S.G. Makarova[1, 2], E.A. Vishneva[1, 2], L.S. Namazova-Baranova[1, 2, 3], A.A. Alexeeva[1, 2], T.V. Turti[1, 3], M.A. Snovskaya[1]
[1] Scientific Center of Children's Health, Moscow, Russian Federation
[2] Sechenov First Moscow State Medical University, Russian Federation
[3] Pirogov Russian National Medical Research University, Moscow, Russian Federation

Food allergies. Recommendations on supplementary feeding introduction in patients with food allergies and risk group children: what and when?

Author Affiliation:
Elena Aleksandrovna Vishneva, leading research fellow at the department of standardization and clinical pharmacology of the Scientific Center of Children's Health (Federal State Budgetary Research Institution), allergist-immunologist at the department of medical rehabilitation for children with allergic and respiratory diseases at the research institute of preventive pediatrics and medical rehabilitation of the Scientific Center of Children's Health (of the Russian Academy of Medical Sciences)
Address: 2/1 Lomonosovskiy Av., Moscow, 119991; **tel.:** +7 (499) 134-03-92; **e-mail:** vishneva@nczd.ru

Article received: 12.05.2014. Accepted for publication: 17.09.2014.

The article is dedicated to food allergies. There still is no accurate estimate of the socioeconomic burden of food allergies and its impact upon the healthcare budget despite increasing prevalence thereof and lack of clear prognostic criteria. The authors present a modern classification of predominant clinical manifestations based on pathogenetic mechanisms of development. They describe therapeutic approaches, propose recommendations on diet broadening for both patients with food allergy manifestations and risk group children, define cross-sensitization and discuss a problem of non-immune reactions to foods.
Keywords: *food allergy, tolerance, food allergens, cow milk protein, therapeutic formulae, panallergens, cross-sensitization, risk group children, elimination diet, supplementary feeding, diet, tolerance window.*

INTRODUCTION

Food allergy (FA) is becoming an increasingly important public health issues because it is a pathogenetic basis of a number of diseases. There is currently no precise socio-economic evaluation for this issue, and the epidemiological data vary considerably [1-4]. A meta-analysis of the studies published from January 1, 2000, to September 30, 2012, conducted in 2014 assessed the trends of incidence and prevalence of FA in European countries [1]. It has been shown that, according to survey data, that FA and its manifestations have a confidence interval (CI) of 17.0-17.6 for 17.3 and 5.7 - 6.1 for 5.9% of the participants (95%) respectively. The incidence of sensitization to food allergens, as measured by titer of specific immunoglobulins (Ig) of class E (sIgE) was 10.1% (95% CI 9.4-10.8), and according to the skin test, it was 2.7% (95% CI 2.4-3.0); a positive result was obtained in a provocative test with 0.9% of the cases (95% CI, 0.8-1.1). An increase in the incidence of food allergy was registered. The prognostic risk factors for development and resolution of FA have not been identified, but the gender, age, country of residence, hereditary background and the presence of comorbid allergic diseases are of doubtless importance [1].

According to the modern definition [2, 3], food allergy is a food product-induced pathological reaction based on immune mechanisms [specific IgE-mediated responses, cellular immune responses (non-IgE-mediated) or a mixed type of reaction]. The term "food hypersensitivity" does not reflect the pathogenic mechanisms of the FA, so its use in relation to an immunologically-mediated reactions to food is currently impractical. Food allergy is a

pathogenetic mechanism of the formation of a number of diseases and/or symptoms, and, consequently, is not a nosological diagnosis. Nevertheless, after the designation of the main nosological entity the full clinical diagnosis is appropriate to include the presence of food allergies, as it is becoming a determining factor for therapy tactics.

In most cases of FA, the causative allergens are food proteins, both simple and complex (glycoproteins), and, less often, polypeptides haptens that are combined with food protein. The molecular weight of most food allergens is 10 000-70 000 Da. The ability of dietary protein to act as an allergen in genetically predisposed individuals depends on the presence of "epitopes", the structures that can cause the activation of Th2 and production of IgE antibodies, in its composition. The number of protein molecules received in the internal environment matters, too. For example, the inconsistency of the barrier function of the gastrointestinal tract leads to excessive contact of immunocompetent cells with the protein antigens and subsequent sensitization.

The nature of the clinical manifestations of food allergy is due to its pathogenic mechanisms that are defined not only as the predominant age of the onset of pathological nosology symptoms, but also as a prognosis and its development peculiarities (Table 1) [2].

Food allergens may be any substances, often proteinaceous in nature, that stimulate the production of IgE or cellular immune response.

