RCPCH The Paeds Round

Allergy and Tough Nuts to Crack

Transcript of podcast – July 2026

[Music starts]

George: Doing oral immunotherapy may bump up the numbers of natural spontaneous resolutions, for most will give you this huge buffer of protection. You actually become allergic usually through your skin and not your mouth.

Emma: If you were going to do a blood test. It won't make sense unless you've got a good history.

[Music ends]

Emma: Welcome, George. It's a real pleasure to speak to you, and today we are here at the RCPCH paediatric podcast of myself, Emma Lim, and my guest today is George du Toit, who is a Professor of Paediatric Allergy in the Evelina Children's Hospital, Guy's and St Thomas' and King's College Hospital in London.

Okay, so George, what made you interested in allergy in the first place?

George: Allergy initially seemed a little dull to me. I trained in Cape Town, initially in general paediatrics, and I thought it was all about hay fever, which actually now I enjoy as a topic, but I've had great mentors, which we'll dream of in paediatrics, so Eugene Weinberg initially; more recently Gideon Lack; and I was drawn into the world of food allergy, and particularly studies which Gideon has led, and we've done over the last two decades into the prevention of peanut allergy, and more recently prevention of other food allergies.

Emma: If we think about, let's think about peanut allergy, as first of all, I mean, the gold standard. The thing that we would all love to do is to prevent peanut allergy, so to not have peanut allergy. So, what are your hot tips for preventing peanut allergy?

George: So, infants are not born peanut allergic, they may have risk factors of a very strong family history, which is not as strong as perhaps we were taught, but it does, it does play a role. Kids born in Western environments, which is obviously where most people listening to the podcast will be practising, or its slightly higher risk, but the greatest risk factor is atopic eczema, so a take-home tip is, if you see eczema, this is a red flag for the potential development of food allergies, because, as per the dual allergen exposure hypothesis, you actually become allergic, usually through your skin and not your

mouth, so if your skin is inflamed and all those dendritic cells and other allergen recognition cells are open to the environment, and granny is kissing and touching you with peanut, but you're not eating it, you are at greater risk. And so, peanut has gone up in consumption in the Western world, largely since the Second World War. It's commonly in our diets, it's very nutritious, and young infants can be exposed to it, so most will not become allergic, but the at-risk babies who are tickled with peanuts, where peanut is touched onto their skin in micrograms, and they've got this inflamed eczema. Not all of them will have eczema, but the majority do have a dry skin and mild to moderate eczema. They will be at risk for the development of peanut allergy if they're not eating it, so the take-home message is introduce it early for prevention of peanut allergy.

Emma: Interesting, so what you're telling me is that eczema is the problem, not allergy.

George: As paediatricians will know, we have a long stream of patients coming into our clinic saying, which food is causing my child's eczema, and whilst for a few children that will be true; that the milk formula that they are on will be aggravating the eczema; in the vast majority of them the question should rather be what kind of eczema, and will my child's eczema put them at risk of food allergy, and the answer to that is an unequivocal yes, and we used to deny that in decades gone by, because it was very hard for dermatologists who taught us to have to deal with both the skin and dietary interventions, but now most dermatologists and paediatricians deal with these hand in hand, that where we see eczema, we are very switched on and alert to the need to prevent common food allergies.

Emma: Okay, George, so apart from insulting all the dermatologists that they currently change things at the same time, I think actually you've made a really important point here. The primary problem is eczema, so if you can keep the skin intact and then introduce peanut into your diet early, so you're only exposed to it through the gut. We will not have peanut allergy.

George: Correct! And controlling eczema in young infants is difficult. As we all know, particularly in firstborn infants, parents worry for various reasons that any medications we apply to the skin will cause harm of some sort, particularly steroid-based medications, and so it's quite a big barrier to get over, and often by the time they come to see us as specialists, they've spent some time seeing GPs who will follow protocols that, for most eczema, are correct, that you can get away with some emollients and some moisturisation, but any significant inflammation early on is going to need an immune modifier of some sort, either Pimec or Limus to the head and neck area, or steroids to the skin. And on your second and third born children in allergic families, that's slightly easier, but with firstborn children, it does take some persuasion and time in clinic, which not all of us have.

Emma: Yeah, I think that's really common for all paediatricians, that parents don't put enough cream of any sort, enough emollients, enough steroids, and that idea that you need to keep that barrier intact, and anything less than that is not good enough, is really, really important. Number one, we need dermatologists.

George: Yes.

Emma: To look after all this eczema and to get perfect skin, including in our firstborn children. And then, the step two is to get peanut into their diet as soon as possible. So, how are we going to do that, George?

