

Latest approaches to the Diagnosis and Management of Food Allergies in Children

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Abstract

Adverse food reactions are a challenge for physicians. As the prevalence of this condition rises, it is important that paediatricians and other health care professionals adeptly diagnose this condition. We begin by discussing the relevant points in history and physical examination, then we discuss the recent effective diagnostic tests and techniques available for doctors and patients, along with several management options. Over the last decade, there have been major advancements in this field and novel mechanisms have been proposed which efficiently modulate immune mechanisms involved. Although results are only prelimi-

nary, they do however, indicate a promising future for patients with food allergies.

Introduction

The term "Food Allergy" is applied to those reactions to food in which immunologic mechanisms can be demonstrated.¹ Food allergy affects 4-6% of the children, with its prevalence apparently increasing with the increasing prevalence of extrinsic asthma and environmental allergies.²⁻⁴ Food allergies, unlike other allergic diseases, are also known to be the only disorder for which there is no specific therapy.⁵ The potential to cause troublesome reactions and their increasing prevalence highlight the necessity of

of accurate diagnosis and treatment of food allergies. Children of all ages present with a variety of symptoms ranging from simple diarrhoea to fatal food anaphylaxis. Parents may attribute these conditions to constituents of the diet. Only a systematic approach will enable the pediatrician to make the appropriate diagnosis in children with potential food allergy.

Taking the history

An accurate diagnosis begins with acquiring a careful history of the illness and hence is an imperative component in the evaluation. Histories of patients, with allergies, provide information that can assist in selecting appropriate diagnostic tests. Moreover, in the primary care setting, it helps in deciding whether a referral to an allergist is needed.⁶ Several significant aspects need to be elucidated. The description of the signs and symptoms that of food allergies need to be ascertained. It is important to know how much time elapsed, after ingestion of the suspected food, before the symptoms appear. How frequently do reactions occur with each food? When was the most recent episode? What quantity of food triggers the allergic reaction and whether quantity of allergin present in the food affects the nature and sequence of symptoms? Note if symptoms are associated with exercise or other factors. What previous treatment was tried and what medications are currently being used? Whether same symptoms occur on repeated episodes. And also determine whether any cross-contacts are occurring, with other foods or with dust mites, or perhaps with some other innate object?

Physical Examination

The physical examination should be directed towards stigmata of atopic disease. The skin should be examined for atopic dermatitis or urticaria.⁷ Chronic diarrhea and recurrent abdominal pain may be found, as signs and symptoms of food hypersensitivity usually manifest in the gastrointestinal tract. In addition, some children present as 'failing to thrive'. The cause of this is usually not a consequence of food hypersensitivity, rather it happens because parents have severely restricted their diets. Respiratory examination may reveal signs and symptoms of chronic respiratory symptoms like rhinitis, sinus disease, recurrent otitis media, chronic cough, and asthma. In the absence of gastrointestinal and cutaneous symptoms, however, isolated respiratory findings are rare.⁸ The entire physical examination may perhaps even be unremarkable, as atopic manifestations are often quiescent.

The history and examination might be sufficient for an allergist to diagnose and propose a treatment plan. However, for the primary care physician, history should mainly clarify whether the patient experienced a true food allergy or not. The physician should then try and classify the reactions by systems and also figure out the involved

mechanisms. IgE-mediated conditions, for example, include immediate (gastrointestinal, cutaneous, respiratory, ocular, or anaphylactic) reactions or immediate/late-phase atopic dermatitis and other allergic gastrointestinal illnesses. Non-IgE-mediated conditions include gluten-sensitive enteropathy and food protein-induced gastrointestinal diseases.

Elimination Diets

Before making referrals to specialist, primary care physicians should attempt the use of elimination diets. The pattern of illness characteristic of food allergy may help determine whether any dietary manipulation is likely to be helpful. The type and scope of the elimination diet depends on the problem and the age of the child. In infants who are solely breastfeed or are on a milk formula diet, a trial of a "hypoallergenic", soy-based, or amino acid based formula may be useful. Maternal avoidance of highly allergenic foods, supplemented by extensively hydrolyzed formula during the first six months of life, along with delayed introduction of solid foods, has shown to reduce the development of food allergy in high-risk infants.⁹ In older children, eliminating one or two suspected foods may be appropriate. If no improvement is seen then it is difficult to say whether further dietary elimination will be helpful. Often elimination of many food items from the diet leads to nutritional deficiencies. To clarify the situation, specific laboratory tests may be ordered or referral to specialists may be necessary.