The so-called group of eight foods that commonly cause allergic reactions includes cow milk, eggs, soy, peanuts, nuts, wheat, seafood, and fish [2, 3, 5].

The allergen of leading clinical significance in the early childhood is cow milk protein (CMP) [3-8]. The peak incidence of true CMP allergy occurs in the first year of life, accounting for 2-3% of infants [6].

Virtually any protein component of milk can cause sensitization, but most often these are β-lactoglobulin, α-lactalbumin, bovine serum albumin, γ-globulin, and α- and β-caseins. The basic milk allergens hardly lose their biological activity after boiling, pasteurization, UHT (ultra-high temperature processing), and drying.

Feeding with infant formulas has a great significance in developing a CMP allergy in infants, leading to excessive intake of foreign protein that provokes an increase of reactive sensitivity of cells and tissues against immature intestinal barrier and the immune response. However, breastfed children may also develop clinically significant CMP allergies due to the penetration of food proteins in breast milk [3, 6, 7].

Prognosis for CMP allergies largely depends on the form of FA. For example, the incidence of building up tolerance to milk proteins in children with non-IgE-mediated CMP allergy in the first year of life can reach 100% by the age of 5. [9] IgE-mediated allergy is associated with a lower incidence of building up CMP tolerance [10, 11]. The least optimistic prognosis for building up CMP tolerance with IgE-mediated allergy is given by J.M. Skripaket al. who have analyzed the largest number of clinical observations (807): 19% by4 and 52% by10 years of age [12].

THERAPEUTIC APPROACHES TO FOOD ALLERGY

The etiological treatment of food allergy includes an exclusion of the allergy-causing products from the diet [2, 3, 5]. For a child allergic to CMP, a diet is formed that completely eliminates cow milk proteins [3, 5-8]. In case of breastfeeding, this is achieved by prescribing a milk-free diet to the child's mother. If mixed or artificial feeding in necessary, extensively hydrolyzed protein-based or amino acid-based mixtures are used. With mild cases of FA and a limited number of cause significant proteins, the elimination diet can be used as monotherapy. When moderate to severe reactions to foods, as well as the chronic course of allergic process, a complex pharmacotherapy is required according to nosological forms and peculiarities of clinical manifestations.

An elimination diet should be accompanied by monitoring of the child's physical development.

INTRODUCTION OF SUPPLEMENTARY FOODS FOR CHILDREN WITH FOOD ALLERGY

The principles of supplementary foods introduction (introduction of new products in the diet) for children with food allergies have some peculiarities. Since the major allergens of the first year are cow milk proteins, the products containing these proteins are not introduced in this age range, including as a part of supplementary foods [2, 3, 5].

It is inadvisable to use goat milk-based formulas and products as artificial feeding mixtures and as a part of supplementary foods in the elimination period of dietary therapy for children allergic to cow milk protein. The high risk of developing allergies due to cross sensitization as well as direct reaction to goat milk proteins is proven [2, 3, 5-8]. It is also preferable not to use moderately hydrolyzed milk protein-based hypoallergenic mixtures [2, 3, 5-8].

Therapeutic extensively hydrolyzed protein-based or amino acid-based mixtures help provide an adequate diet for a CMP allergic infant in the first months of life, so the approximate terms of supplementary foods introduction are the same in sick children as in healthy [3, 6–8]. According to the modern perception of the optimal formation of food tolerance it is advisable to focus on these terms when introducing supplementary foods at not earlier than 4 and not later than 6 months [2, 3]. However, in each case, the time of introduction of supplementary foods is only determined individually based on the clinical picture and the phase of the disease (Pic. 1).

Depending on the nutritional status of the child and stool characteristics, the ***first supplementary product*** to be introduced is *mashed vegetables* or *milk-free porridge* (Pic. 2). Often the first supplementary product is a single fair color vegetable, mashed: zucchini, scallop squash, cauliflower, cabbage, Brussels sprouts, broccoli or a light-colored pumpkin.

In case of body weight deficit, a gluten-free milk-free porridge (buckwheat, corn or rice) may be the first supplementary food product, followed by *vegetables* (**second supplementary food**).

The next, **third supplementary food** introduced into the child's diet at the age of 5.5-6 months, is usually *mashed meat*. It is recommended to use specialized children's canned meat: horse meat, rabbit meat, turkey, pork or homemade mashed meat without broth. Mashed beef and veal is not introduced in the first year to children with CMP allergies.

