

# Understanding the Type 2 Inflammation Connection Podcast

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**Benjamin Prince, MD (Host):** Hi everyone and welcome to a special episode of Allergy Talk, a podcast by the American College of Allergy, Asthma, and Immunology. Today we're going to be discussing the concept of Type 2 Inflammation and how dysregulation with this inflammatory cascade of the immune system can manifest clinically as several interconnected allergic diseases.

The goal of today's session is to increase awareness of type 2 inflammation, but also discuss how knowledge on this subject can potentially lead to making an earlier diagnosis, but also enabling a more directed and personalized treatment approach for these allergic conditions. My name is Ben Prince, and I am an Associate Professor of Pediatrics at The Ohio State University College of Medicine and the Associate Division Chief of Research for the Division of Allergy and Immunology at Nationwide Children's Hospital in Columbus, Ohio.

Today, I have the pleasure of being joined by two of my friends and colleagues who are both Board Certified Allergist Immunologists and experts within this area of type 2 inflammation. The first is Justin Greiwe. Justin, welcome to Allergy Talk. Tell the audience just a little bit about yourself before we get started.

**Justin Greiwe, MD:** Thanks for having me, Ben. It's good to be here. Just to give you guys a quick background, I'm currently partner at Bernstein Allergy Group in Cincinnati, Ohio, as well as Clinical Assistant Professor of Medicine at University of Cincinnati. Ben and I go way back. We attended medical school together, trained in pediatrics at University Hospitals in Cleveland. So, it's good to be here with you today.

**Host:** Yeah, I can't believe it's, we're getting old. It's been a long time. I also want to give a really warm welcome to our second guest, Maureen Petersen. Maureen, thanks so much for coming on the podcast. Tell us a little bit about your background.

**Maureen Petersen, MD:** It's awesome to be here with you two to share in our knowledge of our field. I am an Associate Professor of Pediatrics at the University of North Carolina Chapel Hill. Before joining the UNC faculty, I spent 29 years serving in army medicine and I held roles of the Director of Medical Education along with the Fellowship Director of the Allergy Immunology Training program for the military.

So I'm happy to be here teaching about something that I love.

**Host:** I know you guys have both actually done and contributed a lot to our field, and I know you're still involved in quite a few different things. So I really want to start by taking a quick moment to thank you for taking some time out of your busy schedules to join us. It really is a pleasure to have both of you guys as guests.

As we get started, I think the best way to kick things off is to talk a little bit about what this Type 2 Inflammation is and how it differs from other types of immune responses. Justin, could you give us of a background on that and so that we know kind of what we're talking about?

**Justin Greiwe, MD:** Sure, I'd be happy to. So, Type 2 Inflammation originally evolved as a protective immune response against parasitic infections, which of course were very prevalent throughout human evolution. Of course, now we don't deal with those infections as much with central plumbing and cleaning products.

So this type of immune response involving Th2 cells, IgE antibodies, eosinophils, mast cells is really well suited to combating these large extracellular parasites by prompting responses like mucus production, muscle contraction, tissue repair, anything to kind of expel these extracellular parasitic infections out of our body.

So, again, in modern environments where we don't really need to deal with these infections, this same Type 2 immune response has become more frequently associated with allergic disease. So, it's really our bread and butter as allergists. Again, this is where the immune system mistakenly identifies harmless substances, whether it's pollen or dust or food proteins, as threats and then triggering a really a disproportionate inflammatory response leading to allergic conditions like asthma and eczema and allergic rhinitis and all these conditions we treat regularly. So, this quote misfiring, of this kind of evolved defense, in the absence of any parasitic infection results in chronic allergic

disease. And that's what our patients are suffering from. And just a little bit more granular detail, this Th2 pathway, involves lots of different cells.

As we mentioned, we also talk about different cytokines that are involved, IL 4, IL 5 IL 13, and all these cytokines promote and recruit eosinophils, basophils, mast cells, et cetera, IgE antibodies produced by B cells also bind to allergens causing mast cells to granulate, basophils are involved.

So yeah, this is a disproportionate response to a harmless antigen and really leads to a lot of suffering in our patients. So, with chronic activation of this inflammation, it can lead to tissue remodeling, and fibrosis, long term to the lungs, to the nasal passage, to the esophagus, et cetera.

So that's really important. And then there are other types of inflammation that we're really not going to get into today, whether it's a Th1 inflammation, et cetera. These involve different pathways and defenses. Th1 inflammation is crucial for eliminating intracellular pathogens whereas a Th2 inflammation, as we mentioned, primarily targets extracellular parasites.

So they all involve different cytokines. There's some overlap between, but it's important to kind of have that baseline as we get into some of this discussion on Type 2 Inflammation. and hopefully this will kind of set the stage for our talk here today.

**Host:** Thanks, Justin. That was actually really great. Since going back, thinking back to kind of my initial interest in the allergy world, that always was really intriguing to me how, this kind of inflammatory pathway which mechanistically, teleologically, like going back into time, caveman days, what it was good for, what we needed it for, is not even relevant anymore, and yet it's still causing problems, particularly within our field, but I think that's what we'll learn within a lot of the public as well.

