Food Allergy

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CONTENT OUTLINE

Learning objectives
Background information
- Non-immunologic and immunologic adverse food reactions
- Clinical manifestations of food allergy
- Mechanism and clinical presentation
- Food allergens
- Prevalence of food allergy
- Natural history of food allergies

Diagnoses and management
- Diagnostic criteria
- Differential diagnosis
- Evaluation of food allergy
  - history
  - IgE and specific IgE antibodies
  - non-IgE mediated allergy
- Diagnostic elimination diets
- Food challenges and food reintroduction
- Unproven or inappropriate diagnostic procedures
- Prevention
- Treatment of food allergies

Food allergy summary
Referral to allergy/immunology
Resources
Selected references
Illustrative cases

LEARNING OBJECTIVES

Understand diversity of adverse reactions to foods
Appreciate IgE and non-IgE mediated food allergies
Correlate clinical presentations with special mechanisms of allergy
Learn about food allergens
Understand the principles of diagnosis of food allergy and hypersensitivity
To discuss present prevention and treatment options

BACKGROUND INFORMATION

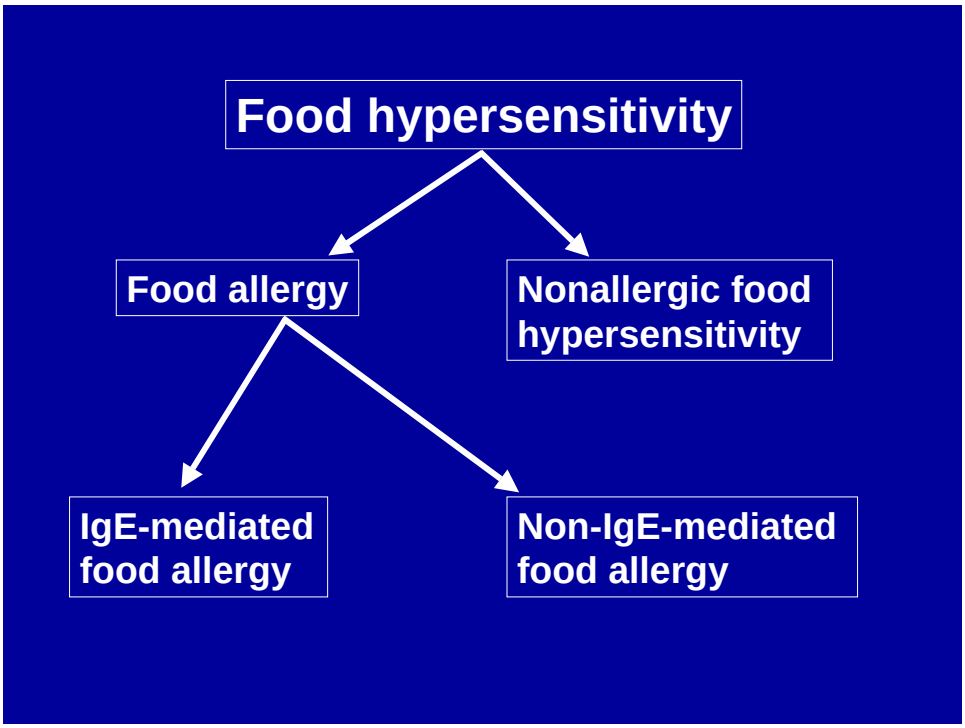
Adverse reactions to foods have both non-immunologic and immunologic causes:

NON-IMMUNOLOGIC REACTIONS (INTOLERANCE)

Pharmacologic/toxic reactions can be caused by caffeine, alcohol, sulfites, sodium glutamate, etc in susceptible individuals. Histamine fish poisoning will occur in any individual ingesting sufficient amounts of contaminated fish.

IMMUNOLOGIC CAUSES: FOOD ALLERGY AND HYPERSENSITIVITY

Food allergy and hypersensitivity have multiple causes and clinical manifestations. (1)
Current concepts have classified all forms of adverse reaction to specific foods as hypersensitivity that can be allergic or non-allergic (when no immunologic mechanism seems to be involved).
Allergic mechanisms in turn are classified as IgE-mediated and non-IgE mediated:



CLINICAL MANIFESTATIONS OF FOOD ALLERGY

There are different ways of classifying the phenotype of hypersensitivity reactions to foods:

By duration of exposure:

1. Acute or episodic
2. Chronic

By location of symptoms

1. Gastrointestinal
2. Gastrointestinal and distal
3. Distal manifestations only: dermatologic, respiratory, systemic, etc.

