

Instilling Confidence Surrounding Early Introduction of Allergenic Foods

✦ Course Transcript ✦

Editor's Note: This is a transcript of an online course released in June 2024. It has been lightly edited for clarity. To obtain credit for participation, [CLICK HERE](#).



Mimi Tang, PhD: What we're hoping to achieve is for you to appreciate why current evidence-based guidelines around allergy prevention and infant feeding have changed. This should

hopefully allow you to discuss common concerns with parents around the introduction of complementary foods, including the allergenic foods and potential risks that they worry about. And finally, to be able to support families in implementing current evidence-based guidelines, taking an opportunistic approach to encouraging families to introduce allergens early, when you see them during encounters.

Let's take a historical perspective. Twenty years ago, the American Academy of Pediatrics Guidelines for Allergy Prevention and Infant Feeding recommended to delay the introduction of highly allergenic foods in infants who were at high risk for developing allergy problems. This included a delay in cow's milk introduction until 1 year of age, delayed egg introduction until 2 years, and delayed nuts and fish until 3 years. Now, the reason these recommendations were in place was because the immunology community applied some basic principles around tolerance induction and we assumed that, in order to become allergic, you had to be exposed to the food and therefore, let's just avoid that until the gut was slightly more mature and able to induce this tolerance response. The fear was that young babies might be less capable of achieving tolerance.

However, this thinking was actually not backed by evidence and, indeed, through the early 2000s, the immunology community became aware of literature which showed that, in fact, developing tolerance to foods is a very active immune response. And indeed, you needed to be exposed to the food in order to develop tolerance. We started shifting our thinking and, in 2008, guidelines were actually updated to remove that recommendation around delaying the introduction of highly allergenic foods. This was similar across the globe and the American Academy

of Pediatrics published updated guidelines in 2008 confirming that there was no convincing evidence to delay the introduction of specifically highly allergenic foods.

At the time that this was released, there was no specific guidance around how to introduce these foods or when. And so, subsequent to that, in 2012, the American Academy of Allergy, Asthma and Immunology Adverse Reactions Foods Committee developed recommendations to support clinicians in their discussions with patients and families around when these allergenic foods should be introduced and also to provide some guidance around how. These recommendations were to introduce complementary foods when the child is ready, between 4 to 6 months of age, roughly when the child can sit up, is showing interest in taking complementary foods, and the way to do that would be to introduce 1 food at a time, but not faster than every 3 to 5 days. And the suggestion was that highly allergenic foods could be introduced after the child had already shown an ability to tolerate the typical complementary foods, such as rice, potato, some vegetables and then, at that stage, it would be right time to introduce these allergenic foods.

In terms of how to do it, they recommended offering an initial taste in the home setting rather than at daycare or out at a restaurant, obviously in case there was a reaction, you would be able to better handle that. And secondly, if there was no apparent reaction, to actually continue that food in gradually increasing amounts to incorporate it into the child's diet. This was guidance that was felt to be very helpful to clinicians.

Now, subsequent to that, the guidance has changed again and I'd like to actually spend a bit of time now studying the evidence for why we have changed the guidelines. In 2015, a pivotal study was published that provided the first level 1 evidence confirming that early introduction of an allergenic food actually is very effective for preventing the development of food

allergy. This was the LEAP study published by a group of researchers from the United Kingdom. What they showed was that if infants were introduced to peanut in the first year of life, sometime between 4 months and 11 months of age, their risk of developing peanut allergy was reduced almost 80% compared to children who had delayed introduction of peanut out to 5 years of age. And this is the data that we show here. Now, the key things to remember from this study are, firstly, all participants in the study were high risk by way of having a history of early severe eczema or a history of egg allergy. And what they showed though was that even in the children who did not have a positive skin test to peanut, there was a benefit with a reduced incidence or prevalence of peanut allergy at age 5, from 13% to 2%. But the benefit was especially striking amongst children who already had a positive skin test to peanut although they were not yet allergic. In this more high-risk group by way of having already developed a positive skin test to peanut, their risk for peanut allergy reduced from 35% to 10%.