George: Correct. So, we have a slight conflict here that recommendations are for exclusive breastfeeding until six months of age, a noble target at which we all fail dismally for 101 different reasons, but it is a noble target, and I do believe in it. However, many children will start becoming hungrier at from four months of age, and the discussion needs to be, what do we advise parents, and when do we advise parents to wean in the real world. The percentage of exclusively breastfed infants in the Western world at six months of age is exceptionally low. So, what is happening? Either these kids are going hungry and then being topped up with a formula, or they were being weaned early, and we know that the window of opportunity for prevention of food allergy starts closing from four months of age, so it was heresy to even suggest a few years ago weaning onto solids from four months of age, but we now do this, and in our studies we show that breastfeeding rates continue, and in fact are higher within a study setting, even whilst you're introducing solids. It is not removing breast milk from a child's diet.

So the ideal way to wean an at-risk baby, if you're asking an allergist, which you are, and there's a fair amount of evidence behind this, is from four months of age, start having the discussion and empowering the mum and dad, and saying if the baby looks hungry, is developmentally ready to swallow, does not have a tongue thrust, is not pushing out early weaning solids out of their mouth, has head control, is reaching for food, is crying for the food that mum is eating in front of their starving baby. Wean your baby, start with regular weaning fruits, but soon after that, particularly if there's eczema present, start off with some major allergens. So, a smooth peanut butter, very easy to swallow. It is safe to swallow. Baby is not going to choke. We are not advocating feeding solid peanuts, and you would start just on the tip of the finger and try and move up to around a teaspoon at least twice a week, we've shown that that that level of allergen is highly protective, indeed, in our LEAP study and subsequent LEAP studies to that, we've been running this for two decades, this was shown to reduce between the two groups, reduce the prevalence of peanut allergy by 81% in high-risk kids, that is a very, very high amount equivalent to vaccinating children effectively.

So, sitting back passively, waiting for the eczema to settle, not feeding the hungry baby, not introducing these allergens very early on, really does represent a missed opportunity, and in fact, as paediatricians, we may have driven this epidemic some two, three decades ago. We were advising parents of eczema in babies to avoid peanut, cashew, fish; wait until two or three years. We thought if we just kick the can down the road, the problem will go away. Well, it didn't. The prevalence of these allergies was doubling, at least for peanut, it was doubling every decade.

Emma: Well, it's interesting. You said two or three decades. I mean, I'm not saying that I'm a little bit older than two or three decades, George, but certainly in - I'm going to say mine and your youth - we were absolutely weaned at four months onto wheat and food, that was the norm. So, four months weaning onto solids was the norm, and it did change to this exclusive breastfeeding for six months.

George: It is an easy scientific error to make that the rate of peanut allergy was going up. Peanuts seemed to be the problem, if we avoid avoided peanut and removed our babies from this problem, that the entire epidemic would go away. But it was a basic scientific error.

Emma: I'm a little bit bitter about this, as a mother of a first child who eliminated peanut from her diet, exclusively breastfed my child for six months, and I'm highly atopic, and now have a firstborn child with peanut anaphylaxis. I am a little bitter about it.

George: Sorry to hear that. It is an emotive thing, and that's how science works. When we were enrolling into this trial, which was about three decades ago, parents were open to this idea of early introduction. Parents often get there first. We've done a provisional study prior to this, so we looked at Jewish kids in Israel and in the UK. So, people separated by a very short period of time, genetically very similar. And in Israel, children are eating this bamba snack, and in the UK, everyone is pessimistically avoiding peanuts, and we showed a tenfold difference, being higher in Israel to children here, but even when you accounted for children there having more sunshine, more vitamin D, being less overweight, all the factors we could think of, even if you're half that rate, it was still far, far higher, but that was a cross-sectional study, and there was a real lesson to scientists in this. People said you can't change weaning guidelines based on cross-sectional data, but that that study did get out in the common media, mums heard of it, and people started acting on it before we then went ahead and did a randomised interventional trial, which took us many years to do, so this is a cross-sectional study that didn't turn out to be right, because when we look to how much bamba, which is this peanut stack that has been eaten in Israel, how much was eaten that was about two grams at the higher level, three times a week, which is about two or more teaspoons per week of peanut butter.

Emma: Interesting, because I've worked in low-resource settings, and absolutely boiled peanut is a very common, very cheap source of protein that is used widely around the world.

