mariam Hanna

Okay, Dr. Wasserman, today I really wanted to get into the dangerous part of SCIT, and thank you for agreeing to discuss it with us. I want to kind of get your way of approaching this, the safety in SCIT. How safe is SCIT?

What are some real-world kind of reaction rates that you quote your patients today?

Dr. Susan Wasserman

Well, you know, look, often these adverse events, these risks are reported differently depending on what you read. If you look at our immunotherapy manual, it says anywhere from 1 to 12 percent of patients can have a systemic reaction to immunotherapy. If you look at the American

Academy data, and they've been looking at this for a long time, since immunotherapy is so central to what we do, what they'll say is about one in a thousand injections can be associated with a systemic reaction, and some of these can be severe.

Near-fatal reactions are reported in something like one in 160,000 shots, and we've probably had about 10 fatalities that have been recorded by the American Academy over about a 10-year period. So, clearly, these things are not super common, the very serious adverse events and death, but they are out there, and for any allergist, it's something that we're very aware of.

Dr. Mariam Hanna

Absolutely. And have these stats meaningfully changed over time? So over the past 100 years that we've been offering this, has this statistic changed?

Dr. Susan Wasserman

Oh, I'd say it has. I mean, you know, hard and good statistics are very hard to gather from all of this. But at the end of the day, when people started to gather this in the early 70s, when data collection was a bit better, there were something like 92 deaths over the course of about 40 years.

Now, in the course of about 10 years, we have something like 8 to 10 fatal reactions. You know, many people do have systemic reactions, but they're mild, they're moderate. But the really serious ones over time have decreased.

They're not zero, but they have gotten better over time. And there are probably good reasons for that as well.

Dr. Mariam Hanna

Let's get into those good reasons. Why do you think these reactions have decreased?

Dr. Susan Wasserman

Well, over time, there has been a lot of education around safety. We now have guidelines. Did we at the beginning?

No, we probably didn't. Not way back when, when all of this started. We've learned how to carefully select patients.

Who are the good candidates? Who are the ones at high risk? We screen people before they get their allergy injections.

Our offices, our clinics are equipped to treat an allergic reaction when they do happen. Symptom recognition, giving epinephrine at the first sign of a problem. We've learned how to do that as well.

We also keep people around for 30 minutes if they pay attention and do what they're supposed to be doing after they get an allergy shot. And of course, the quality of the extracts have probably changed as well. We now have standardized extracts as well, as opposed to sort of making an extract from the contents of a vacuum cleaner bag or whatever used to be done in the old days.

So you know, there are probably lots of reasons why the practice has gotten safer over time. All of that is reassuring, but you know, systemic reactions are still fairly common and unfortunately there are deaths, so thankfully not many.

Dr. Mariam Hanna

Who are the ones that we should be sniffing out and saying, no, maybe you're not a good candidate for this?

Dr. Susan Wasserman

Listen, there are lots of contributors, but number one still has to be uncontrolled asthma. This has to come up every time we decide to examine this question, who is the patient most at risk? And when they've looked at these sort of series of fatalities and severe reactions, asthma is number one.

So clearly before you give anybody an allergy shot, ask them about their asthma control, if they're using their medications, that would be number one. But there are others and they rank a close second, prior systemic reactions. If you have patients who are quite sensitive and they've reacted before, these are your red flags that it may happen again.

And there are other factors as well, people receiving shots in pollen season, which is more of a high risk time as well. And then there's the usual, well, somebody starts to react, do we recognize it? Do we inject them with epinephrine early enough?

And then the usual sort of dosing errors and other more mechanical things that come up in the course of giving allergy injections. But if anybody remembers anything, it's the uncontrolled asthma.

Dr. Mariam Hanna

Yeah. And this is the disease that often tricks us in in health care in general, is not recognizing asthma when it's there, not recognizing control and uncontrolled asthma. Should like, should we be doing, I've seen in clinics, some do spirometry or an FEV1 or a peak flow with each shot.

