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. Disease prevention.

Improved treatments. Disease modifying therapies our options are increasing daily it would seem. As allergists, we need to stay current. The conference halls are filled with the familiar question, what are you doing in your practice? HOW do you deal with this issue? And most importantly WHAT have you been reading? And have you read THIS essential article that's really changed how I approach this issue.

So, today's podcast is all about the top articles of 2023 that we think you should know about. Today's speaker is one who I would personally want to know what he's read over this past year, and what struck him as essentials for our specialty and where we're headed. It's my distinct privilege to introduce Dr. Matthew Greenhawt.

Dr. Greenhawt is a professor in the Department of Pediatrics Section of Allergy and Immunology at Children's Hospital Colorado and the University of Colorado School of Medicine. He holds a medical degree and an MBA from Tufts University, and a Masters degree in health and healthcare policy from the University of Michigan. He has authored numerous peer-reviewed articles, abstracts, and book chapters and is a member of several professional organizations, including the American Academy of Allergy, Asthma & Immunology, American Academy of Pediatrics, American College of Allergy, Asthma & Immunology, and European Academy of Allergy and Clinical Immunology. He has spoken to our Canadian allergists on a number of occasions.

Dr. Greenhawt, thank you so much for taking time out of your schedule to join us and welcome to the podcast.

Dr. Matthew Greenhawt: Thank you.

Dr. Mariam Hanna: Okay, so my request to you was your top five articles for all of 2023 from any part of allergy and immunology. You specifically said, food allergy, and I said, no, we're going through the entire landscape. So we're going to go through your top five articles.

Dr. Matthew Greenhawt: So, I should have prefaced and said that all of my articles that I have chosen, I would have loved to... I mean, I've now read all of these, but did I read all of them before this? Um, sure. But these are coming from the American College of Allergy, Asthma, and Immunology 2023 annual lit review. I looked at all the choices that

my co-presenters had nominated. Each of us gets a topic area, and then there's a 'best of.' So this was one of the top articles chosen from the drug allergies section.

Dr. Mariam Hanna: Let's start first in the world of drug allergies. Dr. Greenhawt, what was your pick for this one?

Dr. Matthew Greenhawt: Yeah, so, I'm about to butcher this poor author's last name. It's Swisherwatchery et al. This was a large meta-analysis looking at the phenomenon of direct drug provocation testing. This is a large systematic review looking at how we can effectively delabel drug allergy in children, which is a huge issue globally, but in particular in the US, with data suggesting that switching costs and other factors that occur when you have to move somebody from a preferred drug to a second or third choice because of a questionable allergy can be associated with $60-70 million worth of costs and stuff when you add everything up between length of stay and additional complications. So this article is a systematic review and meta-analysis looking at the safety of direct drug provocation tests. What this means is it's generally looking to see how well does skin testing predict the outcome? And is it even necessary?

Dr. Mariam Hanna: And what were the key findings with this study?

Dr. Matthew Greenhawt: So, these looked at studies that did provocation testing either with or without skin testing, but they ignored the results and excluded case reports and case series. There were a couple of quirks with it, but across 28 studies and 8300 direct challenges, what they found was that about 5.23% of cases reacted in total. But that includes both immediate and non-immediate reactions. Severe reactions were found in 0.36%. So that's three cases out of those 8300. So what this shows is that if you risk stratify kids, you take a history, you toss out things that would make you think that they have Stevens-Johnson or TEN or some severe cutaneous adverse reaction, that the process of skipping skin testing and just doing a challenge. And they looked at all kinds of challenges; they didn't discriminate the type of challenge that was done, either a one-step or two-step. But it shows that this process is safe. And this sort of reinforces a lot of practice that's been going on for the last couple of years. But still, not everybody is on board. There are still people in my local area where they won't do the drug test or they'll only do it after skin testing. Most of these kids aren't having IgE mediated reactions, so the skin test isn't going to... When it's negative, it's great. If you're reassured by the negative skin test in somebody who's had a rash on day six that burns through antihistamine, it isn't touched. If you can't tell that's non-IgE mediated, that's a problem. Right. But if you're more reassured by negative skin testing for that mechanism, there's an even bigger problem. So we're using the wrong tool for the

wrong job. These kids aren't benefited by skin testing because it's just not the mechanism. They need whatever the drug is, some form of penicillin put back in the mouth. They need to be observed for, uh, you pick the time. I usually do my challenges over about 60 to 75 minutes, show that they don't have an immediate reaction, get them out the door, get that label off the chart so they can move on with their life. So that's why this is important. This is the first actual meta-analysis showing the pooled rates of success. These kids really just need the drug put in their mouth and they need an observation area where they can prove they're either allergic or not. And they don't need very much more from us.

