Samantha

My name is Samantha, I am 42 and I've never really paid much attention to allergies. I am allergic to mosquitoes but my allergy has lessened in severity as I've gotten older and I really don't even take many precautions anymore. And I have an acquired allergy to penicillin that I've had since I was a child. I moved to Florida 5 years ago and had my first interaction with a fire ant. I was leaving work and one fell down my shirt and stung my chest. It hurt and was itchy but I didn't give it a second thought and it really was just a funny story to tell my coworkers. I don't even think I had a welt the next day. About 2 months ago, I was mowing my lawn in flip flops. And I know you're not supposed to do that but it is Florida and it's August and I really don't like wearing shoes and socks. I felt something itchy on my foot, it didn't hurt. And when I looked down, I only saw grass. So I brushed my foot off and just went about my business.

That evening the top of my foot started to turn red and swell, it was itchy. It just looked like maybe a bug bite or I'd brushed up against some plant that I shouldn't have. The next day though I had two little white pustules form and the red area had doubled in size. I still wasn't really worried but by the afternoon my foot was much more swollen and still very itchy and several more white pustules had formed. I went to a clinic and they gave me a 10 day round of antibiotics and told me to go to the ER if it got worse. By the time I got home that evening, part of my foot had kind of a yellowish tint and I wasn't sure if that was from the bite or whatever I had interacted with or because I had been driving or because I had been standing that day. So I just went back to the ER to be sure. There they said it looked like ant stings.

And a few days later I was out mowing my lawn again. Yes, still in flip flops, I had not yet learned my lesson. And I mowed over a fire ant hill that was hidden in the grass and then I stepped on it. I immediately felt pain and itchy. When I looked down, my foot was covered with hundreds of ants all over my left foot and ankle. They were on my right foot, they were all over my mower. When I went to brush them off, they got on my hands and stung my hands. I was able to get them off, I moved away. The pain subsided really quickly but I was definitely feeling the itch. After I regained my composure, I realized I was fine. I finished mowing and weed whacked my fence line. When I went inside, I put ice on my feet and sat down for a few minutes. By now it had been about 20 minutes since I had stepped on the ant hill. And I noticed that I was itching on my bra and my waistline. But I figured I just saw a whole bunch of insects and people get itchy after they see insects.

So I went to take a cold bath and when I got undressed I saw red patches all over my skin, chest, trunk, down my arms, down my legs, front and back. And I was like oh, a rash, because I've never had hives that I remember so I didn't realize right away that's what that was. I was in the bath for about 15 minutes when I started coughing and having difficulty taking deep breaths. And I said this is not normal, I need to go to the ER. So I drove back into town and it's about a 30 minute drive to get to the ER from my house. And they took me back pretty quickly into a consult room. And I was chatting with the nurse while they were starting IV, I was in good spirits and everything. And then all of a sudden my vision started to get blurry. I texted my friend, I need you, ER on 43rd. And after that I don't remember much. But here's what I do remember.

I said several times my vision is blurry, I'm going to be sick, I need a bag, I'm going to throw up. The nurse said several times take a deep breath and try to stay calm. I told her that my hearing was fuzzy, it sounded like I was underwater. I said Please help, I'm going to be sick. And I remember an oxygen cannula going on my nose. I remember the nurses trying to wheel me out in the chair that I was in but hitting a door or a wall several times, they were having difficulty maneuvering the chair. My body convulsed. I don't know what that looked like but it felt terrifying. I heard someone say something about 50-somethings of Benadryl. I felt a sharp jab in my arm followed by pain. And after a while I was able to open my eyes, I saw my friend had arrived. And I said to no one in particular, well that was fun. And no one laughed. So I realized it was maybe more serious.

	A doctor came in and explained that my blood pressure had dropped to 86/54, my heart rate had dropped to 47, and I'd had a false positive to something so they had to do a CT with contrast. After a couple hours, they discharged me with prednisone, doxycycline, famotidine, and epinephrine pens. Obviously I don't go walking through my yard barefoot or in flip flops and I carry my EpiPens in a cute little fanny pack. It kind of stinks but dying is worse. That's my allergy story. Thanks.
Anonymous	My parents found out that I was allergic to peanuts when I was 18 months old. After rubbing bits of a peanut butter and jelly sandwich all over myself, as babies do, I broke out in hives and was rushed to the hospital where my allergy was confirmed. From that day forward I was taught to have the utmost caution around peanuts. And I did. I've been lucky enough to only really go into anaphylactic shock twice. Because it's been so rare for me, I never truly knew what all the warning signs could be for an episode. Only that if I got hives, I had a very short amount of time to use my EpiPen and get immediately to a hospital. And while that advice was helpful for my first run-in with anaphylaxis, it unfortunately wasn't enough for my second.
	In February 2023, I was visiting friends in San Francisco, and we went out as a group for dinner for dim sum. I made sure to ask the wait staff about peanuts and inform them of my allergy while ordering, as I always do when dining out. After my friends and I confirmed in both English and Mandarin that all of the food we ordered was safe, we dug in. As soon as the meal ended, I felt a bit flushed. I went to the bathroom and I couldn't see any hives or swelling so I attributed the flush to digestion and a bit of anxiety and carried on. About 10 minutes into the walk back to our Airbnb I started to feel a little winded and 5 minutes after that I started to feel faint. I figured that I must be having an asthma attack since I couldn't really explain this constellation of symptoms otherwise. I pulled one of my friends aside and asked her if we could sit together at the nearest bus station while I called an Uber back to the Airbnb since I didn't think I could make the last 10 minutes of the walk.
	As soon as we sat down, I started to throw up and I was unable to stop. At this point I still didn't know what my body was reacting to and I was starting to dip in and out of consciousness. The friend I'd pulled aside and a kind business owner from the corner store called 911 when I was no longer verbally responsive. And it was only then that we learned from the 911 operator that I was in the middle of an anaphylactic episode. I had an EpiPen on me but before the operator could finish telling my friend how to use it, an ambulance arrived and gave me a double dose of epinephrine, saving my life. While we will never know with a 100% certainty whether my reaction was due to cross-contamination or peanut butter mixed into a sauce and forgotten, what we do know is that I took every step possible to avoid exposure to peanuts and for whatever reason it wasn't quite enough this time.
	I'm incredibly lucky and grateful for my friend and that business owner, as by the time I'd realized something was seriously wrong, I'd lost the motor skills to do anything about it. Since then I've told as many people as I can about the different presentations of anaphylaxis with the hopes of saving another person's life. After 28 years of caution, I still almost died of anaphylaxis. So I would urge anyone else with a fatal allergy to please stay aware of the different presentations of anaphylaxis. And I would urge everyone else to learn how to use an EpiPen just in case.
TPWKY	(This Podcast Will Kill You intro theme)
Erin Welsh	Just terrifying.
Erin Allmann Updyke	There's so many different ways that allergies terrify me. And these are both just incredible stories and I'm so glad that you're both okay.

Erin Welsh	Yeah, yeah.
Erin Allmann Updyke	Yeah.
Erin Welsh	Thank you so much for sharing those stories with us and with our listeners. We really appreciate it.
Erin Allmann Updyke	Yeah.
Erin Welsh	And wow.
Erin Allmann Updyke	Yeah. Thank you.
Erin Welsh	Hi, I'm Erin Welsh.
Erin Allmann Updyke	And I'm Erin Allmann Updyke.
Erin Welsh	And this is This Podcast Will Kill You.
Erin Allmann Updyke	We're bringing you part two of our allergies episode.
Erin Welsh	We are. I am really excited for this, I gotta say.
Erin Allmann Updyke	Yeah.
Erin Welsh	Like antihistamines and other allergy treatments I feel like have become so much a part of our daily lives or our like medicine cabinets.
Erin Allmann Updyke	Our medicine cabinets, 100%.
Erin Welsh	But how do they work? And also, Erin, the first time I heard of allergy shots, my mind was first like do those work? How does that actually work?
Erin Allmann Updyke	This is not accurate but I feel like I'm really curious about the history of allergy shots because they feel a little bit like homeopathy.
Erin Welsh	Yes!
Erin Allmann Updyke	Even though they're not, like they're not. But it's a little bit like that, right? It's like give the smallest little dose and then...
Erin Welsh	Yes.
Erin Allmann Updyke	So it's... Yeah.
Erin Welsh	Treating like with like.
Erin Allmann Updyke	Right.

Erin Welsh	I mean it actually does have its roots in homeopathy which I'm not going to talk about but that is kind of the way that it all started was like oh, if a lot hurts you, then a little bit maybe you'll get used to it.
Erin Allmann Updyke	Right, yeah. But it actually works in this case.
Erin Welsh	It actually works, I know.
Erin Allmann Updyke	Yeah. So we will talk about how it works and where it came from and all the things for all the treatments, well most of them at least, for allergies today. That's what we're focusing on is how last week... If you haven't listened, by the way, to last week's episode, it's all about what are allergies. What are they even? How do they work? Where did they come from evolutionarily? Why are we stuck with these things?
Erin Welsh	Yeah.
Erin Allmann Updyke	It's a great episode. Check it out. But this week we're talking about what do we do about them once you have them.
Erin Welsh	What do we do about them? But before we get into all of that, we've got some very important business to get into.
Erin Allmann Updyke	We do. It's quarantini time.
Erin Welsh	Erin, what are we drinking again this week?
Erin Allmann Updyke	Well of course we're drinking The Allergy Shot.
Erin Welsh	We are.
Erin Allmann Updyke	This week especially.
Erin Welsh	Yep. It's a shot, right? Like what else could we have done?
Erin Allmann Updyke	Yeah. We could have called it Oral Immunotherapy. Just kidding, it is not but that's what you call it when you give someone oral allergy shots.
Erin Welsh	Good one, Erin. That's a great one.
Erin Allmann Updyke	Why thank you.
Erin Welsh	In The Allergy Shot, it's a pretty simple concoction of rum, orange juice, pineapple juice, and Cointreau.
Erin Allmann Updyke	Delish, check it out.
Erin Welsh	Delish.
Erin Allmann Updyke	The recipe is already posted on our social media channels, so if you're not following us there you definitely should be. Also did you know we're on TikTok?