Is that the level that we're talking about in terms of screening these patients before a shot?

Dr. Susan Wasserman

Look, I would say that in general, that sort of level of caution and vigilance is probably not going to be very pragmatic or reasonable for the vast majority of patients. But clearly, you've got to ask

your patients, have you had a previous reaction to the last shot? Are you experiencing shortness of breath?

Are you sick with a cold? Do you have fever, chest tightness, cough? All of these sorts of things which, you know, question their asthma control is a reason to postpone the shots.

I think probably that doing something like a spiral or peak flow will not be manageable or pragmatic for the vast majority of patients. So maybe the ones that are especially tricky, but then you're going to question whether they should be on this therapy in the first place.

Dr. Mariam Hanna

Fair. Yeah, absolutely. Absolutely.

And back in training, we used to talk a lot about patients on beta blockers as well as ACE inhibitors because of their, well, because of their response to epinephrine more than anything. Should patients on beta blockers or ACE inhibitors still receive SCIT?

Dr. Susan Wasserman

Well, this question comes up a lot. They're so widely used out there, especially if you're seeing adult patients. Every second patient is now on an ACE inhibitor along with their GLP-1 inhibitor and their beta blocker.

So it commonly comes up. And this is sort of a point where you really do have to have shared decision making with your patient. What is the risk benefit of either staying on the medication, changing the medication or coming off the medication in order to be able to receive immunotherapy?

You're right in that the risk of beta blockers that we worry about is that these people will not respond appropriately to epinephrine when it's needed. Neither the epinephrine that you give is an EpiPen nor the endogenous epinephrine that your body's going to produce in order to fight an allergic reaction. ACE inhibitors, you know, don't affect epinephrine per se, but at the same time, they will cause mast cell release so they can compound allergic reactions in addition to causing increase in bradykinin.

Now, you know, it's been hard to collect data and the data has been somewhat controversial over the years because along with blaming beta blockers and ACE inhibitors, these people also have underlying disease. They have cardiac disease. They have renal disease.

How much are these contributors if somebody has an allergic reaction? But weighing everything together, what I think we sort of agree upon now is that the incidence of anaphylaxis or severe allergic reactions is probably no greater with these medications, but the severity maybe. So when you talk to your patient, they may be at no greater risk of experiencing a reaction, but when they do experience it, it may be worse than if they were not on either one of these medications.

So this is the kind of shared decision-making that you need to go to. Now, you know, I would apply those rules more for aeroallergen immunotherapy. I worry less in people on sublingual immunotherapy where there really haven't been any published deaths with sublingual for aeroallergens.

And for venoms as well, I have patients on beta blockers and ACE inhibitors who are receiving immunotherapy for venoms. But that's a different type of patient. They're less atopic with less comorbidities generally.

Dr. Mariam Hanna

Yeah, and it's an excellent point that most of today's discussion is all about aeroallergen subcutaneous immunotherapy and a great differentiator to say kind of risk of disease versus the risk of the medications, severity being worse, not necessarily reaction rate, but the severity of the reaction and response to medications. So these are all great pearls. I also heard prior systemic reaction history.

How big of an element is this?

Dr. Susan Wasserman

We used to worry a lot about large local reactions, but in fact, based on what we know, they don't seem to be very predictive either as to whether somebody is going to have anaphylaxis or not. But it does come up as something which is predictive of future adverse events in anaphylaxis and receiving allergy shots. So again, this is one of those shared decision-making moments.

What is the risk of continuing versus stopping? And you know, it's important to identify the cause of that systemic reaction. If it's a failure of screening because you've missed that asthmatic who's not well controlled, those sorts of issues can be corrected.

If somebody giving that injection has made a mistake, use the wrong vial, use the wrong dose. Again, these are correctable sort of problems that arise in the course of, you know, immunotherapy. So once you identify what the problem is, if it's potentially correctable, then you can work towards finding a solution for that patient if they really want to, you know, stay on immunotherapy.