Dr. Mariam Hanna: So let me ask you one further question on this one. Are we at a point with penicillin allergy and delabeling where the right tool is a direct oral challenge, that it can be put in the hands of primary care, not simply allergists? You talked about being cost-effective in utilization. Are we at a point where we should be doing this at a primary care level rather than a subspecialty level?

Dr. Matthew Greenhawt: Um, I'm going to rephrase and reanswer that, twist it in a different way. Do I think that there are primary care physicians out there who are more than capable of doing a direct challenge in their office and taking us out of this equation? Absolutely. Do I think the majority of primary care physicians right now at this point, if we said 2024, we're done doing this, don't refer to our office. I think a lot of primary care physicians are not going to be comfortable with this yet. I think what we need is some knowledge translation and show the primary care physician that they can correctly identify this situation and they can really become the rate-limiting step in not making them do this. There's always going to be kids where they're not comfortable with knowing we probably are needed for maybe the higher acuity cases in this. And it's going to look a lot like asthma, where not every asthmatic is referred to us because we've worked with primary care for so long to get them comfortable in identifying and treating basic asthma. It's only those cases that are struggling that need to come to us. So maybe it moves into that category. Um, but I do think we need to be very cautious about who we pick and choose. Don't do unnecessary testing just to say, oh, look, it's negative if you can't figure out why it's negative. Right. There's just no validity in that testing in most of the cases.

Dr. Mariam Hanna: Lots of ground to cover, so we're going to move on to the next one. So then we put you on the spot for your next topic. So our next topic is on skin conditions. Dr. Greenhawt, you chose an atopic dermatitis parameter here. Robust publication again, yes?

Dr. Matthew Greenhawt: What was your role with disclosure? I was the joint task force liaison and one of the senior authors on this massive document. This is fresh off the presses. This came out about five days before the end of the year, but this has been in the works. So, this is the updated 2023, because it technically hit impress in 2023, Atopic Dermatitis Practice Parameter. This updates the 2012 practice parameter. It was one of the oldest documents that we had on record and it needed to be updated. So, this was done in GRADE style. And, uh, I must thank our colleagues at McMaster, Derek Chu and the Evidence and Allergy group. But also Gord Gaiat was instrumental in making this possibly the most comprehensive practice parameter that we've done to date. You're seeing a large panel of recommendations. There are 25 recommendations in this. What you're not seeing is about 30 papers that went into this, all high-level systematic reviews and often meta-analyses to investigate each question that got published. This is one of the most comprehensive scopes of work that was done, which includes a huge emphasis on dissemination and knowledge translation because you've got to get these findings out to the people who are going to benefit from them. So, the group that was put together to make the panel wasn't just allergists and dermatologists and people who specialize in atopic dermatitis, but also primary care, a lot of allied health members, and allied and advocacy group members to make sure that the recommendations were not only pragmatic but were going to benefit the patients who really need this the most. So, this is using GRADE methodology in a standard population intervention comparator outcome, or PICO, format with five main management questions to look at. There is this great sort of cartoon pictogram that goes through all 25 recommendations, explaining, for what degree of atopic dermatitis is this applicable for? It gives a very clear recommendation, either for or against. And it gives the certainty of evidence, which means, are, uh, more studies going to really influence the direction and the certainty that you would make this assumption? So, just going through some of the more obvious ones. So, obviously, we are recommending for the use of topical corticosteroids. We're recommending for the use of topical calcineurin inhibitors. One of the side projects of this was a meta-analysis looking into the safety of topical calcineurin inhibitors, because at least in the US and in certain countries, there is a black box warning that says that this has a cancer risk. As it turns out, uh, that probably doesn't belong there, and there's not a lot of evidence to support that. And that was published in Lancet Child and Adolescent Health as a side project. But that was a huge meta-analysis suggesting that that risk is negligible, which is a big finding. We suggest for topical phosphodiesterase-4 inhibitors. Interesting when you get to the JAK inhibitors. So this is a little not intuitive in certain places. So, we're suggesting against topical JAK inhibitors for mild to moderate eczema in children ages twelve and older. But when we go down to the systemic therapies, we actually recommend for certain JAK inhibitors at certain doses. But anyway, going through some of the more highlights, we're recommending against the use of elimination diets. We're recommending for