So, Maureen, now that we know that, can you just take a little time to discuss what does that look like clinically? So we heard all these cells and these cytokines, but when we have dysregulation with this inflammatory cascade, what does that manifest in the patient that we're seeing in front of us in clinic?

**Maureen Petersen, MD:** So, I think it's important to start with talking about the concept of the atopic march, and this term really is describing the progression of atopic conditions that begin in infancy and then can evolve with time. It really is giving us a clinical roadmap of how Type 2 Inflammation might present at different stages of life.

So the earliest sign that we can see is often eczema or atopic dermatitis, and that usually appears in infancy. That chronic inflammation of the skin, causes proteins from the outside to get in, which then can lead to chronic inflammation of the skin and risk to other allergic diseases. Eczema is commonly the first step in the atopic march, and can often precede conditions like food allergies, allergic rhinitis, and asthma. Understanding the pattern is pretty essential because it gives us an opportunity to intervene early. When we're thinking about Type 2 Inflammation, it can manifest not just in the skin, but across other organ systems. And there are really six main diseases that we commonly talk about.

Atopic Derm being the first one, which manifests in the skin and can be characterized by itching, dryness, and inflammation of the skin. We also think about allergic rhinitis. So this, impacts the nasal passages and leads to symptoms like sneezing, congestion, and itchy eyes. Asthma primarily impacts the lungs and causes airway inflammation, hyperreactivity, and wheezing. Chronic rhinosinusitis with nasal polyps is affecting the upper airways. So this leads to nasal obstruction, loss of smell, and persistent sinus infections. Eosinophilic esophagitis and food allergies are the last two Th2, diseases that we'll talk about. EOE impacts the GI tract and can lead to difficulty swallowing, food impaction, and inflammation of the esophagus, whereas food allergies are a more systemic manifestation that can involve multiple organ systems and lead to reactions from anything from mild hives to life threatening anaphylaxis.

But, each of these conditions has the common thread of Type 2 Inflammation. They present differently, though, depending on which tissues are primarily affected. It's important to recognize early signs and knowing the connections because we can better anticipate the course of various diseases and possibly even interrupt that atopic march that I was telling you about.

**Host:** Thanks so much, Maureen. I think that that is such an interesting point that, all of these diseases, right, on the surface, they seem very different. The way that they present is very different. And if you didn't know any better, you wouldn't realize that kind of the mechanism behind them is actually quite similar in this kind of underlying scheme of dysregulated Type 2 Inflammation.

So you mentioned a couple of things, but I would love Justin, if you could take a minute just to highlight, why this interconnection is important, particularly as we think of the management behind these diseases.

**Justin Greiwe, MD:** Yeah, as you mentioned, the interconnectedness drives treatment, and it's different when we talk about very mild disease, you know, things like that, you know, a lot of over the counters and, simple medications

can help with these conditions. But when we get into more moderate, severe, poorly controlled disease, I think that's really where some of these new treatments shine.

And we talk about biologics and small molecules, because of this dysregulated TH2 inflammation driving multiple disease states, you know, it's crucial to really maintain a really low threshold of suspecting other Type 2 Inflammatory diseases when a patient comes in and talks to you because they often have one complaint.

I want to talk about my asthma or my eczema, but they don't bring up multiple other conditions that they have that could be interrelated and could be helped with some of these treatments we have available. So, for example, some patients have very poorly controlled eczema, but also have very poorly controlled asthma as well. And there are some pathways and, treatments, including biologics that can help both of those conditions at the same time.

So it's nice to have these options. And as an allergist, you know, for the last decade or so, this Pandora's box has opened and we've really had an amazing kind of toolbox to treat with lots of different options, more individualized specific therapies targeting patients individual biomarkers.

It's this shift towards personalized medicine that we used to kind of talk about and give lip service to, but we're in it right now. We're in personalized care and that's only going to be improved as we move forward. So, this targeted approach is really important because It's not a blast like a steroid would be.

It's not a shotgun approach. It's more of a sniper bullet in the sense that we're really focusing in on very specific cytokines and kind of cutting the inflammation off at its source. So it's much more targeted and this targeted approach improves outcomes, minimizes side effects and really improves patient's quality of life.

So, we're much more powerful in our recommendations and we can really impact patients lives with a lot of these treatments.

**Host:** Thanks, Justin. I actually, I love that you pointed out, how much things have changed even in the last, like, honestly, five years. We all have lived on this earth for enough trips around the sun that, it's been a while since we went to med school, but I think you guys both can appreciate hearing either when we were in med school or residency or fellowship, how much medical treatments and the medical field is going to change while you practice.

And so certainly it has, but maybe I'm biased, but I truly think with some of these new therapies, over the last even five years, it's revolutionized what we can do and it's pretty amazing and pretty powerful. So yeah, thanks for pointing that out. All right, so, now that we have this understanding of, okay, what is this Type 2 Inflammation? Why is it important?

