

FOOD ALLERGY IN CHILDREN

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ABSTRACT

Food allergy is understood as all the adverse reactions to food products triggered by the immunological mechanism. The immunological reactions include the mediated IgE mechanisms and non-Ig-E mechanisms. It is estimated that the frequency of food allergies in general population is of 3.5-4% and usually come out in patients showing also other atopic disorders. The gastro-intestinal barrier is made up of epithelial cells, mucin cells (IgA secreting), proteolytic enzymes and biliary salts. The factors influencing the digestive tolerance are classified in antigenic factors and factors related to the host. The most important food products determining the most of allergies during childhood are: milk, eggs, nuts, flour and soya. The clinical manifestations in food allergies are the anaphylactic reaction, respiratory, cutaneous and digestive manifestations. The paraclinical diagnosis is different depending on the mediated immunologic mechanism, and the exclusion of the involved allergen is the key element in managing the food allergies.

Key words: food allergy, anaphylactic reaction, allergen

The allergy represents a complex world leading to many interpretations, many conditions being interpreted as allergic disorders. By *food allergy* is understood all the adverse reactions to food products triggered by the immunological mechanism. The adverse reactions to food products include the food allergy and the non-allergic causes. The immunological reactions include mediated IgE mechanisms and non-Ig-E mechanisms. The non-allergic reactions include the *digestive intolerances* due to certain enzymatic deficiencies, intolerance to lactose and intolerance to fructose. The toxic food reactions represent a separate category, they are the result of mediated-histamine reactions caused by the various food toxins. [1]

1. Prevalence

The perception in general population is that

the food allergy prevalence is much higher, but in fact, they affect about 6-8% children of 0-3 years of age. [2] The researchers in their trying to determine a prevalence of food allergies in a certain population, on a group of 1834 subjects, children and adults, found out a 16.6% frequency.

An early survey carried out on a group of 480 children showed that the prevalence of food allergies was 8%, although 28% of the subjects showed allergic type non-specific symptomatology. [2]

In a recent survey carried out on two patient groups, a group with ages to 11 years and the other one with ages to 15 years, showed a frequency of 11.6% and respectively 12.4% of food allergy reactions. Out of these, the cutaneous tests were positive only on 5.1%, respectively 4.9%, and the

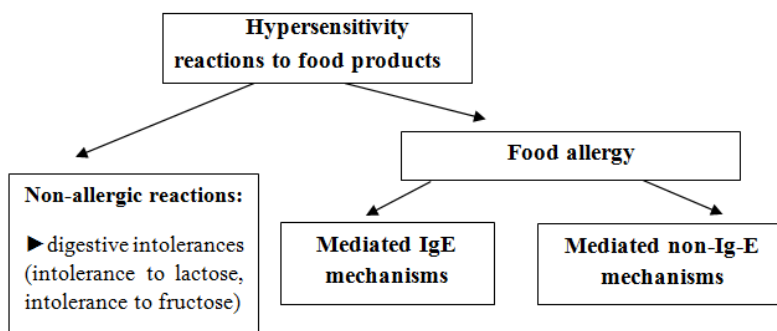


Fig. 1 Food allergy classification

exposure to food allergens indicated a frequency of 2.3% in both groups. [3]

Concluding we may estimate that the food allergy frequency in general population is 3.5-4%.

The allergy to cow milk proteins affects about 2.5-2.8% of children in their 1st year of life (2, 6, 7), the mediated Ig-E type reactions were present only in 60% of cases. The allergy to eggs affects about 1.3% of children [8] and the allergy to nuts affects about 0.8%. Worth mentioning is the fact that after the age of 5, the frequency of allergy to nuts is doubled. [5] The persistence of allergic symptoms varies depending on the involved food product. In case of allergy to milk, 85% of children have no symptomatology after the age of 8, and in the case of allergy to eggs, 66% of children have no allergic reactions after the age of 5. [6] Regarding the allergy to nuts, 20% of children have no symptoms after the age 10 (14-15) and 9% of the subjects recover at the age of adolescence [7].

The allergy to pollen named also *the oral allergy syndrome* represents a complex syndrome which appears by a crossing reaction following exposure to a thermally unstable protein, ingested with the unprepared fruits and vegetables. Of the patients with allergic rhinitis, 23-76% presents also the oral allergy syndrome to at least one food product [7].

The food allergies usually appear on patients with other atopic disorders. A third of the patients with moderate-severe *atopic*

dermatitis, shows food allergies by mediated Ig-E mechanisms and some surveys have indicated a correlation between the atopic dermatitis severity and the food allergy frequency.

The food allergy presence increases the probability of developing an allergic respiratory disorder; the most frequent correlation is with the *recurrent wheezing* [8].

2. Physiopathology

The food allergy represents an atypical response of the immune system at the level of the gastro-intestinal mucosa appeared following its interactions with ingested antigens. The immunological homeostasis is maintained by the immune and non-immune cells and by cytokines within a physical non-specific barrier at the level of the gastro-intestinal mucosa.