allergen immunotherapy for moderate and severe atopic dermatitis. And that probably has the biggest impact overall of any recommendation, because that's something that most allergists participate in. This opens up a whole new set of patients who are eligible for immunotherapy. We suggest against it for mild atopic dermatitis. But between that, the elimination diets and the allergen immunotherapy are probably the two biggest, uh, I think, takeaways from this document. But it's a huge document. It's 40-something pages. There are lots of tables. Um, if any of you have ever had the privilege of knowing or working with Derek, this is very much a Derek paper. It is meticulous. Again, I think this has got to be the most comprehensive guideline that I think I've ever seen. I've been a part of a number of guidelines, but he took this to a whole other level, both he and Linda Schneider from Boston Children's. I mean, the amount of work here is just insane. So, fresh off the presses, read it for your education. If you're having trouble falling asleep, it might work for that, too. Lots of good things from this paper.

Dr. Mariam Hanna: And the visuals at the end of it are actually very useful to print out and plaster in front of your eyes. To say, this isn't based on high-quality evidence that we're making this recommendation, or we're not really recommending that you should be doing that at all. So it's actually great for knowledge translation.

Dr. Matthew Greenhawt: Yeah, and those were intentionally made as patient handouts and stuff, so, um, please do exactly as you said. Those are great materials to share.

Dr. Mariam Hanna: Absolutely. Okay, our next two articles are going to go towards systemic therapies that we seem to be using more and more of within our field or our specialty. The world of biologics is like Pandora's box. That's really opened up, and it's really changed our approach in allergy and immunology. Our first article pertains to eosinophilic esophagitis. Dr. Greenhawt, your selection for this.

Dr. Matthew Greenhawt: So, this is from Evan Dellen and colleagues. This is dupilumab treatment in adults and adolescents with eosinophilic esophagitis. There were a couple of articles from our field published in the New England Journal of Medicine in the last year, and this is one of them. This is important because there are no approved directed therapies specifically developed for the treatment of eosinophilic esophagitis. We are using asthma therapies and other things adapted for it, but there's no specific drug. Dupilumab blocks IL-4 and IL-13. It's a potent T2 inflammation inhibitor with a number of potential applications. This drug has been approved for use in asthma, atopic dermatitis, sinusitis with polyps, perigonodularis, and now for eosinophilic esophagitis. This is the article that cemented this approval. A phase two trial showed that a 300 milligram weekly dose reduced both symptoms and histologic endpoints. This is the result of a phase three trial. For eosinophilic esophagitis, and why you might not see a lot of drugs

making the market, at least in the US, the FDA, and I think the EMA also, has made the bar a little bit higher. Because eosinophilic esophagitis is clinical, pathological, you need to have both histology and symptoms respond. So it's a dual co-endpoint thing. So if you're making endpoints on just symptoms alone, but not histology, you're not going to get approved and it's not going to be a positive trial. So you have to have both. And that's where a number of notable drugs have failed in the late phase two and phase three. Recently, this was looking at two dosing regimens. The first one was 300 milligrams weekly. The second one was 300 milligrams every other week, randomized one to 124 weeks. These patients were largely refractory population, which gets to the implementation side. Basically, they could continue on proton pump inhibitor, but they couldn't start a new one. They could continue stable food elimination, but they couldn't start or continue steroids. But most of these patients had failed through multiple therapies, and that's probably how they enriched the population here. What they showed in this trial was that for the histologic endpoints, either weekly or every two week dosing certainly was successful in achieving the histological endpoints, and so it's effective for that. Where the issue came was that using something called the Dysphagia Symptom Questionnaire, which is what the FDA prefers for symptom scoring for these types of studies, the Dysphagia Symptom Questionnaire score only improved significantly on the weekly, but not on the every two week dose. So it met the dual endpoints only for weekly. So now you've got this drug that for different indications, you've got weekly, you've got every other week, you've got monthly. It's all over the place. The pricing has to go at one level. So people who need it weekly are going to pay four times as much as people who only have an indication where it's monthly. The trial was very safe. Seven adverse events leading to discontinuation. No fatalities. But this showed in the open label, the endpoints continued to hold for 52 weeks. So this is a fantastic drug that is going to become a bedrock of how we manage multiple allergic conditions in allergy. And it's now approved. It's the first biologic agent approved for treatment of eosinophilic esophagitis. We've had patients on this for atopic dermatitis and asthma who have had their life changed. I can't wait to use this more and more in my eosinophilic esophagitis patients. And they're going through the approval steps now down to, I think, age six for eosinophilic esophagitis. So ideally that will come in the next year. But this article really a very nice, well-designed study, and I implore everybody to read and become familiar with this, because I do think that this drug is going to really change how we treat eosinophilic esophagitis.