When potential food allergens cannot be identified, specialists often recommend diets with limited food items and those which are considered "less allergenic". An oligoantigenic diet may contain a grain-rice or corn, 2-3 vegetables, 2-3 fruits, water (possibly apple juice and/or rice milk), salt, sugar, and olive oil¹⁰. If symptoms occur daily, such diet may not be used for a maximum of 2 weeks (avoiding nutritional deficiencies) to see any improvement in the symptoms. If no improvement occurs, it is unlikely that the restricted diet contains the confusing allergic element.

Skin Testing

The main investigation in the diagnosis of food allergy is percutaneous skin testing.¹¹ Several techniques are used for allergy skin testing but research studies indicate that the prick/puncture skin test (PST) is the most useful technique with the most reliable results. The test is performed by placing a drop of the allergen extract, which is being evaluated, on the skin. Several devices are available to puncture the skin and the results read in 15-20 minutes. A wheal of 3 mm or larger is considered positive, signifying the presence of antibodies.¹²

In children more than one year of age, negative skin results virtually exclude IgE-mediated food allergy in most cases. The positive predictive accuracy however is much lower, less than 50%, and often a food challenge is necessary. In children, less than 1 year, negative predictive accuracy is also lower, about 85%, as cutaneous mast cell numbers and sensitization may be too low to detect a response in the skin. For this age group, Hill and colleagues have recommended larger skin tests as highly predictive of clinical reactivity.¹³ Even with a negative skin test, it is important to inquire histories of strongly suspected foods. A study by Burks et al suggests skin testing for foods known to have high negative predictive accuracies, such as egg, milk, wheat, peanut, tree nuts, fish, and shellfish.¹⁴

The atopy patch test method is recently being investigated. The test involves prolonged contact of the allergenic extract with intact skin for 48 hours. Reactions are evaluated 20 minutes after the patch removal and then 72 hours later. Positive result consists of erythema and induration. When compared with prick skin tests, results were more accurate with patch testing in cases of delayed-onset reactions (25-44 hours). However, prick skin testing was better for acute-onset reactions (less than 2 hours).¹⁵ In infants with atopic dermatitis, combined skin prick and patch testing gave the highest predictive value.¹⁶ Despite the promising results, however, patch testing remains an investigational method today.

In Vitro Testing

In vitro testing for food hypersensitivity involves the detection of the presence of circulating IgE antibody using radioallergosorbent test or enzyme-linked immunosorbent assays. These tests in the past have not shown any more accuracy or sensitivity than skin tests. Recently, however, Sampson showed that for foods like egg, milk, peanut, fish, soy, and wheat, cutoff levels of antibodies detected with CAP fluorescent enzyme immunoassay (FEIA) may be used to predict with >95% confidence that food challenge will be positive, thus precluding their use.¹⁷ Similar results were found in Garcia-Ara et al and Boyano-Maritnez et al for young children with cow milk and egg allergy, though using slightly different cutoff levels.^{18,19} In the context of the history and physical examination, CAP-FEIA may be used in the primary care setting. A positive result would then require referral to an allergist, who can then determine if a food challenge is necessary to clarify the diagnosis and further manage the patient.

There are, in addition, other lab tests like food-specific IgG blood testing for food or some combination of IgE and IgG enzyme-linked immunosorbent assay testing that are used in several laboratories across the United States. Others that are marketed, include provocative testing and

neutralization, autogenous urine immunization, electrodermal testing, applied kinesiology and rotary diets. Their use, for the most part, has yet to be validated. Often, very restricted diets based on their results have led to unnecessary malnutrition and eating disorders.²⁰

Food Challenges

The food challenge is currently the most effective way of determining if food allergy truly exists to a particular food. However, it not only poses a risk to the patient but it not practical in the clinical setting. Furthermore, it requires that the patient be stable and with minimum symptoms at the time and be under the supervision of an experienced physician who treat anaphylactic reactions. Among the food challenges, the double-blinded placebo-controlled food challenge (DBPCFC) is the gold standard in the research setting, against which other tests are compared.²¹

The open food challenge is useful to eliminate suspected food allergies. It is used most commonly when the history suggests that reaction to a suspected food is unlikely. One example is that of a child who avoids eggs but eats French toast or pancakes. The open challenge here allows the exclusion of eggs as the source of hypersensitivity.