Mashed light shade apples or pears can be used as the first fruit supplementary foods. However, due to the presence of organic acids, mashed fruit and fruit juices may cause irritation of the mucous membranes and the skin around the mouth, causing a short-term rash. In such cases, the introduction of this product should be postponed. The appearance of such reactions in the spring (during the flourishing of trees) should alert an expert in the search to exclude a possible cross sensitization (see. below).

Supplement the diet with fruit juices is usually also postponed, especially in children with gastrointestinal symptoms or FA.

An example of safe, well-tolerated products with low immunogenicity that can be used in the nutrition of children at risk of atopic disease, and as part of therapeutic diets for patients with allergic diseases is “Frutonyanya” product line (Progress JSC, Russia). Safety and tolerability of this line of supplementary foods (including fruit and vegetables, meat and cereal based products) have been confirmed in a study conducted in the Scientific Center for Children's Health in 2011 [13].

Cross-sensitization to various food products and other allergens (mainly epidermal and pollen) have a great practical significance. Cross-sensitization was previously attributed to the biological proximity of certain animals and plants. However, in recent years proteins were discovered that are widespread in flora and fauna, and that cause cross-allergic reactions to plant and animal species distant in the biological classification. These animal-based "panallergens" include tropomyosin and parvalbumin (Table. 2). In flora, protective proteins are widespread, including pathogenic (e.g. chitinase) proteins, replacement (reserve) proteins, as well as non-specific lipid carriers (lipid transporting proteins), identical in different parts of various plants (seeds, fruits, pollen, tubers; see. Table 2).

The development of supplementary foods enriched with pre- and probiotics, as well as microelements greatly enhances the potential for dietary impact (see. Pic. 2) [14-16].
Food allergens may alter the antigenic properties of a product during cooking. For example, protein denaturation during heating of the product results in the protein losing its allergenicity. That is why cases when heat-processed mashed fruit and vegetables are better tolerated by infants is better than raw mashed fruits or vegetables are often in clinical practice.

The basic principles of complementary feeding introduction

1. Each new product is introduced into the child's diet gradually, allowing 1-2 weeks for adaptation.
2. Only monocomponent products are used. New products are introduced into the diet one by one.
3. The new product is first introduced in the infant's diet in an amount not exceeding 5 ml (g), preferably in the morning feeding, to be able to estimate the tolerance to it during the day (appearance or intensification of skin rash, changes in stool, etc.). In the absence of an allergic reaction, the volume of new product is increased by 10-30 g every day for 5-7 days until the age recommended norm is reached.

At the stage of the diet expansion in remission in patients with severe manifestations of food allergy and suspected multiple sensitization, in order to address the issue of the possibility of the introduction of potentially allergenic food products such as eggs, wheat, soy and other, a specific IgE analysis can be carried out [17].

COMPLEMENTARY FOOD INTRODUCTION TO CHILDREN AT RISK OF DEVELOPING ALLERGIES

Children with family history of atopic disease comprise the risk group The risk is especially high in the cases where at least one of the closest relatives is allergic [2, 3, 5, 18, 19].
In this group, it is necessary to implement measures aimed at preventing an early onset of atopic disease. Nutritional approaches to these children have changed in recent years. Exclusive breastfeeding until the age of 4-6 months is considered an important measure for preventing allergies in children. There has been no convincing evidence of the preventive effect of a strict hypoallergenic diet of the mother during pregnancy in preventing the development allergies in the child: if possible, a full and varied diet is recommended [2, 3, 19]. On the contrary, there is accumulating evidence that the exclusion of certain products in the mother's diet may increase the likelihood of developing allergies and asthma in infants [20]. The results of individual studies show a decrease in the frequency of allergies in infants whose mothers' diet was enriched with omega-3 polyunsaturated fatty acids and dietary fiber [21, 22].
For mothers in the risk group during the breastfeeding period, it is advisable to create a rich and varied diet with a limited use of the most common allergens, including CMP-containing foods.
The use of partially or extensively hydrolyzed mixtures in the nutrition of children at risk of atopic disease receiving artificial or mixed feeding should be a mandatory preventive measure [2, 3, 6-8] in the age of under 6 months; in later age, their effectiveness has not been proven. [2].
For children with high risk of developing atopic disease deprived of mother's milk, it is recommended to use the proven mixtures with reduced allergenic properties. In the Russian Federation, mixtures based on moderately hydrolyzed milk protein are used for prevention of FA; their name containing the word "hypoallergenic" or the abbreviation "HA".
In recent years, based on studies and meta-analyses, the views on the terms of the introduction of supplementary foods and highly allergenic products risk children have been reconsidered. For example, in the 2000s a delayed introduction of a number of products (cow milk - after 1 year of age, eggs - after 2 years, peanuts, nuts and fish - after 3 years) was recommended [23]. In 2009, the results of various studies and meta-analyses allowed The American Academy of Pediatrics to publish certain amendments [24]. There is no doubt that the introduction of highly allergenic products in the diet can only be allowed for children with a good tolerance towards other kinds

