Food Allergy Tests Are Not Screening Tests

✦ 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.

David R. Stukus, MD: I'm happy to address the concepts surrounding food allergy testing. And, as you see from the title, food allergy tests are not screening tests and that is a frequent way that they are misused and abused, unfortunately, but we're going to talk about why that is and the proper way to utilize food allergy tests.

When people come to see me due to concern that their child has a food allergy, I love helping them clarify the diagnosis because that's always the most important part of any evaluation. And when we talk about how do we diagnose food allergy properly, let's just start with some basic definitions because this really sets the stage for everything. And I often explain this to parents in the office setting and more often than not, they'll say, "Oh, well based upon that description, my child doesn't have a food allergy." And I'll say, "I agree with you and I'm glad you're here and let's talk about why."

When we think about some of the definitions and we talk about an allergy, this is an immune-mediated response. Every single time somebody eats the food, their immune system should say, "You don't belong here," and some sort of reaction should occur. The most common type of food allergy that we're going to address mostly today would be an IgE-mediated, immunoglobulin E-mediated, immediate onset hypersensitivity reaction to a food. But of course we can also have delayed onset food allergy, such as cow's milk-induced proctocolitis or food protein-induced enterocolitis syndrome and things like that. But regardless, whether it's an immediate allergy or delayed, ingestion of the food is going to cause symptoms every single time.

This is very different from a food intolerance. Food intolerances are not caused by the immune system going haywire. This is more difficult, due to digestion, and this is not going to occur immediately. It may vary over time. It may vary based upon the amount of food that is ingested or how it's ingested. And the symptoms are often very delayed, often occurring later that day or the following day after ingestion. And these are going to be mostly gastrointestinal symptoms. The most common example, of course, would be lactose intolerance.

We have this term, food sensitivity, which actually is not a medical term. There's no ICD-10 diagnosis for food sensitivity. There's no clearly established clinical criteria. There's no diagnostic test that's been validated to diagnose food sensitivity. We can't really apply any of the principles from a food allergy or intolerance, but unfortunately more and more of these unvalidated food sensitivity tests are being offered which don't measure anything other than a normal response to eating a food, which we can talk about in a little bit.

When we talk about IgE-mediated food allergies, these have increased in prevalence over the last 20 or 30 years and right now, approximately 5% to 8% of children in the United States are affected by at least 1 IgE-mediated food allergy, which affects all races and income groups. There are disparities where lower socioeconomic groups and African American children have higher rates of food allergy and increased prevalence and less access to services and things like that, but this is something that's affecting approximately 1 or 2 children in every classroom, depending upon the size. And when we talk about IgE food allergy, there are 9 foods that cause more than 90% of all reactions. And this would include cow's milk, wheat, egg, soy, peanuts, tree nuts, finned fish, shellfish, and sesame, as well. Now, can you have a food allergy to other foods? Yes, you can, but it's much, much more rare compared to those 9 foods that I just listed.

How do we properly diagnose food allergy? Well, it all starts with the clinical history, and that's the best test. We have to spend the majority of our time really taking a detailed clinical history to see about a pattern of symptoms that occur with ingestion. We should see reactions, these are objective reactions, they should

occur within minutes of ingestion, rarely longer than 1 or 2 hours later, especially when it's IgE-mediated. And, like I said before, it's going to happen every single time. If somebody has concerns about their child being allergic to cow's milk, they really shouldn't be able to ingest cheese or ice cream or yogurt and so on and so forth.

It's almost always going to have to happen through ingestion. Some people can have contact reactions from touching the food if they're allergic to it, but that would be a very rare cause of anaphylaxis and it's extremely rare for somebody to have an allergic reaction to a food just by being near it or inhaling the particles. It can occur in circumstances, but if that's the primary concern, then we should be thinking about other diagnoses and not food allergy.

When somebody does have a food allergy and they eat the food and they have symptoms, it can be any combination of big, red, itchy hives on the skin; they can have swelling; you can have gastrointestinal symptoms, such as nausea and vomiting; and, of course, you can have severe reactions, such as anaphylaxis.