By main mechanism and area involved

IgE-mediated

1. Gastrointestinal	Oral allergy syndrome
	Acute gastroenteritis
2. Cutaneous	Urticaria
3. Respiratory	Rhinoconjuctivitis
	Asthma
4. Generalized	Anaphylaxis

IgE and non-IgE mediated

1. Gastrointestinal	Eosinophilic esophagitis/ Gastroesophageal reflux
	Eosinophilic gastritis
	Eosinophilic gastroenteritis
2. Cutaneous	Atopic dermatitis
3. Combined	Pulmonary hemosideerosis (Heiner syndrome)

Non-IgE mediated

1. Gastrointestinal	Protein-induced enterocolitis
	Protein-induced proctocolitis
	Celiac disease
2. Cutaneous	Dermatitis herpetiformis

Unclassified

1. Allergic colic

By age of presentation

Infant and early childhood formula intolerance and allergy
Adult solid food allergy

MECHANISM AND CLINICAL PRESENTATION

Combining the mechanism and the clinical manifestation, food allergies can present in one of the following ways:

	IgE mediated	Non-IgE mediated	Acute	Chronic
Gastrointestinal				
Oral food allergy	+		+	
Vomit	+	+	+	+
Diarrhea	+	+	+	+
Abdominal Pain	+	+	+	+
Anaphylaxis	+		+	
Skin				
Urticaria	+		+ + +	+
Angioedema	+		++	+
Atopic dermatitis	+	+	+	+ + +
Respiratory				
Throat tightness	+		+	
Rhinitis	+		+	+
Asthma	+		+	+

In general, acute IgE-mediated reactions occur within 30 minutes of exposure while non-IgE mediated mechanisms may occur as late as 3 days after exposure, but this rule is not absolute and late IgE-mediated and prompt non-IgE-mediated reactions may occur.

FOOD ALLERGENS

General characteristics of food allergens

Most food allergens are proteins with a molecular weight 18,000 - 36,000. Smaller peptides may be allergenic.

Allergenicity may be altered by cooking, digestion and interaction with other substances. Fats and oils may decrease absorption.

Sources of food allergens

The source of sensitizing food allergens vary with the age of the patient:

1. Allergens in maternal circulation during pregnancy
2. Allergens in breast milk
3. Allergens in milk and soy formulas
4. Allergens in solid foods

5. Peanut allergens in skin products
6. Fresh apple, peach, plum, hazelnut allergens crossreactive with tree pollens
7. Banana, avocado & kiwi allergens crossreactive with latex

Food allergens causing disease in children and adults

Children: milk, egg, soy, and wheat, peanuts and fish
Adults: peanuts, tree nuts, shellfish, fish

Cross reactivity among foods

Frequently, patients sensitized to one food allergen will also have adverse reactions to other foods. The main mechanism is reaction to shared allergens, as in the following examples:

If Allergic to:	Risk of Reaction to:	Risk:
Peanut*	**Other Legumes** Peas/lentils/beans	**5%**
Walnut	**Other tree nuts** Brazil/cashew/hazelnut	**37%**
Salmon	**Other fish** Swordfish/sole	**50%**
Shrimp	**Other shellfish** Crab/lobster	**75%**

*Although peanuts are legumes, patients with sensitization to peanuts also have a higher risk for sensitization to tree nuts. (2)

Sensitization to one allergen may also increase the risk for additional sensitization to non-cross-reactive allergens, e.g. cow milk protein allergic infants may also develop sensitization to soy protein.

Relationship between clinical presentations and specific food allergens:

Most foods can cause several of the clinical manifestations of food allergy. However, some foods are preferentially associated with some food allergy phenotypes:

1. Cows milk — chronic diarrhea, pulmonary hemosiderosis
2. Egg white — atopic dermatitis
3. Peanuts — anaphylaxis
4. Fresh fruits — oral allergy syndrome

SENSITIZATION, ALLERGY AND TOLERANCE

Normal individuals who have no adverse reactions to foods have developed oral tolerance. Oral tolerance entails immune reactions not associated with the development of adverse reactions. When IgE- or non-IgE mediated allergy develops, this is due to the development of immune reactions that are associated with hypersensitivity. These reactions are mainly the development of IgE antibodies and/or the development of certain forms of cellular immunity.