of supplementary foods, the absence of manifestations of food allergy, otherwise - only after consulting an allergist [25]. There is evidence that the introduction of supplementary foods at the age of 4 months increases the risk of atopic dermatitis in infants of the risk group (by a factor of 2.5 compared with children to whom supplementary foods were introduced at a later age) [26, 27]. At the same time there is no evidence that delayed introduction of supplementary foods (4-6 months later) can reduce the risk of atopic disease in the future [27-30].

At present, the consensus of all the leading scientific community pediatricians and allergists is reached on the optimum timing of the supplementary foods introduction as part of an "early window" of forming food tolerance at the age of 4-6 months [2, 3].

Important rules for introduction of supplementary foods for children at high risk of developing allergic diseases are using monocomponent products and the principle of gradual expansion of the diet (adding no more than 1 product per week) [2, 3, 24, 25]. Timing of the introduction of certain types of supplementary foods match the range recommended for healthy children. Milk-free porridge is introduced, which is allowed to be diluted with a moderately hydrolyzed protein-based mixture (included in the child's diet) [2, 3].

The evidence accumulated to date suggests that it is advisable to refrain from introducing dairy products, eggs, soy, wheat, peanuts, nuts, fish and seafood in the early window of food tolerance. Whole cow milk should be avoided until the child reaches 12 months of age. These highly allergenic products may only be introduced in the diet provided that the infant tolerates other supplementary foods well [2, 3, 24, 25, 30].

NON-IMMUNE REACTIONS

Unlike true FA, pathogenesis of non-immune reactions to foods consists in nonspecific release of neurotransmitters (mainly histamine) from target cells of the allergy [2, 3]. That is why in the first year of life it is customary to avoid histamine-liberating products (citrus fruits, strawberries, tomatoes, spinach, celery, meat by-products) and use heat-treated mashed fruit and vegetables. The most frequent non-immune reactions develop after consuming foods rich in histamine, tyramine, histamine liberators such as fermented cheese, sauerkraut, dried ham and beef sausage, pork liver, canned tuna, herring fillets, spinach, tomatoes, cheese (roquefort, camembert, brie, cheddar), chocolate, cocoa beans, and others.

The cause of non-immune reactions to foods is often not the product itself, but the various supplements introduced to improve the taste, smell, color, or provide a longer shelf life. The most common food additives, often leading to the development of allergic and pseudoallergic reactions include colorants (E102, E104, E120, E122, E124, E132, E133, E155, etc.), sulphites (E220-227), nitrites (E249-252), and glutamates (E621-625).

In addition, it should be remembered that there may also be reactions associated with the presence of contaminants such as pesticides; fluoride, organochlorine, sulfur compounds; antibiotics; products of microbial metabolism; fungi, etc.

Non-immune reaction to food may be clinically similar to the manifestations of the FA, there may be a combination of both in one and the same patient with allergic reactions. For example, lactose intolerance can occur as a separate defect, but in some cases, secondary lactase deficiency accompanies a CMP allergy and is a manifestation of allergic intestinal lesions.

CONCLUSION

Thus, food allergy today is one of the most urgent problems in general pediatrics and allergy in particular. Pathogenesis mechanisms of allergic inflammation cause a wide range of FA symptoms and manifestations. Compliance with an elimination diet is the basis of both diagnostic and therapeutic approach with FA. The modern guidelines recommend adhering to the basic rules when introducing supplementary foods not only for infants with existing FA symptoms, but also for those of the allergy risk group. The optimum age for introducing supplementary foods corresponds to the "early window" of food tolerance formation from 4 to 6 months. Highly allergenic products are only included into the diet in the absence of allergic

inflammation and given a good tolerance towards the already introduced supplementary foods. In cases of poorly controlled atopic dermatitis or other FA symptoms it is necessary to consult an allergist for diagnostic testing, identifying the causative allergens and developing further tactics of pharmacological and nutritional therapy. It should be kept in mind that compliance with an elimination diet should be accompanied by monitoring of physical development of the child, and the nutritional plan should be developed with the involvement of a nutritionist.

CONFLICT OF INTEREST

The authors have indicated they have no financial relationships relevant to this article to disclose.