Erin Welsh	We are.
Erin Allmann Updyke	We are.
Erin Welsh	Yeah.
Erin Allmann Updyke	We have videos there.
Erin Welsh	On our website thispodcastwillkillyou.com you can find so many varied things, right. You can find the notes for each and every one of our episodes which has the sources in case you wanted to read more. You can find links to our bookshop.org affiliate account, or Goodreads list, music by Bloodmobile, links to our Patreon, links to merch, links to savings in case you're like oh I heard a discount code for this podcast. What was that product? What was that code? Check out our website this thispodcastwillkillyou.com. You can find all sorts of things. Transcripts, did I mention that? Transcripts.
Erin Allmann Updyke	You can find them. We've got them. Well then, with that should we get started?
Erin Welsh	I think we should.
Erin Allmann Updyke	Okay.
Erin Welsh	Let's take a quick break and begin.
TPWKY	(transition theme)
Erin Allmann Updyke	It feels like we need to start this section off with the briefest of reviews of how an allergy works just to be thorough. So we're going to basically do my whole episode from last week in like one paragraph. Are you ready for this?
Erin Welsh	I'm ready.
Erin Allmann Updyke	In allergies, you get exposed to an allergen which is almost always some type of protein. It gets into your bloodstream. Your immune system decides to do a wacky thing and start making these IgE antibodies in a process known as sensitization. And then the next time that you're re-exposed to that allergen, these IgE antibodies, which happen to be bound to these cells called mast cells and basophils, they bind to the allergen, causing those cells to burst open and spew forth all of this inflammatory junk. And our immune system goes hog wild. So in mild cases of allergies this might lead to inflammation just near the site of exposure like itchy, runny, watery nose and sneezing when you breathe in cat dander, itchy eyes when you get dust mite gunk into your eyes, or upset stomach and vomiting if you eat a tree nut.
	And in the worst case scenarios, this inflammation triggers an extensive immune response that affects the whole body and can cause anaphylaxis where we see swelling in the mouth and throat and lungs that leads to airway constriction and difficulty breathing. We see dilation of our blood vessels leading to blood pressure drops which is sudden and dangerous. And this is an emergency life-threatening scenario. Was that a good summary of allergies in 30 seconds or less?

Erin Welsh	It was a great summary. Yeah. It made me want to ask more questions and then I was like Erin, this is not about allergies. That was last week, you had your opportunity. Now it's time for the medications part.
Erin Allmann Updyke	Right. So that's the question we're trying to get to today is what the heck do we do about these, how do we treat them? It's probably logical to most people that the treatment is going to vary in part depending on the type of allergy and the severity. Across the board the first answer that most people will get on how do I deal with my allergies is oh, avoid allergens. And A) that's not always possible and B) sometimes there's not really that much data that it's helpful. Like in the cases of things like dust mites, like you can do all these things and there's not necessarily that much data that it helps your allergies that much. Because they're ubiquitous, they're everywhere.
Erin Welsh	Right, right.
Erin Allmann Updyke	So once this allergic response kicks off and starts to run away like a boulder down a hill, what do we do about it? There are three main categories of treatment options that we'll talk in detail about and then there are some others. And then at the end of this episode we'll talk about the really exciting, more novel treatments. But the three main treatments that we'll focus on today are antihistamines, allergy shots, and EpiPens. That's a brand name, so I should say epinephrine autoinjectable devices.
Erin Welsh	Can we say EpiPen because it's such a mouthful.
Erin Allmann Updyke	Yeah, we can say EpiPen.
Erin Welsh	Okay.
Erin Allmann Updyke	Not sponsored EpiPen. Okay. We'll also give honorable mention to steroids and I'll talk about them a little bit as well.
Erin Welsh	Honorable mention.
Erin Allmann Updyke	Honorable mention.
Erin Welsh	Love it.
Erin Allmann Updyke	Steroids. Okay.
Erin Welsh	One of the most important classes of drugs just gets an honorable mention for allergies.
Erin Allmann Updyke	I know, I know. Well you gotta make choices here, Erin. It's a podcast.
Erin Welsh	It's true. It's true.
Erin Allmann Updyke	Okay, so antihistamines, let us start there, shall we? Antihistamines are things like diphenhydramine. That's your Benadryl. Again, I'm going to say a lot of brand names this episode which is not typical for us but that way people know what we're actually talking about. Also things like hydroxyzine. So these are the types of antihistamines that people might think of that they're like oh my god, if I take that I am knocked out, they make you super sleepy.

Erin Welsh	Yeah.
Erin Allmann Updyke	And then you have all these other antihistamines, things like cetirizine, Zyrtec; fexofenadine, I think that one's Allegra; loratadine, pretty sure that's Claritin. I could have gotten those mixed up. Who cares? All of these types of medications, they're called antihistamines because they block histamine.
Erin Welsh	Simple as that.
Erin Allmann Updyke	So histamine is one of the many, many compounds that our mast cells are spewing out when they burst open and release inflammatory juices in response to an allergen. So that is why we can use antihistamines in cases of allergic responses, because you have a ton of histamine floating around and it is very involved in the symptoms that we see. Histamine does literally so much in our body, Erin. It is involved in regulating our gastric secretions in our guts. Histamine is involved in the regulation of our sleep-wake cycle. You might only think of melatonin, it's way more complicated than that. Histamines involved.
Erin Welsh	Well I guess that makes sense considering that some of these knock you out, right?
Erin Allmann Updyke	Yeah.
Erin Welsh	Okay, okay.
Erin Allmann Updyke	We'll talk about why only some of them. But in the case of allergies, histamine is involved in things like vasodilation, so it helps to cause vasodilation of our blood vessels. It also is involved in the smooth muscle constriction that we see, like bronchospasm that we see in asthma but also in the cases of anaphylaxis and allergies. It causes increased vascular permeability, so that leakiness of our blood vessels. Which again in the context of an immune response is forcing all of your blood and all of the immune reactants in your blood to the area for help, right, that's the idea. It also is a big part of the itchiness that we feel. And so antihistamines are really useful in reducing the itchiness from allergies and other things that cause itch when it's a histamine-related itch. Don't ask me how and why, Erin.
Erin Welsh	I was gonna ask again. I was like I just asked this a few episodes ago.
Erin Allmann Updyke	I know you did.
Erin Welsh	Why do we itch? Why do we?
Erin Allmann Updyke	Why do we itch?
Erin Welsh	Yeah.
Erin Allmann Updyke	I don't have an answer. But histamine is involved in the case of allergies.
Erin Welsh	It's histamine.

Erin Allmann Updyke	And so specifically the antihistamines that we use for allergies, they tend to... There's a bunch of different receptors for histamine and they're numbered like 1-4. So the antihistamines that we use for allergies block a receptor that histamine binds to, specifically the H1 receptor. So what happens then is that we're still releasing histamine, there's still plenty of histamine floating around when you're having an allergic reaction if you take an antihistamine but it just can't do its job because that receptor is blocked by the medication. And so this is also like an even wider class of medications because since there are multiple types of histamine receptors, something that you might take for like acid reflux might be something like Pepcid or famotidine, that's an H2 blocker, so it blocks different receptors of histamine. But sometimes if someone is having really severe allergies, they might need multiple types of histamine blockers. So they might be on a whole camaraderie, is that a good word? I don't know. A whole bunch of these medications.
Erin Welsh	Okay. Can I ask a question about histamine receptors?
Erin Allmann Updyke	Sure.
Erin Welsh	So there are multiple histamine receptors that do different things.
Erin Allmann Updyke	Yes.
Erin Welsh	So that if your body is like hey, we need a histamine response because of this allergy or because of this thing, then come join this receptor.
Erin Allmann Updyke	Right.
Erin Welsh	That's exactly how it goes, right?
Erin Allmann Updyke	Yeah, pretty much.
Erin Welsh	But the histamine molecule itself is always the same but it's the antihistamines that are different to match those different receptors.
Erin Allmann Updyke	Exactly. So histamine, think of it as 1 histamine. And this histamine binds to different receptors usually in different parts of our body. So like we have different receptors in our guts than we do in our brain than we do in our blood vessels. And so the medicine that you take is going to block more or less specifically these different types of receptors. But like I said, there are different versions of these, right. So the things like Benadryl or hydroxyzine, these are called first generation antihistamines. And these, there's a few downsides to these compared to the newer ones that we use like the Zyrtecs and the Allegras, etc. First is that they don't last as long so you have to take them more frequently throughout the day because their therapeutic effect is only a few hours as opposed to like 12 or 24 hours. But they also are able to cross the blood-brain barrier which is why Benadryls and things make people so drowsy. Because histamine is important in your brain, histamine crosses the blood-brain barrier.

