

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. A little while ago, I toured the Coca-Cola Museum. I'm not a museum person, but my wandering down history was actually quite amusing. Uncovering the secret recipe and how it has evolved over a matter of decades is actually truly astounding. I wonder if the same thing happened around the discovery of antihistamines, the first generation antihistamine, a miracle drug from runny noses to miserable itch, and as a bonus, a good night's sleep. Look at how we've come in the evolution of allergic rhinitis, seemingly a nuisance, but realizing real health and life impacts from what on the outside would seem like a really benign condition, turns out that we have a lot of impact and can do a lot of things about it. So let me tell you a story. My youngest immunotherapy patient came in with his parents. Classic symptoms of perennial rhinoconjunctivitis, laundry list of medications that have been tried, and then his current regimen, not tolerant to nasal steroids, suboptimal response.

I have this canned spiel that I do now for all my allergic rhinitis patients where we talk about environmental control measures, medical management options ending with the grand finale of them all, immunotherapy. But hold on, I'm not going to tell you my spiel today. I've actually brought this incredible allergist who'll do just that with us because today we're launching you into allergic rhinitis. Bringing you up to speed on the focused Canadian allergic rhinitis guidelines published with our first author, Dr. Anne Ellis.

Dr. Ellis is a professor of medicine and chair of the Division of Allergy and Immunology at Queen's University. She holds the James H. Day chair in Allergic Diseases and Allergy research and is the director of the Environmental Exposure Unit and the Allergy Research Unit at Kingston General Hospital. She's the current president of the CSACI and serves on the Joint Task Force for Practice Parameters representing the American College of Allergy, Asthma & Immunology. Dr. Ellis, thank you so much for taking time out of your busy schedule today to join us and welcome to the podcast.

Dr. Anne Ellis:

Thank you for having me, Mariam.

Dr. Mariam Hanna:

Dr. Ellis, we're going to start with a really simple question. What is your definition of allergic rhinitis?

Dr. Anne Ellis:

So allergic rhinitis is more commonly referred to as hay fever simply because it was initially described as symptoms of runny nose, itchy, watery eyes, nasal congestion, sneezing that happened during the season when you had to hay the fields and collect it. And of course, everybody was getting exposed to other pollens as a result, but in reality, we use that term because it's recognizable by the lay population. But allergic rhinitis is essentially allergies triggered by environmental allergens. So in the springtime tree and grass pollen, in the late summer, early fall, ragweed in Ontario was particularly a troublesome trigger, but we also have year round triggers such as dust mites, cats or dogs. If you happen to live with phyto or fluffy

and you choose not to get rid of them, but again, lots of patients suffer from this common condition. Our best estimates is it's probably about 25%, but probably even higher of the Canadian population experiences symptoms of allergic rhinitis, may or may not present to their physicians for it, but it's definitely very prevalent.

Dr. Mariam Hanna:

So Dr. Ellis, there has been a recent release of Canadian allergic rhinitis guidelines. Can you tell me what was the inspiration behind starting this?

Dr. Anne Ellis:

Well, we had so many advancements in our therapies, particularly you alluded to immunotherapy in your opening presentation, but we now have these really novel sublingual immunotherapy tablets, and we didn't have any kind of real guidance or recommendations as to where they should fit into therapy. We didn't really have any guidelines either for that matter. We had a couple of summary papers that were literally just a review article. So we really wanted to have something that could come across as this is what we recommend for the treatment of allergic rhinitis in Canada.

Dr. Mariam Hanna:

Perfect. And so what we're going to do with the rest of the podcast is we're going to really dissect these Canadian guidelines and see how we can implement them into practice. But the first thing I noticed when I went through it is that you guys looked at publications from 2016 onwards. Was there a particular reason for this timeframe to be chosen?

Dr. Anne Ellis:

So a couple of reasons. One, there's so many articles out there that if we went back all the way to the beginning of any publication related to allergic rhinitis, we would've just been swamped with articles to select and review. There was a lot of things that were published prior to 2016 that were not the highest quality studies. We wanted to make sure that what we had was the best new evidence and just really trying to keep them current and up to date.

Dr. Mariam Hanna:

Perfect, perfect. Okay, so the first part actually addresses how we should test or what can be used for testing. So in Canada, commonly we use skin prick testing as it is widely available in our clinics, whereas in other parts of the world, they'll use serum specific IgE. And this is especially an interesting question for me when we have this shortage of allergists and long wait times, and maybe some of this stuff can be ordered through primary care. So the first question is, is serum specific IgE testing sufficient to identify candidates for immunotherapy? Or is the skin prick test really still needed?