Now, subsequent to that first study, several other studies have been published and these are all showing very similar findings, not just in peanut allergy but now in other food allergies. As for most studies in egg and milk allergy, as in the case of intervention trials for example, and what we see here is a meta-analysis systematic review showing the results from pooled studies of egg, peanut, and milk allergy, showing that earlier introduction of these foods in the first year of life are effective at reducing the risk for developing allergy to those particular foods. The evidence is a little less strong for milk allergy, but this relates largely to the limited number of studies with both studies actually showing a shift towards benefit.

In terms of the systematic review findings, what they showed was that early introduction of egg at 4 to 6 months of age was associated with a halving of the likelihood of developing egg allergy and, similarly, there was moderate certainty evidence for reducing the risk of peanut allergy by introducing peanut around 4 to 11 months of age with the risk actually reducing by 70%.

These findings have led to updated guidelines in the US, as well as around the world. These updated recommendations were first published in 2015 and there have been several iterations of these updated guidelines in the subsequent years. But, to summarize, what these current recommendations advise is to introduce potentially allergenic foods, including egg, milk, peanut, tree nuts, wheat, shellfish, fish and soy, from around 4 to 6 months of age when you're introducing other complementary foods. They recommend this because there is now good evidence that this will reduce the risk of developing at least peanut allergy, but also likely other allergies. If you have any queries, then consult your healthcare provider.

There is now more detailed guidance around how to introduce these foods, but in particular peanut, because of the fear around peanut reactions that exists in the community. And here you can see step-by-step, very graded introduction of peanut which is aimed at minimizing risk. It's very unlikely with this sort of approach that you will induce a serious allergic reaction in a baby, and, moreover, we know that the likelihood of serious reactions in babies is actually low.

Here we talk about introducing first a small amount on the tip of a teaspoon and waiting a period of time, at least 10 minutes, to see if there is a reaction. If there's no reaction, you can then offer a larger amount and continue to offer the remainder of a standard serve of peanut which is around 2 g of peanut protein. The important aspect here—when you first introduce foods—is to have access to observation for at least 2 hours after you've introduced the food so that in the event there is a reaction, you can manage it.

Now, because the LEAP study was conducted in high-risk infants and it did involve some level of screening for existing peanut allergy, the current guidelines in America offer the option to test for peanut sensitization before introducing peanut. I do want to highlight, however, that this is not essential, and many areas around the world, including Australia, do not screen children for peanut sensitization prior to introducing peanut. We do, of course, take a careful history because if there is a history of prior reaction

which would suggest allergy, we would not recommend introducing peanut. However, if there is no history of allergy to peanut, we would simply recommend introducing peanut without prior screening and there is a lack of consensus, even in the United States, around whether or not you would do early screening or not.

Nevertheless, there is this guidance that has been published in 2017 which gives you an algorithm if you did choose to screen for peanut sensitization before recommending introduction. You may screen in high-risk infants. High risk is defined as having either severe early-onset eczema or established egg allergy. In these infants, you could consider doing a peanut skin prick test or a peanut blood test, looking for peanut-specific IgE. If this test came back positive, it does not necessarily mean the child has allergy because we know that at least half of the children with a positive test are not allergic to peanut. This is actually the reason for the controversy around whether or not to screen for peanut sensitization. But in the event the test is positive, you can then apply thresholds that have been published to stratify your patient into whether or not they have high, moderate or low risk of clinical allergy. In those with a high risk of clinical allergy, you would refer to a pediatric allergist for ongoing care. If, on the other hand, it is at a low level—and therefore it is unclear whether the child is likely to have clinical allergy—you may choose to introduce peanut in a supervised setting or through an oral food challenge in your clinic.