I'd like to pause for a moment to note that every single symptom that can occur due to a food allergy reaction can occur for nonallergic reasons as well. This is where it gets very tricky and there's a lot of overlap. We really need to piece together very important details in the history of what was the food of concern, what was the timing of onset of symptoms, what were the symptoms and how long did they last for. For most IgE-mediated food allergy reactions, they're going to occur within 30 to 60 minutes of eating it and the symptoms are going to be gone, with or without treatment, within a few hours. If somebody develops diffuse hives in association with eating a food but those hives last for 3 days afterwards, it was very unlikely to be caused by a food allergy reaction. If somebody comes to you with concerns about lemon causing delayed-onset rash or something like that, I hear you and I believe you but I'm not worried that that's actually a true food allergy because lemon is a very rare cause of food allergy. The detailed clinical history is absolutely the most important part in establishing the diagnosis and we can't get around that.

When should we be doing food allergy testing? Well, we should really be doing food allergy testing when somebody comes in with a history that is very suggestive for them having IgE-mediated food allergy. The food allergy tests that we use, which we'll talk about, really only detect the IgE antibody. For somebody who has a delayed-onset food allergy, those tests aren't going to give us any good information. If you are concerned about those rare causes, such as food protein-induced enterocolitis syndrome and things like that, these food allergy tests aren't going to be very good in establishing the diagnosis.

When we do allergy testing, these aren't positive or negative. We get a range of results. On a skin prick test, we place a drop of the liquid allergen on the skin, typically on the forearm or on the back, we gently scratch through the top layer of the skin to introduce that allergen to those mast cells that are sitting there. Those mast cells, if they have the IgE bound to them, they will be unlocked by exposure to the allergen and they will release histamine. Within about 15 minutes, we will see a hive develop and then the size of the hive at the area of the allergen placement indicates the likelihood that allergy is present. It's not a yes or no answer.

On blood testing for food allergies, we can do serum IgE levels to any food essentially. The results come back as a range and the range is often from 0.1 to 100 kilounits per liter. Just because you have detectable IgE doesn't necessarily mean that you have an allergy. And these aren't good screening tests because we get a lot of false positives whenever we do the testing. The test, by itself, does not diagnose allergy. If you have a highly suggestive history of ingestion causing symptoms on multiple occasions and you have an elevated test, then that would indicate that that person likely does have a food allergy, but we can't do the testing first and then diagnose it based upon that. That would be backwards.

Allergy testing is really important to clarify the diagnosis. It can really help assist avoidance. A lot of people think that they may be allergic to all tree nuts, for example, but they may only need to avoid cashews or pistachios. They can liberalize their diet

otherwise. And then also, once somebody has an established diagnosis of food allergy, that person needs to be followed over time with repeat testing. Generally, we'll do this about every 12 months or so just because we don't expect things to change much sooner than that, but we know, for example, that the vast majority of children with milk, egg, wheat or soy allergy are going to outgrow this by school age whereas, unfortunately, only about 20% with peanut or tree nut allergy will outgrow it. But they still need to be retested over time, especially when they're diagnosed as infants. These are reasons that we should be doing testing.

If we think about what an ideal test would be, if we had an ideal allergy test for food allergy especially, it would be something that's accessible to all of us, noninvasive because we don't want to put children through torture as we test them for things, and then readily available. We want this to be available in all our offices and very inexpensive. We want it to be reliable, meaning that it would have a very high positive predictive value so we could believe the positive results and a high negative predictive value. And we want to avoid false positives. And then we want it to be clinically applicable, meaning we want it to be easy to use, that it should require minimal training in order to interpret it. We'd want to get a better sense of how allergic that individual is because everybody has different thresholds that can trigger an allergic reaction. And we would love to have a test that tells us how severe that person's allergy is as well.

Well, unfortunately, the reality of today's world is we actually don't have these tests. Now, we do have accessible tests, especially with the serum or the blood IgE levels that anybody can order through your local laboratory. But otherwise, those still aren't noninvasive. It requires a blood draw and a needle stick. The allergy tests that we have, whether it's a skin test or a blood test, have high false positive rates, which is not what we want, which leads to a lot of unnecessary avoidance and misdiagnosis. And then the tests that we have currently available don't really give us much of a sense in regard to how reactive somebody is or how severe their allergy can be. Those are some limitations.

