Food Allergies

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Learning Objectives

• Define food allergy.
• Identify food intolerances and pharmacologic and neurologic responses to food.
• Detect IgE food reactions.
• Recognize food protein-induced enterocolitis and eosinophilic gastroenteritis.
• Discern a connection among atopic dermatitis, rhinaria, urticaria, and food allergies.
• Apply proven and acceptable allergy tests.
• Employ a basic approach to treatment of food allergies.
• Interpret food labels.
• Outline appropriate preventions.

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Transcript of the Panel Discussion
as recorded on the Audio CD
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1 Introduction

Dr. Sicherer: My name is Dr. Scott Sicherer. Today we’re going to be talking about food allergy. I’m a pediatric allergist. I work at the Jaffe Food Allergy Institute at Mt. Sinai in New York. I’m also currently the chair of the Section on Allergy and Immunology of the American Academy of Pediatrics.

Dr. Sampson: Hi, I’m Hugh Sampson. I’m professor of pediatrics at Mt. Sinai School of Medicine. I’m Chief of Pediatric Allergy and Immunology and currently the president of the American Academy of Allergy, Asthma and Immunology.

Ms. Groetch: I’m Marion Groetch. I am a registered dietitian at the Jaffe Food Allergy Institute.

Dr. Sicherer: So to get started, Hugh, there’s a lot of confusion sometimes about how we even define food allergies. So, what is the definition of food allergy?

Dr. Sampson: Food allergy is an adverse immunologic response to a food. This is where the immune system misidentifies a food as being a potential pathogen and responds inappropriately. This is in distinction to an intolerance, which does not involve the immune system but may involve things such as enzyme deficiency. Probably the most common intolerance would be lactose intolerance, which 80% of the world’s population has. And then there are also pharmacological responses due to substances in particular foods. For example, high caffeine content in some of the soft drinks that we have may lead to gastrointestinal (GI) symptoms, and some people may even develop diarrhea from that.

Dr. Sicherer: When I have super-spicy foods, my nose goes crazy from that. Some people think that’s an allergy. Can you talk a little bit about that?

Dr. Sampson: That’s really a neurologic response due to the capsaicin in the food and that many people will, in fact, end up getting a runny nose.

Dr. Sicherer: When I think about food allergy as an immune response, I think about two flavors of an allergic response. One flavor has to do with immunoglobulin (Ig) E antibodies. The B cells are making IgE, they’re sitting on the surface of mast cells and the high-affinity IgE receptor basophils in the bloodstream, and you get sort of one pattern of an allergic response from that. And then I think of the other flavor of food allergies and immune responses being a cell response, like T cells are acting and releasing cytokines and basically orchestrating inflammation that then leads to sort of another brand of food allergic problems. And then sort of in the middle are a number of diseases that we have where probably both mechanisms are playing a role. So, let me give you some examples.

For the IgE immediate reactions, which are the ones that we think about most commonly, you have a sudden reaction, usually within minutes of eating the food — it could be an hour or two sometimes. Those IgE immediate responses are the ones that we’re most familiar with. The most severe would be anaphylaxis, a multisystem reaction where it’s progressive and could be fatal. We often think of skin reactions like hives and angioedema, we think of stomach pain and vomiting or diarrhea. Again, all potentially based on IgE responses.

We think about asthma as being part of that, so throat tightness, wheezing, respiratory problems, including nasal symptoms for that matter. All of these immediate types of responses that have to do with IgE antibody getting activated when the food that you’re allergic to comes back into the body.

In that category of IgE reactions, we also have some that are very common but not exactly as severe. So there’s something called oral allergy syndrome or pollen food-related syndrome. What happens there is that a person first gets allergic to a protein in pollen, let’s say birch pollen, and then there are very similar homologous proteins that are in certain fruits or vegetables. So, if the example is birch pollen, then we’re usually talking about pitted fruits, like raw apples and peaches. And if we’re talking about ragweed, then melons, for example, have some similar proteins. And so people who have the pollen allergies sometimes, but not always, get an itchy mouth when they eat the raw fruit. It’s usually not a severe reaction; maybe 1% or 2% of the time these people get more severe reactions.

There’s another less common one, which is food-associated, exercise-induced anaphylaxis. And that’s someone who, for example, could eat wheat and they’re fine, they could exercise and they’re fine, but if they eat wheat and then exercise, then they have anaphylaxis. So those are some of the examples of these immediate reactions.
On the other end of the spectrum we have illnesses that are really just mediated by cells, T cells, for example, releasing mediators. Some of the ones that pediatricians are going to come across would be proctocolitis syndromes. This is the baby who is usually breastfed, has mucous bloody stools; Mom removes milk, for example, from her diet and then the bleeding goes away. These babies usually don’t get anemic, they usually don’t have failure to thrive. It’s just a mess of having blood in the stool, and it responds when the mom removes the food from the diet. If a biopsy was done for a baby like that, there’s basically an eosinophilic inflammation just locally by the rectum.

There’s a much more severe form of non-IgE mediated reaction. Hugh, can you tell us about food protein-induced enterocolitis syndrome or FPIES?

Dr. Sampson: Food protein-induced enterocolitis syndrome is something that we see in infants, typically due to soy or milk formula. In this particular syndrome, the infant may ingest the formula and appear to be relatively fine for about 2 hours, and then all of a sudden starts having repetitive vomiting. These children can get quite sick: they can appear dusky and pale, and in about 15% of the cases they’ll actually develop hypotension. So this is something that we clearly want to pick up.

I think oftentimes it’s not identified early because of this delay in the onset of symptoms. They’re often sent to allergists for evaluation because of the severe symptoms. Typically the allergist may do some standard allergy testing, such as skin testing, and when it’s negative, they think that it’s not related to an allergic response.

Fortunately, most children will outgrow the food protein-induced enterocolitis syndrome. Some of the older textbooks always suggested it would be by 3 years of age; clearly now we’re seeing it progress much longer.

The other thing that we’re seeing now is reactions to many of the cereal grains. It’s not uncommon to have children who have, for example, rice-induced enterocolitis syndrome, barley-, wheat-induced enterocolitis syndrome. We’re even seeing it with some of the other foods, such as chicken, turkey, and some of the others. This is something to be aware of.

Dr. Sicherer: Patients who I’ve seen have actually started with a rule out sepsis workup, essentially because they look shocky and they look like they’re sick. Actually, the white count is high. Do we have any theories as to what that has to do with? It looks like a systemic reaction, but there’s no IgE.

Dr. Sampson: We don’t really totally understand the mechanism, but it is felt to be either a T cell or even one of the antigen-presenting cells releasing cytokines, which is what brings about this delay in the symptoms. The other thing, you’re exactly right; the white count is elevated and in very young infants, they’ll often undergo a sepsis workup, including a spinal tap. And it’s not uncommon to see a few white cells in the spinal fluid as well. So typically what will happen is the children will get put on an antibiotic for a 2- to 3-day period, the cultures will all come out negative, and then people are somewhat perplexed as to what’s going on. But this is a food-induced allergic disorder.

Dr. Sicherer: Another illness that we’re seeing more of, that’s a gut-related disease, is allergic eosinophilic esophagitis or allergic eosinophilic gastroenteritis. This is an illness that we kind of think of as being a mixture of IgE-associated and non-IgE-associated factors. The presenting classical child with this is typically an 8- to 12-year-old boy who is having symptoms that are a little bit like reflux, but also dysphasia. And that’s sort of one of the key features of it: that they’re having trouble when food is trying to go down and it’s getting stuck. And sometimes there’s an impaction, and they have to go to the emergency room and have the food pulled out or pushed down. What we find on biopsy is lots of eosinophils. Classically people have thought about eosinophilia in an esophagus with reflux, but these numbers are much higher, usually over 15 or 20 or 25 eosinophils per high-power field. It tends to happen in kids who have other allergies; they’ll often have some notion of food allergy. And actually, in studies that you did early on, you kind of made that connection, Hugh, with there being a food responsiveness to this disorder. Can you just mention a little bit about that landmark study?