Dr. Mariam Hanna: Do you use symptom scores at the bedside with patients in follow-ups? Do you implement that into your private practice?

Dr. Matthew Greenhawt: Not formally. I think I've learned to adapt how I ask questions about dysphagia. That probably incorporates a lot of what's in that questionnaire, that just over the years and my familiarity with the disease state, that I'm probably doing that

naturally. I think it could be used in clinical practice. It's not like SCORAD or something for eczema, where it's not maybe the easiest thing to translate to the bedside. But the DSQ is not bad. I worry that the DSQ is not really the right tool for the job in this, and that not all patients have consistent dysphagia. There are a lot of problems. The DSQ has tanked more drugs in the last two years than I care to mention. And I do think that maybe we need a different measure because it just may not be sensitive to all phenotypes of eosinophilic esophagitis or something like that. But it's worth kicking the tires on, I think, in clinical practice anyway.

Dr. Mariam Hanna: So, the next one is respiratory health, but it's not asthma. You did not pick an asthma topic.

Dr. Matthew Greenhawt: I know.

Dr. Mariam Hanna: What's our fourth article pick for 2023?

Dr. Matthew Greenhawt: Yeah. All right, so this is another New England Journal article by Bot et al, that is talking about dupilumab use for COPD with type two inflammation indicated by eosinophil counts. In the last ten to fifteen years, COPD has slowly crept into, I think, our landscape, especially with asthma, COPD overlap syndrome phenomenon, and whatnot. And you see a lot of COPD articles being published and talked about within our field. And this article was chosen by our asthma person for the Lit review. So this is another dupilumab study, and this is now literally its sixth indication as a drug. I mean it's a remarkably versatile drug in terms of treating all conditions. But there seems to be some evidence that certain forms of COPD may have some T2 inflammation with this higher eosinophil count. This absolutely makes it a condition of interest for us. This study was looking at can in this T2 dominant phenotype of COPD. Is there a role for dupilumab? So, phase three randomized controlled trial looking at patients who had at least 300 eosinophils per microliter and an elevated exacerbation risk despite being on standard triple therapy. So they were given dupilumab versus placebo every other week. And the endpoints were looking at the annualized rates of moderate to severe COPD exacerbations. And then FEV1 and St. George Respiratory Questionnaire, which is a quality of life measure, and the Evaluating Respiratory Symptoms in COPD severity scores. Almost 1000 patients were randomized and this showed that the dupilumab group had a lower rate of moderate to severe exacerbations. They had greater improvement in their pre-bronchodilator FEV1, improvement in their St. George's Respiratory scores, and improvement in the Evaluating Respiratory Symptom scores. So across the board, this group that received dupilumab did better. So strikingly positive trial. And late last year this was approved for this condition. So is COPD an allergic disease? No, but I think we're learning that there are some allergic features. The other thing we're learning is that the rest of the medical

world identifies us as really the go-to to deal with some of these biologics for administration.

Dr. Mariam Hanna: You're a cost-effectiveness man.

Dr. Matthew Greenhawt: Yes.

Dr. Mariam Hanna: Tell me a little bit about putting biologics, and we could start them as early as six months for atopic dermatitis. And we're talking about different age indications, six different ways that you can qualify for this drug nowadays.

Dr. Matthew Greenhawt: Yeah.

Dr. Mariam Hanna: How long are we going to keep these patients on for? Is that our new approach for managing these conditions?