If, on the other hand, the level of reactivity is deemed to be low, so for example, it is a negative test or a borderline test, you could still offer a supervised feeding in your clinic, or you could suggest the family introduce at home. If a child only had mild to moderate eczema, these children are not considered to be at increased risk for peanut allergy and do not need to be screened for peanut sensitization. They simply would proceed to introduction at home, as would be a child deemed to be at low risk for developing peanut allergy.

Let's talk now about how we implement guidelines. What we know about guidelines is that there are significant barriers to adoption. In the case of food allergy prevention guidelines, I think these barriers

are even greater because there is general fear around the possibility of serious allergic reactions happening, the fear of a potentially life-threatening reaction and the fear of having to manage these in the setting/in the community, where parents are then responsible for looking after their child for that reaction. I think it's important for us to now think about how we can improve adoption of guidelines. In order to do that, we first need to understand barriers. And these are the barriers that I think face us, as health professionals, and the community, in encouraging our families to do what we'd like them to do which is to introduce these allergenic solids early.

The first is actually educating health professionals. It takes a while for new guidance to filter out. I know it's 10 years since the latest guidelines were released, but it can take that long if you don't proactively implement a plan for educating health professionals. You then need to steer health professionals to accept those guidelines and actually support them, and therefore recommend them to their patients.

On a second level, we then need to work on the community, to improve awareness around guidelines at the community level and to then address this hesitancy, that I was talking about previously, about following the guidance. And the last thing that we note is that often guidelines across the country are not well-aligned, and that can be confusing for families. What we want to do is to ensure that there is alignment across all national guidelines for allergy prevention and infant feeding.

What I'd like to move onto now is to share with you some data from Australia which nicely illustrates how addressing the barriers to adoption can actually successfully lead to improved implementation of guidelines. Here is data on the introduction of solids and allergenic solids prior to updates to our guidance. The Allergy Prevention guidelines in Australia were updated in similar time frames to what we discussed earlier for the US. Prior to 2008, we recommended delaying allergenic solids. Around 2008, we published updated guidance that said there is insufficient evidence to delay. We removed the recommendation to delay and then, in 2015/ 2016, we updated guidelines again to actively recommend early introduction.

Let's see what Australians were doing with the original guidance of delaying introduction. They actually followed guidelines pretty well. Most children introduced solids, complementary solids, between 4 and 6 months of age. If we then look at allergenic solids, egg was introduced typically in the second half of the first year of life with the majority having introduced it by 12 months. But in the case of peanut, almost no one had introduced peanut prior to 1 year of age. Now, following our initial recommendations, the updated guidelines in 2015, we ran another population study to evaluate intake of peanut, in particular egg, as well and some other allergenic foods.

What you can see here, from the HealthNuts study, is that there was a very clear adoption of guidelines. We showed that introduction of peanut improved significantly, such that 83% of infants were now eating peanut within the first year of life, including highly, high-risk patients who had severe eczema in the first year of life. We have similar data for egg and cashew. There is a shift to the left in terms of timing of introduction. And now, with most children, were steadily introducing egg in the second half of the first year of life. Now, more than half had introduced egg by 6 months of age. For cashew, prior to guidelines being updated, nobody actually had introduced cashew in the first year of life, but here we see, with the updated guidance, there is a steady introduction of cashew in the second half of the first year of life. The takeaway message, using evidence from our HealthNuts study in Australia, we can show that adoption of guidelines and implementation of guidelines in the community led to improved intake of these allergenic solids.

Now, what we also wanted to do in Australia was to see if we could improve this adoption even further. We wanted to specifically address the barriers by a public health intervention approach and what we did was develop a Food Allergy Prevention Project. This was funded by the national government and allowed us to implement a number of strategies to overcome the barriers that we mentioned earlier. What we wanted to do was to be able to improve introduction of allergenic solids in the first year of life even further

and to optimize eczema management, knowing that eczema is actually a risk factor for food allergy.

