Dermatologic Food Allergy

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The clinical presentation of hypersensitivity reactions to foods can be highly variable and include gastrointestinal, respiratory, cutaneous, or systemic symptoms (anaphylaxis).[1,2] Cutaneous reactions, such as acute urticaria and angioedema, are among the most common manifestations of food allergy. In addition to acute urticaria, however, there is an increasing body of evidence implicating food allergy in atopic dermatitis and contact dermatitis.

Given the increasing prevalence of food allergy, it is critical for the pediatrician to recognize the importance of the various skin reactions related to food allergy.[3] It is important to remember that skin reactions to foods may be immunologic in nature (ie, immunoglobulin E [IgE], cell-mediated, or mixed) or relate

Urticarial rash on the upper arms and torso, an allergic reaction to eating strawberries in a young girl.

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to irritant, toxic, or nonspecific properties of the food (Table 1). This article gives an overview of the dermatologic manifestations of food allergy, including urticaria/angioedema, atopic dermatitis, contact dermatitis, dermatitis herpetiformis, and auriculotemporal syndrome (a "masquerader" of food allergy).

TABLE 1.

Cutaneous Reactions to Foods

Mechanism	Disorder
IgE-mediated	Urticaria Angioedema Flushing, pruritus Acute contact urticaria
Mixed IgE- and cell-mediated	Atopic dermatitis
Cell-mediated	Dermatitis herpetiformis Contact dermatitis
Nonimmune-mediated	Irritant dermatitis

IgE = immunoglobuin E.

URTICARIA

Acute urticaria and angioedema represent perhaps the most common symptoms of food-induced allergic reactions, although the exact prevalence of these reactions is unknown.[1-4] Urticarial lesions represent transient localized areas of edema within skin or mucous membrane tissue. Lesions typically appear as raised, erythematous, blanching, extremely pruritic, well-circumscribed wheals that resolve completely within 24 hours of onset. Angioedema represents transient localized edema within deeper areas of skin or mucous membrane tissue and typically is painful, rather than pruritic.

Acute urticarial reactions to foods, which may also be associated with angioedema, morbilliform rash, flushing, and pruritus, are thought to be IgE-mediated and develop as a consequence of mast cell degranulation within the skin following allergen-specific cross-linking of membrane-bound IgE. Symptoms develop within minutes of ingestion of the responsible food allergen, and thus can provide the pediatrician with a useful diagnostic tool in the evaluation of possible food-associated acute urticaria.

The foods most commonly responsible for IgE-mediated cutaneous reactions in children are eggs, milk, peanuts, and nuts.[5] Diagnosis is based on the demonstration of food-specific IgE antibodies (prick skin test or blood test) and a clinical history of resolution of skin symptoms, with elimination of the food and development of symptoms following challenge. Acute urticaria should be distinguished from both irritant and allergic contact dermatitis, which can result from direct physical contact with a variety of foods, as discussed in more detail below.

The significance of food allergy in chronic urticaria remains somewhat controversial. In general, food allergy rarely is incriminated as a cause of chronic urticaria, defined as lesions that recur at least twice a week for a total of at least 6 weeks.[4-6] There have been some recent reports of pseudoallergic reactions to volatile aromatic components in natural foods inducing chronic urticaria in adults[7] and pseudoallergic reactions to food additives as a cause of chronic urticaria in children[8] and adults.[9] The diagnosis of food allergy as a cause of chronic urticaria can be challenging, and other diagnostic possibilities must be entertained. Referral to an allergy specialist likely would be necessary to determine if foods or food additives are responsible for chronic urticaria occurring in a child.

ATOPIC DERMATITIS

Atopic dermatitis is an inflammatory skin condition that affects 10% to 20% of the pediatric population.[10,11] It frequently precedes the development of other atopic disorders, such as asthma and allergic rhinitis.[12] Atopic dermatitis generally begins in early infancy and is characterized by a typical distribution of lesions, extreme pruritus, and a chronic, relapsing course. Although the pathogenesis of atopic dermatitis is not fully understood, TH2-type mechanisms clearly play a role in at least a subset of children with a positive family history of atopic disease.

Skin lesions in acute atopic dermatitis are characterized by cutaneous

CME EDUCATIONAL OBJECTIVES

1. Describe the common dermatologic manifestations of food allergy in children.
2. Discuss the evidence supporting a role for food allergy in the pathogenesis of atopic dermatitis in children.
3. Recognize that cutaneous reactions to foods may be immunologic in nature or relate to toxic or irritant properties of the food.