Sensitization to food allergens with development of specific IgE antibodies is far more common than the development of allergic manifestations upon exposure to foods eliciting the IgE response. The intensity of sensitization, the quantity and preparation of foods are the main determinants triggering allergic reactions.

The development of other immune reactions to food components is also common. IgG antibodies to food components are so common that their presence is of no diagnostic value to the determine risk for allergy.

PREVALENCE OF FOOD ALLERGY

The prevalence of food allergy is quite variable depending on patient perception (20 - 25%), or confirmation by oral challenges (1-2% in adults; 6-8% in infants and children). Sensitization and allergy to specific allergens depend upon societal eating pattern. Infants have a relatively high prevalence (2.5%) of cow milk allergy. Peanut sensitization is close to 1% in the general population and appears to be increasing without a clear cause for this increase.

NATURAL HISTORY OF FOOD ALLERGIES

The natural history is dependent on the food, the age of sensitization and the mechanism of allergy involved. Allergies to cow milk, egg, wheat, and soy allergy remit in 85% of patients by 3 yrs of age. Ingestions of these foods after allergy has remitted do not tend to re-induce sensitization.

Recently it has been reported that allergy to peanuts also remits with age, although the risk for sensitization and redevelopment of allergy may persist. Allergy to nuts, seafood typically persist for longer periods of time. Non-IgE-mediated GI allergy forms in infants resolve in 1 - 3 years; however, toddler and adult forms appear to be more persistent.

DIAGNOSES AND MANAGEMENT

DIAGNOSTIC CRITERIA

A food **hypersensitivity** is fully identified if an avoidance diet improves the clinical picture and a food challenge reproduces symptoms again.

Food **allergy** is confirmed in the presence of either IgE antibodies or a positive patch test to the food(s) shown to cause an adverse reaction. The mechanism of food allergy is inferred from this information.

Sensitization to a food without allergy is confirmed by the presence of IgE antibodies following ingestion of a food that is well tolerated in the regular diet or in controlled challenge procedures.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of food allergy is as varied as its clinical presentations. Each one of these manifestations, e.g. anaphylaxis, chronic diarrhea, atopic dermatitis, has its own list of diagnoses that need to be ruled out.

Some clinical problems that may be due to food allergy require special mention:
Failure to thrive
FTT with pulmonary infiltrated (Heiner syndrome)
Protein losing gastroenteropathy with hypogammaglobulinemia
Chronic vomiting, gastroesophageal reflux
Recurrent abdominal pain
Recurrent rhinoconjunctivitis.
Pruritus or tightness in the throat, dry "staccato" cough, dysphonia or dysphagia

The differential diagnosis for gastrointestinal manifestations includes enzyme deficiencies that may also cause food intolerance: pancreatic insufficiency; lactase deficiency; other single enzyme deficiencies.

EVALUATION OF FOOD ALLERGY

In patients with a clinical phenotype suggestive of food hypersensitivity, several diagnostic methods contribute to determine a diagnosis of food allergy hypersensitivity and of the mechanism involved:

1. Elimination diet and possibly challenge identifies hypersensitivity.

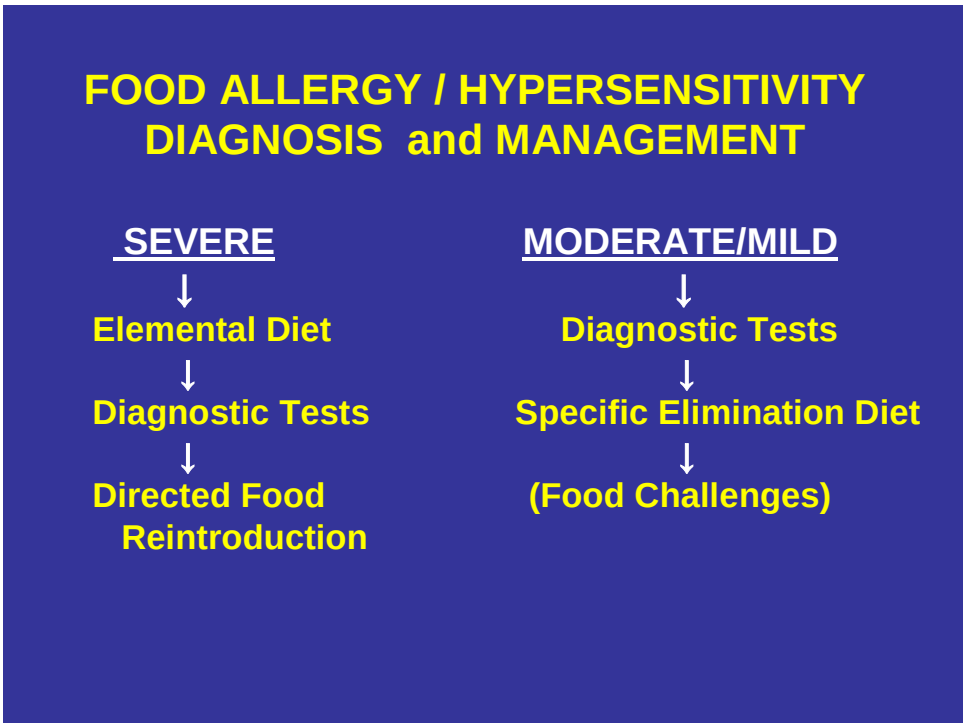
2. Skin and/or in vitro specific IgE testing suggests IgE-mediated allergy.