Dr. Sampson: One of the things we were interested in was whether or not the eosinophils were attracted into the esophagus because of an allergic response. So, the idea was to take 10 children who had very severe gastroesophageal reflux, four of whom already had a Nissen fundoplication performed, and put them on to a very hypoallergenic diet. In this case, we used an amino acid-based formula and then one solid food, which typically was corn. We found that after a period of about 4 to 8 weeks, the symptoms were dramatically improved, that these children who had not really had any appetite were actually expressing desire to eat. And when they were re-scoped and biopsied, we found a dramatic decrease, if not resolution, of the eosinophilic infiltrate. So I think this was one of the first times that anybody had clearly shown that food was the cause of this particular disorder.
Dr. Sicherer: So fast forwarding about 15 years from that, now people describe this more commonly. It seems to have increased, whether it's recognition or epidemiology-wise, it's being recognized more. Our GI colleagues say that they'll often see some characteristic changes in the esophagus, like trachealization of the esophagus, like these rings — also furrows and sometimes white spots — that look a little like *Candida*, but they're really collections of the eosinophils. And the treatment nowadays is either an anti-inflammatory treatment or food avoidance and trying to figure out which foods are causal. This is like one of these mixed disorders, so you might find some positive skin tests, you might not. The foods that are connected to this tend to be the big ones, the ones that we talk about most with food allergy in general — milk, egg, wheat, soy, peanuts, tree nuts, fish and shellfish — as being the major allergens and they also play a big role in allergic eosinophilic esophagitis and, for that matter, the more diffuse version in allergic eosinophilic gastroenteritis.

So that leads me to the last of the mixed disorders that we talk about, which is atopic dermatitis. This is actually another disorder where you, Hugh, were one of the first to really put together some clear-cut connections between food allergies in atopic dermatitis. So nowadays I think we would say that, for example, with moderate to severe atopic dermatitis, from studies that you've done and participated in as well, about a third of kids with moderate to severe atopic dermatitis have a food allergy, and it's usually milk, egg, wheat, or soy, and some of the other ones that I mentioned before. And evaluating for food allergens in someone who has that level of atopic dermatitis becomes important.

There are also some rarer types of immune responses to foods. One is Heiner syndrome, which is a pulmonary hemosiderosis associated with cow's milk protein. These are children who actually develop elevated levels of IgG, get essentially bleeding into their lungs, and are treated by milk avoidance. And we're not going to talk today about celiac disease, although you could consider that a type of immune response to the gluten.

Dr. Sampson: The other thing that I just wanted to point out was, it's not infrequent that we will have young infants referred to us with what appears to be a chronic nasal rhinorrhea. And it's very unusual to have isolated nasal findings as a sole manifestation of food allergy. We frequently will see it when we do challenges, for example, on children with atopic dermatitis, where they'll get skin symptoms and often gastrointestinal symptoms during a challenge, but to find just isolated nasal symptoms is quite uncommon.

Some people suggest possibly 10% of children with asthma may have exacerbations induced by food, but in very severe cases, it certainly is something worth looking at. Findings in a number of studies have shown that children who have both food allergy and asthma are the children who tend to have the more severe asthma.

Dr. Sicherer: A lot of children show up in the pediatric office with urticaria, with hives, and maybe they've had it for days or weeks, and people jump to wondering if it's food allergy. What do you have to say about that?

Dr. Sampson: That's a good point, Scott, because again, not very often do we find somebody, especially with chronic urticaria, where food is the sole cause. So, worth looking at, but fairly low yield in patients with chronic urticaria.

Dr. Sicherer: We've talked about a lot of symptoms. We talked about nose running, hives, wheezing; we talked about stomach issues.

There's a lot of disorders, there are a lot of potential things in the differential diagnosis. What, Hugh, is really the way that you approach these various overlapping symptoms to get to a food allergy diagnosis? What's the most important thing? What do you do?

Dr. Sampson: I think the most important thing is taking a good history. Basically what we're trying to find out is whether there's a good correlation between the ingestion of a food and actual development of symptoms. So some of the things that are very important are which food is it that we're thinking about? Because as you pointed out before, Scott, there are certain foods that are more likely to cause symptoms. And things like egg, milk, peanuts, tree nuts, fish, shellfish, wheat, and soy are going to be responsible for at least 90% of the food allergic reactions that we see.

We also then want to really hone in on the timing. Certainly when you're dealing with IgE-mediated disease, the closer in time that somebody has a reaction to the ingestion of a food, the more likely it is that that really is an IgE-mediated phenomenon. We also want to have some idea of how much of the particular food they ate. That can give us an idea. For example, if it's a very small amount, and we do see someone developing vomiting, skin rash, then it is more likely, again, to be an allergic response. We also want to know whether or not it's happened on more than one occasion. If it's reproducible, then that certainly makes a much stronger case for the fact that it is a food-related event.
So Marion, one of the things that we often do when we're evaluating these patients with our history is we ask them to keep a diary. Do you want to comment on patient diaries?

Ms. Groetch: We always ask our patients to keep a food diary and to save product labels for review prior to their visit. Both provide us with valuable information. Specifically, they help us to identify what foods are actually eaten and tolerated. For instance, a parent might feel that wheat is a problem, because the child may have had an allergic reaction after eating wheat bread for the first time. But with the food diary and the product labels, we might see that the child regularly eats spelt bread, which is just another form of wheat. So then we know to look at other ingredients. Maybe soy, milk, egg, or sesame, all of which are common ingredients in bread. Or maybe we'd be looking at another ingredient in the meal altogether. Maybe the parent put mayonnaise on the bread and didn't know that mayonnaise contains egg. So the food diary and the product labels help us to specifically identify the foods that the patient is eating and tolerating, so the physician can rule those out and focus on the foods or ingredients that are more likely to have caused the reaction.

And then, of course, from the dietician's perspective, the food diary gives me the means by which to assess the nutritional adequacy of the diet.

Dr. Sicherer: Hugh, regarding diagnosis, we're often asked about skin tests and the serum IgE test. Can you review those tests?

Dr. Sampson: Both tests really provide us with very useful information, but we do interpret them a little bit differently. This prick skin test essentially involves taking a small amount of extract, which contains the protein of the food that we're interested in, placed on the skin, then we take a needle and we make a small break or puncture in the skin that allows that food protein extract to permeate and get to the mast cells where the IgE antibodies are attached. If the patient does have IgE antibody on the mast cell that's specific for the particular food, in this case, that we did the prick test on, we will see basically a small hive develop at that site. And we're very interested in what we call the wheal, which is the raised portion, and the erythema. Typically what we'll do is we'll measure the diameter of the wheal, and then we can use that to help us in interpreting whether or not we think that's a relevant response.

Some of the limitations of doing the prick skin test are that the various food allergen extracts that we use are not standardized. So if I perform a test in New York using one reagent and somebody else performs a similar test using a different reagent somewhere else, they don't always exactly correlate. Also, there are some other variables that we see, one being the location where the prick skin test is placed can cause a difference in the size of the wheal that you might see. Also, individuals will interpret these differently. Some allergists, rather than measuring them, do a grading system and there are variabilities in the grading system. But bottom line, what they're doing is they're telling us that this patient has or does not have IgE antibodies specific for whatever foods we're placing on their skin.

I think the other thing to remember, though, is that the test is simply telling us that there's IgE antibody there. It's not telling us that these people are going to have clinical reactions to those particular foods. And in fact, in a number of studies that have been done, when we look at the outcome of the prick skin test to the outcome of an oral food challenge, for example, only about 30% to 40% of those positive prick skin tests actually translate into clinical symptoms or a positive challenge.

Dr. Sicherer: Is it painful? It is something that, you know, in the old days, it was, “oh no, those skin tests.” Is it that way?

Dr. Sampson: No. The prick skin test is really not a painful procedure. Basically, we're putting a number of extracts, which look like drops of water, either on the back or on the volar surface of the arm; then we take a small needle, and the idea is that you either rock or just lightly press the needle.

Dr. Sicherer: So there's no bleeding.

Dr. Sampson: So there's no bleeding. There's really no pain involved. The only discomfort that comes from it is when you do have a positive response, you're going to develop a hive at that site and it is fairly itchy. But it's not injecting anything under the skin, it's not drawing blood; it should not be a painful procedure. And the real benefit of it is that within 10 minutes you know whether or not that patient has evidence of that particular allergic antibody.