Dr. Matthew Greenhawt: Well, part of the dupilumab story for eosinophilic esophagitis is that while it's indicated as a first-line agent, most third-party payers make you fail through a couple of things before they'll even consider it. So, yes, it is an expensive drug. However, it is an incredibly effective drug. And if you use a health economic model of looking at something called value-based pricing, it's a simple concept. Drugs that do more and have better outcomes deserve to be more expensive. There's a difference between a basic beater Toyota and a McLaren, right. These cars cost different amounts of money because you get different experiences. And yes, they may both get you from point A to point B, but certain things have more value and they can charge more money for that. The cost-effectiveness, right. If you're only looking at it over one year, a lot of things aren't cost-effective in that short of a horizon. But when you start to look at things over five years, ten years, twenty years, eighty years, right, the lifetime of a patient, you pay more up front because the drug is more expensive. But if the drug is good enough to prevent things like hospitalizations and exacerbations and all the things that tie up a huge amount of medical costs, and if you never reach those costs over a ten-year period, eventually these drugs often become cost-effective long-term agents, but you have to start them soon enough to realize that. And Marcus Shaker and I, when we do a lot of our work, we model 20 to 80 years. But our push has been to start some of these things earlier on because you nip a small problem in the bud. And yes, you might not need to run over a bug with a huge monster truck tire when a simple fly swatter would do, but if that fly swatter is going to allow that to keep coming back and back and back, then yeah, you should crush it with as big of a gun as is indicated. And if it keeps other outcomes from happening, then again, there's a line that crosses where it becomes more cost-effective. So, yes, it's expensive, but you pay a little bit more upfront to

prevent the downstream stuff. And there have been models that have shown that dupilumab at its current price actually is justified in terms of cost-effectiveness.

Dr. Mariam Hanna: Straight from the cost-effectiveness guru. And we love analogies on this podcast. Okay, from one wonder drug to an old wonder drug that we still find a little bit mysterious. Our next topic is anaphylaxis, and our mysterious wonder drug is epinephrine. What's your article choice for anaphylaxis?

Dr. Matthew Greenhawt: Yeah, so this is an interesting study by Paul Turner's group in the UK at Imperial, looking at the optimal dose of adrenaline auto-injectors for children and young people at risk of anaphylaxis. So this is a phase four study. The drugs have been approved, obviously, but they did a randomized controlled crossover study of looking at two doses of the same. They looked at 300 micrograms or the 0.3 milligram dose of epinephrine in two devices, and then the 0.5 in a second device. 0.5 is not universally available in all countries. I know it is in Canada, but it's not in the US. But essentially, they wanted to see what dose actually works better. You call epinephrine a wonder drug, and my wonder is, I wonder how the hell this thing works. Because everything that we have thought about epinephrine has been disproven in terms of what it's actually doing with this wave of new needleless devices. All these needleless devices, whether it's nasal or sublingual, all of them are asked to do bracketing studies, meaning that the regulatory agencies have pharmacokinetic and pharmacodynamic parameters that they know epinephrine should perform in, and they want the drug to work within those parameters. So they give them brackets and they give them a little leeway, a margin of error for non-inferiority, or it allows them to come close to it. And sometimes that margin of error can be up to 20%. But these companies are all doing the same control experiments. They're doing intramuscular epinephrine with a needle and syringe and a plunge, and they're using different branded auto-injectors as second controls. And what they're seeing is that literally nobody is replicating the old data about the T_max and the C_max. So the time to peak plasma concentration and then the overall level of peak plasma concentration and work by Estelle Simons years ago had set much later than twelve minutes. A couple had been earlier. But basically, what has been shown is that there's not a lot of consistency. And this may have influenced the reason why in the US over the summer, ARS was not given approval, and the FDA asked them to repeat some experiments in looking at some of the data and some of the inconsistencies in the control group and whatnot. So, this is a huge issue that we don't necessarily know how epi works. We know it works, we know it works quite well. But the predictability of that and the reliability of what we're seeing is a little concerning, say a lot concerning, as.

Dr. Mariam Hanna: As a person that causes kids to have allergic reactions all the time. That's like a reason for concern. And we counsel families quite a bit on this.