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lymphocyte-associated antigen (CLA) positive memory T-cells. These produce increased levels of TH2 cytokines, including interleukin (IL)-4 and IL-13, involved with isotype switching to IgE synthesis; IL-5, which plays a role in eosinophil development and survival; and IL-31, implicated in pruritus, dermatitis, and specific chemokine production; as well as decreased levels of interferon (IFN)-gamma, a TH1 cytokine known to inhibit TH2 cell function.[12,13] Langerhans' cells and inflammatory dendritic epithelial cells in the skin of patients with atopic dermatitis display increased expression of the high-affinity IgE receptor (FcϵRI) on their surface and are hypothesized to play a role as antigen-presenting cells important in the pathogenesis of atopic dermatitis.[12]

There is strong evidence to suggest that food allergy plays a pathogenic role in one-third to one-half of childhood atopic dermatitis.[14-18] Sampson[14] found that approximately 60% of selected children with atopic dermatitis undergoing a double-blind, placebo-controlled food challenge (DBPCFC) experienced a positive reaction to food. Among a group of children referred to a university-based dermatologist for evaluation of atopic dermatitis, Eigenmann[15] found 35% to 40% of children with refractory, moderate to severe atopic dermatitis had IgE-mediated clinical reactivity to one or more of six common foods (ie, milk, egg, wheat, soy, peanut, or fish).

Some studies have suggested that the younger the child and the more severe the skin disease, the more likely it is that foods will be implicated in contributing to atopic dermatitis.[19,20] The clinical presentation of food allergy in infants with atopic dermatitis can be variable, and in addition to immediate cutaneous, respiratory, or gastrointestinal reactions, delayed reactions can occur. Breuer et al.[21] found that 57% of children with atopic dermatitis undergoing DBPCFCs developed late eczematous reactions, either isolated (12%) or in combination with immediate reactions (45%).

Thus, it is extremely important for pediatricians to recognize that the prevalence of food allergy in children with moderate to severe atopic dermatitis is significantly higher than in the general population. It is also critical to remember that the clinical expression of food allergy in children with atopic dermatitis might include delayed reactions without an associated immediate reaction, and in fact, acute urticarial lesions in young children with atopic dermatitis are rarely seen when there are extensive eczematous lesions.[2]

Identification of specific food(s) contributing to atopic dermatitis in a child can sometimes be difficult. The clinical significance of a positive skin prick test to foods in young children with atopic dermatitis must be interpreted with caution, as the false positive rate for skin tests can be quite high.[2,4] Determination of clinical significance may require a combination of prick skin testing, evaluation of food-specific IgE levels in peripheral blood and consideration of a DBPCFC to confirm clinical reactivity.[2,4,5,17,18] Although considered investigational, atopy patch testing has been used in some studies as a diagnostic tool in determining the clinical significance of certain foods in atopic dermatitis.[2,4,22,23]

It is important for the pediatrician to be aware that most studies have implicated only a few foods (ie, milk, egg, wheat, soy, peanut, and fish) as contributing to atopic dermatitis in young children.[3,14,16,17,18] Of these, egg and cow's milk appear to be the most common,[24,25] and both have been associated with a worse clinical outcome of atopic dermatitis in terms of both persistence and severity of disease.[25]

In children with documented food-associated atopic dermatitis, it has been demonstrated that elimination of the relevant food allergen improves the skin disease.[5,17,26] The role of dietary elimination for the prevention of atopic dermatitis, however, is an area of some controversy. Exclusion diets for preventing atopic dermatitis are not felt to have a role during pregnancy,[27] and there is no convincing evidence that maternal dietary restrictions during lactation have a long-term preventive effect.[28] There is some evidence to suggest that exclusive breastfeeding for at least 4 months in infants considered "at risk" for atopic disease decreases the risk of atopic dermatitis.[29-31] A recent large cohort study found no evidence for a protective effect of delayed introduction of solid foods beyond the sixth month of life for the prevention of atopic dermatitis.[32]

Atopic dermatitis generally begins in early infancy and is characterized by a typical distribution of lesions, extreme pruritus, and a chronic, relapsing course.

As infants or their mothers risk being placed on restrictive diets, sometimes inappropriately, in the hope of preventing or improving atopic dermatitis, it is critical for the pediatrician to assist families in further evaluation of possible food-associated atopic dermatitis. Referral to an allergy specialist is encouraged to determine the potential clinical significance of food allergens in atopic dermatitis. Before placing any child on a food-restricted diet, a full allergy evaluation is warranted to assure that only those clinically relevant foods are eliminated and close nutritional monitoring is in place.

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TABLE 2.