What was the Food Allergy Prevention Project? This was an initiative of the National Allergy Council, which is a collaboration between our professional society, the Australasian Society of Clinical Immunology and Allergy, that is the American Academy of Allergy, Asthma and Immunology equivalent in Australia, a collaboration between ASCIA and Allergy and Anaphylaxis Australia, the equivalent of your food allergy patient organization in the US, for example Food Allergy Research and Education, but I understand you have many national patient organizations.

The funding for this project, as I mentioned, was through the Australian federal government. And the implementation process was guided by a key stakeholder meeting that we held in March 2017. And what this group came up with—I was fortunate to be part of this group—is we developed 3 different components to the Food Allergy Prevention Project. The first was something called Nip Allergies in the Bub website. This was a website that aimed to share evidence-based information to parents and health professionals in partnership with ASCIA and Allergy and Anaphylaxis Australia.

The second component was an app that we developed for smartphones that was called the SmartStartAllergy app. It was built off the back of another app that we have in Australia that reminds families to see their healthcare provider for routine childhood vaccinations. And what we would do is, at 6 months, 9 months and 12 months, families would receive a reminder through their smartphone asking them had they introduced allergenic solids and, if not, sending them to the Nip Allergies in the Bub website where they would respond to a questionnaire and also receive guidance on how to introduce solids and the importance of introducing allergenic solids for preventing food allergy.

The third component of the program was a support line. We had dedicated health professionals, typically experienced nurses, who were able to take calls from parents and health professionals to support them in implementing the updated guidance. This project was

rolled out as a pilot phase in western Australia, one of our Australian states, in August 2018, shortly afterwards as a national launch in September 2019. And what we were able to do was to evaluate this particular project.

When we evaluated the program, we first looked at the SmartStartAllergy service. If you recall, this was the allergy app on smartphones. And our specific research question was whether having access to this smartphone app actually influenced the rate of peanut introduction in the first 12 months of life. We basically recruited participants via GP practices that were already using this particular app for vaccines. And we divided patients into the intervention group, those that were enrolled into the program before they turned 12 months of age, and a control group who were parents and families who enrolled into the program at 12 months of age or later.

All parents were invited to complete an online questionnaire asking them about peanut introduction at 6 months, 9 months and 12 months of age for the intervention group and, obviously, for those who were already age 12 months, they were only able to respond to the 12-month questionnaire. The specific details that we collected were whether they had introduced the allergenic foods, specifically peanut, as well as other food allergens, parent-reported reactions to these foods, and whether the child was suffering from eczema, whether they had other food allergies, whether there was a family history of allergy problems, and their country of birth.

What we found from our data was that participants were recruited between the September 21, 2018 through April 2022. The introduction of the SmartStartAllergy service increased the likelihood of introducing peanut by 12 months of age from 88% in the control group to 98% in the intervention group. The crude odds ratio was 5-fold, meaning that families who received the prompt from the SmartStartAllergy service were 5 times more likely to introduce peanut by 12 months of age as compared to the families who did not benefit from the SmartStartAllergy prompt. When we looked at the effects in high-risk as compared to non-high-risk babies, we found that the benefit was similar. And we can look at this in a different way, using logistic

regression analysis, adjusting for the high-risk infants' status. We showed that the odds ratio for introducing peanut in the first year of life was the same in the high-risk as compared to the low-risk groups. And here you can see, in the table below, that irrespective of the nature of you being high risk, whether the baby had eczema, severe eczema, the family history of allergic disease, or all 3, you can see that the odds of achieving early introduction of peanut in the first year of life was similarly improved following access to the SmartStartAllergy service.

We summarized the findings from our SmartStartAllergy study, we can say that SmartStartAllergy service, receiving a prompt through a smartphone app at 6 months, 9 months, and 12 months, amongst both low-risk and high-risk infants, significantly improves the likelihood that families will introduce peanut in the first year of life, according to current evidence-based guidelines around peanut introduction as compared to not receiving those prompts. What was interesting is that the control group in this study, the likelihood of introducing peanut in the first year of life was similar to our population-based study that was carried out at a similar timeframe that I showed you from the EarlyNuts study.