George: Correct! The mainstay of many feeding schemes will be peanuts. It's affordable, accessible, safe to swallow if boiled up, and children really do like it. So, and also, if they've got a bit of reflux, it is quite soothing, I always sell that for our silent refluxes, you know, to settle that oesophagus down. It's less easy to chuck up your formula when you have had some peanut butter to melt it all down, and it's extremely satiating. 25% worth is protein, and we know that of the macronutrients, poach protein is really, really satiating. If you want a baby sleeping all night, it's not a bad idea.

Emma: Well, the other thing I was going to say is it's not just peanut. I mean, in fact, you should be introducing all nut butters, not all at once, but in that window of opportunity. It's not just peanut, you can go almond, cashew, walnut.

George: Correct! This point generates a lot of stress because these nut butters are very proteinaceous, young infants also have to eat other foods. We showed at least for peanut that even the upper quartile consumers neither suffered from over nutrition or under nutrition, because you've got to ask yourself, if you feed your baby a bucket load of peanuts, will they stop eating other foods, will they become obese, and we showed that

that did not happen, even in those who ate a lot. But now, if you introduce, to the mix, many other nuts, it's actually quite difficult to do. So, in clinic, what I try and aim to do is what happens commonly. Common things happen commonly, so cashew is very common, sesame, which is basically a nut, it's a seed of a plant very rich in protein. So, I always advocate some of this on a scientific basis, some just extrapolating for cashew butter, a teaspoon at least twice a week, tahini a teaspoon at least twice a week. Cashew is very similar to pistachio, identical nearly, so that will settle that argument. Walnut will do the same with pecan, they are very some similar, so if you can get in peanut, walnut, cashew, and sesame, you will cover many of the allergens. Almond is commonly eaten, very easy to eat, not such a common allergy, but parents normally include that one. It's low hanging fruit, easy to do. Egg, we have shown in the EAT series of studies that eating egg is protective as well. Egg is a bit trickier to give to kids for reasons either maternal, paternal reasons, smell, taste, texture. So, the uptake was slightly lower, but of course it can be done, and it's extremely healthy. But that's a lot of food for a young infant to be eating.

Emma: I know that Louise Michaelis, who's an allergy doc here in Newcastle, has a neat way that she gets everybody to make cupcake smoothies. You put some nut butter on the cupcake, and then you just blitz the whole thing into a kind of smoothie, and then you have egg, wheat, milk, nuts, everything in one drink.

George: There's a whole industry being raised on the back of this, and I'm partly at fault of it. We, I'm very worried that we will over medicalise eating food, but any help parents can get is welcome, because many of these kids are eczematous. People aren't sleeping, they're all exhausted. Feeding a kid is hard to do anyway. And this does put pressure on parents, and you all know this in clinic. Parents have read about it before they come and see you, and they really want to do the right thing.

Emma: Excellent, so I think if everybody's listened this far, and if you do all this, then you don't need to listen to the rest of the podcast, because you will have no allergy, but let's just say that there was still some allergy. One of the things I think is most important is making a good diagnosis, and for me that always comes down to taking a good history. But what are your clues for general paediatricians sitting in clinic, when people come and say, ‘my child's allergic to x, y, and z’.

George: Make a most basic and very important point is clinical history trumps all. If you tried peanut, particularly if you tried it twice, and you were well beforehand, your child was well soon afterwards, that availed hives, swelling, vomiting, but then melted away over a few hours, that's peanut allergy. I can't think of a differential diagnosis other than that. However, most of the infants you see have not eaten cashew or sesame or walnut, so you have no pre-test probability to work with. You then are stuck with this diagnostic dilemma of having to do a skin break test if you have access to it or blood tests if you have access to those. Children with eczema of high total IgEs, which can give rise to some IgE noise in the system, and particularly if genetically prone towards high total IgE, such as folk of East Asian or South Asian heritage, which, as many of the patients we see, so you can do testing, but like many tests, that the tests will be most helpful when negative, so your negative predictor predictive values are high, or strongly positive, because your positive

predictive values will be high, but you have a lot of noise in the middle, and you've got to be cautious of broad expansive testing if you can't sort that noise out, so if you have a three millimetre sesame tahini test coming back with no clinical history, you can't just leave that family hanging, and you may have done more harm if you say 'just avoid this' unless you go to an oral food challenge. So that is the gold standard diagnostic test in a safe and controlled and supervised setting, feeding the child the food, but not everyone has access to that. If the kids were just to eat these foods without any testing, would they come to severe harm? So, most of the population eats foods without testing, and children, thankfully younger children, are seldom coming to severe, life-threatening harm. It does happen. It's very occasional, so you're stuck with a sort of dichotomy, you know, risk benefit ratio.