3. Patch testing suggests non-IgE-mediated allergy.

The practical sequence of steps to confirm the presence of a food allergy varies according to the history of adverse food reactions and to the severity of the clinical manifestation.

As shown in the algorithm below, the conventional steps in the diagnosis of mild to moderate food allergy involve the use of a complete medical history and allergy resting to guide a diagnostic elimination diet and challenge confirmation. Some indirect markers of food allergy may be helpful in this approach. When the problems is severe and this history does not give

clues that allow the elimination of some specific food(s), the use of an elemental diet followed by diagnostic tests and guidance of food re-introduction is the most effective approach.



HISTORY

Disease phenotype: A clear clinical description of the type of reaction is essential.

Timing of reaction: immediate vs. protracted. It is important to note that the presence of immediate skin test reactivity and/or IgE antibodies to a food component does not prove the pathogenic role of the food in causing the patients disease phenotype.

Atopy: Personal history of eczema, hay fever, asthma

Family history of eczema, hay fever, asthma and/or food allergy

IgE AND SPECIFIC IgE ANTIBODIES

IgE concentrations

We recommend measuring total IgE in addition to determinating the presence of specific IgE antibodies. Very low or absent total IgE concentrations rarely if ever are seen in patients with specific IgE sensitization. Elevated IgE concentrations are frequently seen in food allergy patients and their presence helps in monitoring the patients' response to treatment. Some patients with food allergy have extremely elevated IgE concentrations.

Specific IgE antibodies

Specific IgE antibodies against food proteins are an essential component of the diagnosis of IgE-mediated food allergy. IgE antibodies can be detected through prick skin testing or in vitro testing. These are complementary tests. They usually correlate well, but sensitization to some foods may be detected only with one or the other method. When one method reveals sensitization of similar intensity to several foods, the other methods may give better information about the intensity of the reaction elicited by the foods that are positive. The positive and negative predictive values for both methods are related to the type of food and the intensity of the reaction or the concentration of IgE antibodies. Not all antibodies to the many allergenic food components can be detected by either method.

Percutaneous skin testing with food allergens:

Prick skin testing is safe and can be performed at all ages, including in infants in the first few months of life. Intradermal skin testing is not recommended due to a high incidence of false positive reactions. The negative predictive value for food challenge outcome is high, over 85%, but the positive predictive values are much lower; there are many positive skin tests to foods that are well tolerated by the patient. (3)

Specific IgE antibodies in vitro:

The preferred method to detect specific IgE antibodies in vitro is a chemiluminescence (CAP) test. This test has shown to have good reproducibility and to give reliable results over a wide range of total IgE concentrations. The positive and negative predictive values also vary according to the food tested and the antibody concentration detected. (4)

Histamine and tryptase

Histamine and triptase levels are helpful in establishing if a patient in shock is experiencing anaphylaxis caused by mast cell mediator release.

NON-IgE MEDIATED ALLERGY

Patch testing

Non-IgE mediated food allergy can be detected through the direct, prolonged application of foods to the intact skin. Patch testing is being increasingly used, in particular in the diagnosis of non-IgE mediated allergy causing eosinophilic gastroenteropathies.

Peripheral and local intestinal eosinophilia

Evaluation of peripheral and tissue eosinophilia through intestinal biopsies are an important part of the diagnosis food allergies. If tissue eosinphilia is present and IgE antibodies are negative, a non-IgE-mediated allergy needs to be investigated. Patch testing may help identify the offending food component.