Dr. Sicherer: So there's a visual that you can discuss with a parent, what you're seeing right then and there.

Dr. Sampson: Right. And sometimes that's very helpful.
to have that immediate visual, because then the parent does understand that their child may, in fact, be allergic to that particular food. And when it comes to compliance of trying various elimination diets, I think that really has a profound effect on them.

18 **Dr. Sicherer:** So what about the blood tests?

**Dr. Sampson:** The blood test is really looking at the amount of circulating IgE antibodies that an individual has. And there is a correlation between the amount of IgE that you detect in the blood and the amount of IgE that's actually bound to the surface of mast cells in various target organs. The advantage of this test is that it can be standardized. So, for example, a company will make standard reagents that, regardless of where they're used, will result in the same answer. So when we’re trying to correlate levels of IgE antibody in my practice with levels in someone else's and the correlation they might have to reactivity, it’s much easier to do that.

The other thing that you have to be aware of is that just because there is measurable IgE antibody, does not necessarily mean that the person is going to have a reaction. And this leads to a problem where we’ll see patients that will come into our office, referred to us for evaluation, where somebody has done a large screening procedure, where they've looked at 40 different tests. And when that happens, it’s very common to see multiple positives that are not going to correlate or translate into true clinical reactivity. And worse is when they’re actually told to avoid all the foods where they either see some evidence of IgE in the blood or a small positive skin test.

19 **Dr. Sicherer:** So to boil that down: you’re a pediatrician in the office; a child comes in, they’ve had a sudden reaction to egg. You say, “Okay, I want to confirm this so I’m going to check off this food panel.” And then they come back with a positive test to egg, but also a positive test to milk and wheat and soy. So what you’re saying there is that they shouldn’t have done those tests or are those tests meaningless? Like, what do you make of all that?

**Dr. Sampson:** Well, I think one of the things that we would really encourage people to do is to take the history. If you have the history where somebody has what sounds like a fairly clear-cut reaction to egg — so say it’s a young child with atopic dermatis and egg is the most common cause of reactions in individuals with atopic dermatis. We know from previous studies that these individuals may have other sensitivities. We might be selective in picking a few foods. So, for example, we know that children with atopic dermatis and sensitization or re-

action to egg are at a higher risk to have a peanut allergy. So we may want to check and see do they have evidence of IgE antibody to peanut.

**Dr. Sicherer:** Assuming they’re not already eating it.

**Dr. Sampson:** Correct. And then we know that someone with reactivity to milk also may be at higher risk for a few other foods. So you want to be selective. You don’t want to just order a huge battery of 30 or 40 tests, because often times what’s going to happen is you’re going to have low levels of IgE antibody to 10 or 12 foods; then you’ve got to decide what do you do with that? You don’t want to have them avoiding all those foods, because that certainly becomes a nutritional hazard as well as extremely difficult, but then you can't ignore it either.

**Dr. Sicherer:** So you said sort of twice that the higher the level is, the more likely it is that there would really be a reaction. And would you correct me if I said that that’s sort of the case for the skin test, too. I mean, a much bigger skin test, the more likely that there really is a clinical reaction.

But for the pediatrician who’s ordering these tests, sometimes though people will ask me, “Well, gee, you know, what am I looking at here? There’s this ASM, there’s this category 0 to 5 or 1 to 6, and then there’s units per liter and there’s different brands.” What do you do about all that?

**Dr. Sampson:** One of the things that we looked at — and other people have been looking at as well — is whether or not, as you say, there is a correlation between the amount of allergic antibody or IgE antibody they have in the blood and the likelihood that they would have a reaction. Just as you brought up with the skin prick test, there are some studies that show that the larger the skin test, the more likely it is that somebody's going to be reactive. And we’ve shown, and other people have shown now, that the greater the amount of IgE antibody in the serum, the more likely that we will see reactivity.

And we published a study where we looked at a number of the common foods and found what we called 95% diagnostic decision points. And what this means is that if you have a certain amount of IgE antibody that exceeds a particular number, then it’s greater than 95% likely that these people will react. So with milk we found, for example, that if an individual had 15 kilounits per liter or greater of IgE antibody to milk that it was greater than 95% likely that they would react. To egg, we found that it was greater than 7 kilounits per liter; peanut was
greater than 14 kilounits per liter. If we look at the nuts sort of as a general group, it appears to be about 15 kilounits per liter is the 95% diagnostic decision point. And with fish, about 20 kilounits per liter.

**Dr. Sicherer:** So it's important each food is a little bit different. And was that a broad range of ages or is this something that you look at age-wise?

**Dr. Sampson:** When we look at other immunoglobulin levels there is age variation and with IgE, that's true as well. If we look at young children, so children less than 1 year of age, for milk allergy, it's been shown that 5 kilounits per liter is really the diagnostic decision point. And with children who are less than 2 years of age, looking at egg allergy, it's less than 2 kilounits per liter. So there is some age variation.

Now the other foods have not been as well studied looking at age, and then we do have foods, for example, soy and wheat are very common allergens. And unfortunately, there's not a really good diagnostic decision point for that. We know that if you have levels greater than 30 kilounits per liter, it's about 75% likely that you'll be reactive.

But I think the other thing to remember is the closer you get to that number, the more likely it is that you'll be reactive. So if someone, for example, had 12 kilounits per liter and you had a strong history or a strongly suggestive history that they might be milk allergic, that would certainly make it highly diagnostic, even though it had not hit that 95%.

Dr. Sicherer So you had started off saying that history is the most important thing, and I guess you're turning back around and saying that the testing is also important, but it has to be in the context of the history. So you're thinking of what happened to this person, what are they eating or not eating. Marion had talked about looking at the food diaries to see if maybe they're eating something that the parent didn't even realize they were eating and then having a problem from it. And all of that sort of gets put together as you're deciding whether they're really allergic or not.

**Dr. Sampson:** Right.

**Dr. Sicherer:** So it's pretty complex.

**Dr. Sampson:** You really need to interpret both the skin test and the blood test in the context of the clinical history.

**Dr. Sicherer:** So it's important each food is a little bit different. And was that a broad range of ages or is this something that you look at age-wise?

**Dr. Sampson:** You really need to interpret both the skin test and the blood test in the context of the clinical history.

**Dr. Sicherer:** By the tone of your voice when you say “other,” I guess you’re meaning the tests that we don’t typically do as traditional board-certified allergists. This includes what the American Academy of Allergy, Asthma and Immunology and the College of Allergy, Asthma and Immunology politically correctly sort of call “unproven in experimental tests,” That includes muscle strength testing, which is also known as applied kinesiology: having someone hold a food and then checking if they're strong or not. And for a child, maybe the mom would hold the baby and hold the jar of a food and see if the mom’s strength is different.

So there is also provocation neutralization, which sometimes is done putting drops under the tongue or small injections of things and seeing if you can provoke symptoms, which are usually subjective ones. And you know, if you start to blind the reagents the people are using, then you end up with studies that say it didn't really matter whether you were using real stuff or not. So there's a lot of subjective and suggestion involved in these.

Probably the one that's most available for people to sort of check off the box and send off to a lab is IgG testing. And so we've been talking a lot about IgE — the immunoglobulin that binds on the high-affinity receptors on the mast cells and basophils, and causes a lot of the different food allergy problems that we've talked about — but IgG actually is another immunoglobulin, obviously. And as far as most studies would say, it's not associated with disease. In other words, people who are healthy and are eating foods have IgG to the foods that they're eating. Part of the story is that our immune system does see what we eat and sort of, in an intelligent way, ignores it; it is something that we call oral tolerance. We don't consider those types of tests, IgG testing, to be helpful in trying to make a food allergy diagnosis.

**Dr. Sampson:** One of the things with the standard tests that we do, the prick skin test or the serum IgE levels, is that it does not end up being diagnostic; that we have, for example, a child with atopic dermatitis or a child with recurrent asthma who has levels that indicate the presence of IgE, but no clear-cut history that they actually have had a reaction. Sometimes we'll ask to eliminate the food from the diet and see if there's any change, and that can be helpful. But again, many times it's really not totally predictive. And in fact, in studies where they cor-
relate what appears to be a positive response by elimination diet with the outcome of a double-blind oral food challenge, we see that only about 40% of those are really predictive. One of the things that we often have to do is actually perform some sort of oral food challenge to determine whether or not they're reactive.