	But the medication can also do that and then block those receptors and then cause sleepiness in your brain. They also tend to be a little bit less specific. So you said like okay, these different medications are blocking different receptors. Yes but some of them are better at that than others. And so some of these older antihistamines block a wider range of not just histamine receptors but other things as well which is why they tend to have more side effects across the board and interact with other medications. The newer antihistamines that we use for allergies which are called second generation antihistamines, Zyrtecs, Allegras, not sponsored, these don't cross the blood-brain barrier. And so they have less sedating side effects. They're more specific for those H1 receptors and they tend to last longer, so you can take them maybe once or twice a day.
Erin Welsh	Okay. How do you know which ones to take?
Erin Allmann Updyke	Oh I don't know if I want to answer that question. I have answers to that question but it feels like a doctor question.
Erin Welsh	This is not an advice podcast.
Erin Allmann Updyke	This is not. I have a lot of like those caveats in this episode in particular. We are not your doctors, this is not medical advice. But it really will depend. All of these antihistamines can be used to treat a lot of the symptoms of allergic reactions, right. They're not treating the allergy at all. They're just treating the symptoms by blocking histamine from having an effect. But so no matter what the type of manifestation, be it allergic rhinitis, hives, food allergy where you're not having anaphylaxis of course, itching, all of these symptoms that histamine is involved in in the whole suite of allergic reactions that we talked about last week, they can help be mediated by antihistamines.
	Which one you choose will depend on what your allergies are and which one you respond better to. Because some people respond better to some than others. What's really interesting is especially when it comes to things like Benadryl, some people have like paradoxical effects where it makes them really agitated, especially kids which is why it's usually not recommended to give kids those because they can either be way too sedating or make them super hyper, which is not fun. But all of these can potentially have a role. And sometimes people will respond really well to one for a long time and then it will just like stop working.
Erin Welsh	Yeah.
Erin Allmann Updyke	And then they have to switch to another one.
Erin Welsh	Why?
Erin Allmann Updyke	Why? We don't really know.
Erin Welsh	Okay. But you can get used to a certain antihistamine.
Erin Allmann Updyke	Absolutely, yeah.
Erin Welsh	Interesting.

Erin Allmann Updyke	And is it just because all of your receptors are so saturated that then your body is like well I'm just not gonna... Like I'm going to upregulate my receptors or what is it? We don't really know. But for some reason, at some point, that particular type of antihistamine for some people might not work as well and if they switch to another one, which all of these are just different shapes of molecules binding to the same receptor, then it usually will work for them. But across the board, antihistamines are rarely the only thing that is used to treat allergies. So let's keep going, shall we?
Erin Welsh	Yeah.
Erin Allmann Updyke	Steroids, honorable mention, have a role to play in the treatment of allergies. Allergic rhinitis especially, so like nasal and eye and your face symptoms from allergies really benefit from specifically nasal sprays that have glucocorticoids. And the reason is because steroids are general anti-inflammatories. They are blocking not just histamine, they're blocking your whole inflammatory response.
Erin Welsh	Right.
Erin Allmann Updyke	So they're incredibly effective at calming down the inflammation in this tiny area that is your nasal passages. And they tend to be very safe and well tolerated because even though steroids might sound scary, in the case of nasal sprays they're not super well absorbed systemically so they're really locally treating this inflammation. So they're really awesome and like generally recommended as first line treatment for things like allergic rhinitis. Not all nasal sprays are steroid nasal sprays.
Erin Welsh	Okay.
Erin Allmann Updyke	And so I think it can be really easy to get confused between all the different types. And there are some nasal sprays that you can really only use for like a day or two at a time before you start having pretty severe side effects from the nasal spray.
Erin Welsh	Oh wow. Like what would those side effects be and why?
Erin Allmann Updyke	It's because they're not steroids, so they're working in a way to just constrict your blood vessels. It's for when you have like really bad sinus infection or something and you just need to dry up your sinuses.
Erin Welsh	Right.
Erin Allmann Updyke	They'll do that but then they can cause rebound, worsening of symptoms, and blah, blah, blah. So those are not what I'm talking about. The types of medicine I'm talking about are things like Flonase and Nasacort, those are the brand names in the US, but they're things like fluticasone and mometasone. Those are the steroids that are in it. There are also antihistamine nasal sprays that people can use, which again are going to do the same thing as your oral antihistamines except locally just in your nose. Same thing with eye drops, there are antihistamine eye drops. Those tend to be less effective than steroid nasal sprays because they're more specific. They're only targeting the histamine rather than a more generalized inflammatory response, the way that steroid nasal sprays are. Doesn't mean there's no downside to steroid nasal sprays. The biggest side effect tends to be that it can increase the risk of nosebleeds for some people.
Erin Welsh	Okay.

Erin Allmann Updyke	And they usually take some time to work, so they're not like automatic. It takes several days for that steroid to build up in your nasal passages to actually then reduce that inflammation.
Erin Welsh	Got it.
Erin Allmann Updyke	We use steroids also topically for things like eczema or other allergic dermatitis-type reactions, so topical ointments and creams that contain steroids are phenomenal. But in terms of oral medications, like we were talking about the scorched earth philosophy.
Erin Welsh	Yeah.
Erin Allmann Updyke	That's steroids, right.
Erin Welsh	Yeah, yeah.
Erin Allmann Updyke	They're just wiping out your entire immune response.
Erin Welsh	Indiscriminate.
Erin Allmann Updyke	Exactly. So in cases of severe allergies or a severe allergic reaction, then yes, there might be like a short course of steroids but they're really not a great option for long-term treatment for oral steroids. Another honorable mention, I will say it so that no one gets mad that I didn't, is a medicine called montelukast. Singulair is the brand name.
Erin Welsh	Okay.
Erin Allmann Updyke	It's controversial enough that I'm not going to go into it but it's used mostly for asthma plus allergic rhinitis. So when you have both of those things together. This, unlike antihistamines, blocks another inflammatory bazhuzh called leukotrienes.
Erin Welsh	Bazhuzh.
Erin Allmann Updyke	Bazhuzh.
Erin Welsh	You can find it in the index of a medical textbook, right?
Erin Allmann Updyke	Yeah.
Erin Welsh	Yeah.
Erin Allmann Updyke	It's one of the other things that your mast cells spit out in the case of allergies is a leukotriene. And so this medication blocks some of those. But it has the potential for more severe side effects and we're learning more about the like neuropsychiatric potential side effects of this medication. And so it is used but not as commonly and in very more specific indications compared to these other medicines we're talking about today.
Erin Welsh	Okay.
Erin Allmann Updyke	Which include, for the next one, allergy shots.

Erin Welsh	Yeah.
Erin Allmann Updyke	So how does an allergy shot work? Allergy shots are something that we use really for, again, a wide range but as far as all allergies go, a narrow subset, and yet it is a wide range of different allergies. Mostly inhaled allergens, things like danders, mites, cockroaches, pollens, also bee stings, fire ants, and other venoms. And this process most often is done subcutaneously. So it's called subcutaneous immunotherapy, SCIT. And essentially what happens is the person has to go usually weekly, sometimes even more frequently, like a couple times a week to start. And an allergist will inject teeny tiny amounts of the thing that they're allergic to underneath their skin.
Erin Welsh	It's just like Iocaine powder in 'The Princess Bride' but it works.
Erin Allmann Updyke	I don't... I have watched that movie but I don't remember. Can you tell me about it?
Erin Welsh	He's built up a tolerance to Iocaine powder? Wesley.
Erin Allmann Updyke	Oh okay, now I do remember.
Erin Welsh	Yeah.
Erin Allmann Updyke	So he doesn't die.
Erin Welsh	He puts it in both of the drinks.
Erin Allmann Updyke	Yeah.
Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah, I do remember that now. Thank you.
Erin Welsh	Yeah.
Erin Allmann Updyke	It's just like that, Erin.
Erin Welsh	That's how allergy shots work.
Erin Allmann Updyke	It is literally what that is. So you start out weekly or multiple times a week and then you slowly are building up the amount of allergen that this person is being exposed to. And over time you space it out to less frequently, every couple of weeks, every month, every few months, and this goes on for usually a couple of years, at least many, many months. And then eventually you can stop doing the shots altogether and people don't have allergies or have significantly less of a response to allergens.
TPWKY	(transition theme)
Erin Welsh	Erin, why does that continuous exposure result in decreased sensitivity rather than increased sensitivity?

Erin Allmann Updyke	It's a really good question. I think if we fully understood why this works, then we'd have a lot better treatment for all of our other allergies and we don't. But what we do know what is happening. So what is happening is that this very minute, really, really, really small amount but frequent and repeated exposure, what it does is it kind of retrains our immune system and it induces a level of tolerance. So the way that I think of it is this repeated exposure over time trains our immune system to be like hey, listen... Remember in last week's episode we talked about door number 1 and door number 2 and how allergies, they're opening too much of door number 2? So what this process is doing is telling our immune system, listen, we've opened up enough of door number 2. Like we've done it, it's overplayed, chill out with that over-response. And then what our immune system does is it starts to shift to the production of IgA and IgG antibodies and away from the production of IgE antibodies.
Erin Welsh	And what do IgA and IgG do?
Erin Allmann Updyke	Well they don't trigger this mast cell type response, right. It means that our bodies can still see and flag these allergens because we have these other antibodies to them but we're never going to trigger that severe immune response unless you have IgG antibodies. And so we are shifting production to where we can be like yes, immune system, recognize this, you can remember this allergen but you don't need to freak out about it.
Erin Welsh	Okay.
Erin Allmann Updyke	Unsurprisingly this can also backfire and can induce anaphylaxis because you are literally exposing somebody on purpose to something that their body has already been trained to identify and attack. So it's like Owen Grady is training velociraptors, that's like the process of... Have you seen Jurassic World?
Erin Welsh	No.
Erin Allmann Updyke	Really?
Erin Welsh	I stopped at Jurassic Park III.
Erin Allmann Updyke	Okay well everyone else is going to know what I'm talking about. Imagine someone trying to train a velociraptor, right. Like it might work because they're very smart, right. And so they might learn okay, don't attack this thing. But you also could get your arm bit off. And that is why allergy shots are always done in a very highly regulated and monitored setting under direction of an allergist and it's not something that people do like at home.
Erin Welsh	Right. You have to wait in the office and make sure a certain amount of time...
Erin Allmann Updyke	Exactly.
Erin Welsh	Yeah.