Dr. Anne Ellis:

So the whole reason this question evolved actually was due to the COVID-19 pandemic when our offices were closed and we couldn't see patients in person to do skin testing. But that didn't stop the onslaught of referrals for people who were suffering from allergies. I ended up ordering

a lot of serum specific IgE at the time, and I wanted to know was I actually doing the right thing? Is this actually good enough or am I missing the boat here? What we found in the literature was, in fact, if you've got detectable specific IgE greater than 0.35 kilo units per liter or even better, greater than 0.7 kilo units per liter, that turns out to be just as good as a skin prick test for identifying people specifically for candidates for immunotherapy. That's the way we phrased the question. It's helpful for people who, as you said, live in remote areas and don't have access to allergists.

Some of us have very, very long wait times and it is an option. Now across the country, coverage for this test is variable. Not all provinces will cover the cost, and it does run up there from time to time. I know the last time I checked in Ontario anyway, it was \$35 per allergen. So some patients that's out of reach for them, but if you're in a province that covers it and you're selective and you're not doing a massive panel, it could be a way to avoid having to wait two to three years to see an allergist to get a skin prick test.

Dr. Mariam Hanna:

That's a great point. Now, I often wonder if there's a role when a patient comes in and has negative skin testing in my office, like with these patients where I think they have local allergic rhinitis. Is there a role in still ordering serum specific IgE for them?

Dr. Anne Ellis:

My personal experience, they're always still negative. So if the skin prick test is negative, the specific IgE is negative. All the patients that I assessed during the pandemic with specific IgE who's had undetectable IgE, I brought them back two years later when we were open again. Their skin prick tests were negative. So my own personal experience is a good correlation between negative skin test, negative IgE, positive skin test, positive IgE. You don't need to go to the extra expense of ordering the specific IgE if you've got negative skin tests. That's an allergist of one experience, but that's what I've come across.

Dr. Mariam Hanna:

We like these allergist pearls on this show. So all right, next question is particularly around patients and prescribers. So in the era of shared decision-making, this is the big buzzword these days and medication efficacy, what should be our first line treatment, second generation antihistamines or go straight to nasal corticosteroids?

Dr. Anne Ellis:

So what we did with the guidelines and the figure is going to be really helpful. Obviously I can't show it on a podcast, but we literally put all of the first line agents across the top and just rank them based on efficacy. And it depends there on patient preference. So good first line options are second generation antihistamines, but nasal corticosteroids are more effective, even more effective as if you have a combination intranasal corticosteroid, intranasal antihistamine. So we said these are all good first options. We rank them based on efficacy and we do throw in leukotriene receptor antagonists with a caveat that it's only been studied in seasonal allergic rhinitis and only short-term use, and it's the weakest of all of them. But again, some patients would rather take an antihistamine than put a spray in their nose, and so that's where, as you

mentioned, the shared decision making comes in. But they're all possible options at the very beginning. You can go straight to the big guns if you want, with the combo nasal spray, or you can start simple based on what your patient wants to do.

Dr. Mariam Hanna:

Okay. But starting simple could also mean just going to the pharmacy and picking up an over-the-counter antihistamine. So let me sidetrack you because this is a common topic that you and I sometimes have discussed in the past. First generation antihistamines, Dr. Ellis, like Benadryl or even Atarax in this publication, they don't go into it too much, but do you want to comment about it?

Dr. Anne Ellis:

So the reason why we didn't harp on it in the new guideline is because we already have a position statement that's been out since 2016 stating that the CSACI does not recommend the use of first generation antihistamines for the treatment of allergic rhinitis, and we strongly favor second generation agents. One because they're safer first and foremost. Secondly, because they work better, they last longer, they're more potent. Why would you use one of the first, the one that was invented in 1964 that didn't go through FDA approval when we have all these great second generation agents that have a much safer profile and have gone through rigorous randomized controlled trials to prove they're actually better than placebo?

Dr. Mariam Hanna:

Yeah. See, that's the question I'm left with. Why? Why would you even bother? Why? I'm going to go back to the big guns that you alluded to, a nasal antihistamine with nasal corticosteroid formulation. This is often viewed as big guns. I always call it the Rolls-Royce of the nasal sprayers in comparison to my Honda Civic model, which is like a nasal corticosteroid alone. So in this next question, your team looked at a combination of nasal antihistamine nasal steroid versus nasal steroid plus oral antihistamine, and are they in fact equivalent approaches or do they even out in the long run? Do you want to comment about that one?

Dr. Anne Ellis:

Yeah, we did find that if you're using the combo spray, that works slightly better than taking a nasal steroid spray plus an antihistamine. Turns out if you're actually using your nasal corticosteroid properly, adding in an oral antihistamine may not be doing all that much extra for you, whereas the combo spray covers it all right off the bat.

Dr. Mariam Hanna:

Oh, so it's even better, is what Dr. Ellis is, -

Dr. Anne Ellis:

Yes.