As I've mentioned several times now—and will again until everybody makes sure they understand—both skin tests and blood tests have high false positive rates. These are not screening tests. You can't just test for everything and see what comes back. Food allergy panels need to go away. There's no indication to ever order a panel of random foods on any patient, regardless of why they come to see you. If you're concerned about specific food allergies, take a detailed clinical history to determine what foods cause the symptoms and then you can order those specific tests. So we need to have a history of ingestion, exposure, and know what's happening. We can't predict who's going to develop food allergies, so we can't just place a bunch of these allergy tests on babies to see who will develop it. And we don't know the severity of it, so nobody should be telling their patient that they have a severe food allergy based upon the level of IgE in the blood or based upon the skin test size.

We also want to make sure that if somebody has a really good clinical history of having a reaction, especially if it's something like peanuts or tree nuts, and even if they have a negative skin test, we should follow that up with either a blood test or ideally an oral food challenge. Unfortunately, we can have very low rates of false negative testing, but if somebody has a really good story, especially if they have a history of severe reactions, we want to follow that up and do our diligence to properly diagnose them.

When we talk about the interpretation of these, we really don't have good cut-off levels for the vast majority of foods, especially food IgEs. There's some very old data that have been done that tried to offer some predictive values for different numbers for different foods. It's important to recognize this has only been established for a handful of foods, like egg, milk, peanut, fish, soy and wheat. The numbers mean different things for different foods. For instance, with soy and wheat, people generally won't experience reactions unless they have a very high IgE level towards those foods in their blood, whereas people may have a higher risk for having actual allergy to fish, with a lower IgE level. But, even then, it's not 100%. The positive and negative predictive values are all over the place when it comes to all of these tests and the thing that's missing from here is we don't

know what the predictive value is for things like sesame or for fruits and vegetables and things like that. The more of these IgE tests that are being done, the more they're being misinterpreted because people mistakenly attribute any detectable IgE to meaning that that person has a food allergy and, as we've already discussed, that's not the case.

Why do we see such high rates of false positive food allergy tests? Well, there's a couple of reasons. When it comes to cross-reactivity, from a clinical standpoint there's no clinical cross-reactivity between peanuts, which are legumes, and tree nuts, which grow on trees. Just because somebody had a reaction to peanut doesn't mean they're allergic to tree nuts. But if you do enough tests, oftentimes you will see some of that cross-sensitization on the testing. Keep in mind also (and we'll talk about air allergens in a second) a lot of our patients who have food allergies—they don't exist in a void—they also have other allergic comorbid conditions, such as allergic rhinitis to tree pollen and things like that.

In regard to tree nuts, very few people are allergic to every single type of tree nut. We do see high degrees of cross-reactivity between cashews and pistachios as well as walnuts and pecan. Whereas we have low cross-reactivity with almond and these tree nuts and hazelnut and things like that. There's really no cross-reactivity between finned fish and shellfish. These are very different in regard to the type of protein that causes allergic reactions. Many people with shrimp allergy are completely fine if they eat finned fish, such as salmon or tuna or tilapia. Whereas we do see high rates of cross-reactivity amongst the finned fish, as well as amongst the shellfish. Very few people who are allergic to shrimp are able to eat crab or lobster.

Peanut and soy have very little clinical cross-reactivity. They are both legumes, but if you have somebody with a peanut IgE that's very elevated and if you start testing for other legumes, they're almost always going to come back detectable. Does that actually mean that they're allergic? No, it just means you're getting false positives on the testing because there's such similarity with the peanut as far as the assay is concerned. Same thing with wheat and other grains, and then cow's milk and other types of mammalian milk.