Erin Allmann Updyke	Now there also are newer options to do this without having to poke somebody and this process is called sublingual, usually it's called sublingual immunotherapy. And that's when you are exposed to the allergen under your tongue and so it absorbs into your mucous membranes of your mouth rather than under your skin. It's approved for some allergens, a smaller subset of allergens than subcutaneous immunotherapy. And again, we don't know exactly why but is it because like absorption isn't as good? Whatever it is, we don't have as good of protocols for all the allergens for sublingual immunotherapy. But it is possible for some. So especially for kids, that's a great option because getting shots is scary.
Erin Welsh	But you can't get shots for food allergies.
Erin Allmann Updyke	Oh Erin.
Erin Welsh	Or can you?
Erin Allmann Updyke	You're right.
Erin Welsh	Oh okay, dang.
Erin Allmann Updyke	So everything that I just talked about, it's for the types of allergies that mostly are like allergic rhinitis or rhinoconjunctivitis or venom's toxins. It's not for food allergies. And it's not for lack of trying. There have been so many studies where people have tried to use subcutaneous immunotherapy or sublingual immunotherapy for food allergies. They haven't panned out, mostly because especially with subcutaneous, people were just having really severe reactions. So like the reactions were more severe and then more dangerous and so nothing ever got approved. Asterisk because we'll talk more at the end of this episode about some newer therapies that are similar to this for food allergies.
Erin Welsh	Okay. What a teaser. Wow.
Erin Allmann Updyke	I know. But until very, very recently, like this year really, the only real advice for people with food allergies was avoid it, avoid it, avoid it, avoid it, along with an EpiPen. Which brings us to our third and final medication that we use to treat allergies.
Erin Welsh	Epinephrine autoinjector.
Erin Allmann Updyke	There you go. I am really interested to hear the history of this.
Erin Welsh	It's a good one.
Erin Allmann Updyke	But what I'm going to talk about is like what the heck is in an EpiPen or an epinephrine autoinjector. Well it's epinephrine. That's easy.
Erin Welsh	Yep.
Erin Allmann Updyke	Epinephrine, the other name for it that people might have heard of is adrenaline. And so epinephrine or adrenaline, it's literally the same thing, two different names. Why?
Erin Welsh	It's bizarre. I mean it's like a little bit in the history but mostly it was just like someone liked this and someone liked that.

Erin Allmann Updyke	That's what I figured. Two different people came up with that again.
Erin Welsh	Yeah.
Erin Allmann Updyke	We picked one. This is a hormone that we make in our bodies. And this hormone is our fight or flight hormone, it's our fight or flight response hormone. So epinephrine is the thing that makes your heart pound when you get anxious. It's the thing that makes you feel jittery when you're feeling jittery when you're anxious or when you're nervous or when you're super excited. Epinephrine acts on these receptors in our body, across our entire body, called alpha receptors. And these receptors are present on our blood vessels and they serve to constrict our blood vessels. Anaphylaxis, like we talked about last week, dilates our blood vessels. So when we give this drug, we constrict them. Boom, logic.
	But epinephrine does even more than that. It also works on these receptors called beta receptors and we have a lot of these on our heart. And when epinephrine binds to these receptors on our heart, it makes our heart beat faster and it makes our heart beat harder. So it's pumping blood through these more narrowed vessels. It also, through these beta receptors in our lungs, relaxes the muscles in our airways to reverse that bronchoconstriction or bronchospasm that we see. So that is why epinephrine is the medicine, it is the medicine to treat anaphylaxis, like point blank period, this is what you use.
Erin Welsh	Okay. I kind of have a silly question.
Erin Allmann Updyke	There's no such thing.
Erin Welsh	Okay well, so let's say that you know that you are really, really allergic to bee stings and you see a bee. Presumably does that mean that your adrenaline would shoot up? Would that make you less likely to have an anaphylactic reaction?
Erin Allmann Updyke	Erin, that's not a silly question. That is such a fun question.
Erin Welsh	Or like a snake bite. You see a snake and you're like ah! And then it bites you and you're freaked out that the snake bit you.
Erin Allmann Updyke	Yeah!
Erin Welsh	And then your body is like anaphylaxis time and then your body is also like but we just saw a snake so...
Erin Allmann Updyke	Erin, this is such a fun question in the context of the history and like the toxin hypothesis from last week.
Erin Welsh	Yeah.
Erin Allmann Updyke	I have no idea.
Erin Welsh	I have no idea either.
Erin Allmann Updyke	I have absolutely no idea. Like I don't even know how you would study that. Like if someone is anxious before they... Yeah, I have no idea how you would study that.

Erin Welsh	Right.
Erin Allmann Updyke	Because we can't even do like placebo controlled trials on epinephrine because it would be unethical, right.
Erin Welsh	And how durable is an adrenaline spike?
Erin Allmann Updyke	Right.
Erin Welsh	Versus anaphylaxis, etc.
Erin Allmann Updyke	Yeah, right. And is it just that in anaphylaxis, do you just not have enough endogenous adrenaline? Are you just not making enough epinephrine and that is why, right? Because here's the other thing, and this is where epinephrine gets a little bit weird, these beta receptors, they also do vasodilation which is what is happening in anaphylaxis. So if you give someone some epinephrine but not enough, like a lower dose of it, then those effects can override and be stronger than the vasoconstriction effects on the alpha receptors. And so the dose is actually really important in epinephrine.
Erin Welsh	Okay, okay. So each EpiPen contains a dose specific to the person that it is prescribed for?
Erin Allmann Updyke	Absolutely not, Erin. That would be personalized medicine and we don't have that.
Erin Welsh	Wait, so...
Erin Allmann Updyke	An epinephrine autoinjector, EpiPen, I will throw out other trade names, Anapen, Emerade, Fastjekt, that's what one is called in German, love that. These devices are fixed dose injectors. In the US they're mostly in two doses. For kids, they're 0.15 mg and for adults they're 0.3 mg. That's it, those are the two dose options. And you get prescribed them based on weight. So babies and small kids are going to get the small dose, everyone else is going to get the big dose. Which means some people might be overdosed, some people might be underdosed. But across the board... I know, your face is like that sounds horrible.
Erin Welsh	Why? Yeah.
Erin Allmann Updyke	But it's also like across the board, even though there are potential side effects, how long those side effects last are usually not that long and so these are the doses that are considered across the board safe. And so you give the dose that is closest to that person's weight based on their weight.
Erin Welsh	Why would we not have a finer system for doing this?
Erin Allmann Updyke	Oh my gosh, Erin, that is a question for pharmaceutical companies and who's making the most money off of this and I do not know how to answer that.
Erin Welsh	But there's already price gouging going on.
Erin Allmann Updyke	Yeah.
Erin Welsh	With EpiPens or epinephrine autoinjectors, excuse me.

Erin Allmann Updyke	Yeah.
Erin Welsh	I don't know which companies are doing the price gouging but it does happen.
Erin Allmann Updyke	I don't have an answer to that. But these doses work for most people. When I say like underdose or overdose, it's not a large segment of the population.
Erin Welsh	Okay.
Erin Allmann Updyke	It's more likely that somebody might be underdosed but at least you're still buying time.
Erin Welsh	Okay.
Erin Allmann Updyke	It's also the case that many people, regardless of whether it was the perfect like weight-based dose or not, might need more than one. Because this epinephrine doesn't last for very long, the effects are very rapid onset but transient, and so a lot of times they will help but then that's not enough. So you're going to need multiple doses. People might even need an infusion of epinephrine running over a really long time period, like multiple hours, before their body is really out of the woods.
Erin Welsh	Wow, yeah.
Erin Allmann Updyke	So in general, one of the benefits of these auto-injectors is that they are standardized across the board. So no matter what pen you can find, if someone needs one, you can use it, right? It's the same dose for everyone, so it's easy in that way. They're also designed to deliver the epinephrine directly into the muscle and we usually use the thigh muscle because it's a nice juicy beefy muscle that has a ton of really good blood vessels and really good blood supply, which means that the epinephrine gets delivered in a really predictable way to the blood as opposed to intravenous which you can have much higher side effects, plus then you have to find somebody's vein, which in an emergency isn't easy to do. And subcutaneous administration, so just putting it into the skin or like just under the skin rather than into the muscle, what happens is that you have so much local vasoconstriction from the medicine that you don't have as much penetration quickly into the bloodstream. So it doesn't work quite as well. Still better than nothing,
Erin Welsh	And seconds matter.
Erin Allmann Updyke	Seconds absolutely matter.
Erin Welsh	Yeah.
Erin Allmann Updyke	These pens also are designed to work through clothing, so they can be delivered incredibly rapidly, you don't have to worry about like exposing someone's thigh, you just can get the medicine in.
Erin Welsh	How do you know when to use one?
Erin Allmann Updyke	That is a really good question, Erin. And that is... It is not something I can fully answer. And there have also been studies, and there's a paper that I'll link to in our sources, about like pros and cons of at what point in an allergic response. Like do you wait for things to get more severe or do you not? And the thing is that even when there are cases where yeah, maybe you could have waited, the side effects of epinephrine generally are less severe than the risks of waiting.