IgG and IgA anti-gliadin antibodies

Measurement of these antibodies helps with the diagnosis of celiac disease. Celiac disease needs to be differentiated from other forms of wheat allergy, including IgE-mediated allergy.

DIAGNOSTIC ELIMINATION DIETS

A diagnostic elimination diet can be directed to one or more foods or it may involve the use of an elemental diet to determine the presence of food hypersensitivity.

Specific elimination diets

These diets avoid foods identified through the history of food reactions and knowledge of cross-reactive foods and the results of allergy testing. When multiple foods are involved, it is possible to use known association between some foods and specific disease phenotypes to eliminate foods most likely to cause the clinical disease manifestation.

Disease phenotype:	GERD	cows milk
	Eczema	egg, milk, wheat
	Anaphylaxis	fish, shellfish, peanuts, tree nuts
	Oral food allergy	fresh fruits

Family history is useful in exceptional situations of multiple members being allergic to the same food.

In the latter case, the specificity for some foods is achieved through immunologic testing or sequential reintroduction of foods.

Elimination diets usually need to be maintained for 4-6 weeks before attempting challenges when challenges are important to reduce the stringency of a diet. However, clinical improvement can usually be expected within a few days.

Elemental diets

Elemental diets can be used in severe chronic conditions suggestive of food hypersensitivity, if the history and allergy testing does give enough information to design a specific elimination diet. Elemental diets should be clinically effective within 1-3 weeks.

Elemental diets for infants include elemental formulas. For older children and adults, they include special diets, like rice, chicken and other meats.

FOOD CHALLENGES and FOOD REINTRODUCTION

Food challenges are used to confirm the causal relationship of a food and disease symptoms, or to rule out the persistence of risk for anaphylaxis in patients with known anaphylactic reactions to specific foods who may have outgrown the risk for anaphylaxis.

They can be open or single or double blind, placebo controlled.

Patients with anaphylaxis or severe allergic reactions should be tested in the hospital.
Patients with chronic symptoms only that are not severe may be challenged at home by reintroducing eliminated foods gradually, usually at three-day intervals.

If there are doubts about the diagnosis or the skin tests are negative, plan a careful reintroduction of food to obtain proof that there is reappearance of symptoms upon food exposure.

If the patient improves on a multiple food elimination diet or an elemental diet, test each food by reintroducing separately.

Indications to perform a food challenge

1. To identify individual food component in reactions to complex foods.
2. To determine if foods being avoided can be reintroduced when skin test is negative:
   - After having been positive in the past, or
   - When IgE sensitization was never confirmed by skin and/or in vitro IgE tests
3. To determine if foods to which there are positive IgE antibodies cause allergic reactions.
4. To determine which food components of a complex elimination diet needs to be eliminated permanently and which ones can be re-introduced safely. The patient should remain asymptomatic and on a minimum maintenance medication.

Goals of a food challenge

1. To design proper food elimination diet, without unnecessary restrictions.
2. To eliminate need for anaphylaxis prevention, even if it may be advisable to continue elimination diet, e.g. for peanuts.

T**ype of challenge**

1. Open label food challenge. This is the preferred challenge in children
2. Double blind study or single blind study: Placebo should be used if the patient has psychological abnormalities or a history inconsistent with food allergy, e.g. exacerbated symptoms with minimal food exposure.

Food reintroduction

This refers to the re-introduction of foods that were eliminated from the diet but for which no allergy was documented by appropriate testing. The intention is to simplify the diet and improve nutrition, not to prove an adverse reaction. It is usually done with foods that can be assumed to be safe.
If the problem that led to the elimination of foods was not an anaphylactic shock, this may be attempted at home.

UNPROVEN OR INAPPROPRIATE DIAGNOSTIC PROCEDURES

A. Multiple food elimination diets for diagnostic purpose
B. Intradermal skin testing with food components
C. Provocation-neutralization testing (Intracutaneous, subcutaneous, sublingual)
D. IgG RAST antibodies against multiple food components
E. Cytotoxic food tests
F. Lymphocyte blastogenesis, IL-2 production

PREVENTION

Primary prevention (Prevention of sensitization)