For those with aeroallergen sensitization or allergic rhinitis, they can have false positives on testing for food. Dust mite and cockroach look very similar to shellfish in regard to the IgE assay, whereas clinical reactions in these folks are very rare. Anybody who's allergic to birch tree pollen, which is a predominant cause of allergic rhinitis in the spring, can easily have false positive testing for peanut, a variety of tree nuts, different fruits, soy, basically anything that grows on a tree and may come back detectable because the assay thinks it's measuring birch tree pollen, but that person may not actually be allergic to that. Same thing with grass and things that grow in the ground, such as wheat, and then anybody with tree pollen allergy can easily have false positive testing to tree nuts.

In recent years, there are newer types of IgE tests available, such as component tests. These have been developed for a wide variety of foods. What the component tests do, instead of looking at just the overall protein that can bind to IgE, it really breaks down into specific antigens. And for instance, when it comes to peanut, there are some antigens, such as Ara h1, h2, h3 and h6, that are more likely to cause clinical reactivity as opposed to Ara h7, h8 and h9 which is more cross-sensitization with birch tree pollen. And this has been established for other types of tree nuts, also for egg and milk and things like that. But here's the problem. These are often widely marketed as great screening tests for patients which, again, it's not a screening test. These are often widely marketed as saying that it can predict the severity of reaction, which it can't. This can only predict which of those patients are more likely to have a clinical reaction at all compared to just false-positive testing.

When should we be doing component testing? Well, again, if they have a history that's clear for allergic reactions, there's probably no reason to do component testing. If, for some reason, somebody had panel testing done and we're trying to tease out if they were actually clinically reactive or had cross-sensitization, then we can use this to help clarify that. But again, the predictive values for these have really not been well established and they should never be used as a screening test.

How can we use all of this information? That was a lot that we covered in just a very short period of time. But, as you can see, there are some common areas and ways why these tests can easily be misinterpreted.

Before we move on, I think it's really important that we address all the unvalidated tests that you may have come across or that I know all of our patients are being bombarded with. And there's a couple of key principles to understand. When validation matters. These IgE tests that we were discussing, they were validated, meaning that we see differences in people *with* a condition, compared to those who don't have a condition. We see the same results in the same person over and over again when we do the tests. And they've gone through very stringent criteria to make it a validated test. But there are unvalidated tests, such as IgG food sensitivity tests. These are widely marketed, but they have never been validated and it's never been demonstrated that they actually diagnose anything, let alone food sensitivities. We have no data that show that a population with certain symptoms will have different IgG results to foods, compared to a population that doesn't have those symptoms, for instance. There are alternative forms of tests, like mediator release tests. There's something called an applied kinesiology or muscle testing. There's people that offer electrodermal analysis, hair and urine analysis. I mean, the list goes on and on. If you get questions about this or if you have questions yourself, please take a moment to think through—is this a validated test or not? And when it comes to food allergies, really it's only the skin prick and serum IgE tests that are validated and useful.

How can we use this to really benefit our patients? Well, 1, we can avoid over-testing or, 2, we can utilize what is the gold standard and this is something that I do every day as a pediatric food allergy specialist. We do oral food challenges. Oral food challenges are an opportunity where, in the office setting, we feed small amounts of the food. We gradually increase the amounts that they're eating over time and we monitor. And then if no signs or symptoms of allergic reaction occur after eating a full serving of that food, then that indicates that person's not allergic to that food. Even if symptoms do occur, there's benefits because we get to identify what's that person's threshold. Many people are led to believe that even trace amounts are going to cause a severe reaction, which is rarely the case. We know that, for instance, 50% of the population allergic to peanuts need to eat two-thirds of 1 peanut kernel before they have any reaction at all. Now, that doesn't mean that they're not allergic to peanut if they can tolerate a whole peanut. It just means that they're sort of already bite-proof. On the flip side, that means 50% of the population is allergic to very small amounts. And we need to identify those individuals and help them better understand how to avoid those other types of exposures.