Erin Welsh	Okay.
Erin Allmann Updyke	So usually across the board, the recommendation is if you have a known, like especially if you've ever had anaphylaxis before or if you have had severe enough reactions where maybe it's not anaphylaxis but you're really at high risk of anaphylaxis, then the recommendation is once you see signs of a systemic response and not just like oh, just one hive or something like that, then you give it. Because the risks of waiting often outweigh the risks of the medication itself.
Erin Welsh	Okay.
Erin Allmann Updyke	But again, it's going to be... I'm not your doctor.
Erin Welsh	Yeah.
Erin Allmann Updyke	So this is not medical advice. Also not medical advice, I feel very strongly that everybody should learn how to use one of these pens even if you don't have allergies because allergies are so common. So there's lots of great YouTube videos out there. Most of them are really similar even though all the pens look different. Some look like a box, some look like a pen. Never, ever, ever, ever put your finger over the top. Anyone. You hold it like it's a, I don't know, a turkey leg. Not like a...
Erin Welsh	I honestly can't think of anything else, so that's perfect.
Erin Allmann Updyke	Yeah, thank you.
Erin Welsh	It's how you hold a turkey leg. You're not gonna hold the end over the top of the turkey leg.
Erin Allmann Updyke	You can die that way. Anyways. And we'll talk more about other newer options for epinephrine administration because also injecting, like shoving a needle into your leg or your child's leg, that's traumatic.
Erin Welsh	Yeah.
Erin Allmann Updyke	So there are some really awesome newer options. But one of the biggest issues, you mentioned cost, Erin, these pens can be incredibly expensive. I went on GoodRX and I looked them up and the cheapest one I could find in the US is $140 for two pens if you don't have insurance or if your insurance doesn't cover. That's not cheap.
Erin Welsh	No, it's not cheap.
Erin Allmann Updyke	But an even bigger problem in terms of access is that according to the World Allergy Organization of a survey of all of its member states, this type of epinephrine autoinjector is only available in 60% of the countries that they surveyed. 60%.
Erin Welsh	And then I would still imagine like we talked about oh do you wait, do you not wait, how do you know when to? And I wonder for how many people cost is a factor in that.
Erin Allmann Updyke	100%.

Erin Welsh	Right.
Erin Allmann Updyke	Because then if you use it... And they also degrade within 12-18 months, so they have to be replaced. So you need a new one even if you don't use it.
Erin Welsh	Yeah.
Erin Allmann Updyke	You have to carry it with you all of the time because you have no idea when you might be exposed to something that could give you an anaphylactic reaction. I mean they are life saving medication and it is incredible and we need better options and more affordable options. So we'll talk about that a little later. But Erin, first tell me how did we come up with all of these different medications?
Erin Welsh	Oof. Yeah. There's a lot of story to cover, so let's take a break and then I'll get started.
TPWKY	(transition theme)
Erin Welsh	If you look in my bathroom cabinet, you will find, among a million other things like cough drops and ibuprofen, about 10 different types of antihistamine medications.
Erin Allmann Updyke	Wow, that's a lot.
Erin Welsh	That's a lot, yeah. Drowsy, non-drowsy, generic, name brand, in a cold medicine combo. 10 is I don't really think it's an exaggeration. Maybe it's more like 8 but honestly there's a lot. I'm ready for when someone visits during ragweed season and asks if we have any Claritin or Wal-itin which is what we actually have, which is the Walgreens version.
Erin Allmann Updyke	Is that the Costco brand?
Erin Welsh	No, it's Walgreens.
Erin Allmann Updyke	Okay.
Erin Welsh	I don't know if we would go through a Costco size thing of Claritin.
Erin Allmann Updyke	Costco Allertech, have gone through many, many a bottle of children's Allertech.
Erin Welsh	My husband gets allergy shots every Saturday. I think he's actually down to every other Saturday because they seem to be helping.
Erin Allmann Updyke	So exciting.

Erin Welsh	Yep. And while I don't personally own an EpiPen, I probably should, just in case, I have family and friends who do. Considering the extremely high prevalence of allergies around the globe, it's not all that surprising that medicine has put together a stocked and diverse tool kit for dealing with this condition. But it is pretty amazing even considering the limitations of these treatments, because even though allergies were only described and linked to an exposure roughly 150 years ago, even though we don't have a full grasp on why we develop allergies in the first place and how to prevent them entirely, we do have effective treatments and plenty more promising ones on the horizon. So what I want to do today is talk about the big three, as we've already discussed, to pay them homage, right, in order of their development. So we'll start with allergy immunotherapy, AKA allergy shots, I know, spoilers.
Erin Allmann Updyke	I love that that one's first.
Erin Welsh	I know. Antihistamines and epinephrine autoinjectors, AKA your EpiPens.
Erin Allmann Updyke	Okay.
Erin Welsh	And let me just acknowledge that these treatments are not perfect, right. They don't work for everyone, they aren't the only ones out there, and there is certainly room for improvement. Because allergy remains a debilitating condition for many people even with these treatments available or even with the threat of allergies out there, right. But in most respects, allergy treatment is a huge medical success story and it's one that I'm excited to tell in three chapters. Chapter one, thank you vaccines. In last week's episode, I mentioned that English physician John Bostock was the first to describe allergy in 1819, hay fever, and that it was Charles Blackley in 1870 who first linked hay fever to a specific exposure, in this case grass pollen. Blackley's evidence was pretty compelling. He stuck grass pollen up his nose out of season to show that it still caused symptoms, he correlated pollen counts with prevalence and severity of hay fever symptoms, and his conclusions were simultaneously corroborated by a physician in the US who was inhaling ragweed to induce his symptoms.
Erin Allmann Updyke	Wow.
Erin Welsh	Sounds really pleasant, right?
Erin Allmann Updyke	Honestly hardcore, good for you.
Erin Welsh	Very hardcore.
Erin Allmann Updyke	I would not subject myself to that, sorry.
Erin Welsh	Despite this, many scientists still doubted that grass pollen could cause such a response and that it must be some undescribed microbe or good old hysteria. Fortunately others were convinced enough to take matters into their own hands, like William Dunbar, who as a hay fever sufferer himself was personally invested in understanding what caused his seasonal symptoms. So Dunbar confirmed Blackley's findings by injecting undiluted grass pollen extract into himself and his colleague who also had hay fever. So just like a shot of undiluted straight up grass pollen.
Erin Allmann Updyke	Oh my god.
Erin Welsh	Yeah.

Erin Allmann Updyke	And then he was miserable.
Erin Welsh	Yeah, yeah. Both he and his colleague had awful systemic reactions. Like I can't imagine. And instead of that experience dissuading them from pursuing this area of study, they were like more, we must keep doing this.
Erin Allmann Updyke	Oh my god.
Erin Welsh	And granted they didn't inject themselves with like full on pollen again. Instead they took the diphtheria antitoxin approach and they tried to produce pollen antiserum by injecting horses with grass pollen. They then turned the serum into powder which could be applied to the eyes and nose prophylactically during hay fever season.
Erin Allmann Updyke	Did it work?
Erin Welsh	Results were mixed.
Erin Allmann Updyke	Okay.
Erin Welsh	Some people got worse, they developed a sensitivity to the horse serum itself, something that had been known to happen with other serum antitoxins. Dunbar didn't give up hope though and he took one of these patients who had developed this sensitivity and started them on a pollen exposure journey. Over many weeks he injected teeny tiny amounts of grass pollen extract, alternating with horse serum, trying to get them desensitized to both. And at the end of 15 increasing dosages, the patient had become much more tolerant of pollen. During that first hay fever season, they reported much more mild symptoms compared to previous years.
Erin Allmann Updyke	Wow.
Erin Welsh	Dunbar published his results in 1903. 1903!
Erin Allmann Updyke	Wow.
Erin Welsh	Right? And he wasn't even necessarily the first to try out this concept. A few other small reports came out in the five or so years before. But it was Dunbar's paper that would catch the eye of one young researcher, Leonard Noon. Noon was on board with hay fever being caused by grass pollen, specifically quote "a soluble toxin found in the pollen of grasses. It is also undoubted that hay fever patients sometimes become cured of their idiosyncrasy. The most reasonable explanation of this phenomenon would seem to be that the cured patients have had the good fortune to develop an active immunity against the toxin to the action of which they have been liable for so long." End quote.
Erin Allmann Updyke	I love this, Erin.
Erin Welsh	And so using this logic, Noon rounded up some human volunteers and tested their sensitivity to pollen by dropping a little bit of pollen extract into their eye.
Erin Allmann Updyke	Oh god.
Erin Welsh	Sounds horrible. And also I just wanted to note that the pollen had been collected by his sister, which I Just love. Like I love that detail so much.

Erin Allmann Updyke	He's like hey sis, go out. No, no, no, this grass, just this one, yeah, yeah, yeah, okay.
Erin Welsh	This grass. Just that one right there.
Erin Allmann Updyke	Collect it all, just bring it back to me. It's cool. A glass tube is fine. Here.
Erin Welsh	And then in the winter and spring outside of hay fever season, he proceeded to administer very precise doses of this pollen extract to his two groups, those with and those without hay fever. And he increased the concentration of these doses slowly over the weeks. He experimented with different intervals between injections and found that longer intervals could actually make the patient become re-sensitized and shorter intervals seemed to meaningfully reduce symptoms. Unfortunately Noon was not able to see his experiment to the full conclusion, nor would he live to see his landmark research honored in the decades to come as the first allergen immunotherapy trial. Noon had tuberculosis and over the course of the study he grew sicker and sicker and he eventually had to turn his work over to his friend John Freeman to finish carrying out. Noon published what would be his last paper, 'Prophylactic Inoculation Against Hay Fever', in 1911. And he died two years later at the age of 35.
Erin Allmann Updyke	Oh that's so sad.
Erin Welsh	From tuberculosis. Yeah, it is. Freeman continued this work for the next few years and showed that using this immunotherapy approach in 30% of participants, hay fever was effectively cured.
Erin Allmann Updyke	Wow.
Erin Welsh	In 35% symptoms were greatly improved, in 24% slightly improved, and only 12% had no improvements whatsoever.
Erin Allmann Updyke	Wow.
Erin Welsh	That's pretty impressive.
Erin Allmann Updyke	Yeah.
Erin Welsh	Noon and Freeman's work was truly foundational for the field of immunotherapy. Not only did it demonstrate that long-term improvement was possible for at least one type of allergy, it also provided a roadmap for healthcare practitioners to try this out on their patients and for researchers to tweak the protocol, testing it out with other allergens, developing a combo shot, improving safety, standardization, and so on. And I'm not going to go into those later improvements. Instead I wanted to focus on these early years because I want us to consider the timing. The time from description, identification of cause, and effective treatment happened lightning fast for hay fever in science years. But if we place it in the context of what else was happening in the science world at the time, it's clear to see why or at least partially why. Vaccines.