So, for paediatricians, I would say, if you're going to do these tests, as with any of the tests you do, ask yourself, what are you going to do with the result? If it's negative, you're going to be bold, obviously. If it's strongly positive, you're going to be very cautious and take that forward, but the majority of your tests may lie in a grey zone. So, if you take peanut, for example, far more children will return a low positive test to peanut and be able to eat peanut than not be able to eat peanut. So, therein lies the art of allergy, putting all these factors, the pre-test probability, the risk factors together, the allergy test together, and then the talent. Maybe AI will sort this out for us soon.

Emma: You're very optimistic. You're very optimistic. Okay, I'm just going to pull apart some of that, because there's quite a lot in there. So, let's say, for example, you've got this child with eczema. You want to decide whether you can start weaning them, so you might say, 'Let's do a panel of skin prick tests on the common allergens'. So, you might try milk, egg, wheat, and some nuts, and peanut will be in there. Now, you may get as you said, if it's normal, great, eat everything, hurry up.

George: Yes, Emma. If it's hugely positive, so if you get a great big wheel that is larger than not your standard or negative, your standard piston.

George: Yes, Emma. But if you get a large positive test, bigger than your standard positive, that confirms, but this is still sensitisation, because they haven't eaten anything yet. So, as you said, if they're sensitised, ideally, they have an oral allergy test. They come into the hospital and get given a bit, a bit of whichever food they're sensitised to, and they're fine. The majority of them are fine. And then they need to go home and carry on eating that food, not stop. However, the problem is it's the enormous full clinics and children waiting for these tests, so I guess the question is, so your argument is, can you pick out the low-risk ones who could start eating without skin prick tests?

George: Red flags would be eczema, family history to a degree, a single food allergy. So, if they've already reacted to egg and now, you're stuck with a low peanut, I would worry a bit more, because it just shows that this immune system is capable of developing allergies. And we know if you take egg allergy, for example, 30% or more will have an additional allergy, so I would worry a little bit more in that scenario. The appearance of the skin prick test, sometimes you get a large flare, a very angry looking three-or four-millimetre wheel. I sometimes dismay that a child's nutritional destiny, allergy destiny, is determined of 1, 2, 3,

or 4 millimetres of a little wheel. It's like when we do drug tests, you know, it comes down, and these things are not symmetrical, so you've got to measure this very carefully. So, there's a little bit of art around the skin prick test. It also depends on the allergen. Peanut performs well, cashew performs well, soy performs terribly. Milk, we like to use fresh milk very often. All the extracts have got better. Sesame does not perform well, so we do tahini, so you do, if you're doing this test, you want to work with them, like with any medical test, fairly frequently to get a feel for what is reliable and what isn't. What seeds and nuts have in common is they are proteinaceous. It's the protein and the seed storage proteins within that you become allergic to, so that the testing can perform much better than then for vegetables, for example. If a strawberry and you had a two millimetre, that really wouldn't worry me, because that is largely carbohydrate, we know it's not going to cause severe reactions, so be cautious of panels, ask your pre-testing questions to yourself and the family you know with great certainty. Families often will see these skin prick testing sheets as if it's a menu and want to order all these things as a bit safer but that's not always the case.

Emma: Excellent, yeah, I completely agree. Don't tick everything on the box, think about what you want. Now we talked about skin prick test, but we started off this whole conversation about peanut allergy. What about blood tests and your rust tests? Because you've got a lot more choices for peanut than you used to have, so we're sticking with diagnosis here. What, when you're thinking about a general paediatrician, somebody comes in, says my child had a bit of peanut butter, their lips swelled up, but nothing else happened. Let's say you can't get a skin prick test, but you can get blood. What do you think they should be asking for?

George: So, if you look at a peanut, 25% is protein, and of that protein, there are many sub proteins, and they don't all behave the same, so you get a primary peanut allergy, that's the one that comes on early, that often will stay with you, that can cause anaphylaxis, and then some of the kids, people will see do not have the primary, but they live longer and they develop pollen allergies. Within pollen, there are proteins that are also found in peanuts, and so when these older kids eat peanuts, they may develop a secondary reaction, which is much milder. It's in their mouth, it's a fuzzy, spiky metallic taste that doesn't cause anaphylaxis. They don't need adrenaline in their plan, and that's occurring to a protein that is similar to pollen. The seed store, the nasty guys, the seed storage protein, so there's an Ara h2, it's Arachis hypogaea 2. You can order that commercially in your lab, so you can order a total IgE. If that is negative, it implies that the sub proteins are likely to be negative. If that is very low, you can dig a little bit deeper. So, you, you've done your peanut total IgE, it's low, you dig a bit deeper, and you order your Ara h2 to peanut. If that is raised, then your probability, particularly with that history you just provided, is very, very high of having peanut allergy. If that is negative and your child is older, an 8, 9 or 10, years old, then you can do what's called an Ara h8 protein, that's the pollen protein, it's a heat labile protein that's damaged by heat, and this is a very common phenomena, and people will see this in their clinics, no matter what conditions they see.