Table 1. Classification of food allergy manifestations (PA) [2]

Pathology	**Peculiarities of the development of clinical manifestations**	**Age**	**Prognosis**
IgE-mediated reactions			
Oral allergic syndrome (food allergy caused by sensitization to pollen)	Itching, swelling of the light is limited to oral	The onset of manifestations after the establishment of pollinosis (less often in children than adults)	Both persistence and seasonal dependence are possible.
Nettle rash/angioedema	Ingestion or contact	Children suffer more often	Depends on the causative allergen
Rhinoconjunctivitis/asthma	Can accompany FA manifestations (rarely) Manifestations are possible when inhaling the allergen aerosol	Infants and children suffer more often than adults (with an exception of professional diseases)	Depends on the causative allergen
Gastrointestinal symptoms	Nausea, vomiting, abdominal pain and diarrhea caused by eating	Any	Depends on the causative allergen
Anaphylaxis	Rapid progressive multisystem response	Any	Depends on the causative allergen
Anaphylaxis with food allergies induced by exercise	Food only triggers anaphylaxis in case of further exercise	Children, adolescents	Persists
Mixed IgE-mediated and cellular responses			
Atopic dermatitis	Associated with food allergies in 30-40% of children with moderate and severe AD	More common in young children	Usually permitted at an older age
Eosinophilic gastrointestinal pathology	Symptomatology depends on the gastrointestinal tract involvement in the process, and the degree of eosinophilic inflammation	Any	Predominantly persists
Manifestations mediated by cellular responses			

Food induced proctitis, proctocolitis, enterocolitis	Mucus and blood in the stool	Mostly infants	Usually permitted at an older age
Food induced enteropathy	Chronic symptoms: vomiting, diarrhea, growth retardation, apathy Repeated impact after restriction: vomiting, diarrhea, hypotension (within 2 hours after administration)	Mostly infants	Usually permitted at an older age

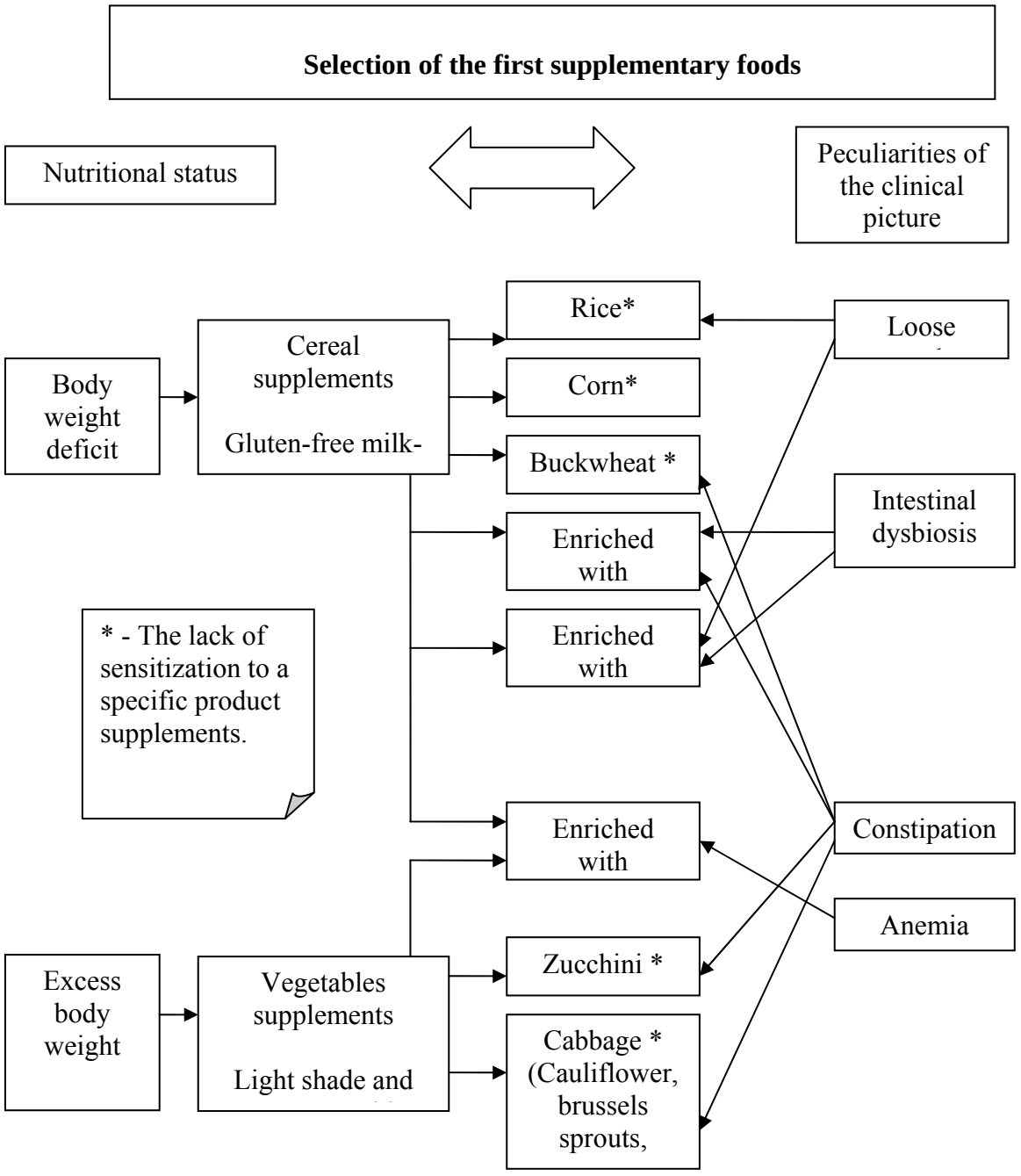
Note. AD - atopic dermatitis.