	Although the smallpox vaccine had been around since the late 1800s, no other vaccines were developed until the end of the 19th century, around the 1870s and 1880s, which is right when Blackley's work on hay fever came out. And with the growing number of vaccine success stories and the development of antitoxin, everyone with a remote interest in microbiology or immunology began trying their hand at developing a vaccine. And using the germ theory framework to describe what happens with an allergen exposure, along with the concepts of immunity, immunization, susceptibility, toxin, antitoxin, and so on. It seemed entirely reasonable that if vaccines worked for pathogens, introduce a little bit to prevent someone from getting sick in the future, then maybe that could work for allergens. Voila, allergy shots.
Erin Allmann Updyke	Yeah.
Erin Welsh	So in a sense we have vaccines to think.
Erin Allmann Updyke	That is so interesting, Erin. I really love that.
Erin Welsh	I just can't believe how old it is.
Erin Allmann Updyke	Yeah.
Erin Welsh	Like it makes sense but it's also like I just can't believe it.
Erin Allmann Updyke	It's also just like so, so, so interesting immunologically that it works and that it works the way that it does.
Erin Welsh	Yeah.
Erin Allmann Updyke	And it makes me have so many more questions about our immune response and like tolerance vs resistance. You know what I mean?
Erin Welsh	Oh tolerance vs resistance is such a fascinating question.
Erin Allmann Updyke	It really is. And it's like ugh.
Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah.
Erin Welsh	And it doesn't work like vaccines in a way either, right.
Erin Allmann Updyke	Right.
Erin Welsh	Like vaccines sensitize you to something.
Erin Allmann Updyke	Exactly. It is like the opposite of vaccines.
Erin Welsh	Yeah.
Erin Allmann Updyke	But also the same as vaccines, right. Because it is shifting your immune response to be an IgG response which is what we see with vaccines. But they A) didn't know that of course.

Erin Welsh	Right.
Erin Allmann Updyke	And B) it is because you already had an abnormal, well is it abnormal, we don't know, but you had this IGE response and you're having to shift it. So it is tolerance rather than this like prime ability to resist in the future.
Erin Welsh	Resistance. Yeah.
Erin Allmann Updyke	What?
Erin Welsh	Yeah. I know.
Erin Allmann Updyke	It is so weird.
Erin Welsh	It's weird and I love it.
Erin Allmann Updyke	I love it. Ugh I love it.
Erin Welsh	Are you ready for our next chapter?
Erin Allmann Updyke	I really am.
Erin Welsh	Okay. Chapter two, thank you, pharmacology. Just as allergy shots were a product of their time and the excitement surrounding vaccines, antihistamines came out of an era that saw the birth of modern pharmacology. By the mid to late 1800s, the fields of chemistry and biochemistry had made huge technological advancements that allowed scientists to isolate and refine more and more compounds, especially those from living organisms. The goal of this work was basically to understand how stuff works, link a compound to its function. Then if a certain compound did something interesting or helpful, like quinine treating malaria, you could take steps to either isolate larger quantities of it from natural sources or try your hand at producing it artificially. It sounds like a straightforward process but in reality this type of work often led researchers down unexpected roads, which is exactly what happened for Henry Dale and George Barker.
Erin Allmann Updyke	Okay.
Erin Welsh	Dale and Barker were working at Sir Henry Wellcome's research lab in England, like of Wellcome Collection, Wellcome Library, when they turned their sights to ergot. Wellcome became interested in the commercial potential of ergot as a medication to speed up labor during childbirth and reduce postpartum bleeding, both of which ergot had been shown to do but no one really understood how.
Erin Allmann Updyke	I love this. We talked about ergot way back in...
Erin Welsh	Dancing plague.
Erin Allmann Updyke	Dancing plague. That's right.
Erin Welsh	Yeah. We should do just an ergot episode really.

Erin Allmann Updyke	Okay. I mean we say like we could make anything into an episode, so like I don't know.
Erin Welsh	I mean this could have been three additional episodes, let's be real. But ergot on its own is not something you really want to mess with. And so the key was to find the compound that had these desired effects, isolate it, and then turn it into a medication with fewer side effects than straight up ergot. So Dale, Barker, and another researcher, Laidlaw, began this process of isolating various compounds from ergot and then injecting them into various animals. One compound in particular caught their eye, beta... I'm gonna try to say this. Beta imidazole ethylamine. Or as we know it, histamine.
Erin Allmann Updyke	Okay.
Erin Welsh	So glad I don't have to say that again. It was brutal. Histamine had been isolated previously but Dale and Laidlaw were the first to look into what it actually did. And what they found was pretty compelling. It caused all the things you talked about, Erin. Vasodilation, the contraction of smooth muscles in the airways, in the uterus, in the intestines. It increased heart rate and stimulated contraction. Overall, injection with histamine induced a response in animals that looked a whole lot like anaphylactic shock. Which they pointed out at the very end of their 1910 paper as a possible avenue for future research.
Erin Allmann Updyke	Wow. 1910!
Erin Welsh	1910. I know. Anaphylaxis, by the way, had only been described eight years prior in 1902, which is pretty early, by Richet and Portier.
Erin Allmann Updyke	Yeah.
Erin Welsh	Dale and Laidlaw's paper went a long way towards linking histamine and allergy/anaphylaxis but the connection wasn't quite complete. This compound from ergot can cause this reaction but does it have biological significance? Like is this something that animals regularly encounter?
Erin Allmann Updyke	Right.
Erin Welsh	The answer to that would arrive in 1927 when Charles Best of insulin fame-
Erin Allmann Updyke	Okay.
Erin Welsh	He was one of the people who... Yeah.
Erin Allmann Updyke	Yeah.
Erin Welsh	He isolated histamine from liver and lungs, showing that this compound is produced regularly in animal tissue and that it plays a strong role in allergy and anaphylaxis.
Erin Allmann Updyke	This is so fun, Erin. I can't tell you how much I love learning this stuff that I've never learned about, like where we got antihistamines from.
Erin Welsh	I know. Also I love, I think it's so fascinating to read about that period of science where it was just sort of like throwing a dart.
Erin Allmann Updyke	Right.

Erin Welsh	And being like cool, let's check out this compound.
Erin Allmann Updyke	Yeah.
Erin Welsh	And it does this thing. Let's look at this microbe. It's just everything.
Erin Allmann Updyke	Yeah.
Erin Welsh	Yeah. Open questions.
Erin Allmann Updyke	So many.
Erin Welsh	Once this link was made between animals produce histamine on the reg and it seems to be linked to allergy and anaphylaxis in some way, then the logic followed that if you could find a way to block the action of histamine, you could reduce those unpleasant and deadly effects that it caused. But how do you do that?
Erin Allmann Updyke	Yeah.
Erin Welsh	You look for compounds that bind to histamine receptors, blocking histamine from binding.
Erin Allmann Updyke	I mean straightforward when you say it like that.
Erin Welsh	Straightforward, right? Easy enough. I mean but in a way it was only 10 years after Best isolated histamine from animal tissues that the first antihistamines emerged. So it was 1937 is when Daniel Bovet, who identified the first antihistamine and then was later awarded a Nobel Prize for his efforts. 1937 is when that happened.
Erin Allmann Updyke	Wow!
Erin Welsh	And they were on the market by the mid 1940s.
Erin Allmann Updyke	Wow!
Erin Welsh	I know.
Erin Allmann Updyke	That's so much earlier.
Erin Welsh	Same, same.
Erin Allmann Updyke	I think of the 1950s as like medicines didn't exist. Which I know is inaccurate.
Erin Welsh	We barely had antibiotics. Yeah. That's true.
Erin Allmann Updyke	Wow.
Erin Welsh	But yeah, the first antihistamine. I feel like Benadryl was 1946, something like that.

Erin Allmann Updyke	Wow.
Erin Welsh	Yeah.
Erin Allmann Updyke	That is so cool.
Erin Welsh	And again, these are the first generation.
Erin Allmann Updyke	Right.
Erin Welsh	I could tell a whole separate story about the research that followed from this first generation of antihistamines, how we discovered the second generation histamines, all the different receptors, the recognition that they could help with things like motion sickness, the discovery that some antihistamines could have potentially harmful cardiac side effects, the identification of their sedative effect. I mean there's a lot more to the history of antihistamines.
Erin Allmann Updyke	Ugh. I would read that book, Erin.
Erin Welsh	Well I'll have to save that story for another day because we've still got the last of the big three allergy treatments to get into. And that is the epinephrine autoinjector/the EpiPen.
Erin Allmann Updyke	Love it.
Erin Welsh	Chapter three, thank you, Sheldon.
Erin Allmann Updyke	Sheldon?
Erin Welsh	Sheldon.
Erin Allmann Updyke	Okay.
Erin Welsh	The EpiPen is one of the most powerful medical devices you hope you never have to use. It has saved countless lives from anaphylaxis since its initial introduction and millions of people around the world rely on EpiPens to save their lives from severe allergic reactions. We owe the existence of this amazing device to two separate but equally crucial developments in medicine. The discovery of adrenaline/epinephrine and the invention of the autoinjector. Let's begin with adrenaline. Again placing ourselves in the late 1800s when alongside the fields of vaccinology and pharmacology, the study of hormones was also kicking off. Two researchers, George Oliver and E. A. Schafer, ground up a bunch of adrenal glands from various animals, swirled them up with some alcohol and glycerin, and injected it into dogs just to see what would happen.
Erin Allmann Updyke	Oh my goodness. Okay.
Erin Welsh	Yeah, not great. This idea didn't come out of thin air though. Several other researchers had attempted something similar but no one had thoroughly characterized a typical response. Usually it was just death.
Erin Allmann Updyke	Yeah.
Erin Welsh	Because it was like not very purified hormone extract.