So, hay fever will affect about 25% of the children we see, no matter what kids you see. They'll come into clinic, and they may have a clear nasal crease across their nose, and they

may be sneezing. The pollens are high, even today tree pollens are, and if you ask the history, for example, if they are grass allergic, and you said, 'Can you eat raw tomato?' Many of them will say no, and the parents will say they used to eat this, but they will eat cooked tomatoes, such as tomato sauce, bolognaise, pizza, champion foods, and what's happened there is this structural protein in tomato that is actually a pollen protein is damaged by heat, so when that tomato is cooked, they're tolerating it, when it's raw, they are not, and that's all because of their pollen allergy. That's the secondary phenomenon. So, to come back to your question, I've taken a bit of a journey here. But you also need to understand your blood tests fairly well, because for many children you will get low positive blood tests that may be due to secondary phenomena and not primary troublesome phenomena, and so again you just want to want to learn a little bit more about how these tests behave, and we can test they call components.

We can test these components to peanut, to hazel. Hazel's a very common one that can cause a primary allergy, and if you escape that and you develop birch pollen allergy when you're older, which many kids do, then hazel, particularly raw hazelnut, but not your roast, roasted hazelnut in Nutella, champion food once again, but the raw hazelnut will tickle in their mouth, that is called the oral allergy syndrome, or the pollen food syndrome.

Emma: Okay, so if you were going to do blood tests, you cannot let me go back to a basic trend, if you were going to do a blood test, it won't make sense unless you've got a good history. So, you must take a good history from the child. Have they ever had peanut or whatever your allergen is? What happened when they had it? That is the first thing. The second thing is to think about, are they an atopic in other ways, have they got eczema, are they Southeast Asian, have they got a high IgE, and then there were all these subclasses of the Ara h proteins that could give you a better clue to whether they're going to have lifelong peanut allergy.

George: Yes, better to the binary question, are they allergic? Yes or no. Parents will often ask, does this test size strongly associate with severity, and it does loosely associate with reaction severity, but not close enough that you can make them worry any more or any less. Once a diagnosis of a primary significant allergy is made, you need to prepare them for severe reactions, which thankfully are rather rare.

Emma: So, this is why it's not going to put you out of business at the moment, because there's lots of this around. So, we've talked a bit about diagnosis, we've talked about taking a history, skin prick test, blood tests. So now let's think a bit about treatment.

So, we're all used to thinking about the treatment of allergies, thus excluding the food from the diet, having symptomatic treatments, so the treatment of adrenaline, if you get an accidental exposure. So, what's new in your allergy toolbox?

George: So, the two aspects to discuss within this topic, probably the easiest and quickest is that the adrenaline tools we have. So, many people are going to be asked by their patients about the EURneffy largely online because in America it's traded as Neffy, so you can administer adrenaline for severe reactions through a needle, and then there's been EpiPen injects for some time now, and most folk will be familiar with that, the problem with the needle devices, it's a needle, it scares people and may delay administration. It's

quite a long device to carry. If you carry one, you need to carry two, because you may not administer the first one properly, or it may misfire, or you may need two doses. We only have two doses, the higher dose being point three milligrams ideal when you're 30 kilos, but what if you have a large child at 60/70 kilos, or far higher? That's a rather low dose. So, there are problems with the adrenaline devices, injectables, and they expire a lot. So, they cost society a lot of money, and it's a big hassle for parents having to go back to the GP to get these filled again, and you need to carry a lot, for you know, if families are separated, then that's a problem, and they need them at school, and so we're all familiar with that. The newer device is a nasal squirt device called Neffy. It has no needle; it squirts up your nose. As medics, we all familiar with this with migraine medicines and opioid overdose medicines, so we know you absorb medications very well from the nasal mucosa.

It would simply, for the same indication, so severe reactions squirt this up a child's nose, and the early data that gave rise to the FDA and MHRA approval showed it was equivalent, at least in normal healthy volunteers, to the intramuscular device, and I'm very excited by this, because it's smaller, it withstands greater temperature flexes, it's more likely, I think, to be used slightly earlier, which may halt that immune cascade that occurs during anaphylaxis stabilise those mast cells and basal pulse from releasing all those mediators, so it's more likely to be used, more likely to be carried. Not having a needle is a big benefit, but it's not for everyone. Some families are wedded to the needle device, believing that this will be optimal, and that's fine. There's choice, which is wonderful. Asthmatics have the choice of 20 different asthma products, and probably in a year or so's time, if the FDA approve it, there will be a sublingual strip of adrenaline, so that the choice will expand. So that is new. We use non-sedating anti histamines for mild reactions, and we now have two routes of administration of adrenaline for more severe reactions.