Dr. Mariam Hanna:

Perfect. Perfect. Okay. And then the leukotriene receptor antagonist, again, you've alluded to this already, did they have a greater benefit than oral antihistamines in allergic rhinitis? We alluded to this one already.

Dr. Anne Ellis:

So they're technically not as good as second generation antihistamines, leukotriene receptor antagonists. So again, we only have one left in Canada. It's Montelukast. It's an interesting class. In some people it works really well, but it only works really well in 25% of the population. The good news is you'll know within a day or two at most, I usually say a week, but if you haven't noticed any improvement within a week, it's not going to work and you can save your money.

Dr. Mariam Hanna:

Perfect. Now, do you provide counseling around Montelukast side effects? What's your spiel there?

Dr. Anne Ellis:

Yeah, so it is important to realize there's now a black box warning against Montelukast for things like hallucinations and even suicidality. So I don't recommend using them in anyone who has a history of depression, anxiety. You can deal with the nightmares as another known side effect by dosing it in the morning rather than at night, which is what the product monograph tells you to do. I've asked the inventor, why did you dose it in the trials at night, and they don't have a good answer for me. So if it is an effective therapy and patients prefer to take it rather than using a nasal steroid spray, I just indicate move it to the morning and dose it then. But I don't use Montelukast very often in allergic rhinitis. I tend to focus on antihistamines and nasal steroid sprays.

Dr. Mariam Hanna:

Perfect. And can we predict who the 25% of the population is that would respond to it?

Dr. Anne Ellis:

Sadly, no, but the good news is you'll know fast.

Dr. Mariam Hanna:

Perfect. Okay. So we have talk about immunotherapy, and I too am excited at how rapidly sublingual immunotherapy has evolved over this past decade. Are we at a point now where based on efficacy we should consider sublingual immunotherapy first line over the traditional allergy shots, subcutaneous immunotherapy?

Dr. Anne Ellis:

So what we've done with the guidelines is really made sure it's clear that you don't have to wait for severe disease to introduce immunotherapy, especially in patients who have comorbid asthma. We know that it does have, well, they don't have technically the indication for asthma. We know that sublingual immunotherapy as well as subcutaneous immunotherapy improves

asthma outcomes. We also have shown with the systematic review that we conducted for this guideline is that the efficacy of SCIT and SLIT really can be considered equal. So we have clinical equipoise.

So it really comes down to what you're allergic to and if what you're going to be allergic to can be covered by the tablets, that often will lead to patients choosing that route due to convenience of home dosing, the improved safety profile, the fact that you don't have to go to the doctor's office once a week during that buildup phase, which is traditional for the subcutaneous or so-called allergy shots as you referred to. The downside to sublingual immunotherapy is we can only treat trees, grass, ragweed, and house dust mite with the tablets. So when it comes to animals or molds, then we'd have to revert back to the subcutaneous route if we think those are actually important and we can't mitigate your allergic rhinitis symptoms due to cat, dog or mold in other ways.

Dr. Mariam Hanna:

That's an important caveat to say if we think that those sensitizations are important or relevant to your allergic rhinitis symptoms that you have. So not necessarily needing to treat all but to treat relevant allergies. I mean, this is an area where sometimes I find in Canada we differ a little bit from other parts around the world. Is that true?

Dr. Anne Ellis:

Absolutely. So we pride ourselves on taking a good history and figuring out when are you actually getting your symptoms? What season is your actual worst? Because yes, we have these four tablets, but some patients don't want to take four tablets. So when I have people who really just say, I'm just so sick all year round, so then they're not even sure that the seasonal allergens that they've clearly come up positive to on their skin prick test. I'm like, okay, well let's just start with a house dust mite tablet because you're sensitized to that. It's there all year round. Maybe we can dampen down all of your other sort of minor seasonal exacerbations, which you're not even reporting to me with just monotherapy. But other times it's very clear that first thing when the trees start budding, you're miserable. Then we're definitely going to make sure we include the tree tablet. And then again, we just go through the history of when are you actually getting symptoms? We can figure out what are the ones that are actually going to be needing to be treated as opposed to just, we're not going to treat a skin test. We're going to treat symptoms.

Dr. Mariam Hanna:

Okay, not included in the guidelines, but I have to ask because I've recently learned there's a large proportion that order an epinephrine autoinjector for patients that are on sublingual immunotherapy. Is that needed?

Dr. Anne Ellis:

In the United States, unfortunately, it is. It's an FDA mandate. In Canada, it's optional. And honestly, I have never ever seen a systemic reaction to the sublingual tablets. Prescribing an epinephrine autoinjector may increase a patient's anxiety around a side effect that really doesn't exist, so I don't do it. Some practitioners feel more comfortable, and so that's their choice and

it's the patient's choice too. So you just have to have a discussion. Whereas for subcutaneous immunotherapy or allergy shots, particularly because so many of my patients are not getting their injections with me, I don't know where they're going, I'm much more likely to prescribe an epinephrine autoinjector to somebody who's getting an injectable immunotherapy because the risk of anaphylaxis is measurable and known with that treatment, whereas the risk for the sublingual tablets is minuscule.