The single-blinded food challenge involves administering the challenge without the knowledge of the patient or the parent. For example, suspected nuts can be hidden in chocolate pudding or elemental formulas and given to the patient. This single-blinded approach works when certain symptoms are expected or if it is likely that the challenge will be negative, if not influenced, by the patients beliefs.

Recently, recipes have been developed for soy, peanut, milk, hazelnut, wheat and egg for DBPCFC in children.²² The DBPCFC, for which there is no standardized protocol, essentially involves preparation of foodstuffs in a form that neither the patient nor an observer can distinguish as the active or the placebo.²³ This method challenges subjective symptoms and eliminates biases of everyone involved, something necessary even in clinical practice. Unlike the open challenges and single-blinded challenges, however, DBPCFC is not that easy either to arrange or to administer and it also requires the expert opinion of a specialist.²⁴

Management

With the offending source identified, avoidance is the most important therapeutic option for children with food allergies and is an effective measure in dealing with the signs and symptoms.²⁵ It is important to prescribe an elimination diet as it important to prescribe just any medication in the primary care setting, continuous education about avoidance of certain allergens must be given. Patient and family must learn how to read labels, adapt recipes, and

educated other family members, child care providers, camp counselors, and teachers. Decisions such as which restaurant to go to and where to go to on a vacation, will take on a new meaning. Family decisions must be centered on avoidance of the child's food allergen.²⁶ Despite such measures, however, accidental ingestions of food allergens continue to occur due to the ubiquitous presence of certain foods such as peanut, soy, milk, and egg, compounded by poor labeling practices and cross-contamination during processing. In a study that followed 83 children with peanut allergy, Vander Leek et al reported that 60% had a total of 115 documented adverse reactions cause by accidental exposure to peanuts during follow-up.²⁷ Several studies that reviewed fatal food-induced cases reported that the patient unknowingly ate the food to which they were allergic.^{28,29}

Emergent treatment of accidents includes assessment of severity, treating systemic symptoms with intramuscular adrenaline, antihistamines, and systemic steroids; and treatment of persistent bronchospasm with inhaled or nebulized bronchodilators. Severe reactions may also require intravenous fluids, vasopressor support, and endotracheal intubation.³⁰ Self-injectable epinephrine, i.e. EpiPen, may even be prescribed for the future to patients along with clear instructions for when and how to use the life-saving medication.

In addition to the above recommended management, very recently several promising immunomodulatory approaches have emerged for future treatment of food allergies. Humanized monoclonal anti-IgE antibodies have been engineered that bind to circulating IgE and prevent IgE deposition on mast cells, thus disrupting the process that plays the central role in the pathophysiology of atopic disorders like food allergy. Preliminary reports indicate that anti-IgE therapy in patients with peanut allergy significantly increased the amount of peanut protein necessary to induce allergic symptoms.^{31,32} If confirmed, such anti-IgE may be used to treat patients with any IgE-mediated food allergy.

Probiotics, live bacteria that improve the hosts' intestinal microbial balance, reduced severity of atopic dermatitis symptoms in infants with cow milk hypersensitivity and prevented development of atopy in at-risk infants.³³

Regarding peanut allergies, for which there is no curative therapy, traditional Chinese medicines have proven to have anti-allergic properties. Chinese herbal formula FAHF-1 completely blocked peanut-induced anaphylactic symptoms and markedly reduced mast cell degranulation and histamine release in a mice model.³⁴ Another approach involves using engineered recombinant proteins that are forms of major allergenic proteins with reduced ability to bind to IgE. Their use in mice sensitized to peanuts resulted

in significantly decreased symptoms on oral peanut challenge.³⁵ This technique might someday prove effective in humans with peanut allergy as well.

In conclusion, as the prevalence of food allergies rises worldwide, it is important that physicians are able to accurately diagnose and manage this problem at the primary level. Patient's history is the most significant aspect of the evaluation; this is followed by physical examination, which often reveals signs of allergic reaction. Besides elimination diets, we must also take advantage of the increased diagnostic accuracies of skin tests and latest in vitro tests. We must also continue to educate all those involved in the care of the child. Moreover, prepare them to handle an emergency - such as anaphylactic shock. As novel and effective methods emerge for modulating the immune system, we can say that the future is promising for those suffering from food allergies.

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