Emma: Excellent news. That is excellent news, really. And you're right, the cost both in environmental terms, in financial terms, and in pain and worry of adrenaline intramuscular injections, is huge.

I have one question: if you have these intranasal devices we know that you're more likely to get an allergy if you have a concurrent infection, so all the children are snotty all the time, all winter, six months of the year, which is great, because they're being exposed to viruses and it's like motivating their immune system to get going, but does that cause a problem.

George: That was thought of in the licencing, so people said most peanut or nut allergic kids that perhaps would need an adrenaline at some stage are likely also to be aero allergen allergic to pollen or dust mite and have big swollen turbinates and local inflammation, and so what they did is take pollen allergic individuals and put them into a pollen exposure chamber, so induce hay fever, and the medication uptake was equivalent, in fact a little bit better, because you have some sort of vasodilation and uptake of the medication, and then they did the same with a viral head cold, so people, when they had a head cold, were administered the device, and then that was compared with when they didn't have a head cold. So that question has been answered, but of course some people will have made significant nasal abnormalities where they can't easily breathe very few in truth. Everyone worries about septum deviation, but kids can breathe through the nose,

even with fairly more acceptable deviation, so they should be able to take it up. Nasal polyps in kids, we don't often see, it's more sort of a cystic fibrosis territory in adults, but of course, if your nose is full of polyps, you're going to battle to administer this medicine. I'm not sure that'll affect many kids, at least.

Emma: So, is this available through NICE yet for everybody? **George:** It's not been through NICE, but it's been through MHRA approval, and it is filtering down through the medical approval system. So, GP should have access to this within the coming months. It's over, because it expires over to two-and a-bit years. It works out cheaper for the NHS, so there's a win on that front.

Emma: Excellent, such a hot topic. So, apart from, that's the acute treatment of peanut allergy, but if you've already got an allergy, so we can't prevent it. Is there any way we can cure you from it?

George: So, cure is a strong word, it's implying disease remission. In other words, eating ad lib and the disease is gone. So, we are not talking about cure yet, but disease moderation. So, some decade and a bit ago, we set off on the peanut journey, trying to treat. This is not talking about prevention anymore, not treatment, treat individuals, and there was a company behind this product, is called Palforzia. It was just peanut protein. It eventually made its way through licencing, which was good for our field, because we now had an FDA MHRA approved product. It had some credibility, was very, very well studied, and what we learned from that peanut protein product, that giving small increments over time would give you a huge buffer of protection, because you would be eating around one peanut, 300 milligrams of peanut protein a day, and if we challenge these kids, many of them could go far higher before they had a reaction. So that was wonderful data.

The problem was it was very cumbersome for the NHS, and indeed, in America as well, so it required at least 12 visits, clinic space, lots of hand holding, and so whilst the product itself wasn't phenomenally expensive, for that there was an insignificant cost to it, it was everything around it that tripped it up, and very few patients could gain access, so the Evelina turned out our waiting list was years, which was just cruel, and the kids were getting older and older, so more and more NHS clinics, and certainly there's a whole private industry around this now, but the NHS clinics are slowly moving towards using other products, and that is where we're going to go. We've learned a lot from doing it in a rigorous way, and we now need to learn about doing it using other everyday products, but with strict controls, hand holding, patient education, emergency plans, contact telephone numbers, because at the end of the day, you're feeding children what they're allergic to, so you don't want to take a chance, and, like you said, there are lots of co-factors: exercise, jet lag, taking ibuprofen, all the kids with menstrual cycles, alcohol, all these things can facilitate the uptake of a protein, and you may tolerate it for a while, and then that same dose may trip you up for one or more of those reasons. And a good example for anyone who's had a sip of alcohol in their lives, you would know that a glass of champagne sort of bubbles into your head quite soon afterwards, you can feel that effect, and that just shows how rapidly things can actually enter your bloodstream, which peanut can do as well, with or without alcohol and other cofactors.

So, if you start this in young children, in many of them, their tests will get smaller and smaller over time. And what we do then is we do it's called free eating, but it's not really free, because you still need to eat it. It just implies you can eat a much higher amount, and you don't have to do it daily. That's for the lucky few, and for the very lucky, the test will go away entirely. Now, that may have happened anyway. Some 10 to 15 percent of kids are young kids, will likely grow a peanut allergy, but that's not many, and we know from studies that that happens, but treating them that percentage is higher.