But regardless of what you find, even if it's a total error, the next dose should be lower than what you gave in advance. And again, that's judgment. Is it one dose?

Is it two dose? Do you go back to the beginning of the vial? And now more and more people are receiving shots in walk-in clinics.

No family doctors who are the main administrators of most of these shots, frankly, more so than the allergy community. So I think that the, you know, the landscape for sort of having some of these reactions is growing, even though the practice overall seems to be safer.

Dr. Mariam Hanna

Speaking about administration errors with immunotherapy, is it the buildup that's more risky or maintenance that's more risky, or it really doesn't matter?

Dr. Susan Wasserman

Based on what we know, buildup is riskier. You know, you're starting to give somebody injections where with every injection you're going up to a higher dose. And sometimes those doses are, you know, significantly higher than the amount of allergen that they would have received before.

So at the end of the day, yes, maintenance is safer. These are doses that the patient has tolerated for a certain amount of time, and maintenance appears to be more of a risk. And, you know, based on some of the numbers out there, the risk of reacting during maintenance varies anywhere from double-dose risk to about five times.

Dr. Mariam Hanna

Okay, double to five times increased risk. What about speed of updosing? So, you know, we're talking about cluster, rush versus standard immunotherapy.

Does that affect safety as well?

Dr. Susan Wasserman

Oh, it would definitely. I mean, you know, with any rush protocol, you're giving multiple injections over a certain period of time. You're building up that dose, you know, really to get to the maintenance as quickly as possible.

What's the incentive for going that route? Well, if somebody lives out of town, they don't have an allergist, you really want to get up to where you're going. In the aeroallergen space, I almost never do this.

I never rush anybody. I think that there's inherent risk. And for something like aeroallergens, it really is never, in my opinion, super critical to get up to that maintenance that you might consider for something like venoms, for instance.

So, you better be in a place where somebody is prepared to treat systemic allergic reactions if they are on cluster or rush.

Dr. Mariam Hanna

And have a really good reason to do cluster or rush.

Dr. Susan Wasserman

Absolutely. Yeah.

Dr. Mariam Hanna
Yeah.

Dr. Susan Wasserman
100 percent.

Dr. Mariam Hanna
Okay. What about high aeroallergen load versus just like polysensitize, treat everything that's positive on the skin test versus not? Does that increase likelihood of systemic reactions?

Dr. Susan Wasserman
Sure. You know, look, in reference to what you said before, you don't treat every skin test. At the end of the day, you need to have somebody who shows some sort of clinical symptomatology to the allergen in question that you have a positive skin test to.

So, we don't treat everything. Now, the more things that you load into that injection, do you have a higher risk of reactivity? And believe it or not, it really has not been a consistent factor in identifying people who do have allergic reactions.

We don't tend to practice like that for reasons of efficacy. And you know, we tend not to mix certain things that may break down allergens like mold and cockroaches and other things that have proteases. But the simple answer to your question is that allergen load has really not played any consistent role in reactors that we've identified.

Dr. Mariam Hanna
Okay, we talked about it earlier in that now we stipulate that patients should wait in the waiting room for 30 minutes. I've on occasion had the staff call the patient back to the office, actually, because they've wandered away. When do most severe reactions occur?

Is it within 30 minutes or are we talking delayed past that?

Dr. Susan Wasserman
Look, 30 minutes got established because most severe reactions did occur within that 30-minute window. But you're still talking only about 75 percent of reactions. It's entirely possible that somebody will go out there and have a delayed reaction.

So, you know, in order to make this practical, less of a barrier to sort of err on the side of capturing as many people as possible who may react, we say 30 minutes. But that doesn't mean that somebody may not have a reaction on leaving your office. Probably about 25 percent of them.

Also, look, we do give people instructions. Don't have an allergy shot and then ride a mile on your bike to get home. I mean, don't exercise immediately after the shot.

So you do have those people who don't hang around. You send them to the waiting room. They disappear.