Table 2. Proteins that contribute to the presence of cross-sensitization to allergens of different origin

Proteins	**Food products and non-food antigens that induce cross-allergic reactions**
Tropomyosin	Crustaceans (shrimps, lobsters, crabs, crayfish) Arachnids (house dust mites) Insects (cockroaches) Shell fish (squid, oysters)
Parvalbumin	Fish (all kinds), amphibians meat, white poultry (rarely)
Bovine IgG	Milk Beef, lamb, venison
Lipid transporting protein	Peach, apricot, plum, apple, cereals, peanuts, walnuts, almonds, pistachios, broccoli, carrots, celery, tomatoes, cantaloupe, kiwi
Profilin	Peach, cherry, plums, celery, birch pollen, zucchini, latex
Chitinase I	Latex, banana, avocado, kiwi, chestnut, papaya, tomato, cherimoya, passion fruit, mango, wheat
Phenylcoumarin ether reductase Isoflavone reductase	Birch pollen, apple, peach, orange, lychee, strawberry, persimmon, zucchini, carrots

Pic. 1. Principles of introducing supplementary foods in children of the first year of life with food allergies

Период острых проявлений пищевой аллергии	*Period of severe FA manifestations*
Новые продукты прикорма не вводятся	*New supplementary foods are not introduced*
1. Диагностический этап диетотерапии	*1. The diagnostic step of nutritional therapy*
2. Элиминационный этап диетотерапии	*3. The elimination step of nutritional therapy*
4. Этап расширения рациона	*2. The diet expansion step*
Введение гипоаллергенных продуктов прикорма по индивидуальной схеме	*Introduction of hypoallergic supplementary products according to an individual plan*
Ремиссия	*Remission*
Подострый период заболевания	*Subacute period of the disease*



Note. * - The lack of sensitization to specific supplementary foods.