Erin Allmann Updyke	Right. Lots of ways that that could kill a dog. Just saying.
Erin Welsh	Yeah.
Erin Allmann Updyke	Yeah.
Erin Welsh	Absolutely. Oliver and Schafer were the first to actually say okay, this is what happens.
Erin Allmann Updyke	Okay.
Erin Welsh	They noted that the dogs receiving the adrenal gland extract had elevated heart rate, vasodilation, increased blood pressure, and reduced respiratory rate. It's kind of a messy suite of symptoms.
Erin Allmann Updyke	Yes.
Erin Welsh	It's not necessarily-
Erin Allmann Updyke	Your adrenal glands are messy.
Erin Welsh	Yeah, there's a lot of stuff going on there.
Erin Allmann Updyke	They make a lot more than just adrenaline.
Erin Welsh	Yeah. Inducing this type of response, they recognized, could come in handy. But first you needed to find out exactly what was triggering this response or the different parts of this response. Several researchers set to isolating the responsible compound and in 1901, Jōkichi Takamine would ultimately claim the title, calling the substance adrenaline, which Parke, Davis & Co, later owned by Pfizer, patented in 1903.
Erin Allmann Updyke	What?
Erin Welsh	I don't know. Yeah. Yeah, I know.
Erin Allmann Updyke	So that's why we call it epinephrine because...
Erin Welsh	Trade name. Yeah. Once people were able to synthetically produce adrenaline in 1906, it quickly became one of the most studied hormones over the first few decades of the 20th century as researchers sought to identify possible therapeutic targets. Among those, asthma and hay fever. Since at least 1859, physicians had observed that quote "asthma is immediately cured in situations of either sudden alarm or violent fleeting excitements." End quote.
Erin Allmann Updyke	So when you're activating the sympathetic nervous system, Erin.

Erin Welsh	And so researchers figured look, here's this thing adrenaline that causes the same sensations as sudden alarm or violent fleeting excitements. Maybe we inject it into people with asthma and hay fever and just see what happens. And in the first few years of the 1900s, that's exactly what Solomon Solis-Cohen, Jesse Bullowa, and David Kaplan did, finding that both oral and injected doses of adrenaline relieved symptoms of both conditions. But a major question remained. Well I mean several major questions remained, like what is adrenaline doing at a cellular level? But for the purposes of this history, the main unanswered question was what is the best way to get adrenaline into someone? As a treatment for hay fever and asthma, you really had to get adrenaline into someone as fast as possible to be effective, which meant injection, specifically intramuscular injection, over oral tablet or other kinds of injections. But how many people are lucky enough to have a syringe and vial of adrenaline on hand during an attack? And even if you are, like drawing up the liquid into the needle while your throat is constricting, not an ideal delivery system. Especially when, as we talked about, every second counts.
Erin Allmann Updyke	Yeah.
Erin Welsh	By the 1930s, researchers had developed nebulizers which helped to solve the problem for people with asthma but getting adrenaline into someone going into anaphylaxis was still a huge challenge. Fortunately a solution was on the horizon but it wasn't initially created with adrenaline in mind. During the Cold War, a big fear was that troops would encounter nerve gas which acted rapidly to incapacitate or kill, like nerve gas would be within seconds, right. And so the military was understandably very motivated to find a way to deliver an antidote as quickly as possible.
Erin Allmann Updyke	Oh my gosh, Erin.
Erin Welsh	I know. Sheldon Kaplan, an engineer working at Survival Technology Incorporated... What a name for a company, right?
Erin Allmann Updyke	What a name. Survival Technology. Does it still exist?
Erin Welsh	But Sheldon had just the thing. One of his projects at the company was redesigning the Atro-Pen, which was an autoinjector that had limited usefulness since it used stainless steel to hold the medication rather than glass, which was thought to be too fragile, and I think that this was developed with astronauts in mind.
Erin Allmann Updyke	Okay, okay.
Erin Welsh	But again, you could only do certain medications because some medications when they come into contact with stainless steel, not a good thing.
Erin Allmann Updyke	They interact. Yeah. Okay.
Erin Welsh	But this problem didn't stop Sheldon. He rebuilt the pen entirely using glass and developing a system to carefully calibrate the dose. Sheldon's new pen was called the ComboPen.
Erin Allmann Updyke	Okay.
Erin Welsh	And this is what the military used to deliver antidotes to nerve gas.
Erin Allmann Updyke	Wow.

Erin Welsh	But Sheldon saw the great potential that this pen had outside of the military for the general population. He reworked it to contain adrenaline, epinephrine. And the world's first epinephrine autoinjector, developed in 1976, was officially approved by the FDA to treat anaphylaxis in 1987.
Erin Allmann Updyke	Wow!
Erin Welsh	I know. He had the vision, right. Like he saw this and was like there's so much more that we can do with this.
Erin Allmann Updyke	Wow!
Erin Welsh	Yeah. The EpiPen would go on to become a household name and make pharmaceutical companies billions of dollars, thanks especially to price gouging yet again. But Sheldon Kaplan never received any money for his invention, even though his name is on the patent. And I bet that most people have never heard of this incredible inventor whose work and brilliance has saved untold lives.
Erin Allmann Updyke	Oh wow.
Erin Welsh	So let's give it up to Sheldon Kaplan.
Erin Allmann Updyke	Give it up for Sheldon. Oh my goodness.
Erin Welsh	And there have been so many interesting developments and, like you talked about, different delivery systems like a box vs a pen.
Erin Allmann Updyke	Right.
Erin Welsh	And there have been studies looking at well if you conceal the needle, it makes people more likely to use it because it's less scary.
Erin Allmann Updyke	Also I am sure, and I don't know enough about the history of development of other medications, but we use similar types of delivery systems for so many medications now. It's not just epinephrine, right.
Erin Welsh	Yeah.
Erin Allmann Updyke	It's even all of the Ozempics of the world, semaglutide is the non-brand name. Right? Like all of these kinds of medications. Insulin pens, like all of these things that have the ability to deliver a fixed dose amount in a way where you in a lot of cases have very minimal contact with the needle part of it. Wow, that is so interesting, Erin.
Erin Welsh	Yeah. So all from Cold War, nerve gas, the genius of Sheldon Kaplan.
Erin Allmann Updyke	I love it.
Erin Welsh	I know.
Erin Allmann Updyke	How fun, Erin.

Erin Welsh	Yeah.
Erin Allmann Updyke	Also 1987. I don't know if that feels early or late. I don't know. But I love to know that date.
Erin Welsh	Yeah. I don't know how I feel about it. I'll search my soul.
Erin Allmann Updyke	Yeah, same.
Erin Welsh	Yeah.
Erin Allmann Updyke	Well.
Erin Welsh	Well. Erin, that was a quick tour through the histories of some allergy treatments and I know that we've got a lot of interesting potential on the horizon. And so I'm going to turn it over to you to let us know where we might be going with allergy treatments today.
Erin Allmann Updyke	I will do that right after this break.
TPWKY	(transition theme)
Erin Allmann Updyke	So we talked already, Erin, cause you asked like well allergy shots, food allergies, what's up? Okay, well let me tell you. There is a very new, and by very new I mean it was approved in the US in 2020, oral immunotherapy, OIT as opposed to SCIT or SLIT for subcutaneous or sublingual, this is oral in your mouth immunotherapy for peanut allergy. It exists, Erin!
Erin Welsh	Yes, nice.
Erin Allmann Updyke	Peanut allergy affects in the US 1.2% of the entire population and 2.5% of kids. And peanut allergy specifically is associated with like a disproportionate amount of anaphylaxis cases that end up in the emergency room. So that is why peanut allergy has been the one that people have been studying to try and come up with treatment for. So this new treatment that exists, I didn't even write down the brand name cause I didn't and now I forget, but it's a powder and it's made from peanuts, like it's just made from peanut protein, Erin. But it's used as oral immunotherapy in a very similar type of desensitization therapy. And the difference between this and just feeding a kid peanuts to try and desensitize them are a few things. One, it's been very well studied to be safe and well tolerated. Two, it is made to have a very specific and predictable level of allergen exposure, right. That is why it is approved and safer than just trying to eat peanuts to desensitize yourself.
Erin Welsh	Right.
Erin Allmann Updyke	And the therapy regimen itself seems pretty complex. It is multiple exposures per day, it is daily exposure, it's not like subcutaneous immunotherapy where you just go like weekly exposures or something like that. And so it often starts in an allergist's office or in your physician's office with these monitored, very well controlled exposures, and then has to continue at home where you're doing this every single day, often multiple times a day. And then every time that you increase the dose, which happens slowly over weeks to months, every time you increase that dose, you've got to go back to your allergist's office to do that safely under guidance to make sure that you don't have an anaphylactic reaction. But it exists, Erin.