These are not people who I would recommend continuing with. They're not reliable. And they put both of you at risk.

And there are also things regarding, you know, exercise and other things that may potentiate reactions the patient should be told about. But that varies.

Dr. Mariam Hanna

Okay. And is that 25 percent significant enough that we should be changing our practice to say, like, an hour of observation? 30 minutes is already hard enough.

Dr. Susan Wasserman

You know what? Look, I'd say that based on what we know now, there's probably not enough out there to say the practice should change for everybody.

But if you do identify a patient who wants to continue their shots and they have a history of reacting beyond that 30-minute window, these are the patients that you're going to watch for a longer period of time.

Dr. Mariam Hanna

Fair enough. Now, we've touched about epinephrine multiple times. Does every patient need to have their own epinephrine autoinjector with them?

Dr. Susan Wasserman

You know what? I think that my practice over the years has changed. Maybe I was a bit more cavalier in not giving everybody an epinephrine autoinjector.

And we've been lucky because as allergists, most of our patients carry them anyway. They're food allergic. They're severe asthmatics.

They happen to be equipped. But now I think just based on everything that we know and the fact that adverse events do happen, I feel better equipping people with EpiPens, frankly, when they leave the office. I think it's a safer practice.

I don't do so with sublingual immunotherapy. And, you know, anybody who's had a prior systemic reaction, anybody who has asthma, especially if there is any sort of tendency to a lack of control, people who are getting injections outside of my office, which is the majority, I mean, I would equip those as well. And anybody on a cluster or rush buildup, definitely, they should be equipped with EpiPens.

So, you know, I just outlined a number of situations which is probably going to apply to many patients who are on immunotherapy.

Dr. Mariam Hanna

Yeah. Essentially the majority, if not all.

Okay. Each guideline has their own kind of response to a missed dose or prolonged gap between injections. Where is the art in this one or the finesse? How do you decide?

Dr. Susan Wasserman

Well, you know what? The correct response is going to be the individual patient as well. If I have somebody who's been on maintenance for years and has really not had a problem and they've been tolerating it well, et cetera, I mean, at the end of the day, I may not reduce that patient if they're a month late on their shots.

I may give them the same shot. But what I find particularly useful, I mean, the American Academy laid it out according to days. How many days missed versus the amount of reduction of the allergy shot?

And I would advise people to look at that. You know, there is some guidance behind it, and I find it very useful. Once, though, you get up to something like, you know, six to eight weeks even on maintenance, then really you either have to go back to the beginning of the maintenance or, you know, more than two injections back prior to restarting again.

So the longer you wait, the more you have to reduce.

Dr. Mariam Hanna

Now, one of the things about aeroallergen immunotherapy, and we're going to compare it to venom for a second, is that the patients when they are on maintenance for an extended duration of time, whereas venom will start stretching out dose frequency, aeroallergen ones don't typically. Why is that?

Dr. Susan Wasserman

Good question. I mean, I can't say that I know the answer, and I don't know if anybody's ever studied stretching out the interval. I mean, clearly, you know, even if you look at this missed dose guideline, you can miss a week or two and not go back.

So you can stretch out the interval that much. But to maintain tolerance, you do need good, steady exposure to that allergen. And the population who receives aeroallergen injections are different than your venom population.

These people are more atopic. They have comorbidities. They're on medications.

They're a higher risk group in general. So I tend not to fool around with it too much. We pretty well, you know, stick to the schedule.

And I will back down with missed doses. If it's a week or two, then you're usually okay. Venoms, we can go as long as a three-month interval sometimes.

So, yeah, it's a different animal.

Dr. Mariam Hanna

It's a different animal altogether. I gotcha. Okay, how often is unrecognized asthma exacerbations involved?

Dr. Susan Wasserman

Well, you know, if you look at these series in the fatality series, you know, about 60 percent were uncontrolled asthmatic. So did they walk in like that? And because of a failure of prescreening, nobody picked them up.