REFERENCES

1. Nwaru B.I., Hickstein L., Panesar S.S., Muraro A., Werfel T., Cardona V., Dubois A.E.J., Halken S., Hoffmann-Sommergruber K., Poulsen L.K., Roberts G., Van Ree R., Vlieg-Boerstra B.J., Sheikh A. EAACI Food Allergy and Anaphylaxis Guidelines Group. The epidemiology of food allergy in Europe: A systematic review and meta-analysis. *Allergy*. 2014; 69: 62–75.
2. Muraro A., Werfel T., Hoffmann-Sommergruber K., Roberts G., Beyer K., Bindslev-Jensen C., Cardona V., Dubois A., duToit G., Eigenmann P., Fernandez Rivas M., Halken S., Hickstein L., Høst A., Knol E., Lack G., Marchisotto M.J., Niggemann B., Nwaru B.I., Papadopoulos N.G., Poulsen L.K., Santos A.F., Skypala I., Schoepfer A., Van Ree R., Venter C., Worm M., Vlieg-Boerstra B., Panesar S., de Silva D., Soares-Weiser K., Sheikh A., Ballmer-Weber B.K., Nilsson C., de Jong N.W., Akdis C.A. EAACI Food Allergy and Anaphylaxis Guidelines Group. EAACI Food Allergy and Anaphylaxis Guidelines. Diagnosis and management of food allergy. *Allergy*. 2014; 69: 1008–1025.
3. Baranov A.A., Namazova-Baranova L.S., Borovik T.E., Makarova S.G., Yatsyk G.V., Skvortsova V.A., Turti T.V., Vishneva E.A., Alekseeva A.A., Roslavtseva E.A., Zvonkova N.G., Lukoyanova O.L., Snovskaya M.A. *Pishchevaya allergiya. Pod red. A.A. Baranova, L.S. Namazovoi-Baranovoi, T.E. Borovik, S.G. Makarovoi. Ser. «Bolezni detskogo vozrasta ot A do Ya»* [Food allergies. Edited by L.S. Namazova-Baranova. Series "Diseases of Childhood from A to Z"]. Moscow, 2013.
4. Prescott S., Allen K.J. Food allergy: riding the second wave of allergy epidemic. *Pediatr Allergy & Immunology*. 2011; 22 (1): 156–160.
5. Namazova-Baranova L.S., Alekseeva A.A., Altunin V.V., Antonova E.V., Arshba E.A., Akhmedullina D.I., Bakradze M.D., Baranov A.A., Botvin'eva V.V., Vazhnova I.M., Vishneva E.A., Voznesenskaya N.I., Volkov K.S., Galitskaya M.G., Gaivoronskaya A.G., Gevorkyan A.K., Goryachkina L.A., Deev I.A., Dvoryakovskii I.V., Dmitrienko E.G. et al. *Allergiya u detei: ot teorii — k praktike. Pod red. L.S. Namazovoi-Baranovoi. Ser. «Sovremennaya pediatriya: ot teorii — k praktike»* [Allergies in Children: from Theory to Practice. Edited by L.S. Namazova-Baranova. Series “Current Pediatrics: from Theory to Practice”]. Moscow, 2011.
6. *Diagnostika i lechenie allergii k belkam korov'ego moloka u detei grudnogo i rannego vozrasta: prakticheskie rekomendatsii. Pod red. A.A. Baranova, L.S. Namazovoi-Baranovoi, T.E. Borovik, S.G. Makarovoi*. [Diagnosis and Treatment of Allergy to Cow's Milk Proteins in Infants and Toddlers: Practical Advice. Edited by A.A. Baranov, L.S. Namazova-Baranova, T.E. Borovik, S.G. Makarova]. Moscow, Pediatr, 2014. 48 p.
7. Koletzko S., Niggemann B., Arato A., Dias J.A., Heuschkel R., Husby S., Mearin M.L., Papadopoulou A., Ruemmele F.M., Staiano A., Schappi M.G., Vandenplas Y. Diagnostic Approach and Management of Cow’s-Milk Protein Allergy in Infants and Children: ESPGHAN GI Committee Practical Guidelines. *JPGN*. 2012; 55: 221–229. Doi: 10.1097/MPG.0b013e31825c9482.
8. Vishneva E.A., Namazova-Baranova L.S., Turti T.V., Torshkhoeva R.M., Alekseeva A.A., Levina Yu.G. Allergy to cow's milk proteins. Approaches and treatment algorithms. *Voprosy sovremennoi pediatrii = Current Pediatrics*. 2012; 11 (3): 65–69.
9. Savilahti E.M., Savilahti E. Development of natural tolerance and induced desensitization in cow’s milk allergy. *Pediatr Allergy Immunol*. 2013; 24: 114–121.
10. Saarinen K.M., Pelkonen A.S., Makela M.J., Savilahti E. Clinical course and prognosis of cow’s milk allergy are dependent on milk-specific IgE status. *J Allergy Clin Immunol*. 2005; 116: 869–75.