24 So, Scott, why don't you just review what you think about in your decision to have somebody do an oral food challenge.

Dr. Sicherer: A feeding test or an oral food challenge is when we give a food to the child where we're not sure whether they're really allergic or not based on the history of the test results that we have. As an allergist, I make decisions about whether it’s safe to do that. A parent makes a decision as to whether they want to do that, and we do it under a strict supervision. So it’s really sort of the “gold standard” to find out if someone could tolerate the food or not, but I think that it really belongs in the toolbox of the allergist for the most part. But what we’ll do is just a gradual feeding of the food. If I feel that they don’t add up, that there’s definitely an allergy and the family agrees that they feel that it would be important to get this food back into the diet — and that includes things like nutritional issues, social issues, the age of the child, the willingness of the child to eat the particular food, and many other issues — we’ll start with a tiny amount of the food and then just gradually increase the amount and watch them under physician supervision. I wouldn’t undertake it if I thought there was a high risk of a reaction, but the family might feel that if I can kind of say there’s a 50/50 chance here, often that they will want to have us do a doctor supervised feeding which, depending on my risk assessment, I’ll do perhaps in an office setting or maybe even in a hospital setting if I feel that there may be a higher risk.

25 But, Marion, sometimes we mask the challenges, meaning we hide the food in another food. Can you review why and how we do that, briefly?

Ms. Groetch: Sure. We would definitely decide to mask a challenge if the patient or if the parent had a lot of anxiety about trying the new food. Sometimes their anxiety about the challenge might cause them to have some subjective symptoms that mimic an allergic reaction, and then it's hard to tell if the child is actually reacting to the food or if they're having anxiety symptoms. Masking challenges is really quite easy. There are many ways to mask or to blind a challenge. For instance, for a wheat challenge we might add a dose of wheat flour to oatmeal, applesauce, or to a pudding. Powdered milk or egg can be added in the same way or to mashed potatoes. If the child drinks soy milk, we can mix some cow’s milk in with the soy milk; usually at a 50/50 ratio, it’s undetectable. And, these are all common ways to blind a challenge.

Peanut has a very strong scent, so it’s the most difficult to mask. We could add peanut flour to a tomato-based meatball; that masks it pretty well. Or another thing we can do is to add peanut flour to chocolate with some added mint extracts so the child thinks that they’re eating a minted chocolate bar.

So those are ways to mask a challenge. And we do a masked challenge either single blind or double blind. In a single-blinded challenge, only the patient is unaware which food is the placebo and which is the actual challenge. But in a double-blind, placebo-controlled food challenge, which is, of course, considered the gold standard for food allergy diagnosis, neither the patient nor the clinician who administers the food challenge knows which is the challenge food and which is the placebo. This eliminates not only the patient bias, but also the clinician bias.

26 Dr. Sampson: Scott, when you were talking about doing the food challenge and some of the considerations, again, you have to go back to the history. So, for example, if you had a child in whom you’re suspecting enterocolitis syndrome, you would perform the test a little bit differently than if you thought it was IgE mediated. How do you go about making those kind of decisions?

Dr. Sicherer: If I’m expecting there to be a sudden reaction, then I’m going to plan my day a little bit differently than for enterocolitis syndrome, where the reaction actually classically happens about 2 hours after the ingestion. So both the dosing is a little bit different, and the expectation of what might happen is a little different. And as you mentioned before, I wouldn’t be relying on a positive skin test to tell me whether or not someone’s going to react with an enterocolitis syndrome.

27 Hugh, once a diagnosis is made and treatment then has to start, can you just review the basic approach to treatment of food allergy?

Dr. Sampson: Right now, the only proven treatment for food allergy is strict elimination of the food that you’ve shown them to be allergic to and then preparing them to treat an allergic reaction should they accidentally ingest the food. In the area of avoidance, we’re trying to educate them how to read labels correctly, how to identify situations that put them at higher risk for accidental cross-contamination of a food. So, for example, eating at a
buffet where there are foods on the buffet that you may be allergic to, you put yourself at high risk of taking any of the foods because of the possibility that people are scooping food out of the different dishes with the same spoon and causing cross-contamination.

We also try to educate them on types of restaurants that may be a problem. So, for example, an individual who’s peanut allergic really is putting themselves at high risk if they’re eating, you know, in Chinese restaurant or some of the other Asian restaurants.

Dr. Sicherer: What’s the treatment if someone has a reaction?

Dr. Sampson: If they have a reaction, one is, we need to educate them on how to identify the kinds of symptoms that mean they’re having a reaction, then we typically will give them an emergency treatment plan. In that plan, it does describe the kind of symptoms and it talks about the medication that they should be using. The medication of choice for any significant reaction is self-injectable epinephrine. We would prescribe some form of epinephrine, either the EpiPen® (Dey, L.P., Napa, CA) or Twinject® (Sciele Pharma, Inc., Atlanta, GA), which will give them a set dose of epinephrine should they have a significant reaction.

Typically, we also will give patients liquid antihistamine in the form of either diphenhydramine or hydroxyzine, which has a fairly rapid onset, but really is only effective in treating some of the mild skin symptoms. So if the patient is having any kind of significant respiratory symptoms, throat symptoms, or there appears to be multiple organs involved, we always insist that they use epinephrine.

Scott, when you review the treatment plan with your patients, what kinds of things do you stress?

Dr. Sicherer: By the time I get to, “It’s time to talk about epinephrine,” usually the families are swimming in too much information as it is. And I think that their primary concern is, this is a dramatic thing, it’s a shot. And so they start to almost panic right then, even when we’re just first talking about it.

I also know from studies that we’ve done that a lot of times people will come into the office having been prescribed the self-injector and not know how to use it. We did a study where we also looked at physicians, and the physicians did worse than the parents did when it came to actually showing how it works. So one message is to make sure that you review how to use the self-injector devices with your parents. I tell people to practice once a month with a trainer, because they make these trainers that don’t have actual medication in it. They have to, of course, be careful they’re using the trainer and not the regular one.

Because there’s some fear with using the epinephrine, I also try to emphasize that this is a medicine people used to use to treat asthma episodes before. You’d come into the emergency room and, “Hey doc, you know, I’m having asthma.” “Alright, here’s your shot of adrenaline and go sit down.” “Oh, it’s coming back.” “Here’s another shot.” It wasn’t such a big deal in those days. And especially for kids who are not too worried about any kind of side effects other than a little heart racing and maybe a little jitteriness.

We actually recently published in Pediatrics decisions about dosing because these units are in two fixed doses, 0.15 mg or 0.3 mg, and there’s a little wiggle room as to when you might trade off. But we had suggested switching from the small size, the 0.15, to the 0.3 mg one at about 55 lbs. But that might be adjusted, depending on the child’s personal severity of previous reactions and some other issues of deciding on whether they’d be better off with a slightly higher or slightly lower dose.

Put written emergency plan into ref material.

I like to review with the families when they would use it. So not only do I give them a written emergency plan, but I also discuss it with them, “Gee, would you use it for this scenario, that scenario?” A lot of times I’ll start them off with a little story of “you’re in the bakery, you’re not going to buy any peanut cookies for your child, but there are these free samples out. Your child grabs a piece and you didn’t realize it. You go, ‘Johnny, what are you doing?’ And you shake your child, it’s like, ‘Get that out of your mouth.’ And the next thing you know, the child’s not breathing. What do you do?” And the parents, you know, 99% of the time say, “Well, I’ll inject the epinephrine because they’re having a breathing problem.” And I was like, “Well, what if your child didn’t have a food allergy and they had cookie in their mouth; you shook them and they suddenly stopped breathing?” “Oh, choking.” So I try to have people think about what are the circumstances that they’ve eaten a food; they usually don’t stop breathing immediately, there would be a progression of symptoms. So I go through these different scenarios as well.