Dr. Matthew Greenhawt: Yeah, no, we do. But I would say this is that we know it works. I've never not seen epinephrine work. The timing or whatnot, those are nuances that we can fine-tune. Like, I'm still going to give it, whether it works at 5, 12, or 20 minutes, that's my best bet. And it works better than antihistamine. But anyway, so in this study, right, so this is a twelve-patient crossover study of two devices. They all got a 300 microgram or 0.3 milligram injection of device one. Then they either got the 0.3 or the 0.5 of device two. These are all at least teenagers, 40 kg food allergy. The needle length was 16 mm in the first device, and it was 23 mm in the second device. And there's some literature about needle length and pressure. And does it get into the intramuscular component, does it hit the bone? Some of Harold Kim's work and stuff on that. But anyway, so what they found in this study, and this is where people should pay attention. So the 0.5 dose had a greater and longer increase in heart rate, stroke volume, and cardiac output versus the 300, the 0.3, right? And that's intuitive, right? So maybe the 0.5 is the better dose overall. What they found, though, was more interesting when they started to compare the performance of the 0.3 milligram devices. One device showed one sort of rise in heart rate and stroke volume, but then the other one. So they both increased the heart rate, but one device showed an increase in the stroke volume. The other one showed a decrease in stroke volume and cardiac output. In cardiac terms, we call that negative inotropic effects. That's not what you want to see. You give Epi. You're saying your stroke volume should go up, your heart rate should go up. Therefore, stroke volume times heart rate equals cardiac output. Systemic vascular resistance should go up, everything should go up to support getting more blood around to perfuse your organs so that you don't go into shock. And what this is showing is that one of these devices actually causes a temporary pause in looking at the abstracts, the published abstracts from control studies of all three non-injectable devices that are looking at approval. This has been shown, it's not necessarily widely talked about, but there is this dip that's seen and that's concerning. I throw this out there not to scare people, but to understand that we cannot be dogmatic about what we say about epinephrine. We can say that epinephrine is the most effective treatment in anaphylaxis. That's true. We can say that this works better than antihistamine. That's true. We can't say that the effect is immediate. Right. And we can't say that. If it hasn't hit in five minutes, reinject, because that doesn't match up with the parameters that we're seeing in these studies. So we need as a field to stop being so dogmatic and do more studies to understand. Now, are we going to be doing randomized controlled trials and withholding epinephrine in patients in Anaphylaxis? No, I mean, we know it works, right? We have to look at these different ways of performances, and that's why this sort of bracketing and equivalency pathway for approval. You take a lot that epinephrine is. Epinephrine is epinephrine, and that anyway it gets into the body that it's going to perform. And I think the FDA got cold feet, honestly, in looking at some of the control

data and saying, oh, we don't really understand this too well, so let's do more. This is showing that not all devices act the same. We need to be careful. It's certainly showing that the higher dose is probably better, but I think most people knew that. But is 300 sufficient? Right? Yes, it probably is. 500 might be better, but not all countries sell the device. If anybody attended my talk at the college where part of it was. It is supposed to be a little bit of a tongue-in-cheek thing about what do we know about epinephrine? And how many epinephrine devices should we be prescribing? I went to town on it, and I used this article as an example of just how little we actually understand about epinephrine and how it works. My take home would be that I think in the next two years we will learn a lot more. We may rewrite some things and some past assumptions. We just can't be so dogmatic about what we say about epinephrine. I think we want our patients to use it. We'd like them to use it more promptly than on a delay. Delay may not matter that much. Asthma may not matter that much. I mean, I think if you have somebody with poorly controlled asthma who waits an hour and a half to use their epi after a severe ingestion of peanut, yeah, you may end up in trouble. But most people who treat promptly waiting five versus 15 minutes isn't going to be critical. It probably won't make a difference at all. But we need to understand epi a little bit better before we hammer down on saying, you've got to do this and this and this and this, and we may have to be willing to eat some crow on some past assumptions as well, which is not necessarily a strength of our field in terms of reversing what we said dogmatically in the past. So I'll get off my soapbox now.

Dr. Mariam Hanna: Be willing to eat some crow. I learned new allergies, too, as we do this. Okay, Dr. Greenhawt, 98% of your time is spent on food. You did not provide me with your top food article of the 2023 year. And I must know. I can't let you go at the end of this episode without hearing what your food allergy pick would be. So what food allergy article publication stood out to you in 2023?

Dr. Matthew Greenhawt: This is shameless. And I don't care because I'm taking this shot. It was the epitope study in the New England Journal where I was the lead author. That, to me, was the best article. But it's a very...

Dr. Mariam Hanna: I heard a thing or two about this epitope study. Why don't you run us through it really quick?