One of the questions is why would having access to a smartphone app actually help a patient follow guidance and actually adhere to the instructions? The reason you ask that question is that other studies that have used a smartphone app prompt haven't been as successful at achieving adoption. We think there's a number of differences with our SmartStartAllergy approach. The first is that we were directing them to a website endorsed by an expert body, the Australasian Society of Clinical Immunology and Allergy. When patients are actually directed to a website with this endorsement, they are more likely to actually follow the guidance that's available in that website. The second is we found that patients actually like going to a website to read information. They are able to do that at their leisure, they feel more in control, they can read through it at their own pace, and so they are more likely to actually take on board the information that they're reading, rather than dismissing it. The third is that this website was very specifically designed to deliver the information that patients are

actually interested in. Because we had that stakeholder forum when we developed this Food Allergy Prevention Project, we were able to very carefully tailor the website to the way that patients like to see information. We believe that those particular aspects of our Food Allergy Prevention Project and the SmartStartAllergy service were key to achieving the significant benefits that we showed in the use of our smartphone app.

The next question to ask is if these changes to guidelines, and improved adoption of these guidelines, have led to any actual benefits at the community level in relation to incidence and prevalence of peanut allergy. And here we can draw on evidence generated from Australia. We have conducted a number of studies that have examined whether or not rates of peanut allergy and peanut anaphylaxis have been changed following the introduction of our guidelines in Australia. Starting with this particular study, my colleagues and I published an examination of food anaphylaxis admissions across Australia in 2022. What we did was we accessed national admissions database and we looked at food-specific anaphylaxis rates over the course of 20 years, from 1999 to 2019.

We looked at different age groups and we examined 3 different time periods related to the changes in guidelines. In 2008, there was a removal of instruction to delay introduction of allergenic solids, similar in timing to the US update. And then in 2016, there was a second update to actively introduce allergenic solids from around 4 to 6 months of age. Here we looked at food anaphylaxis admission rates across Australia for those 3 time periods, and we examined rates of admission for different age groups who may or may not have benefitted from those guideline changes.

Children who did not benefit from any of the updates to our guidelines. They were born prior to 2008 and adhered to the original delay introduction of allergenic solids advice. What you can see in this group is that there is an exponential increase in food anaphylaxis admissions over the course of time paralleling what we know of food allergy and food anaphylaxis rates across Australia, the US, and the rest of the world. What you can see, there is, no, this is the baseline that you're comparing against.

If you then shift your attention to children aged 10 to 14 in the solid red line and to children aged 5 to 9 in the dotted red line, these children benefitted from the 2008 updates in the case of the 10- to 14-year-olds and to the more recent updates in the case of 5- to 9-year-olds. In both cases, you can see that there is a fleshing in the right of food anaphylaxis admissions over the course of the 3 periods. And it's actually most striking for those in the 5- to 9-year age group where they do show an initial exponential increase, and then a flattening as they benefitted from the increased—the recent guidance change.

An interesting question is, as we recommend introducing solids earlier, are we increasing rates of anaphylaxis? And what we can see is we do cause a spike in the rate of anaphylaxis admissions amongst children aged 1 year or less. Because we're recommending introducing allergenic solids sooner, we do see a higher rate of anaphylaxis in this age group. But, when you look at the overall prevalence of anaphylaxis admissions in the full 0- to 4-year age group, so for all children aged 0 to 4, there is no overall spike. What that tells us is that there isn't an increased prevalence of anaphylaxis overall. There is, however, a shift in the admissions from slightly later on in the first 4 years of life to earlier on in the first year of life, in line with the timing of introducing the solids.