Dr. Mariam Hanna:

Perfect. If immunotherapy should be considered earlier and we shouldn't wait for severe disease, does that mean that now all patients should be seen by an allergist when they have allergic rhinitis and offered these options?

Dr. Anne Ellis:

I think certainly if over the counter and primary care interventions are not doing the trick or patients just don't want to be taking medications year after year, all year round or even just every spring, I think it's always worth finding out exactly what your triggers are and having a discussion about disease modifying therapy such as immunotherapy and the two different ways we can offer it now.

Dr. Mariam Hanna:

Okay, so now I'm going to ask you a harder question. We've talked today about serum IgE testing can be quite helpful and quite equivalent to using skin prick testing and it can be ordered in the community. Can immunotherapy be ordered by non allergists and started that way?

Dr. Anne Ellis:

That's a really loaded question. Certainly not. I would never recommend injectable immunotherapy be prescribed by someone in primary care, simply because the formulations are more complicated, the risks are higher. It really does require specialist attention. If, however, you're simply looking at treating house dust mite and you've got a positive IgE, you're comfortable with the local side effects that are common from the sublingual tablets, and you're happy to actually do what the product monograph says, which is you must have the first dose in the office. You must monitor them for 30 minutes and be prepared to treat local allergic symptoms.

So again, making sure you have second generation antihistamines in your office, preferably have a supply of the suspensions because they're very effective if you give them rapidly for those local side effects. I wouldn't be averse to that, particularly if you're in an area where either you don't have an allergist at all or your wait times are excessive. I think that's the only way we're going to improve overall better care of our patients with allergic rhinitis, is opening up the doors a little bit knowing that there are certain areas of the country that are well serviced by allergist and others not so much.

Dr. Mariam Hanna:

That's a perfect response, Dr. Ellis. That's perfect. I have to touch on eosinophilic esophagitis. Do you see it with sublingual immunotherapy? When do you screen, how do you counsel patients?

Dr. Anne Ellis:

So I have not yet personally seen it, but I am aware of the case reports that have been emerging. It seems to be a bit more of an issue in the pediatric population. It's really important to make sure that children taking sublingual immunotherapy, make sure they're actually letting it dissolve. They're not chewing it or swallowing it. It's really important to make sure they hold in their mouth and it dissolves. Don't eat or drink anything for three to five minutes afterwards. And then I do on a yearly basis, I will ask questions like, have you had any issues with swallowing, feel like food's getting stuck in your throat? Again, it's certainly not a common side effect, but it's something we're aware of and we do screen for it now.

Dr. Mariam Hanna:

Dr. Ellis, these are fantastic guidelines. I actually love that we have our own Canadian allergic rhinitis guidelines that cover these key issues. So with this wrap up, you can cover whatever you like. But time to wrap up Dr. Ellis with today's three key messages that you want to impart to patients, physicians on today's topic, allergic rhinitis. Dr. Ellis, over to you.

Dr. Anne Ellis:

Well, thank you so much again for inviting me to talk about these new updated guidelines. Big caveat, they're not yet published. They're still undergoing peer review, but they won't be too long. I think the three things I would like people to take away is first and foremost, don't suffer in silence. If you're having problems with allergies and allergic rhinitis, don't be afraid to talk to your family for your primary care provider to ask to see an allergist for the opportunity to discuss all these options. Secondly, if you do have milder disease and you're just going to the pharmacy, please avoid sedating antihistamines like Benadryl. Choose one of those second generation agents. They're all effective. They've all been well studied. We even have two that are available by prescriptions, so they'll be covered by your health insurance if you do have a drug plan. Talk to your pharmacist.

They have prescribing powers now for minor ailments, including allergic rhinitis. They may be able to help you move on to the Cadillac of the nasal sprays as you refer to it, or as I like to call it SYMBICORT for the nose because you get that immediate benefit from the antihistamine and then the steroid kicks in to actually reduce inflammation. And I think mostly don't be afraid of using these disease modifying therapies. They're safe, they're effective. They will actually let you get away with using less medication, and they can have disease altering powers in the long run. So I think it is worth, the time has come to not wait until people are on the floor and they can't stand it anymore before we go to immuno. So I'm excited for when these guidelines are actually published and we'll be able to share them when it'll be published in our Canadian Journal, which is open access, which means anybody can read them.

Dr. Mariam Hanna:

Anyone can read them, available at your fingertips. Thank you, Dr. Ellis for joining us today on today's episode of The Allergist.

Dr. Anne Ellis:

Thank you for having me.

Dr. Mariam Hanna:

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