Erin Welsh	And okay, so what is the success rate for this?
Erin Allmann Updyke	Great question. Not perfect. I don't have an exact number. The biggest downside with this and another medicine that we'll talk about in a minute is that it doesn't seem to produce as long-lasting effects as allergy shots do.
Erin Welsh	Okay.
Erin Allmann Updyke	But it does have significantly increased tolerance for peanuts. Does it mean that somebody is going to no longer have a peanut allergy? No. Does it mean that they're going to be able to accidentally have peanuts or to have a little bit of peanuts in something they didn't know had peanuts without having a severe reaction or dying? Yes. And that is huge.
Erin Welsh	Right. And I imagine that it probably helps to then reduce a little bit of the anxiety and fear of a peanut exposure.
Erin Allmann Updyke	Exactly, Erin. Exactly. And along those same lines, there's another new medication that is really exciting and mere months ago, February 2024, was approved in the US for treatment of food allergy more broadly, not just peanuts. And this is called omalizumab. This is a monoclonal antibody. Anytime you see a medication like on TV that ends in -mab, -mab is monoclonal antibody.
Erin Welsh	Monoclonal antibody. Wow.
Erin Allmann Updyke	Yeah.
Erin Welsh	I just made that connection.
Erin Allmann Updyke	So this is a medication that targets, wait for it, IgE antibodies. So we are using an antibody, an IgG antibody, to find and target IgE antibodies in our body. What?
Erin Welsh	What?
Erin Allmann Updyke	I know.
Erin Welsh	That's wild.
Erin Allmann Updyke	It's incredible, Erin. It's so interesting. I love it. And the way that you do this is very similar to allergy shots in that people had to be getting shots multiple times. You don't do like a small dose and build up kind of a thing but you have to have multiple doses over a pretty long time period. The study that I read that was the phase 3 trial of this drug before it got approved was like 16-20 weeks and then they were even checking like if we went for longer, would it have a better effect, etc. And what's incredible is that this showed in this trial where they took people who had at least two food allergies, so peanut allergy plus at least one other, and the ones that they ended up studying were egg, milk, cashew, wheat, hazelnut, walnut, that's just what people who happened to be in the trial. 67% of people with multiple food allergies, including peanut, were able to tolerate by the end of the study at least 1000 mg of peanut protein, which is equivalent to four peanuts. Four peanuts. So that also I think gives you a sense of just how little peanut it takes for many people with peanut allergy to have severe reaction. Because in order to be included in the trial, they would have reacted to less than 100 mg of peanut protein.

Erin Welsh	Wow.
Erin Allmann Updyke	Right?
Erin Welsh	Yeah.
Erin Allmann Updyke	So by the end of the study, 67% of people were able to tolerate at least four peanuts worth of peanut protein. 44% of participants tolerated up to 25 peanuts by the end of this trial.
Erin Welsh	That's awesome.
Erin Allmann Updyke	It's incredible. And they saw similar results for cashew, egg, milk, wheat, hazelnut. Some of these were statistically significant, some of them weren't. But here's the other thing I want to say. I feel like in a recent episode we talked about the difference between like is it significant clinically? Is it significant statistically?
Erin Welsh	Yeah.
Erin Allmann Updyke	So 67%, depending on who you are, that might sound like a lot. Like okay, there's like an almost 70% chance that if I have food allergies, if I can get access to this medication, I might not be as allergic as I am now. But that means there's also like a 33% chance that I wouldn't, right? But if you break down that 33%, there was a portion of those people who did respond to the medication as in before they maybe would respond to like 1 mg or a couple of milligrams of peanut protein and by the end they didn't react until they hit maybe 300 mg of peanut protein. So it wasn't statistically significant for the purposes of the study.
Erin Welsh	Right.
Erin Allmann Updyke	But that might be the difference between I take one bite of a cookie and I realize I'm starting to have a mild reaction and I can stop vs I take one bite of a cookie and all of a sudden I'm going into anaphylaxis.
Erin Welsh	Yeah.
Erin Allmann Updyke	So clinically that is still significant. There was about 14% of people in the study who were true failures, as in they did not, sorry, they weren't failures but they did not have any improvement in their response to this medication.
Erin Welsh	Which is interesting in and of itself. Like why not?
Erin Allmann Updyke	It is. It is.
Erin Welsh	Why are some people...
Erin Allmann Updyke	Why?
Erin Welsh	Why does the treatment work for some people but not others?

Erin Allmann Updyke	Exactly. And so we don't know the answer to that because it does not work for everyone but it works for a pretty good proportion of people. So this was just approved. And again, like you mentioned, Erin, the potential that this has to improve the lives of people, even though it does not mean that they're not having an allergy at all, and we still don't know because this is so new and these trials weren't that long, how long is this tolerance going to last? We don't know. Are you going to have to get this medication again? If so, is it going to work as well? There's still a lot of unanswered questions. But this medication has been shown to be safe and to be effective in increasing tolerance to so many of these food allergens, including these multiple food allergens. And that has just such a huge potential for impact on not only alleviating anaphylaxis, saving lives, but also on reducing that anxiety and that's something that's not like... Maybe we didn't even emphasize it quite enough in last week's episode just how severe that amount of stress can be.
Erin Welsh	Right.
Erin Allmann Updyke	To never know when you are going to be exposed and how severe your reaction might be. Who's going to believe you at a restaurant and who's not?
Erin Welsh	Right. The fact that there are people who are like I don't believe in allergies... I mean it's not surprising given just the current state of everything in the world but what?
Erin Allmann Updyke	I know, I know.
Erin Welsh	That's the hill?
Erin Allmann Updyke	And it's not just food allergies too.
Erin Welsh	Right.
Erin Allmann Updyke	Like we talked a little bit last episode about allergic rhinitis, how it can contribute to things like difficulties in schools, anxieties.
Erin Welsh	Yeah.
Erin Allmann Updyke	All of these allergies have been shown to have significant effects on people and their families, especially for families with kids with food and other allergies, it can lead to social isolation. These are big deals. And so the fact that we have treatments that can help to alleviate that is major. And there's one more that I want to throw out there. And that is nasal epinephrine.
Erin Welsh	Oh nice.
Erin Allmann Updyke	Even newer, Erin. This medication was just approved in August of 2024 by the FDA.
Erin Welsh	Awesome.

Erin Allmann Updyke	This is a no needle way to get epinephrine straight into your bloodstream in the case of an anaphylactic reaction. And I found it on GoodRX for only $199 which is pretty surprising considering it's not generic because it was just approved. This is a really exciting, like really, really exciting medication. And I'm sure there's a really interesting history of this because I will link to a really cool paper that went into like what it took to be able to develop this because we needed not only the type of nasal sprayer that could spray out a fixed dose of a medication, so that technology had to develop. We also then had to develop a medication that could help other medicines be more well absorbed by your nasal mucosa so that we could more reliably get... Remember I said how like if it's absorbed into your skin, it's not going to work as well as in your muscle?
Erin Welsh	Yeah.
Erin Allmann Updyke	So we had to have another medicine to help it get into your bloodstream and so we have that now.
Erin Welsh	Wow.
Erin Allmann Updyke	And so nasal sprays for so many medications, I think they're going to just take off. And so this is one where now there is a nasal version, which means that it's going to be easier for people to use, no needles, easier to give your kid because you don't have to poke them, which means kid might be less afraid of it. Like there's just so many incredible things that are now possible because there's a nasal spray version of an EpiPen. It's called Neffy. But all of these are new treatment options. What we still don't have is prevention, aside from what we talked about in last week's episode, the LEAP trial and the EAP trial, which I looked it back up, stands for Inquiring About Tolerance. And these are big deals because we know that early exposure, repeated exposure can reduce the risk of food allergies, especially peanuts. But for other types of allergies, we still just don't know. There's a lot of work being done. Does treating eczema early in life help to prevent allergies? Studies are so far pretty inconclusive.
Erin Welsh	Right.
Erin Allmann Updyke	But there's a lot of people doing so much incredible research trying to understand what are those immunologic triggers and what can we do to try and prevent these allergies from starting in the first place. At the same time that we're trying to develop better treatments for people who already are living with allergies. It's an exciting time in the world of allergy research.
Erin Welsh	It really is.
Erin Allmann Updyke	Yep.
Erin Welsh	It seems like there is going to just be more and more incredible developments and we're going to look back at this time and go oh wow, we didn't have... Like we have so much right now.
Erin Allmann Updyke	Yeah.
Erin Welsh	But we're going to have so much more in the future.
Erin Allmann Updyke	I know.
Erin Welsh	To bring people hope.

Erin Allmann Updyke	It's pretty exciting.
Erin Welsh	And relief.
Erin Allmann Updyke	If you want to know more to learn so that you can be one of those future researchers, oh my gosh, thank you, we'll direct you to some sources.
Erin Welsh	Oh wow, I have so many for this. I don't even know where to begin. So I'll just shout out a few in particular and list the rest on the website. I'm going to shout out that one by Noon and Cantab from 1911 called 'Prophylactic Inoculation Against Hay Fever'. For the antihistamine and histamine section I'll shout out a paper by Ostrom from 2014 called 'The History and Progression of Treatments for Allergic Rhinitis'. And then for the epinephrine autoinjector, how about a paper by Arthur from 2015 titled 'Epinephrine: A Short History'.
Erin Allmann Updyke	I have also a number of papers. A couple that I really liked that were more broad overviews was a paper from 2008 from Nature Reviews Immunology called 'Treatment Strategies for Allergy and Asthma' and then an update from 2023 also from Nature Reviews Immunology called 'Allergy and Immunotherapy: Past, Present, and Future'. But I have a whole bunch more specifics on antihistamines, more specifics on food allergy treatment and epinephrine. You can find the list of the sources from this episode and all of our episodes on our website thispodcastwillkillyou.com under the EPISODES tab.
Erin Welsh	Thank you again so much to the providers of our firsthand accounts and for being willing to relive those experiences through sharing your story.
Erin Allmann Updyke	Yeah, thank you so much. We really appreciate it.
Erin Welsh	Thank you to Bloodmobile for providing the music for this episode and all of our episodes.
Erin Allmann Updyke	Thank you to Tom Breyfogle and Lianna Squillace for the audio mixing.
Erin Welsh	Thank you to everyone at Exactly Right.
Erin Allmann Updyke	And thank you to you, listeners. We hope that you enjoyed this two-parter and that you learned a little bit or a lot about allergies and how they work and why we treat them.
Erin Welsh	I certainly learned a lot.
Erin Allmann Updyke	Me too.
Erin Welsh	And a special thank you of course to our lovely, generous patrons. We appreciate the support that you give us so, so very much.
Erin Allmann Updyke	We do, we do.
Erin Welsh	Well until next time, wash your hands.
Erin Allmann Updyke	You filthy animals.