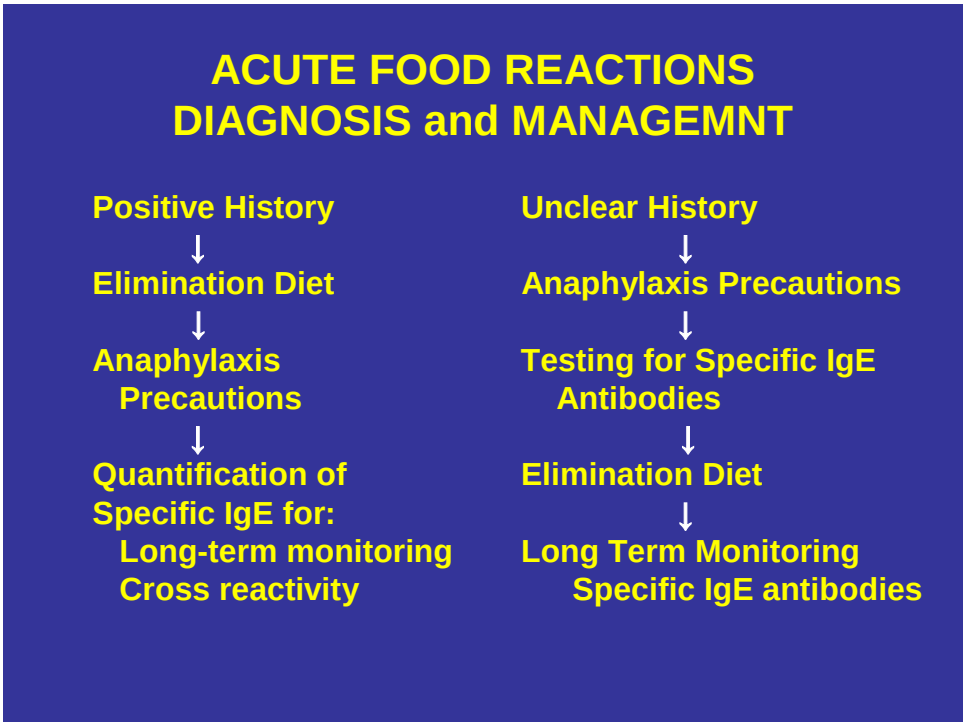
The prevention of sensitization to foods is a topic that is attracting much attention because of the probable role of early induction of food allergy in the “allergic march” to rhinitis and persistent allergic asthma.

Many strategies for prevention of primary food allergies have been explored. There is general agreement that the best prevention method is to encourage breast feeding and to use hydrolised, "hypoallergenic" formulas when supplementation is needed. (5) In addition, delayed introduction of allergenic solids like nuts, egg, and chocolate is recommended.

TREATMENT OF FOOD ALLERGIES

The mainstay of food allergy treatment is an elimination diet whenever possible. If only one or few foods are implicated, an elimination diet is realistic and does not put the patient at risk of malnutrition. We usually maintain the elimination diet for 2-3 years before retesting and deciding on the reintroduction of the food(s) avoided.

When severe acute reactions or anaphylaxis are involved, the following steps can be followed:



In these cases, the elimination diet has to be very strict and patients need to be advised about hidden allergen sources, including possible crossreactive foods.

Since complete avoidance of offending foods is nearly impossible, patients also need Epi-Pen prescriptions and instructions. A medical alert bracelet is also recommended.

For the long-term of some food allergies, antihistamines have some beneficial effects.

Systemic and topical corticosteroids are helpful in atopic dermatitis and asthma.

Immunotherapy has been tried for peanut allergic patients, but the risk is too high to make this treatment acceptable. Several immunomodulatory approaches are under active investigation. For patient with a high risk for peanut-induced anaphylaxis, the use of monoclonal anti-IgE antibodies may be of some benefit.

FOOD ALLERGY SUMMARY

Multiple causes/multiple manifestations
Can cause life threatening reactions
Frequently over/or under-diagnosed
Relatively high frequency in childhood
Requires awareness by general practitioners
Can be managed effectively after proper diagnosis
Importance of avoiding persistent sensitization and allergic march

REFERRAL TO ALLERGY/IMMUNOLOGY

INDICATIONS FOR REFERRAL

- Anaphylactic shock related to food ingestion
- Chronic symptoms suggestive of food allergy
- Perioral food allergy, recurrent vomiting, chronic diarrhea
- Unexplained failure to thrive, chronic pulmonary infiltrates
- Atopic dermatitis
- Adverse reaction to complex foods
- Adverse reactions to one or several foods
- Elevated IgE and/or eosinophilia
- Positive specific antibodies to food components

