

**S.O. Zubchenko, S.R. Maruniak**  
*Danylo Halytsky Lviv National Medical University Ukraine, Lviv*

# Prevalence associative links of co-factors impact on food allergy manifestations

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**Topicality.** Today throughout the world is noted increase in the prevalence of allergic diseases. Quite a large percentage of the total amount of this disease falls on the formation of allergic reactions associated with the consumption of different foods, manifestations of food allergy (FA). According to the nomenclature of the European Academy of Allergology and Clinical Immunology, food allergy – is altered reaction to food products, caused by immunological and non immunological mechanisms [12]. Great importance in the formation of sensitization to food products has genetically determined penchant to allergies, in addition there are other risk factors – co-factors.

**Analysis of recent researches and publications.** Co-factors – allergen-independent factors that intensify the clinical manifestations of allergic reactions, including those associated with the consumption of food products. [15] Some, for example, serve as a trigger for starting of allergic reactions, when sensitized body gets even minimal doses of allergen necessary for their actual launch without co-factors [10]. According to many scientific studies found that often co-factors for the initiation of allergic reactions are physical activity, alcohol, drugs, primarily – nonsteroidal anti-inflammatory agents (NSAIDs) and related infectious diseases [9].

In modern scientific literature one can term: intensifying (stimulating) factors, related factors, additional factors, inductors, coordinators, x-factors. Thus, the specific term is not defined and not accept the classification of co-factors. Simons (2012, WAO) suggested to consider two types of factors: the first related to the patient (age, menstrual cycle, concomitant diseases, etc.), others – in fact co-factors (physical activity, concurrent medications, infections or stress) [16]. Other scientists have proposed to consider

four types of factors: lifestyle factors, receiving medications, concomitant diseases and factors specific to individual patients (individual) [17]. According to the German group of researchers led by Worm W. offered to single out as co-factors age of the patient and history of atopic [13].

In addition, there is no consensus on the leading mechanism of influence of co-factors for launching or intensifying manifestations of FA. Long-term studies have shown that there are three groups of mechanisms, of which the first is the most common:

1. Reverse of acquired clinical tolerance: long after the formation of clinical tolerance, allergic reactions can suddenly recover due to the impact of co-factors [3].

2. Reducing the threshold of sensitivity to allergens: allergic reactions occur only after consuming large quantities of food (allergen) and under the co-factor allergic reaction may occur at lower doses of allergen.

3. Increasing severity of FA: increases the severity of the reaction caused by the same dose of food or for the first time observed the development of anaphylactic shock.

Pathogenesis of initiating of clinical allergic symptoms depend on the type of co-factor. Research in this area continues.

At present described action mechanism of physical activity as an amplifier manifestations of allergic reactions, whose influence on different data amounts to 52 % [7]. Determined that due to activation of the sympathetic nervous system during physical activity a redistribution of blood begin from the internal organs and intestines to the skeletal muscles, heart and skin. [6] Absorbed peptides of food with allergenic properties are tolerant to a specific mast cells that are found in the intestine [18]. This is the reason for the lack of visible

symptoms when a person is at rest. Under the conditions of physical activity, absorbed allergen transported to other phenotypically different mast cells in the skin or skeletal muscle, increasing the probability of severe allergic reactions [11].

From scientific sources we know that effect of NSAIDs on the course of FA ranged from 9 % to 38 %. The most studied mechanism of action as a cofactor – aspirin. Aspirin can cause dysfunction of the gastrointestinal epithelial barrier initiate enhance its permeability, which leads to intense absorption of gliadin (the main protein of wheat with major allergenic properties) and increase its concentration in the blood (which depends on the dose of NSAIDs). Thus, this drug can accelerate the development of allergy symptoms, for example, in gliadin-sensitized patients [4]. Proved that probable role of aspirin and other NSAIDs in allergic reactions related to protein – lipid carriers (Eng. Lipid transfer protein, LTPs). The mentioned group of proteins often presented in plant foods, including peach (the main allergen Pru p3), nuts (the main allergen Ara h 9, Cor a 8) and so on. LTPs – often associated with systemic and severe allergic reactions to food and oro – pharyngeal urticaria [2]. In addition, LTPs are not sensitive to heat, so causing the reaction to the finished food. It was established that the combination of physical exercise and aspirin can significantly increase the risk of anaphylaxis in patients with mild FA.