We can learn severity of reactions because we're actually watching them eat the food and we can see what types of symptoms can occur. And we can really clarify the diagnosis. Now, the downside is these aren't offered, even by allergists, out in the community on a widespread scale because they take a lot of time. You have to have the staff support in order to do these, and these families are in the office for at least 3 or 4 hours per food. If reactions occur, we have to stop everything that we're doing and treat that patient and make them feel better. And it really does require expertise. It's sort of a double-edged sword because it's the best test that we have, but it's really hard to implement in the clinical practice on a regular basis.

When we talk about oral food challenges—and we won't have the opportunity to talk about treatment, at least in this talk—you will hear about that in others, the terminology is really important. We think about food challenges, and this applies to desensitization with oral immunotherapy as well, we really want to talk about what's the eliciting dose or the reactive dose and this is the dose that somebody ate that immediately preceded their symptoms. Every single dose that they ate prior to that challenge. And typically there's 5 or 6 steps in each challenge. If they didn't have symptoms until a certain point, whatever that dose was when their symptoms occurred, that's their eliciting or reactive dose.

Prior to that, you can add up the amount that they ingested without reaction and that can be called their cumulative dose of which they tolerated or if you

include the dose that caused the reaction, that's your cumulative reactive dose. But altogether, this can be very helpful in helping people better understand thresholds and really understand essentially how allergic they are.

Even when symptoms occur during a food challenge, there can be benefit to that. There are studies that have shown that quality of life actually improves after a challenge. We basically take the guesswork out of everything. Families with food allergy have gone to an if/then sort of mentality of, well, what happens if they're exposed to this trace amount, what happens if it touches their skin, what happens if, if, if, then what? Well, we can answer a lot of those questions. We can actually show them, in a very safe way, you watched your child eat this much and here were the symptoms that occurred. We remove the stigma from it. Even when epinephrine is administered to make people feel better due to reactions during the food challenges, families are thankful for that because they got to see how fast the medicine worked, they got to see that it wasn't nearly as scary as they thought it was in administering the auto-injector, and things like that. And then, of course, whenever they are successful, it's a game-changer. This is the best part about my job. If we can get food back in the diet that people are avoiding, or especially remove the fear that people have regarding specific foods and demonstrate that it's very safe for their child to eat that food, that's a huge win. It's also part of their identity, so we have to address that because, especially for adolescents, they lived their whole lives, for years and years, thinking that even small amounts of their food allergen is going to send them to the hospital. And when they pass their challenge, they're no longer allergic, it's a very positive way that we can support them and talk about how they can integrate that in their life. It's a very powerful experience.

What are some of the key educational concepts that are essential for patients and parents? Really, it's understanding proper diagnosis. Telling somebody to avoid a food in their diet is no longer a benign recommendation. We're reading more and more and learning more and more about disordered eating habits and, especially when you do these large panels of food sensitivity tests—which, by the way, the IgE tests that I mentioned and described in detail have high rates of false positives—they're not screening tests, IgG food sensitivity tests are, IgG's a memory antibody. This is not involved in an allergic response at all. It is a normal immune response to foreign food-specific IgG towards that food when you eat it. All that these tests are measuring are basically foods that people have eaten in the past, but then they're being turned around and misinterpreted as saying this is showing you have a sensitivity to these foods. That is not the case at all. We want to educate families about all the marketing that's out there and educate them about how to properly diagnose and then manage their food allergy.

I see a lot of families that are just scared to feed their baby. We talked about flip-flopping guidelines and how, as a medical establishment, we've just really scared parents everywhere about feeding their babies. But all the evidence now does support early introduction of allergenic foods into a baby's diet around 4 to 6 months of age, once they're already eating other solids, and then, most importantly, keeping it in the diet consistently to promote tolerance. A lot of families or even referring physicians still ask for screening prior to introduction, but we don't want to do that. There's no evidence that supports screening and doing testing prior to introduction. It can actually cause more anxiety. Parents may be led to believe that they need to have the testing done before just feeding their baby which is a very safe thing to do and there's a lot of distrust in these flip-flopping guidelines, but that's what science is. It's very messy and this is the evolution of the evidence.