Was the severe asthma, did it develop just during the course of, you know, the anaphylaxis which took place with the shots? You know, clearly they are a key contributor. And, you know, I would venture a guess that it was missed, that unless you do proper screening in advance, that these people are not being picked up and that we're not asking about previous reactions that they may have had after the allergy shot.

Dr. Mariam Hanna

Absolutely. Absolutely. And should clinics be tracking systemic reaction rates at this point?

Dr. Susan Wasserman

The allergy clinics need to. Look, it's part of the quality control that all of us should be doing. And if you look at, you know, adverse reactions, poor outcomes, failure of process is big.

People didn't prescreen. People didn't have the necessary medication available at their fingertips. There was no process for early recognition for or for administration of medication.

At the end of the day, if you want a process that works well and that's reliable, you have to track what you're doing and you have to improve. And, you know, even things like simulation exercises within a clinic or office, which probably never take place but are always recommended, should probably be done as well. So, yes, we should be tracking.

Is there enough of it? No.

Dr. Mariam Hanna

Fair enough. Okay, one myth about SCIT. Safety that needs to go.

What's one myth that you want to bust right now, Dr. Wasserman?

Dr. Susan Wasserman

You know, I think that SCIT does have a bad reputation. I think that people do think that this is something that allergists do because somehow it's a big moneymaker. Everybody goes out and they're on allergy injections.

And this is such a dangerous therapy. But in fact, the safety aspect of SCIT, you know, we really have made progress. And that part is not emphasized enough.

It's one of the few therapies that we do that can change or remodel the immune system. And we have to remember that. There's nothing else that we do that is able to do that.

So we have to play up the benefits. This is not a dangerous therapy. There will always be that tricky patient, you know, who will be hard to immunize no matter what you do, even if you do everything right.

But if you do practice, you know, safe screening of your patients, if your office is equipped, if you have careful patient selection, this is a safe and very effective therapy, which is probably underutilized within our own community.

Dr. Mariam Hanna

Fair enough. Okay. And then on the tail of that, one change every allergist should implement immediately, right now, as soon as they finish listening to this.

Dr. Susan Wasserman

Well, I hope that, you know, along with the sort of benefits of immunotherapy and the fact that there's many benefits to be had, that we are paranoid enough and vigilant enough to make sure that we're totally prepared. When you least expect it, something may arise. And that's the message.

I mean, we do need to be prepared to treat adverse reactions and to make sure that everything is in place so that we do have good outcomes.

Dr. Mariam Hanna

Perfect. All right. Time to wrap up and ask today's allergist, Dr. Susan Wasserman, for her top three key messages to impart to patients and physicians on today's topic, subcutaneous immunotherapy. Dr. Wasserman, over to you.

Dr. Susan Wasserman

My top three. Well, okay, you know what? I'd say, Mariam, that the first thing is not safety-related directly.

But see your allergists. I mean, our allergy patients should not be suffering in silence. It's not only about what you can grab off the counter at the pharmacy.

Ask to see your allergist, because along with this does come safety. You will be tested. Your prescription will consist of allergens that are relevant to you.

And hopefully, you'll be immunized in a safe fashion with all of the safeguards that we've talked about. So that would probably be number one. Number two, well, I'd say, yeah, maximize safety, as we said before, and put all those things in place.

That's something that we really ought to be doing in our own offices. Number three, patients need to take some responsibility as well. I mean, they have to know when a shot should not be given.

They should take control of their asthma. They should report adverse reactions. You know, allergy shots are very much sort of a hands-on type of approach to patient treatment.

You're going to be seeing them very often, and that patient has to be confident that anything that they've experienced should be reported, and that they have to look after their other comorbidities. And that would probably be it.

Dr. Mariam Hanna

Perfect. Thank you Dr. Wasserman for joining on today's episode of The Allergist.

Dr. Susan Wasserman

It's been a pleasure. Thanks for the opportunity.

Dr. Mariam Hanna

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