And lastly, people wonder about how do you store this? A lot of times they might imagine you’re supposed to refrigerate it. But really, it’s a spring-loaded device, so you just keep it at room temperature and don’t have it at ex-
Dr. Sampson: Scott, one of the things that we’re often asked about are the younger children, so the children who weigh less than 15 kg. You know, even occasionally those who weigh less than 10 kg. What do you tell those parents to do?

Dr. Sicherer: We actually did a study on that as well, and 80% of pediatricians were willing to prescribe the 0.15-mg dose to a 10-kg baby, so about a 1-year-old baby. Where it gets a little bit dicier, because you’d be exceeding 150% of the dose, is smaller than 10 kg.

But Estelle Simons did some studies looking at an ampule and syringe method of giving epinephrine, which would be another option, drawing up exactly what you needed. But unfortunately, even under circumstances of no stress of a child with a reaction, parents had a lot of trouble and made even logarithmic errors in trying to draw up a little bit. So I will usually discuss with the families about the issues of dosing for the infants. I will usually prescribe the 0.15 mg dose anyway, unless the parents happen to be emergency medical technicians (EMTs) or just really into the ability to draw it up with a syringe and needle.

So, this is a scary topic and one of the things is about food allergy possibly being fatal. And we certainly want to give education to our patients about how to prevent a fatal reaction. And you’ve actually done several studies on food allergy fatalities. What have we learned?

Dr. Sampson: One of the things that we’ve learned from looking at these anaphylactic reactions to food, one, how common they are. Food allergy is probably the leading single cause of anaphylaxis that is treated in emergency departments. There was a recent study that came out looking at a survey conducted by the Food and Drug Administration (FDA) where they showed that there are at least 125,000 cases of food allergy treated in emergency rooms in the United States each year. So this is a very common finding, and I think we have to be very much aware of it.

The other thing that was a little bit disturbing in the FDA study was the fact that less than half of these cases were actually accurately diagnosed as being due to food allergy. But some of the things that we’ve learned by looking at the very severe and fatal reactions are the fact that asthma is a very high risk factor for somebody potentially having a severe reaction. Also, it seems to be most common in teenagers and those in their early 20s. And I think one of the strongest correlations is the delay in the use of epinephrine — that most of the fatal cases have not received epinephrine until very far along in the reaction or never received it at all.

The other finding that was somewhat surprising was the lack of hives or lack of skin symptoms in many of the fatal cases. And it’s really unclear to us whether or not the person attending to this patient didn’t appreciate the fact that they had anaphylaxis because there were not skin symptoms or whether there’s really something different about individuals who don’t develop these urticarial reactions.

Many of these patients will actually experience what we call a biphasic response, where they will have their immediate response, they’ll be treated, they seem to be doing fine. Then, anywhere from 90 minutes to several hours later, they go back into a major anaphylactic reaction. And unfortunately this second phase is often more difficult to treat.

Now one of the things that I mentioned, Scott, was the age, and the teenagers do seem to be the group that is at higher risk. I know you’ve done some studies looking at this. Do you want to just tell us a little bit about what you saw in these studies?

Dr. Sicherer: In your studies, which triggered my studies, it was teenagers who were at highest risk; they didn’t have their epinephrine and presumably were worried that they weren’t following the rules. Maybe they were eating more risky. And sure enough, by doing surveys of the teenagers we found out a few things.

One was that they didn’t always carry their epinephrine, and they admitted to it. And some of the circumstances where they said that they didn’t have it were times when they didn’t think they’d be eating; times when they were doing sporting events; if they had clothing that was too stylish and they didn’t have anywhere to put it, so they had small purses or they had tight clothing and it was going to embarrass them to have it sticking out. They also assumed some things, like maybe they could eat a food if they just taste-tested it a little bit first and then ended up in trouble if they ate it. Or they just wanted to be like their friends and just eat what their friends ate and then took risks in that way.

That translates to, what can we tell pediatricians to talk to their patients about? I think some of the things that
you mentioned would be: it’s important to have the epinephrine and to use it when you need it; it’s important if you’re having a reaction to get to an emergency room, and so that might mean calling 911. Because of the biphasic response, it’s important to stay there for 4 hours or more to make sure that the symptoms aren’t coming back. It’s important not to assume things. And for the teenagers in particular, an issue for pediatricians: we want to make sure that the pediatricians go through some scenarios with their teenage patients — showing how, for example, you might not expect to eat when you’re playing soccer; but what if you’re just drinking water and your friend was eating a peanut butter bar, then drank your water. Now you’re drinking the water, and then all of a sudden it’s an issue. And part of the reason they were taking risk was embarrassment. They actually, when asked what’s the most important thing that we could do for you, they said “educate my friends about food allergy.” Because in order to fit in better, if the friends know about their food allergy, that makes it easier for the teenager with food allergy. They go to the restaurant together and all of a sudden their friends are asking questions and that they know how to use the epinephrine and such.

So, these are all some of the things that I think are important that we learn from that study to try to improve the safety for especially the teenagers who have these food allergies.

34 Now, Marion, avoiding a food is the key to treatment, really. The first thing about avoiding the food is label reading. Can you review what’s going on with labels these days?

Ms. Groetch: Labels have changed in the last couple of years, exclusively because of the Food Allergen Labeling Consumer Protection Act or FALCPA. That came into effect in January 2006, and it mandated that food products must clearly list on the package label, in plain English language, any intentional ingredient derived from the eight major food allergens, those being milk, egg, wheat, soy, peanut, tree nut, fish, and crustacean shellfish.

So previously, patients had to learn, for instance, all of the terms that meant milk, such as casein, whey, sodium caseinates, or lactalbumin, and a whole long list of others. But now if any milk ingredient is in a product, the word milk must also be on the product label, and that goes for any of the eight major food allergens. Also, if a major allergen is in a vague labeling term like flavoring or spice, it would have to be identified.

But unfortunately these labels are not perfect yet. We have to keep in mind that FALCPA covers only products that are regulated by the FDA. So fresh meat products are not regulated by the FDA; they’re regulated by the United States Department of Agriculture (USDA), so they need not comply with the new labeling laws. Major allergens, therefore, can be hidden in a flavoring or a spice of a fresh meat product and not be disclosed. We see this mostly with things like ground meats and fresh sausages. But this, of course, doesn’t apply to frozen and packaged meats like hot dogs or frozen chicken nuggets. These are regulated by the FDA.

Another pitfall of the labels is that if you have a patient who’s allergic to a food that’s not a major allergen, such as clam — because remember, we said it’s crustacean shellfish that’s considered a major allergen — or something like sesame or garlic or mustard, these allergens may still be hidden in a product under vague labeling terms like flavoring or spice. So the patient with this type of allergy will need to contact the manufacturer because all the information they need might not be on the label.

And then, of course, there’s always the issue of unintentional ingredients or the presence of allergenic ingredients due to cross-contact or contamination, and this may or may not be listed on the product label. More and more manufacturers now are addressing issues of cross-contact with advisory statements such as, “may contain peanut” or, “manufactured in a facility that also manufactures soy products.” Our patients also need to know that these statements are voluntary, so the absence of an advisory statement does not mean that the product is safe. It just might mean that the manufacturer chose not to use it.

So consumers with food allergies still need to call the manufacturer to determine if the product is safe or at risk of cross-contact.

Dr. Sicherer: That would be if they’re very sensitive, probably, right?

Ms. Groetch: Yes, if they’re very sensitive, but certainly we know that some of these products do actually contain the allergen. So although it might not be a large amount in the product, it certainly could be enough to cause a reaction.

We also know that these statements are not regulated, so we can’t apply a degree of risk to the various statements in use. So although “may contain traces of peanuts” implies a greater risk than “manufactured in a facility that also manufactures peanut products,” that might not necessarily be the case. The manufacturer chooses a statement and it might not be based on any degree of risk.
we try to teach our patients to read the entire label, not just the ingredient list, and to avoid products that have advisory statements.