11. Elizur A., Rajuan N., Goldberg M.R., Leshno M., Cohen A., Katz Y. Natural course and risk factors for persistence of IgE-mediated cow's milk allergy. *J Pediatr*. 2012 Apr 4 [Epub ahead of print].
12. Skripak J.M., Matsui E.C., Mudd K., Wood R.A. The natural history of IgE-mediated cow's milk allergy. *J Allergy Clin Immunol*. 2007; 120: 1172–7.
13. Turti T.V., Namazova-Baranova L.S., Borovik T.E., Davydova I.V., Snovskaya M.A. Nutritional possibilities of prevention of atopy in children during weaning. *Voprosy sovremennoi pediatrii = Current Pediatrics*. 2012; 11 (4): 38–46.
14. Makarova S.G., Borovik T.E. Balabolkin I.I., Katosova L.K., Lukoyanova O.L., Semenova N.N., Stepanova T.N. The modern view of the role of intestinal biocenosis with food allergies in children and approaches to its correction. *Rossiiskii allergologicheskii zhurnal = Russian Journal of Allergy*. 2012; 5: 36–45.
15. Makarova S.G. Prebiotics as functional food component of the child. *Voprosy sovremennoi pediatrii = Current Pediatrics*. 2013; 12 (5): 8–17.
16. Borovik T.E., Netrebenko O.K., Semenova N.N., Makarova S.G., Skvortsova V.A., Sergeeva S.N., Zvonkova N.G. Innovative approaches to feeding children with food allergies and those at high risk for the development of atopy. *Pediatriya = Pediatrics*. 2011; 90 (3): 91–99.
17. David M. Fleischer, Jonathan M. Spergel, Amal H. Assa, Jacqueline A. Pongracic. Primary Prevention of Allergic Disease Through Nutritional Interventions. *J Allergy Clin Immunol*. 2013; 1: 29–36.
18. Greer F.R., Sicherer S.H., Burks A.W. American Academy of Pediatrics Committee on Nutrition; American Academy of Pediatrics Section on Allergy and Immunology. Effects of early nutritional interventions on the development of atopic disease in infants and children: the role of maternal dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas. *Pediatrics*. 2008; 121: 183–191.
19. Muraro A., Halken S., Arshad S.H., Beyer K., Dubois A.E.J., Du Toit G., Eigenmann P.A., Grimshaw K.E.C., Hoest A., Lack G., O'Mahony L., Papadopoulos N.G., Panesar S., Prescott S., Roberts G., de Silva D., Venter C., Verhasselt V., Akdis A.C., Sheikh A. EAACI Food Allergy and Anaphylaxis Guidelines Group. EAACI Food Allergy and Anaphylaxis Guidelines. Primary prevention of food allergy. *Allergy*. 2014; 69: 590–601.
20. Bunyavanich S., Rifas-Shiman S.L., Platts-Mills T.A., Workman L., Sordillo J.E., Camargo C.A. Jr., Gillman M.W., Gold D.R., Litonjua A.A. Peanut, milk, and wheat intake during pregnancy is associated with reduced allergy and asthma in children. *J Allergy Clin Immunol*. 2014 May; 133 (5): 1373–82.
21. Palmer D.J., Sullivan T., Gold M.S. et al. Effect of n-long chain polyunsaturated fatty acid supplementation in pregnancy on infants' allergies in first year of life: randomised controlled trial. *BMJ*. 2012 Jan 30; 344: e184.
22. Makarova S.G., Vishneva E.A. Long-chain polyunsaturated fatty acid classes ω-3 and ω-6 as essential nutrients in different periods of childhood. *Pediatricheskaya farmakologiya = Pediatric pharmacology*. 2013; 10 (4): 80–88.
23. Committee on Nutrition. American Academy of Pediatrics. Hypoallergenic infant formulas. *Pediatrics*. 2000; 106 (2 Pt. 1): 346–349.
24. Committee on Nutrition American Academy of Pediatrics. Complementary Feeding. 6th ed. American Academy of Pediatrics. *Elk Grove Village, Il*. 2009.
25. Fleischer D.M., Spergel J.M., Assa'ad A.H., Pongracic J.A. Primary prevention of allergic disease through nutritional interventions. *J Allergy Clin Immunol*. 2013; 1: 29–36.
26. Fergusson D.M., Horwood L.J. Early solid food diet and eczema in childhood: A 10-year longitudinal study. *Pediatr Allergy Immunol*. 1994; 5 (6 Suppl.): 44–7.
27. Zutavern A., von Mutius E., Harris J. et al. The introduction of solids in relation to asthma and eczema. *Arch Dis Child*. 2004; 89: 303–308.

28. Zutavern A., Brockow I., Schaaf B. et al. LISA Study Group. Timing of solid food introduction in relation to eczema, asthma, allergic rhinitis, and food and inhalant sensitization at the age of 6 years: results from the prospective birth cohort study LISA. *Pediatrics*. 2008; 121: e44–e52.
29. Tromp I.I., Kiefte de Jong J.C., Lebon A. et al. The introduction of allergenic foods and the development of reported wheezing and eczema in childhood: the Generation R study. *Arch Pediatr Adolesc Med*. 2011; 165: 933–938.
30. de Silva D., Geromi M., Halken S., Host A., Panesar S.S., Muraro A., Werfel T., Hoffmann-Sommergruber K., Roberts G., Cardona V., Dubois A.E.J., Poulsen L.K., Van Ree R., Vlieg-Boerstra B., Agache I., Grimshaw K., O'Mahony L., Venter C., Arshad S.H., Sheikh A. EAACI Food Allergy and Anaphylaxis Guidelines Group. Primary prevention of food allergy in children and adults: systematic review. *Allergy*. 2014; 69: 581–589.