SUBSPECIALTY SERVICE

- Anaphylaxis: etiology and treatment
- Identification of relevant food allergy
- History and appropriate testing/interpretation of test results
- Food elimination and challenge
- Dietary management and instructions
- Food avoidance for causal foods and cross-reactive foods: common antigens or increased sensitization risk
- Monitoring of sensitization
- Reintroduction of food after prolonged avoidance
- Assessment of persistent risk for anaphylaxis

RESOURCES

The Food Allergy Network
10400 Eaton Place, Suit 107
Fairfax, VA 22030-2208
Phone: (703) 691 3179
Fax: (703) 691 2713

Food Allergy and Anaphylaxis Network (FAAN)
FAAN Web site at www.foodallergy.org/Advocacy/FDA.html
[InternetShortcut]
URL=http://www.foodallergy.org/schoolpr.html
Modified=003F3BCFD0DFBD01B6

Food Allergies:
Creating a safe classroom for your child - Copy and distribute in your office waiting area.
http://www.aaaai.org/members/academynews/patient_update_handouts/0902.pdf
(Adobe Acrobat required to download)

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ILLUSTRATIVE CASES

PATIENT 1

Diagnosis and management of cow's milk allergy and peanut anaphylaxis

Milk allergy:

- Urticarial rash after introducing cow's milk at 7 months of age
- Perioral skin rash and abdominal cramps after reintroduction of cow's milk at one year of age.

Peanut anaphylaxis

- Anaphylactic shock after ingestion of a small amount of peanut butter at 14 months of age

Allergy/Immunology evaluation revealed an elevated IgE concentration and positive skin tests for milk and peanuts.

A comprehensive management plan for his peanut anaphylaxis was provided. This plan included

detailed anaphylaxis prevention and treatment instructions and dietary recommendations to avoid all peanut products. Early signs of anaphylaxis were explained and the recommendation of immediate use of EpiPen rather than Benadryl was made to the parents. Information about hidden sources of peanut allergens and instructions to avoid tree nuts were also provided. For the patient's milk allergy, it was recommended to follow a dairy product elimination diet until re-evaluation at 2 and 3 years of age.

Long term follow-up. At 3 years of age, a repeat skin test was negative for cow's milk but still positive for peanuts**.** A gradual reintroduction of dairy products was well tolerated.

A reevaluation at 6 years of age revealed that he had had no known peanut ingestion or anaphylactic shock. Prick test revealed persistent mild reactivity to peanuts but in vitro IgE antibodies to peanuts (CAP test) revealed concentrations below risk level for peanut anaphylaxis. An open challenge with increasing amounts of peanut products was performed in Short Stay Unit at Children's Hospital without eliciting an allergic reaction or anaphylaxis.

Based on this open challenge results the indication to carry Epi-Pen was discontinued. However, we recommended to avoid peanut products and tree nuts on a permanent basis.

Comment

When this patient came to us, the most important issue was the management of peanut anaphylaxis. Since the history of peanut anaphylaxis was clear and peanut sensitization was confirmed by skin testing, a comprehensive plan of peanut avoidance and prevention of anaphylaxis could be developed immediately. When the cause of an anaphylactic reaction can't be readily identified by history, elimination diets can be developed only after the possible causes have been identified through skin testing and in vitro measurement of specific IgE antibodies.

The in vitro test now offers information about antibody concentration that helps in assessing the risk for severe food reactions. The IgE concentrations that are associated with a high positive predictive value for severe reactions vary for each food allergen; this information is essential for the follow-up of patients and to determine at what point an open food challenge can be safely performed, and to determine if the continued use of EpiPen is warranted. In this patient, it was possible to discontinue the recommendation to carry EpiPen, but permanent peanut and tree nut avoidance was recommended. Peanuts are legumes and have a low incidence of cross reactivity with other legumes, but patients sensitized to peanut allergens are know to have a higher risk of becoming sensitized to tree nuts.

Dairy products were reintroduced sequentially when the skin test became negative. A negative skin test has a high negative predictive value for the absence of reactions upon exposure to the food tested. Since this patient did not have severe, acute manifestations of milk allergy, the reintroduction of dairy products ending with ingestion of cow's milk was performed at home. Sensitization to cow's milk, egg, wheat and soy remit in approximately 85% of patients by 3 years of age. Attempts to reintroduce these foods too early without prior testing may extend the state of sensitization. In older patients allergy to peanuts, nuts and seafood typically persists.

PATIENT 2

Food allergy in breast fed infants, atopic dermatitis and the allergic march from food allergy and dermatitis to respiratory allergies.