**Dr. Sicherer:** Probably to read the label each time they buy it because things can change.

**Ms. Groetch:** Every time they buy it, it can change.

**Dr. Sicherer:** So another concern for families is school. Hugh, what do you tell people about school?

**Dr. Sampson:** One of the most important things in dealing with schools or even summer camps is that the parents work with the school or the summer camp to set up an action plan for their child should there be an accidental ingestion. I think one of the best things that's happened since I started practicing food allergy was the origination of the Food Allergy and Anaphylaxis Network. I give all my patients their number, 800-929-4040, or the Web site www.foodallergy.org, because FAAN has a large number of different resources to help people deal with various situations. For example, they have a whole manual on how to deal with the schools; who to notify, who to get involved in the action plans, and a lot of really good practical advice.

One of the things that they review and that we often will review with the patients is, the amount of supervision a child needs is really dependent on how old the child is. So if you're working with somebody who's at a pre-school level or in a kindergarten, where children tend to be a bit sloppy with their meals, you may have to ask for hand washing after meals so that a child who ate a peanut butter sandwich doesn't have the peanut butter on his hand, touch the hand of a child who is peanut-allergic and who then sticks the hand in their mouth.

So with this kind of interaction with the school, going through it carefully, emphasizing the need not to share foods either in the cafeteria, in the classroom, or on buses, and to be cognizant of kinds of projects that they might do at school where food's involved. For example, we often run into problems where they make bird feeders with peanut butter to stick the grain on. So just thinking with the school about those kinds of situations can generally make a very safe environment.

Scott, there's been a lot of concern about casual contact, and there have been some cases in the news about casual contact. I know you've looked at this; what do you think about some of these episodes?

**Dr. Sicherer:** We did a study actually having to do with casual contact with peanut butter. And just to take a step back, if someone ate peanut and then was passionately kissing another person who had a peanut allergy, they're basically putting the protein into their mouth. So I wouldn't call that casual exposure. That actually is something that I talk to many patients about, especially the teenagers, because if they're milk allergic, whatever it is, if their partner has had the food and they're sharing saliva, then they're getting the food and they could react. And actually 10% of adults with food allergies report reactions like that, including some severe ones.

But casual exposure would be smelling or touching. And so if grandma ate peanut butter and kissed Johnny on the forehead, is that going to cause anaphylaxis? What we did was, we took children who were severely peanut-allergic and had peanut butter and a placebo placed on their skin for a minute, taken away. We also had them sniff placebo, it smelled like peanut butter, for 10 minutes. No one reacted with those exposures. A third of the kids who had the peanut butter rubbed on them had a little redness there, but there was nothing beyond the site of contact. And for the sniffers, well, one of the 30 children who we tested actually did have some throat problems, but that turned out to be with placebo so it was a panic attack.

So I think what we learned was, there could be some level of relaxation in terms of families that are worried, oh, their child's going to walk into a room where someone's eating a Snickers bar and suddenly have an anaphylactic reaction. I would not expect that to happen. However, as you pointed out, we still have a concern about the youngest kids. And so when we're talking about sloppy eaters, and kids who might be sucking on the same toys, and things like that, it's a whole different story. That younger age group could turn a casual contact into a non-casual one and would be more of a problem, so we worry about that aspect.

**Dr. Sampson:** Another thing we're frequently asked is, what about peanuts on airplanes, and what about going into a restaurant where they're cooking fish and you're fish-allergic?

**Dr. Sicherer:** There are studies actually where aerosolization of foods has been looked at in a double-blind setting as well, and reactions have occurred from cooking foods like scrambling eggs, frying fish or shellfish. Obviously, if you had a powdery peanut substance and got it into the air, that would be different. If we were boiling milk, for example, that would be another example, and there are other examples of that.
Usually the symptoms from those kinds of exposures are respiratory symptoms, so similar to someone who has a cat allergy or a pollen allergy. Typically we’re talking about red eyes, sneezing and, for someone with asthma, possibly wheezing. Not to say that this couldn’t become a more serious symptom, but it’s in the context of those that we talk about.

So for airlines, for example, people popping open dusty peanut snacks may present some into the air. We actually have a study with almost 4,000 people with peanut allergy, children mostly, and there were very few described reactions from smelling in that circumstance. They’re mostly these milder symptoms. There were a few people who described more severe symptoms. They were actually adults who described what I would have to say sounded like panic attacks. So it’s something that I sort of give a balanced presentation to my patients about. It’s something to think about; it’s probably not a very high-risk thing. They might be able to get a peanut-free flight, but I’m not sure I would not travel because of these concerns.

So let’s move on to restaurants. Marion, we probably hear a lot about reactions in restaurants, and we also have some studies showing that, for quality-of-life purposes, it’s one of the biggest issues for families with food allergies, that it impacts their quality of life. We also have studies that are showing that people in restaurant reactions have errors where, for example, they may not present their allergy just right to the person in the restaurant, and also the restaurant personnel may not understand about food allergy.

What do you advise people in terms of getting a safe meal in a restaurant?

Ms. Groetch: I think the most essential ingredient in obtaining a safe meal in a restaurant is clear communication with the staff. So there are a few basic tips that we generally recommend. First and foremost, they have to inform the staff that there’s a food allergy, not just that they can’t have peanut. Sometimes a patient will go into a restaurant and say, “Oh, does this have milk in it?” without actually saying, “We have a milk allergy at our table and a small amount might be enough to cause a reaction.” So they need to communicate that there is a food allergy.

It’s probably best to speak with the manager or even preferably the person who will be preparing the food. The wait staff might be ignorant about ingredients in dishes, and you wouldn’t want this important information to be relayed through a third party. Obviously dining during peak hours will make this difficult, so going during off hours or calling ahead to speak to the person who will be preparing the meal is a good idea, and then providing some written materials such as chef cards, which list all the ingredients that need to be avoided. These can be downloaded through the Food Allergy and Anaphylaxis Network Web site at www.foodallergy.org. And then choosing simple foods prepared simply, so no dishes with complex sauces or soups or even desserts, which may have hidden ingredients.

In addition to discussing ingredients, it’s important also to discuss cross-contact risk. So the chef or the cook really needs to understand that in order for a meal to be safe, it must be prepared using clean cooking equipment and utensils, and the food should not come in contact with other foods. So you wouldn’t want a hamburger for a child with a milk allergy to be grilled on the same grill as other burgers including a cheeseburger, or you wouldn’t want a salad for a child with a nut allergy to be assembled using the same tongs as a salad that was assembled with nuts on it.

Dr. Sicherer: So it sounds like you have to educate the restaurant where you go for a meal.

Ms. Groetch: You need to educate the restaurant; you do. So clearly communicating if there’s a food allergy, what ingredients to avoid, and then how to avoid cross-contact are all essential elements.

Dr. Sicherer: Well, Hugh, for many children we expect actually good news in the end, that they’re going to outgrow their allergy. Can you describe a little bit about the natural course of food allergy and also how we evaluate for that?

Dr. Sampson: Happily most children who develop allergy to milk, egg, soy, wheat, and many of the common foods will outgrow it; studies would certainly suggest that at least 80% to 85% of milk- and egg-allergic children will outgrow it. One of the things that we’re seeing more recently is the fact that it seems to be taking longer for these children to outgrow it than we saw in the past. So studies done in the late 1990s would suggest that children would outgrow it by 3 to 5 years of age, things such as milk and egg, whereas now we’re hearing reports where it’s more into the teenage years.

On the other hand, young children who develop allergy to peanuts or tree nuts, fish, or shellfish, often don’t outgrow it; at least in about 80% of the cases, it turns into a lifelong food allergy.

As far as trying to determine when somebody does outgrow it, we will look at things like the serum IgE level
to a particular food; we’ll often monitor that. We expect to see the serum IgE levels fall over time, and that does seem to correlate with them in this so-called outgrowing process. We also sometimes will employ a skin test because we’ve seen that some children will have a significant drop in their IgE level, and yet when we challenge them they would be reactive.

If you have any significant concern that somebody’s allergic, you want to see what the skin test response is because that’s going be the most sensitive indicator that IgE antibody is still there.

Marion, one of the things that we always worry about, especially when we have children who are allergic to more than one food, is the nutritional restrictions that this might place on them. What would you suggest us pediatricians might do to approach this topic?