The gastro-intestinal barrier is made of *epithelial cells, cells with mucin* (IgA secreting), *proteolytic enzymes* and *billiary salts*. The immune response is mediated by *Peyer patches* (lymphoid structures organized at the level of the small intestine and rectum), IgA secreting, dendrite cells, macrophages showing antigen, the major histocompatibility complex (MHC) class I (MHC I), class II (MHC II), T lymphocytes, intestinal epithelial cells and other cytokine producing cells.

The stimulation of the immune system and the production of IgE type antibodies are determined by the intact food protein intake. During childhood, this phenomenon is

avored by a series of factors: increased intestinal permeability (immaturity of the gastro-intestinal barrier), insufficient production of gastric acid, reduced pancreatic and intestinal enzymatic activity [9].

The factors influencing the digestive tolerance are classified in antigenic factors and factors related to the host (age, genetic factors, gastro-intestinal flora). The most important antigenic factors are the antigen form (the soluble form increases the tolerance) and the dose (the increased sole dose and repeated small doses increase the tolerance). The cells involved in mediating the immune response are the T lymphocytes CD4+, CD8+, NK1.

The breastfed children develop an important immune response to food proteins in the first months of life, fact proved by the rapid increase of circulating antibodies together with the introduction in alimentation of milk and soya formulas.

The genetic factor influencing the digestive tolerance is sustained by surveys showing an increased concordance of the allergy to nuts in the case of monozygote twins [10].

The role of intestinal flora in digestive tolerance is demonstrated by the favorable clinical evolution of the patients with allergic diseases to which probiotics were administrated. The recent surveys show the fact that the breastfed children naturally fed by their mothers receiving probiotics much rarely develop allergic diseases, especially atopic dermatitis [11].

3. Food allergens

The most important food products determining the most of allergies during *childhood* period are: *milk, eggs, nuts, flour and soya*. Regarding *adults*, the most allergic food products are *nuts, walnuts, fish and clams* [1]. There are two important classes of *food allergens* determining the mediated IgE reactions.

Class I contains allergens sensitizing the GI mucosa; they are thermally stable and have a weight range between 10-70 kDa. This class comprises milk casein, nuts allergens, ovalbumin [12].

Class II contains thermally unstable allergens that can be ingested with the unprepared fruits and vegetables [13]. This class of allergens affects mainly the adolescents and adults

It was demonstrated the existence of a similarity between the tridimensional structure of the pollen epitope and of the epitopes from certain fruits and vegetables, explaining in this way the appearance of the oral allergy syndrome by mediated IgE crossing reaction [14].

4. Reaction mechanisms

There are 3 main reaction mechanisms:

4.1. Mediated IgE type reactions

In an allergic reaction, by coupling the IgE antibody to Fc fraction of receptors at the level of mastocitary and basophil cells, chemical mediators are released such as histamine, leucotriens, cytokines, chemokines and protease [15].

The mediated IgE reactions have *two phases*:

- immediate from several minutes to 1 hour;
- latent from 6 hours to 24 hours after allergen exposure

4.2. *Mediated non-IgE reactions*, where T lymphocytes have the main role (mediated by cells);

4.3. *Mixed reactions* mediated both by cells (LyT) and humoral (IgE).

5. Clinical manifestations in food allergies

5.1 Anaphylactic reaction

It represents a very severe systemic allergic reaction with fatal potential. The anaphylactic reaction is accompanied in most of the cases by cutaneous symptoms such as: rash, angioedema, erythema but the absence of these reactions does not include the

diagnosis. For example, the cardio-vascular collapse cases can appear without cutaneous reactions [16]. As any other mediated IgE mechanism, the anaphylactic reaction may comprise the 2 immediate and latent phases (in children, 6% of reactions are two-phased) but it could not be demonstrated a correlation between the final severity and the intensity of initial symptoms.

5.2 Cutaneous manifestations

5.2.1 *Acute rash and angioedema* are the result of a mediated IgE mechanism, being the most frequent manifestations of food allergy [1]. They can have an evolution to become chronic in case the symptoms persist more than 6 weeks.

5.2.2 *The atopic dermatitis* is the consequence of an immunological mixed reaction – IgE and cellular. Usually it begins in childhood and it is characterized by periods of acutization and remission. The lesions are maculo-erythematous and papulovesicular with pruriginous character located at the face, scalp and extension areas level. A third of the children with moderate severe atopic dermatitis show also food allergies. The most frequent allergic food products associated with atopic dermatitis are the eggs, milk, flour, nuts, walnuts and soya. Two thirds of the children with atopic dermatitis and food allergies show intolerance to eggs.

5.2.3 *Herpetiform dermatitis* appears by the cellular mediated mechanism. The cutaneous lesions are polymorph, pruriginous, characterized by erythema, placards, papules and vesicles. It is frequently associated to intolerance to gluten (celiac disease) and the patients with herpetiform dermatitis may show IgA type anti-transglutaminase antibodies [17].

5.2.4 *Contact dermatitis* is a cellular mediated cutaneous manifestation that can be triggered by exposure to food products.

5.3 *Respiratory manifestations* are carried out by the 3 immunological mechanisms.