Alcohol and allergic reactions are often linked, although the literature have not enough data on the mechanism of the effect of alcohol on the development of allergic reactions. According to a Spanish study on the effect of ethanol accounted for 12.5 % of all cases the impact of co-factors. Found that patients suffering from alcoholism, have higher serum levels of total and specific IgE antibody class compared with those that do not consume alcohol [5]. Determined that the ethanol molecule has a very low molecular weight, to initiate the development of the immune response. It is believed that ethanol acts as a part of haptens, although specific IgE to ethanol-protein conjugate today could not be determined. Ethanol can also directly affect the mast cells, causing their degranulation. This was confirmed in a study of biopsies of skin damaged urticaria after taking alcohol. [14] On the one hand, alcohol as an organic solvent, increases the permeability of biological barriers, including the intestinal wall, which can lead to falling in the blood toxins or undigested food proteins. The latter, acting as a classical allergens can trigger urticaria. On the other hand, strong drinks, as from a dose of their use, inhibit the enzymatic activity of the pancreas, especially in the use of large quantities of food or fatty food. An important function of the pancreas is digest proteins, by the way of destruction of peptide chain to the certain aminoacids. Getting into the blood, some aminoacids have no immunological activity and used intracellularly for the synthesis of their polypeptide chains. While absolute or relative lack of pancreatic enzymes consumed during meals foreign protein is not divided into individual aminoacids.

Since it formed large peptide complexes that do not pass through the intestinal barrier, however, is absorbed in high permeability due to the effects of alcohol.

According to the literature, much lower threshold hypersensitivity to food allergens was 2-2.5 % of patients during acute infection. Consider that it is caused by increased of body temperature that intensify blood circulation and increase allergen getting through physiological barriers. The presence of gastrointestinal infections accompanied by inflammatory changes appropriate mucosa, which in turn can lead to accumulation of large undigested proteins. Thus, the latter penetrating through the wall, come into contact with sensitized lymphoid structures. Also today, discussed some possible immunological mechanisms [8]. In the literature there is evidence that even the early stages of clinical infectious diseases or light infections were co-factors of FA manifestations.

Thus, consideration of co-factors are an important factor in the conduct of patients with symptoms of allergic reactions, including FA to gain the effectiveness from treatment and prevent serious complications.

**Aim.** To determine the prevalence of co-factors impact on the course of allergy in patients with symptoms of food allergy.

#### Materials and methods

To achieve the goal organized a comprehensive search of the scientific literature via PubMed, Scopus and ScholarGoogle. The works were selected by the following keywords: augmenting factors, co-factors, food allergy, risk factors, physical activity [1-18]. After working through literature a special questionnaire that contained a variety of issues regarding the manifestations allergopathological alterations (data depth allergic history, objective and subjective data, etc.), including their likely effect on the formation of a number of co-factors was developed. The questionnaire filled in all patients who were under the supervision of doctors Advisory Allergy and Clinical Immunology of the Lviv Regional Medical Center within 2013-2015 years and had at least once in their lives manifestations of food allergy. Patients performed the general laboratory, instrumental and specific immunological tests, namely: skin prick tests (SPT), determination of total and specific serum immunoglobulin IgE (sIgE). Prick tests performed by allergen extract (Diater, Spain) determination of total IgE i sIgE was performed by ELISA using test kits «Euroimmun». **For the detection of species-specific allergen components used** immunofluorescence method ImmunoCAP ( «Phadia AB», Sweden). All researches were carried out in stages by A WAO-ARIA-GA2LEN consensus document on molecular-based allergy diagnostics [1]. Material of the study was serum.

#### Results and discussion

Revealed that during the said period was 104 patients with recurrent manifestations of allergic reactions to food, including 57.2 % of men and 42.8 % women, aged 5 to 64 years. Most patients reported allergic reactions to the appearance of several types of food (an average of 3-4 different). The

most common were allergies to vegetables and fruits (apples, pears, carrots, celery, etc.) – 72 %, nuts – 37 %, peanuts – 19 %, wheat products – 13 %, fish – 3 %.