**Ms. Groetch:** Nutrition is always an issue in our pediatric population, but especially when the diet is restricted as it is in food allergy. So it’s not enough for pediatricians to say, “Avoid all milk and milk products.” In a typical toddler diet, milk and milk products provide about 30% of the overall nutrition — namely calories and protein and fats — as well as almost all the calcium and vitamin D, in addition to other nutrients like riboflavin, pantothenic acid, B12. And a diet that eliminates wheat without providing for a substitute might be low in iron, folate, B vitamins, fiber, and complex carbohydrates.

So when a major food group such as milk or wheat is removed from the diet, provisions have to be made to substitute for the nutrients lost to that elimination diet.

So while many pediatric practices are dealing with an obesity epidemic, in food allergy we tend to have the opposite problem — children who aren’t growing properly due to these diets. We really need to make sure that we are offering substitutes. Research has shown that children with milk allergy or two or more food allergies are shorter, based on height-per-age percentiles, than those with only one food allergy or no food allergy. So as pediatricians you want to ensure adequate growth. This will give you a gross picture of the potential caloric and protein intake. But also keep in mind that we might not see immediate signs and symptoms of inadequate micronutrient intakes, but we know that there are long-term consequences. So ensuring that alternatives to the eliminated foods are recommended, that these are tolerated, and that they’re accepted by the child is very important. And a trained dietician will not only be able to provide clear avoidance education, but also help the family to provide a diet that’s nutritionally adequate within the context of the allergy-restricted diet.

**Dr. Sampson:** Scott, it’s not uncommon that we will have patients referred in to us who are avoiding whole classes of food. So, for example, somebody who has peanut allergy may have been told that they need to avoid all members of the bean or legume family, so they’ll be avoiding soybeans, green peas, beans, lentils. We did a study looking at that and found that only about 20% of children who were allergic to peanut actually reacted to another member of the legume family. How do you deal with this issue, and what are other kinds of large family avoidances that we run into?

**Dr. Sicherer:** Just getting back to the peanut issue, as you studied a few years back, 19 of 20 people could tolerate all these other beans. There are some beans for which there have been reports since then that have been more problematic. So, for example, lupine or lupin, at least from reports from Europe, seems to be a bean that about half of the people with peanut allergy might react to. And although we haven’t seen a lot of it in this country yet, it’s being used more in this country — lupine in pastas and flours and things like that — so it’s a bean that they grind up and use in that way. So it gets to be really tricky.

There are other foods, tree nuts, so families will be like, “Well, if I’m allergic to peanut do I avoid tree nuts?” In some sense, yes, because there may be issues about cross-contact, and personally I’ll individualize with the family, “Now is it easier for you? Is it safer for you if you’re not allergic to the tree nut, should you be avoiding them?” Because a peanut allergy — they’re in brownies together and bakeries or whatever it is, so there might be some argument made to do that.

On the other hand you have a family that says, “I want my child to eat walnut,” so then the question is, do they have a tree nut allergy? And so the tree nuts act like their own food sometimes as well. Walnut and pecan are very similar, cashew and pistachio are similar, almond and hazel are similar to each other, but not necessarily among those different groups, even within the tree nut family. So we might individualize or we might decide whether it’s worth individualizing, depending on the age and the preferences of the family. But there’s a higher rate of cross-reactions in the tree nuts.

So for fish: if you’re allergic to fish, you’re often allergic to all of the fish because there are some major proteins in there that are shared with all the different fish. On the other hand, you find some people who are just allergic to one kind — tuna or swordfish. So we might individualize, but the rate of having issues with multiple ones is much higher. Same thing for shellfish: there are major al-
lergens called *shrimpomycin*; it’s in shellfish. Occasionally someone might be just allergic to crabs and nothing else, but most of the time they’re allergic to multiple types.

With milk and milk-related foods, it’s also something that pediatricians need to be aware of in that if you’re allergic to cow’s milk, studies show that about 92% of the time you’re going to react to sheep’s milk and goat’s milk, so you don’t want to pick those as a substitute. On the other hand, mare’s milk or donkey’s milk usually is okay, but it’s hard to find so that’s usually not an option.

One thing that’s important for pediatricians with milk allergy is they might want to say, “Let’s try sheep’s milk or goat’s milk,” but 92% of the time you react to those. Now only 8% of the time do you react to mare’s milk or donkey’s milk, but those are hard to find, they don’t like to be milked so that’s usually not an option. When we’re talking about milk allergy, also about 10% with a severe milk allergy react to beef and that’s even variable depending on how well you cook the beef, so that’s also a little consideration.

And I should also mention that partially hydrolyzed formulas are not a good choice if you have a milk allergy because people will tend to react to that, whereas the extensively hydrolyzed casein formula would be and it’s labeled as hypoallergenic for milk allergy. It’s usually tolerated in that setting. And then there’s a bunch of things that cross-react among fruits and vegetables, but usually those are mild symptoms.

Lastly, if you start testing somebody for allergy to related foods, the tests are often positive. So in the same study where only one of 20 with a peanut allergy reacts to a bean, more than 50% of those people will test positive to various beans. So that could be really misleading and should not be depended upon when you’re trying to figure these things out.

Now, Marion, we’re seeing a rise in food allergy, we think — at least we know that we are for peanut allergy. It seems like all types of allergies — asthma, atopic dermatitis, even allergic rhinitis, and food allergies are on the rise. The American Academy of Pediatrics (AAP) revised statements that they had originally made in 2000 as a list of recommendations on allergy prevention through diet, and now we have a new report in 2008. Can you update us on this new report about prevention of atopic disease through dietary changes?

**Ms. Groetch:** The new guidelines do differ somewhat from previous recommendations. I think a subtle difference between the original AAP report published in 2000 and the new report published in January 2008 is how at-risk infants are defined. So the 2000 report defined at-risk infants as having two first-degree relatives with an allergic disease. That’s a parent and a sibling or two parents. And the 2008 guidelines define at-risk infants as having one first-degree relative with an allergic disease. So the new guidelines define at-risk infants somewhat more broadly.

The most significant difference, I would say, between the two guidelines is that the new report is sensitive to the notion that when there’s a lack of evidence of benefit, both the physician and the patient should be aware of that lack of evidence. So the new guidelines support approaches based on clinical research to date that are generally proven protective in infants at risk. And those are exclusive breastfeeding for 4 to 6 months of life, delaying the introduction of solid foods until 4 to 6 months of age. And then if not breastfeeding or if using supplemental bottles, using an extensively hydrolyzed casein formula instead of cow’s milk or soy-based formula for the first 4 to 6 months. The report also said that partially hydrolyzed whey formula might also be protective if somewhat less effective. Now you mentioned before that the partially hydrolyzed whey formulas are not hypoallergenic, but in this case for prevention they might be effective. And if cost is an issue, you would use the partially hydrolyzed whey formula over soy milk or cow’s milk.

The report then goes on to say that the approaches that have been tried, but remain unproven, are avoiding allergenic foods during pregnancy, avoiding allergenic foods during breastfeeding, with the possible exception of some reduced atopic dermatitis. And then the last area where we currently have no significant evidence of benefit is avoiding introduction of solid foods beyond 6 months of age, including those that we consider highly allergenic. So in other words, beyond 6 months of age, normal infant feeding guidelines apply; that means beginning with one new single-ingredient food at a time for a period of 5 days and watching for symptoms of allergy.

**Dr. Sicherer:** So I think it would be fair to say that these new lists of evidence or non-evidence are a little bit different as an approach, but on the other hand, they’re not saying that peanut butter’s a weaning food for a 6-month old.

**Ms. Groetch:** You’re going to be looking at foods that are age-appropriate, the pureed foods, but also looking at the nutritional needs of that infant. So we know that breast milk is low in iron and we are probably going to be looking for an iron-enriched or an iron-fortified grain as the first food.
Dr. Sicherer: And this is about prevention. So again, if a child already has atopic dermatitis or already has had a reaction to a food, it’s likely all bets are off; you need to think about testing and what exactly should be added.

So it’s a little bit depressing that right now we’re talking about avoidance and treatment with things like epinephrine as the treatment of food allergy, but, Dr. Sampson, there’s a lot of study going on for treatments in the future. Can you give us a little about that?