The main manifestations through mediated IgE mechanism are: rhinoconjunctivitis, larynx edema, cough and bronchospasm. The bronchial asthma is carried out by mixed mechanism and represents an increased risk factor in the emergence of the anaphylactic reaction. The respiratory manifestations can appear during inhalation of food antigens present in the vapors resulted following heat preparation of food products.

The Heiner syndrome appears following a mediated non-IgE reaction, the main involved allergen being the proteins from milk and consists of recurrent pneumonia, haemosiderosis, digestive hemorrhage, iron deficiency anemia and growth fail. The removal of milk from alimentation leads to symptom disappearance [18].

5.4 Gastro-intestinal manifestations:

5.4.1 *Immediate gastro-intestinal hypersensitivity reaction* is carried out by mediated IgE mechanism and includes acute symptoms such as nausea, abdominal pain, colic, vomit and diarrhea. The patients that associate the atopic dermatitis and food allergies with chronic exposure to antigen can show chronic vomits and growth fail.

5.4.2 *Oral allergy syndrome (Pollen-food allergy syndrome)* is a mediated IgE type manifestation appearing by a cross reaction due to the structural similarity between the pollen epitopes and some proteins from thermal unprepared fruits and vegetables. The allergy to the birch pollen can give a cross reaction with the proteins from apples, carrots, tomatoes, celery, kiwi, pairs, chestnut, almonds and nuts. The grass allergy can give cross reactions with tomatoes, watermelon and kiwi [19]. The main symptoms have a rapid debut, are of short duration and consist of oral pruritus, angiodema of lips, tongue, palate and pharynx;

5.4.3 *Eosinophilic esophagitis* appears by a cellular and humoral mixed mechanism and represents the most frequent type of

eosinophilic gastro-enteropathy. It is manifested by dysphagia, intermittent vomits, food refusal, abdominal pain, irritability, sleep disorders. The certitude diagnosis is morphopathologically applied (more than 24 Eo on field) [20].

5.4.4 *Allergic eosinophilic gastro-enteritis* appears by a mixed mechanism and can start at any age with the following manifestations: diarrhea, abdominal pain, anorexia, nausea, vomits, weight loss and growth fail [20]. Some patients have anemia and hypoalbuminemia, secondary to digestive hemorrhage and to exudative enteropathy. The biopsy reveals important eosinophilic infiltrate at the mucosa level.

5.4.5. *Allergic procto-colitis* is mediated non-IgE and appears during the first weeks of life. The symptomatology includes blood in stools and mucus to an apparently healthy child, the usual triggers being the cow milk and soya proteins.

5.4.6 *Enterocolitis induced by food proteins* appears via a mediated non-IgE mechanism. Most frequently, it starts in the first months of life. The involved proteins are casein, β -lactoglobulin, soya proteins but can also be involved other food products like rice, oat, chicken and fish meat. The symptomatology includes irritability, severe vomits, diarrhea, mucus and blood in stools, so that in breastfed children dehydration, lethargy, acidosis, hyponatremia appears. In severe cases, methemoglobinemia may appear. About 50% of the breastfed children allergic to cow milk proteins have allergy also to soya [21].

5.4.7 *Celiac disease* represents a chronic inflammation of the small intestine carried out by cellular immune response to gluten. The main haplotypes associated with celiac disease are HLA-DQ2 and HLA-DQ8. It is frequently associated with herpetiform dermatitis and the patients have a high risk to develop type I diabetes mellitus and auto-

immune thyroiditis [22]. Children with celiac disease not observing a strict gluten free diet have a high risk to develop non-Hodgkin lymphoma with T cells [22]. The symptoms include vomits, diarrhea, anorexia, growth fail and the disease can evolve in severe or subclinical forms. The certitude diagnosis is carried out by duodenal biopsy indicating the villositary atrophy, crypt hyperplasia and lymphoplasmocitary infiltrate.

6. Diagnosis

The positive diagnosis involves the clinical diagnosis and paraclinical diagnosis.

Clinical diagnosis is carried out a rigorous anamnesis (history of atopic disorders, disease history, symptomatology association with ingestion of a food allergen etc) and objective examination (signs and symptoms specific to cutaneous, respiratory and digestive affection).

Paraclinical diagnosis

For mediated IgE type reactions a skin-prick test is carried out; the specific IgE antibodies dosage (23), RAST radio-alergo-sorbent-test), oral food load test.

For mediated non-IgE type reactions - patch test, diet of eliminating the involved allergen, oral load test, biopsy.

Other tests: Upper digestive endoscopy, intake tests, stool analysis.

7. Therapeutic conduct

The elimination of the involved allergen is the key element in food allergy management. The main food allergens are: milk, eggs, nuts, walnuts, flour, soya, clams and fish. The parent and patient training in order to detect the hidden allergens is very important as 50% of the allergen ingestion is accidental (24).

Medication therapy in acute allergic manifestation consists in epinephrine manifestation (anaphylactic shock – 0.01 mg/Kgc), corticotherapy and antihistamines in cutaneous and oral manifestations.

Immunostimulation with allergen can be subcutaneously and sublingually carried out.

Future therapy consists in monoclonal anti-IgE antibodies, immunotherapy with recombined proteins and traditional Chinese medicine.

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