A 5-month-old black female with severe generalized skin rash since the second month of life was referred for an allergy/immunology evaluation. The patient was exclusively breast fed. A complete blood count and IgE measurement had revealed eosinophilia and an elevated IgE concentration for her age, but identification of possible allergens were not pursued and the skin rash was treated with topical medications only.

Laboratory test at 5 months af age revealed persistent eosinophilia and very elevated IgE concentrations (Table 1).

Table 1.

	3 Months	**5 Months**	**8 Months**	**12 Months**
WBC X 10^3	10.3	11.6	6.8	7.7
Eosinophils, %	22	19	17	15
IgE, I, U/mL	33	484	501	588

Skin prick testing revealed positive reactions to wheat, egg and fish. CAP testing revealed that she was also sensitized to cow's milk protein although skin testing was negative. Both parents were clinically healthy and had no evidence of allergy. Their IgE concentrations were not elevated and skin tests with foods and inhalant allergens were all negative.

An aggressive management of this patient's atopic dermatitis had failed to improve her condition; a dietary management of her food allergies was imperative. Several options were considered: a maternal diet avoiding all foods to which the patient was sensitized was considered almost impossible to implement. Since she was already sensitized to milk, partial whey hydrolysates were not indicated. However, extensively hydrolysed milk or even elemental formulas probably would be helpful if the patient had additional gastrointestinal allergy manifestations and failure to thrive. We opted for a soy-based formula despite the risk for eventual sensitization to soy. On this formula the patient improved significantly without any additional systemic or topical medication. She continued to tolerate this formula well and her IgE concentrations and eosinophilia remained stable.

After the first year of age, this patient developed symptoms of rhinits and recurrent wheezing that were associated with dermatitis exacerbations. She had become sensitized to mites and some

mold. Mite and mold prevention measures and management of her rhinitis and wheezing were added to her treatment.

Comment

Breast feeding is the best protection against developing food allergies in infancy. However, breast-fed babies can become sensitized to foreign food components in human breast milk, as this patient clearly demonstrates. One of the manifestations of food allergy is atopic dermatitis. This is an allergic disease that is most often caused by IgE and non-IgE-mediated food allergy and also by inhalant allergy. The principal inhaled allergens causing atopic dermatitis are dermatophagoides (house mite) allergens. The latter are usually implicated when symptoms of respiratory allergy are also present.
The patient described here had several risk factors to follow the "allergic march" from food allergy and atopic dermatitis to allergic rhinitis and asthma: elevated IgE, eosinophilia and early sensitization to food and/or inhalant allergens. Indeed, at the time she was evaluated her immune system was already committed to a T helper cell 2 predominance and development of further sensitization and allergic manifestations. Earlier intervention, close to the onset of symptoms, may have been more successful in preventing this development. Still, appropriate management of her allergies significantly improved her clinical condition without need for more aggressive treatment with systemic steroids or other immunosuppressive agents.

PATIENT 3

Eosinophilic gastroenteritis can be caused by\ non-IgE mediated allergy. Non-IgE-mediated sensitization can be detected by patch testing.

A three-year-old boy with chronic diarrhea and formula intolerance since infancy was referred for an allergy/immunology evaluation. After onset of diarrhea at 3 months of age he was placed on an elemental formula that improved his diarrhea. However, diarrhea started again after introduction of solid foods although he continued to avoid milk, egg and soy.

Examination of his past medical record revealed persistent peripheral and mucosal eosinophilia documented by biopsies. He had low normal total IgE concentrations and negative specific IgE antibodies to all foods tested. Patch testing in our clinic revealed negative reactions to milk and egg and positive reactions to soy, oatmeal, wheat and rye. He improved on an elimination diet adjusted to the results of the patch test.

Comment

A non-IgE-mediated eosinophilc gastroenteropathy with manifestations that range from eosinphilic esophaigitis to eosinophilic colitis should be suspected whenever there is persistent tissue eosinophilia at the site of major symptoms, with or without peripheral eosinophilia. In these patients, if no IgE sensitization can be documented, patch testing is indicated.

The history rarely reveals the possible food that causes adverse reactions since temporal relationship between food ingestion and symptoms is less clear than for acute IgE-mediated

reactions. Symptoms may take up to 3 days to appear after a food challenge. Conversely, an elimination diet may take up to 4 weeks to take effect due to the chronic inflammation of the gastrointestinal mucosa. The natural history of these types of reactions has not been well defined, but it is clear that patients may eventually grow out of this form of allergy too.