Contact Allergy to Foods

Reaction Type	Mechanism	Timing	Examples
Contact Urticaria	IgE-mediated	Immediate	Raw or processed foods, including fish, meats, fruits, vegetables, spices, milk, egg, and oatmeal
	Nonimmune-mediated	Immediate	Vasoactive substances in preservatives, flavoring agents, and food additives
Allergic Contact Dermatitis	Cell-mediated	Delayed	Multiple fruits, vegetables, and spices
Irritant Contact Dermatitis	Direct toxic effect	Immediate	Citrus juices, garlic, mustard, onion, pineapple, spices, peppers, and food additives
Protein Contact Dermatitis	Mixed IgE- and cell-mediated	Immediate, chronic/recurrent	Animal proteins, grains, fruits, vegetables, plants, spices, and enzymes
Phototoxic Contact Dermatitis	Cell-mediated	Delayed	Plants, vegetables, and fruits
Photo-allergic Contact Dermatitis	Cell-mediated	Delayed	Spices (garlic), celery
Systemic Contact Dermatitis	IgE- or cell-mediated	Immediate or delayed	Spices, garlic, raw cashew, balsam of Peru, and other flavoring agents

DERMATITIS HERPETIFORMIS

Dermatitis herpetiformis (DH) is a chronic, pruritic, papulovesicular skin disorder associated with celiac disease, an immune-mediated enteropathy caused by sensitivity to gluten.[33] Skin lesions of DH are distributed symmetrically on extensor surfaces of the elbows, knees, buttocks, shoulders, and scalp. Although it is an immune-based disease, this is not an IgE-mediated disorder but rather a cell-mediated response to gliadin (Table 1) found in wheat, rye, and barley.[2,33]

The pathogenesis of celiac disease involves deamidation of gluten by tissue transglutaminase (TG) and the production of autoantibodies, including antibodies to TG. The exact mechanism producing skin lesions in DH is unknown; however, circulating antibodies to both tissue TG and epidermal TG are present,[34] suggesting that epidermal TG is the autoantigen in DH. Maintenance of a gluten-free diet is the ideal long-term treatment for childhood DH, with a majority of patients demonstrating clearance of skin lesions in 1 to 6 months after starting dietary restrictions.[35]

CONTACT DERMATITIS

Contact dermatitis refers to inflammation of the dermis and epidermis that occurs as a result of direct contact between a substance and the surface of the skin. Contact allergy has been reported to occur with a wide range of foods, spices, and food additives and may be related to an immune-mediated reaction to a food or a direct toxic effect of the food coming into contact with the skin.[36,37]

Contact allergy to foods is perhaps most commonly seen in food handlers (primarily as hand eczema) but may also involve the face, particularly around the mouth in children and adults. Seven different types of contact dermatitis have been described;[36] these include contact urticaria, allergic contact dermatitis, irritant contact dermatitis, protein contact dermatitis, phototoxic contact dermatitis, photoallergic contact dermatitis, and systemic contact dermatitis (Table 2).

Evaluation of contact allergy to foods in children can be extremely difficult. Although it is important for the pediatrician to obtain a thorough history of exposures, the diagnosis cannot be made by history alone, and referral to an allergist as well as a dermatologist may be necessary to confirm the diagnosis and identify the offending allergen.

AURICULOTEMPORAL SYNDROME

The auriculotemporal syndrome, also known as Frey's syndrome or gustatory sweating syndrome, is an uncommon disorder characterized by recurrent episodes of localized facial flushing, rash, sweating, or a combination that occurs within a few seconds of eating.[38] Symptoms develop in the distribution of the auriculotemporal nerve (the area anterior to the ear and on the check) and typically are unilateral. This does not represent a food allergy; however, symptoms are triggered by foods that increase salivation, such as fruits, candies, spices, and hard foods that might require more mastication.

In adults, the syndrome usually develops as a complication of surgery or trauma involving the parotid gland. In children, the syndrome generally develops before age 12 months, is most commonly first seen when solid foods are introduced into the diet, and has been attributed to obstetrical trauma to the parotid area with a forceps delivery.[38]

Botox A injection has been reported as a safe and effective treatment for patients with this disorder.[39] Even though it is rare, it is important that pediatricians be aware of this syndrome, as its tempo-

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ral association with rash and flush in the context of eating can be confused easily with food allergy.[3]

SUMMARY

Cutaneous reactions to foods represent one of the most common presentations of food allergy in children. IgE-mediated (urticaria, angioedema, flushing, pruritus), cell-mediated (contact dermatitis, dermatitis herpetiformis), mixed IgE- and cell-mediated (atopic dermatitis), and nonimmune-mediated (irritant contact dermatitis, Frey's syndrome) reactions to foods have all been reported. It is important for the pediatrician to recognize the variety of skin reactions potentially related to food allergy and to consider timely referral to an allergy specialist for further evaluation and definitive diagnosis.

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