63 people who filled out questionnaires had verified diagnosis in the past, namely 67 % – hay fever, 48 % – perennial allergic rhinosinusitis, 32 % – atopic dermatitis, 11 % – atopic asthma. Another 37 persons who applied for advice first, were gradually made all the necessary specific allergological diagnostic tests, including (if necessary) component diagnostics. Note that from them in 5 (4.8 %) patients allergic diagnosis is not confirmed, then was diagnosed with various disorders of functioning of the digestive system and is recommended to consult appropriate professionals. It is obvious that in these patients manifestations of «undesirable» reactions to food products were functional in nature. In 2 (2.02 %) patients based on component research verified true FA to peach (major -Pru p 3), peanuts (major allergen -Ara h 3). In 97.97 % – against the main diagnosis – cross-linked FA with detected minor allergens – proteins of different species with a similar structure (most often – known pollen-food syndrome).

Analysis of survey data remaining 99 patients showed that co-factors influence on the course of FA was noted in 34 patients (34.3 %), including 20 (20.2 %) patients gain associated manifestations of allergic reactions to foods with co-factors from questionnaire and 14 (14.1 %) patients showed allergic reactions after consumption of a particular food only after the action of co-factors.

15.1 % noted the combined effect of co-factors and in most cases – a combination of regular receiving NSAIDs with increased physical activity or alcohol consumption.

According to the results of research (Table 1), the most common co-factor defined receiving NSAIDs -21.2 %: 8.1 % – only NSAIDs and 6.1 % – NSAID in combination with alcohol acceptance or combined with increased physical activity.

These patients reported different severity of clinical symptoms, from mild manifestations of urticaria to angioedema (compared to the combined effects of NSAIDs + alcohol). In second place precipitating factor advocated consumption of alcohol (usually wine) – 13.1 %, of which only alcohol 4.04 %. Symptoms in these patients was mainly in the form of urticaria with different localized skin rash (35.3 %) or oro-pharyngeal urticaria (24.2 %). Effect of physical activity was identified in 10.1 %, of which only enhanced physical activity at 3.03 %, mostly in the form of skin manifestations. Less commonly the effects of stress on the

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<i>Table</i>		
<b>Analysis of the prevalence impact of co-factors on the symptoms of allergic reactions to food (by personal data)</b>		
<b>Co-factors</b>	<b>Severity of FA</b>	<b>Prevalence (%)</b>
NSAIDs	+ / ++	8 (8,08 %)
NSAIDs + alcohol	+ / +++	6 (6,06 %)
NSAIDs + physical activity	++	6 (6,06 %)
Alcohol	+ / ++	4 (4,04 %)
Physical activity	+ / ++	3 (3,03 %)
Stress + alcohol	+ / ++	2 (2,02 %)
Intestinal infection	+	2 (2,02 %)
NSAIDs + physical activity + alcohol	++ / +++	1 (1,01 %)
Menstruation	+	1 (1,01 %)
Other medicines	++	1 (1,01 %)

background of alcohol consumption – 2.02 %, intestinal infections accompanied by fever – 2,02 %, other medicines – 1.01 % (receiving b-blockers) and menstrual period – 1.01 %. The combination of the impact of three co-factors identified in 1.01 % of individuals.

### Conclusions

1. Based on questionnaire data revealed that the prevalence of co-factors impact on the manifestation of food allergy was 34.3 %.

2. The most common co-factors determined regularly receiving NSAIDs (21.2 %), alcohol (13.1 %), increased physical activity (10.1 %) or a combination of these co-factors.

3. Association co-factors impact symptoms of food allergy accompanied by different clinical symptoms, but with the advantage of urticaria (35.3 %) or oro-pharyngeal urticaria (24.2 %).

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*S. O. Zubchenko*

*Ph.D.*

*Danylo Halytsky Lviv National Medical University*

*st. Pekarska, 69-B, Lviv, Ukraine, 79010*

*tel.: +38 (067) 670-66-43*

*e-mail: svitlana\_zu@meta.ua*