Dr. Matthew Greenhawt: Yeah. So this is a randomized controlled trial of an epicutaneous patch containing 250 micrograms of peanut versus placebo in children ages one, two, and three. And this is really the first evidence that showed that non-oral treatment for food allergy in children could be successful. This is a product made by DBV. There's a huge unmet need for treatment in very young. This is not for everybody. Parents want options of a non-oral way to desensitize. So this is a phase three,

multicenter, double-blind study of 362 children ages one to three with challenge-proven peanut allergy. They had to react to 300 milligrams or less to qualify for the trial. And then they were stratified based on if they reacted at under ten milligrams, their change in dose was much lower than if they reacted between 33 hundred milligrams. What it showed was that 67% versus 33.5% who were randomized to the patch met the primary endpoint. That is a whoppingly positive result, 64%. No matter what, their triggering dose was able to increase up to about 1000 milligrams, which is four to five kernels of a peanut M&M or something like that, before a reaction was triggered. So in terms of telling parents what's a palpable amount, they're going from a sliver or a half or barely a whole peanut to several peanuts before that reaction goes, this was done very safely. There were four cases of anaphylaxis out of 244 patients, and three of those kids put the patch back on within 48 hours and had no further incidents. So it's really hard. Some 99.2% had some sort of patch site reaction or whatnot that improved. But overall, it also showed that if you looked at the change in severity of reaction at baseline to the month twelve challenge, you saw a significant shift, a decrease in the amount of severe reactions and an increase in the amount of no reactions or mild reactions. So it's also attenuating reaction severity as well as providing desensitization. The take-homes is that this is really the first non-oral thing shown to be effective in very young children. We just presented the year two data at the college meeting that showed continued response with them wearing it another twelve months. So after 24 months, it continues to burn on. And the rollovers from placebo mimicked the first year of the trial. So again, highly effective and ideally, this will become a tangible option for these very young kids who maybe don't want to do immunotherapy or maybe don't want an injection or something like that. So, yeah, I was the lead author on this. I made the New England Journal. So to me, this was a very important article, but that's probably more in terms of inflating my own ego on that. But, I mean, again, you don't see too many food allergy articles in the New England Journal. This was one of them that they chose this year.

Dr. Mariam Hanna: I think it's a fair choice, Dr. Greenhawt, I'll give it to you. I think it's a very fair choice.

Dr. Matthew Greenhawt: If I weren't in this study, I would have said that one was there, too.

Dr. Mariam Hanna: I was asked to give the fellows in training talk about food immunotherapy because, as this is something that I participate in quite a bit. And the first disclaimer I did, despite all the food immunotherapy that we do in the office, is to say, in five to ten years from now, I think food immunotherapy will look so different, and I think the OIT for everyone type mantra will seem somehow barbaric and crude. And I

think what's going to happen is very similar things on different landscapes. You touched on a lot of really important topics that are really going to change our management here, what biologics are going to do to the face of allergy, anaphylaxis, and how we manage and discuss around the use of epinephrine and proper doses and devices, and then going to atopic dermatitis, the era of avoidance, the era of wet wrap them like a mummy. And that'll work, right? This is all going to dramatically change. And, Dr. Greenhawt, you've done a wonderful job of summarizing an entire day's worth of articles into one episode. So I thank you so, so much for joining us on today's episode of The Allergist.

Dr. Matthew Greenhawt: Well, thank you for having me. I hope it's been educational. I tried to pick some meaningful ones here that have broad applicability and whatnot and things that we can implement into practice either tomorrow, today, or in the near-term future. So anyway, thank you.

Dr. Mariam Hanna: All the links to today's review articles that were covered through Dr. Greenhawt are going to be included with today's show notes. This podcast is produced by the Canadian Society of Allergy and Clinical Immunology. The Allergist is produced for CSACI by Podcraft Productions. The views expressed by our guests are theirs alone and do not necessarily reflect the views of the Canadian Society. This podcast is not intended to provide any individual medical advice to our listeners. Please visit www.Csaci.ca for show notes and any pertinent links from today's conversation. The 'Find an Allergist' app on the website is a useful tool to locate an allergist in your area. If you like the show, please give us a five-star rating and leave a comment wherever you download your podcasts and share it with your networks because THIS year it’s all about the right tools, understanding crows, and what kind of car was that again that we talked about?

Dr. Matthew Greenhawt: A McLaren.

Dr. Mariam Hanna: Oh, a McLaren, we’ve got you covered.

Thank you for listening.

Sincerely, The Allergist.