So, to answer your question of cure, doing oral immunotherapy may bump up the numbers of natural spontaneous resolution. For most, will give you this huge buffer of protection, but it's not for everyone. It can cause symptoms, gut symptoms, you can have anaphylaxis. Some 10 to 15 percent of kids on this journey will need adrenaline, and that's very frightening for some people. Tummy ache is a common side effect, particularly in older children. So, it's not a benign intervention. It's not a new intervention. Philip Schofield, some many decades ago, described a case, and it's a beautiful thing to read, if anyone's interested and it is open access on Google. It's called 'A Case of Egg Poisoning', so that term preceded the allergy understanding, and it describes exactly what we do, is giving increments of an allergen to induce tolerance. So that's very exciting. That's where a lot of us are putting our energy into at the moment, there is more Emma.

There are biologicals around the corner, as with, I guess, many of the guests you bring on board, there are biological, so we can zone in now. We've had on the Lizumab, so Zola commercially, and it's Omnico, there's a buyer similar, which is excellent, because it reduces the price that has been licenced by the FDA, not yet by MHRA, for food allergy. It's licenced for many other conditions, but this is like a sponge that mops up circulating IgE and it is not allergen specific, because remember, your peanut allergic is likely to be allergic to many other things, and have hay fever, and have eczema, and asthma, so it sort of cures-all approach. The problem is it's an injection, monthly. It's not obtainable on the NHS for this indication yet. If you do it in private, it's expensive, but it's the forerunner, and there are now many other biologics with very impressive early stage two findings.

So don't lose hope, there's very exciting therapy, some of these are oral therapies, and they've got a good safety record already in diseases like chronic urticaria, so there's hope for our patients, and there will be choice, increasing choice.

Emma: Pretty interesting, what you're talking about peanut therapies, and eating peanut on a regular basis is obviously great, but it's not without risk, and it's not without side effects. And I guess there are other pragmatic ways to go about this. So, do you remember I was telling you about my first atopic child? They did a peanut oil challenge and had to drink lots and lots of peanut oil soaked into things. The outcome of that is that they happily travelled around Thailand, where all the food is covered in peanuts, by themselves as a young person without any problems with their EpiPen, which is actually a very high-risk place. So, I was thinking there are pragmatic ways where you might not be cured, the quality of your life is better.

George: So, families vary enormously. A fair proportion of the families I serve will not be as brave a parent as what you were, and let their kids go to Thailand, and that's neither right

nor wrong. It's just where you are as a family, which occurs many diseases that we manage. But your point is, can you empower people for that journey? Well, now, I mean, there are biologics, we'll discuss in a minute, around the corner that may help provide protection whilst you travel to higher risk countries, but in truth, in many parts of the world now, particularly nice holiday fun destinations for young kids will have cashew or peanut or sesame, and egg and milk are ubiquitous, but if people are worried about aerosolised exposure, reactions whilst they fly or on trains, you can reassure them by saying you've had many skin prick tests growing up, sitting in a room full of nuts, or whatever you're allergic to, we've pricked it into your arm, and you've been okay, and that's reassuring for some of them.

It's not enough for everyone, and so, for those families, I've done milk challenges, where we blow milk at the patient, or let them inhale some steamed milk. Now, that'll be enough to set off some of your patients, but not all. I've tried to mimic kissing, because parents worry teenagers of snogging each other, and you can put two fingers in milk, and then apply it to the body initially periphery, and I've done those challenges, so yes, you can empower them, bit more risky for milk. For peanut oil, so most cooking oil, sesame oil, peanut oil is very common, if the oil is refined, which most of the oils in the UK we use will be refined. There's very unlikely to be protein in it, because it burns, it doesn't make a good oil. But very occasionally, very occasionally, parents do tell me they've reacted to one of those oils, and very often they are of East Asian heritage, and they've procured that oil from a more traditional route where there is residual protein in it, so it's like with every step you take with a kid, you know, it is risk benefit. So most peanut oils will be safe. We don't tell patients that. The same is true of sesame, and a few of those sesame seeds is unlikely to set your child off, because the sesame is in a shell, they will eat it and poop it out and not see the allergen, but a peanut is raw and exposed, and there's a lot of protein in a peanut. So, in clinic, we deal with families, depending on how medically adverse they are to doing this. Will peanut oil be therapeutic? No, there's not enough oil in it. So, I wouldn't feed your kid increasing amounts of peanut oil to treat them, but good on you for embracing travel. I see some families that just haven't flown. I tell families nuts don't fly.