If we walk away from the take-home message here, there appears to have been an impact on food anaphylaxis admission rates in Australia following updates to guidelines which we know were associated with earlier introduction of at least peanut, egg and cashew, which I showed you earlier. What about community prevalence of peanut allergy? Here, the data's less clear. We can see a slight, modest reduction in prevalence of peanut allergy in the community. This data comes from our large EarlyNuts study surveying thousands of babies in the community and the HealthNuts study surveying 5,000 children in the community. EarlyNuts was conducted approximately 10 years after HealthNuts, so we were able to interrogate these 2 population-based studies and examine prevalence of peanut allergy.

Now, when we adjust for the different demographic distribution of patients in the 2 studies, we see the modest reduction in peanut allergy prevalence. However, overall, the impact is small. We see a reduction from 3.1% to 2.6% peanut allergy at age 1 year over the course of 10 years, following the introduction of our guidelines. One might ask, well, hang on a minute, why is there only such a modest improvement in peanut allergy prevalence whereas in the clinical trial, the LEAP randomized trial that led to all of these changes in our guidelines, showed a halving in the risk of peanut allergy prevalence? We think there are a number of reasons for this. First and foremost, recall that the LEAP study was conducted in high-risk children only and what we don't know is whether these effects would equally be applicable to children who don't have eczema and who don't have egg allergy.

Secondly, the introduction of peanut in LEAP was between 4 months and 11 months, and they then waited 5 years before testing for peanut allergy. In the HealthNuts and EarlyNuts studies we measured it at 12 months, and it's possible that if we had waited to 5 years, we would see a greater reduction in peanut allergy prevalence. The third thing to consider is that the dose and frequency of peanut intake in our real-world community in Australia might be very different to the introduction amount and frequency that was required in the randomized LEAP trial. In the randomized trial, children were asked to intake 2 g at least 3 times a week. That is a much bigger amount, or a substantial amount, and we do not know whether our community intake of peanut in Australia matched that level of peanut intake.

Addressing the first point of risk and whether the benefit of early introduction is equal amongst children who have eczema, for example, as compared to those who don't, we were able to examine this very question in our data from HealthNuts. What we were able to show in HealthNuts is that having earlier introduction of peanut is only leading to a reduced prevalence of peanut allergy amongst the children who had early-onset eczema. From our data, it would appear that children who don't have eczema do not benefit necessarily from early introduction of peanut. It is primarily those children with early eczema who

are considered at higher risk for developing peanut allergy that benefit from an earlier introduction. And if you recall, that is 1 of the reasons the US guidance for children who are not considered at high risk recommends that you can simply recommend introduction of peanut as the family desires.

Okay, so what are the key learnings from our Australian experience and the data that we can share from Australia? The first is that peanut introduction by 12 months appears to be effective at preventing peanut allergy. There's a striking reduction in anaphylaxis admissions and a more modest reduction in peanut allergy prevalence in the community. Secondly, parents are more likely to follow advice if it's backed by expert recommendation through a readily available website and supported also by some information around how to introduce the food. In Australia, our smartphone app, SmartStartAllergy, that prompts parents to introduce peanut at 6 months, 9 months and 12 months, seemed to be effective in further enhancing the likelihood of introducing peanut in the first year of life. This suggests that you could take an opportunity when you see patients at 6 months, 9 months, to ask these questions and prompt families on a regular basis to introduce peanuts.

National admissions data in Australia gives us reassurance that the recommendation to introduce peanut, at least, earlier in the first year of life does not lead to an overall increase in anaphylaxis rates. It does shift the presentation of anaphylaxis in already allergic children who introduce peanut to an earlier time point, but it does not seem to increase the likelihood of severe reactions in those already allergic to peanut when you introduce peanut early.

The key takeaways for your practice are that early introduction of allergenic foods can improve tolerance to those foods and reduce the likelihood of developing allergies. Consistent messaging is very important and technology with reminders can be leveraged to improve introduction of allergenic solids alongside opportunistic reminders at patient visits during the first year of life, perhaps centered around vaccination visits.