And, you know, in these specialized treatments that we have, Maureen, I'd love if you could talk a little bit about why this is important for the primary care provider, which is like kind of who we're talking to right now. And then also if you could just dive in a little bit to like how a board certified allergist could be even helpful for that primary care provider in managing these patients.

**Maureen Petersen, MD:** Sure. So primary care providers are really the front lines when it comes to diagnosing and managing patients with Type 2 Inflammatory diseases. They are going to be the ones that recognize the conditions in their patients and often, they're caring for families where more than one family member may be impacted by these diseases like asthma, eczema, or food allergies.

Their role is really critical because they're not just diagnosing, but they're coordinating the care of these patients. And potentially multiple family members. It's important to partner with a Board Certified Allergist Immunologist because we can really make a significant difference. You know, as a specialist, Justin referred to us having a toolbox and we do because we have advanced training and experience in managing a full spectrum of Type 2 Inflammatory conditions.

So it's almost like a one stop shop for the patients of the primary care provider. We are able to tailor therapies, we can help with streamlining their care in a way that can really improve their quality of life. Additionally, we typically have more time to spend with patients versus the primary care provider.

And this allows us to help educate a patient about their disease. Educating a patient about their disease helps them to be better adherent to therapies and ultimately have better outcomes. So working closely with primary care providers helps us to offer comprehensive, collaborative approach that really benefits the patient and the care team.

**Host:** I couldn't agree more. And, as I think back to Justin's earlier comment about how, you know, that patient comes to you for like one reason, whether it's asthma or eczema or whatever it might be, but when I even think to the patients

that I see in clinic on a day to day basis, it's rare that I just treat that one condition.

And in my experience, I've had, you know, as I'm sure you guys have had as well, numerous patients that are overly thankful and grateful that we don't just deal with that one condition they came for. They didn't realize that we could do all these other things, at the same time to make them feel a lot better.

You also pointed about, like, the task that that pediatrician has or that, primary care provider has, and I'm certainly not jealous of them. One of the reasons why I didn't go into primary care was, they have that task of not getting lulled to sleep by, well child visit or well care visit after well care visit and missing that diagnosis.

And then also, seeing all those patients, but at the same time be expected to give really high quality patient care and education. And, you know, I'm thankful for the time that we can actually have with the patients that we see. As we wrap things up, we're getting kind of to the end the podcast.

I did want to just take a couple of minutes to highlight a brand new resource that was recently put together by the ACAAI, supported by Sanofi and Regeneron for actually primary care providers and patients to promote a better understanding of how various allergic conditions that we talked about today are related on the basis of underlying Type 2 Inflammation.

Justin, could you just take a few minutes just to talk to us a little bit about what this new resource is and, kind of what it entails?

**Justin Greiwe, MD:** Sure. Yeah, the college did a good job putting together these two micro sites where patients and primary care providers can go to get detailed information, information about everything we talked about today, all the conditions and the Type 2 Inflammation and kind of patient perspectives on living with these conditions.

In addition to written content, there are several educational patient journey videos specifically focused on EOE. So these resources are highly vetted, evidence based, and they're great tools, to utilize and really convenient to help patients understand their disease better. And there's even links to board certified allergists near where they live.

So overall, again, these resources are really reliable, evidence based, patient focused, emphasizing this collaboration between us and primary care. So, I think that's really important, and we hope that you guys check it out.

**Host:** Yeah. I mean, I, I think I can say we all, all three of us were fortunate enough to help participate in putting this resource together. So we might be a little bit biased, but I really do think it came out really great. And it is really good tool, I think, for those specific populations the primary care provider and the patient to have at their fingertips.

Maureen, as you kind of like sit back and kind of think about this resource or resources like this, what do you think, like, why are things like this that are developed really kind of so important for those populations? Can you tell us a little what your thoughts are on that?

**Maureen Petersen, MD:** I would say, Ben, that, as an educator, that in this world where it's so easy to do a Google search, it's that much more important to have really high quality, evidence based resources available for our patients and also for the primary care providers that we support. Just like what I said a few minutes ago, that having a patient be educated on their disease, not only helps them to be compliant, but it gives them a better outcome.

And as we continue to support primary care providers, we're able to make a bigger impact, to more patients. So I think having those resources at someone's fingertips are incredibly useful.

**Host:** I agree. I'm sure both of you guys, have had this happen and I actually encourage patients to bring me things that they've researched already, because that, I mean, that tells me that they're already taking control and trying to understand their disease. So I encourage that, but sometimes it's really interesting to see what you can find on the internet.

And it's not always, not always correct. So I think, again, I agree that this high quality evidence that's available to everyone is really important.

Well listen guys, I think that's all the time we have for today. I want to again extend a huge thank you to both Justin and Maureen for joining us on this special episode of Allergy Talk. Please email any feedback, questions, and suggestions to [allergytalk@acaai.org](mailto:allergytalk@acaai.org). The ACAAI is presenting this podcast for educational purposes only.



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Thanks again for joining us. Have a great rest of your day.