It's very difficult to get nuts to aerosolise. It creates great angst. Milk does fly. You can actually aerosolise milk, and you can fish. That smell of cooked fish does have allergen in it, but you will never hear announcements on aeroplanes about fish or milk, or people worry about peanuts and nuts. Your kid just doesn't eat those foods that contain those nuts. That's harder for younger babies, because they will scavenge off the seat if something's lying around, or if some person is trying to play with your gorgeous, playful child through the chairs in front, that they may try and feed, they shouldn't feed other people's kids, but it happens. It's very worrying for parents.

Emma: Yeah, I think that is an interesting point, that in all of medicine it is very personalised, that what is risky for one person is not risky for another. Obviously, it's very risky being the child of a paediatrician, because we have a bungee jump, go to Thailand, but I'm interested that you also say that there are new treatments, and that the monoclonal antibodies may well change, change the world. Frankly, it's really interesting.

You've told us about monoclonals and the treatment of allergy, but bringing this back to the beginning, we talked about prevention.

So, we have said the red flag is really bad eczema. These are the children who have atopic families, they've already got bad eczema, they're going to get sensitised, so treating their eczema and using monoclonals could potentially be the beginning of prevention and potentially cure for food allergies.

George: Correct, switching off that eczema very early on is critical. So, we have some medicines that do that, and they need to be trialled also to assess if that produces food allergy, so the SEAL study, sealing up the skin barrier. Gideon Leck is leading on that, is looking at that question now. And there have been the patchy PACI study, if people want to look it up, did try that putting steroids liberally early on to young infants to try, but there were some health concerns associated with that, so the caution that we all have about liberal use of steroids in young infants is worth sticking to until knowledge pushes us in a different direction, but what if we can switch off that eczema with biologics, the MAPS are now licenced down to a very young age, in a six and even four months of age, and so we've looked at setting up a trial with this, and parents' provisional studies show parents are open to this. If you say to them, "You have two options: treat the eczema early or don't, of course they're going to treat it. You can go with traditional steroids, and which a lot of people are very cautious of, and in truth, they are not always successful in significantly controlling the eczema, or we can try a biologic, some of these biologics for a while, so we used to worry in the early days it is going to influence your vaccination, which is yet to come. You know, live vaccine responses are safe with this, but many of them carry certainly the ones have been around for a while. We are certain are safe as some of the other medicines we use, and this would just be wonderful. The problem at the moment is we can't access things like the MAP easily on the NHS for all our eczematous kids, and they normally have to get over other hurdles. They have to have trialled more potent the cyclists forward and miss a trick, a lot of parents don't want to do it for many other reasons, so it's a little bit frustrating at the moment, but these trades do go off patent, so if you take something like Omalizumab, the generic Omnico is cheaper, and this will facilitate more broadly.

Emma: Exciting times, citing times, George, that's really that was really fun, actually always enjoyable talking to you. I was really engaged in this discussion about allergy, really positive about what the future might hold, and how actually things are really changing, and that's a very exciting time.

So, if any of our listeners are really interested in allergy and paediatric allergy, apart from listening to you, where should they go?

George: So, there are two patient support groups, and you could signpost these to your families: Allergy UK and the Anaphylaxis Campaign. So, there are distinct entities are very, very helpful.

If you want your patients to train themselves up in the Neffy, okay. This is a commercial website, but patients going to ask you, Neffy has a website that is very good. If you want to signpost patients with regards to weaning strategies early on. The more recent

Australasian guidelines have just been updated two or three weeks ago, and they speak to the introduction of multiple allergens, no formula milk in the first two weeks. The first guideline, that's a different topic, but there's some novel findings there all based on science, and I think very helpful. Our own allergy society is the British Society of Allergy Clinical Immunology (BSACI). There are many resources there, such as emergency plans for your patients that need to carry adrenaline devices, and then, of course, we also have a very strong European EAACI society. But if folk want to train up, we do a lot of courses in the Allergy Academy, so search that. We have courses coming up. I must prepare the talk after this, and those are the strong societies that I have just referenced, if people want to look for resources.

Emma: Thank you very much. And I have to give you a five-star rating on your PPIE, because it's really interesting doing these podcasts. A lot of the times you had said to me, we did this because patients and parents were interested in this. Patient parents asked us, could we do this, and so it's really good to hear research led by public, parents, patients, and families, which doesn't often happen as much in other areas as in allergy. So that's really, really exciting. It's been a real pleasure to talk to you, George. I've had a lovely time, so maybe you should come back, and we could talk about something else. George: Brilliant. Thank you. I'll see you on the journey.

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