Dr. Sampson: Sure. I think one of the hopeful things is that there are a number of different treatments that are being looked at in clinical trials. A couple approaches, which actually were used decades ago, that are being re-looked at are things such as oral immunotherapy and sublingual immunotherapy for food allergy. In oral immunotherapy, basically you’re starting off with very small amounts of the particular food that the individual is allergic to at a level below which they would react, and then you slowly build it up over time. And it appears that you can desensitize them in a sense that they can then ingest larger amounts without having any significant reaction. Similar findings are being suggested with sublingual immunotherapy.

There are also some new molecular techniques that are being used to alter the allergenicity of the protein, such as peanut, and those will be looked at for use in vaccines to try to reverse the particular food allergy.

There are also some general methods that may be useful in treating. One study was done looking at anti-IgE antibody or omalizumab-like antibody for individuals with peanut allergy, and it was shown that you could markedly increase the threshold of peanut that someone would need to ingest before they would experience a reaction. There are even some less traditional methods being looked at. There’s a trial started now using an herbal formulation that would, at least in the animal model, totally prevent the development of anaphylactic symptoms when the animal ingested, in this case, peanut. So there’s definitely some hope on the horizon. At the moment it’s still strict avoidance and preparation for accidental ingestion. But hopefully in the next 5 to 10 years we’re going to be able to treat some of these disorders.

Dr. Sicherer: That’s terrific news. One of the things that you mentioned was the anti-IgE, and that’s actually being used in asthma because it’s available.

Dr. Sampson: Right now we’re not recommending the use of omalizumab or anti-IgE for food allergy. The study that was done was actually done with a different preparation, very similar, but not the same, so you can’t necessarily extrapolate the finding. But the other thing that came out in that study was, there are probably in the neighborhood of 25 to about a third of the patients who really did not get any protection from the use of the anti-IgE preparation, so there is going to be a significant number that would not be protected.

There are studies that are being planned to look at that so we may be able to better understand or better identify the people who won’t get a benefit while on anti-IgE, but these are things that have to be studied. So right now we would not recommend that people be put on it for food allergy.

Dr. Sicherer: This is Scott Sicherer from the Jaffe Food Allergy Institute. I want to thank my colleagues, Dr. Hugh Sampson and Ms. Marion Groetch, for helping us out in this interesting discussion about food allergy, and I want to thank the American Academy of Pediatrics for hosting us to do this.

Narration Close
References


Test Questions: Food Allergies

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Print Name: _____________________________________________

AAP ID #: ______________________________________________

1. An 18-month-old female infant has had moderately severe atopic dermatitis since age 3 months without improvement despite excellent compliance with treatment regimens. She was exclusively breast-fed until age 6 months when solids foods were introduced and diet advanced according to standard diet recommendations for normal infants. Her parents inquire about allergy testing to foods currently in the diet and those not yet introduced.

   In patients with atopic dermatitis, which food is the most common cause of an allergic reaction?
   1. Egg
   2. Milk
   3. Soy
   4. Wheat

2. As increasing numbers of patients in your practice are diagnosed with food allergies, increasing numbers of parents ask whether their child is likely to outgrow his/her food allergy.

   Which of the following food allergies in young children is unlikely to be outgrown?
   1. Egg
   2. Milk
   3. Peanut
   4. Soy
   5. Wheat

3. The mother of a 1-year-old child suspects that he is allergic to tomatoes. He recently ate a very large tomato for the first time and shortly thereafter was noted to have reddening of the skin around the mouth and on the chin. He did not appear very bothered by the reaction and only occasionally rubbed a hand over the area. Which of the following features in this child’s history would support a potential immunoglobulin (Ig) E-mediated food allergy?

   1. The quantity of food ingested was substantial
   2. The reaction occurred very soon after ingestion
   3. The reaction occurred on first exposure
   4. The suspicious food is one of the eight foods that cause 90% of food allergies

4. Which of the following is the major benefit to performing skin prick testing?

   1. Easiest testing method that confirms presence of allergy
   2. Quick evidence that patient has specific IgE antibody
   3. Quick testing that does not cause pain for the patient
   4. Well-established standards for interpreting results

5. Several months after starting high school, a 15-year-old previously healthy girl is seen for routine health maintenance.

   She seems to be enjoying her new classes and friends. The patient reluctantly reports a recent onset of “stomach aches” sometimes accompanied by an episode of diarrhea. She currently has two or three episodes of diffuse abdominal pain or discomfort each day, most often occurring after drinking one or two cans of soda pop. Between episodes the girl reports feeling “just like normal.” She previously did not have soda often because her old school did not sell it. There are no other complaints and no abnormal findings on examination. Which of the following is the most likely etiology for the girl’s gastrointestinal complaints?

   1. Food allergy (non-IgE)
   2. Food intolerance
   3. Neurologic response
   4. Pharmacological response
   5. School adjustment

6. A 1-month-old infant who is exclusively breast-fed develops bloody stools with mucus. She is well-appearing without pallor or other abnormal findings on examination. The hemoglobin and hematocrit are within normal limits. Elimination of milk from the mother’s diet led to resolution of the infant’s symptoms. Which of the following mechanisms is the most likely explanation for the infant’s problem?

   1. Food allergy cell mediated
   2. Food allergy IgE
   3. Food intolerance
   4. Food toxin

7. Which allergic disorder is often misdiagnosed in young infants on presentation for overwhelming sepsis because of hypotension, very ill appearance, repetitive vomiting, pallor, and duskeness?

   1. Allergic eosinophilic esophagitis
   2. Angioedema
   3. Food protein-induced enterocolitis syndrome
   4. Heiner syndrome

8. A 10-year-old boy is a new patient whose family recently moved from a distant part of the country. The entire family is enjoying the many excellent Mexican restaurants in the area. Like his parents, the boy enjoys spicy Mexican foods, but they seem to really bother his nose, which gets sore and runny. The mother tells you she thinks her son developed allergies following the move and exposure to many new things in the environment. Which of the following is the most likely explanation for the boy’s new nasal symptoms?

   1. Allergic rhinitis
   2. Food intolerance
   3. Neurologic response
   4. Oral allergy syndrome
   5. Pharmacological response

9. Which of the following tests is considered the “gold standard” for diagnosing a food allergy?

   1. Allergy blood testing
   2. Allergy skin testing
   3. Double-blind placebo-controlled food challenge
   4. Single-blind placebo-controlled food challenge
   5. Unmasked food challenge

10. Which age group appears to be at highest risk for severe and fatal anaphylactic reactions from food allergy?

    1. Adolescents
    2. Infants
    3. School-age children
    4. Toddlers
## Evaluation Form: Food Allergies

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<thead>
<tr>
<th>Question</th>
<th>Very Satisfied</th>
<th>Very Dissatisfied</th>
<th>Strongly Agree</th>
<th>Strongly Disagree</th>
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<td>1. Overall satisfaction with this issue.</td>
<td>5</td>
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<td>2. This issue was an effective use of my time.</td>
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<td>3. This issue was effective in achieving its stated learning objectives.</td>
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<td>4. This information will be useful in improving my ability to diagnose and manage patients in my practice.</td>
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<td>5. This information was effective in enhancing my professional knowledge and skills.</td>
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<td>6. Faculty had command of the subject matter and gave a clear and logical presentation.</td>
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<td>7. Do you feel the content was free of personal bias? Yes No If no, please explain:</td>
<td>Yes</td>
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<td>9. What topics would you like to see in future issues of PREP Audio?</td>
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The concept of change in knowledge, competence and practice performance as a result of participation in an educational activity supports the value of continuing education and learning in practice to enhance medical care. These questions are aimed at identifying the knowledge and/or skill you have developed and will apply in practice.

**Based on the content presented in this educational activity, I have found the following:**

10. I have identified a need for more knowledge in regards to the following, noted below, as there is a difference between what I currently know and what I would ideally like to know.

11. I have identified a practice performance issue I need to improve. It is:

12. Name a major barrier to implementing the practice improvement identified in question 10.

13. In reference to the knowledge and/or practice improvement, I am going to implement the following change: ____________________________________________________________ within the timeframe noted below:

   □ 1-2 months  □ 3-6 months  □ 7-12 months

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