From our standpoint, it can lead to improper interpretations, so we get a lot of false positives and we're going to tell people to avoid a food that their child may not be allergic to. Oh, by the way, if we have somebody who's sensitized but not allergic, meaning they have a false-positive allergy test, and we don't feed them that food, that then creates food allergy. Or worse, if somebody's eating a food without having reactions and they have a false positive and you tell them to take that food out of their diet, that will cause them to develop food allergies. That's us doing harm. There's a lot of time constraints for this and then, from a systemic standpoint, it's just going to delay introduction while people are waiting to be seen. It

can take 2 months or 3 months to see an allergist and, in that period of time, they could've eaten all these foods and they may actually miss that window of opportunity where you have somebody who is sensitized, but might be tolerant of it. We need to be very thoughtful about why we're doing food allergy tests and why we're recommending it.

In the evaluation, we always want to be able to stratify into what's low, moderate, and high risk, to develop food allergies. Now, the absence of risk factors does not mean you cannot develop a food allergy, but by and large, a family history of food allergies really isn't a very strong risk factor. Even those families that have older siblings or older children to that infant or young child that you're seeing in the office, that's not a very strong risk factor. In fact, there's some evidence that shows that younger siblings of children with food allergies have a lower risk of developing food allergy. How old are they? It'd be pretty unlikely for a new food allergy to develop in a 12-year-old. It can happen, absolutely, but then you'd have a really good story for it. And then, really the strongest risk factor, especially in infants, would be those with truly persistent moderate to severe atopic dermatitis or eczema and this isn't those children that have like a little tiny patch that keeps coming back. This is significant body surface area being covered and this is despite very good skin care from the family. We're talking about avoidance of triggers, daily skin care with thick moisturizers, use of a good, potent, topical corticosteroid to treat the inflammation. Those infants that still have persistent atopic dermatitis, despite that, those are the ones that are at highest risk to develop food allergy, which is even more of an argument to get them to start eating the food as soon as possible and keep it in their diet. Those are the ones that we really want to target and try to prevent food allergies from developing. And we don't have to screen them with testing first because infants with eczema often have very high rates of false-positive testing because they have a lot of total IgE floating around in their system. The specific IgEs often are inaccurate.

We also want to identify anxiety in these families. If they come to the office and they're very anxious about feeding their baby, we can address that. We can talk about the risks and benefits of testing and then really asking them, "Well if we do the testing, how is it going to change anything?" And feel free to borrow a spiel that I use on a regular basis and it goes along the lines of, I'll say, "There's no medical indication to test before introducing any food to your baby. I meet enough parents to know that some just need to see a negative result to give them that confidence to feed them. I'm happy to test for select foods and I need your help figuring out what that is if a negative result will help you go home and feed your baby today. But if we do see an elevated result, I'm not going to diagnose food allergy in your baby who's never eaten that food or had a reaction to it, but maybe we'll have you come back here and we'll actually introduce it in the office to gain some confidence."

There's an art to what we do. I'm not saying that there's completely against testing, but we have to be very, very thoughtful and absolutely acknowledge the harm that can come if we get a bunch of false positives and we diagnose multiple food allergies in a baby that doesn't actually have those allergies. That's a real problem.

The key takeaways that hopefully you get from this introduction to food allergy testing, we really have limited tools in our tool belt. We have good tests when they're interpreted properly, but the best test is always the detailed clinical history. Focus on that. That's something all of us can do. And when the pretest probability from the clinical history suggests this isn't a food allergy, we don't need to do other testing. It's simply not indicated and we can address those concerns and clarify the diagnosis. There are a lot of other reasons why children can experience symptoms that are associated with eating foods that have nothing to do with allergy. And, as I mentioned, all the symptoms that can occur due to food allergy can absolutely occur for nonallergic reasons. It's up to us to provide an accurate diagnosis.

As we talked about, there's major limitations with current skin prick and blood IgE tests. They can't predict severity of the reaction, they only can predict the likelihood of allergy being present which then ties back to the pretest probability gained from the clinical history. And then the best tests that we have—and it's

really the most empowering tool that we have—are oral food challenges which require a lot of understanding of how to do them and experience and expertise to help families navigate that. But that absolutely is a tool that we have that can help everybody.