International Journal of Research in Agricultural Sciences
Volume 4, Issue 1, ISSN (Online): 2348 – 3997

Food Allergy, Classification, Symptoms, Diagnosis and Prevention – Review

Wedad Q. AL-Bukhaiti[1*], Anwar Noman[1,2],Amer Mahdi[1,3], AL-Farga Ammar[1,4]
[1]State key Laboratory of Food Science and Technology & School of Food Science and Technology, Jiangnan University, 1800 Lihu Avenue, Wuxi 214122, P.R.China
[2]Department of Agricultural Engineering, Faculty of Agriculture, University of Sana`a, Sana`a, Yemen
[3]Department of Food Science and Technology, Faculty of Agriculture, Sana'a University, Sana'a, Yemen
[4]School of Food and Biological Engineering, Jiangsu University, Zhenjiang 212013, PR China
*Corresponding author email id: wedadqasim@yahoo.com

Date of publication (dd/mm/yyyy): 14/01/2017

Abstract **— Food allergies, defined as an immune response to food proteins, affect as many as 8% of young children and 2% of adults in westernized countries, and their prevalence appears to be rising like all allergic diseases. In addition to well-recognized urticaria and anaphylaxis triggered by IgE antibody-mediated immune responses. In this review, we highlight on the Food allergy: Classification, Symptoms, Diagnosis, and Prevention, because of the importance of this issue and its impact on human health.**

Keywords **– Food Allergy, Classification, Symptoms, Diagnosis, Prevention**.

I. INTRODUCTION

A food sensitivity is an abnormal physiologic response to a particular food. That same food is safe for the vast majority of consumers to ingest. Food Allergies have Probably affected human beings since the dawn of time. The first well recorded case histories of food - allergic patients appeared in the early part of the twentieth century, but food allergies were largely ignored until even more recently [1]. Cow's milk (CM), hen's egg, wheat, and peanut allergies are the most common food allergies [2].common self-reported food allergy [3]. Reactions to foods are not new and have been described for two thousand years. The ancient Greek physician, Hippocrates, describes a reaction to milk in the 1st century. Anaphylactic reactions to egg and fish have been described as earlier as the 16th and 17th century [4].

Allergic diseases are regarded as a relevant health problem in all society. Allergic or hypersensitivity reactions to foods are triggered by the immune system, while food intolerances are due to lack of enzymes or induced by pharmacologically active substances in the food [5]. In the last two decades great efforts were undertaken to identify the allergenic proteins from plant derived and animal foods, to study their physicochemical characteristics and their interaction with immune cells. Consecutively, allergen databases were built and maintained to provide extensive information about allergens (e.g. www.allergen.org). It became evident, that only a minority of all known protein families contain food allergens [6]. plant food allergens the most relevant protein families are the 2S albumins, seed storage proteins identified from seeds (e.g. sesame seeds, sunflower seeds . . .) and nuts (e.g. hazelnut, walnut, brazil nut . . .) and peanut, followed by the non-specific lipid transfer protein (nsLTPs) representing the major allergens in fruits like peach and apple and tree nuts [7]. In addition the major allergen from fish, parvalbumin, is present in the majority of fish species [8].

II. CLASSIFICATION

Food allergy may be due to IgE-mediated, non IgE-mediated or a combination of IgE- and non IgE-mediated reactions. Clinically it can involve the skin, gastrointestinal tract, respiratory tract and/or cardiovascular system. The prevalence of food allergy varies from 1 to 10% in children less than 5 years of age, dropping significantly in the adult population, as some allergies are outgrown [9-10].Food sensitivities can be divided into two major categories: food allergies, which are abnormal responses of the immune system to certain food components; and food intolerances, which are any form of food sensitivity that does not involve immunologic mechanisms. The distinctions have practical implications from both a clinical and a regulatory perspective [1].

Adverse food reaction is a broad term representing any abnormal clinical response associated with ingestion of a food and they are further classified as food intolerance or food allergy based on the pathophysiological mechanism of the reaction. Food intolerance refers to an adverse physiologic response to a food and may be due to inherent properties of the food (i.e. toxic contaminant, pharmacologic active component) or to characteristics of the host (i.e. metabolic disorders, idiosyncratic responses, psychological disorder), they may not be reproducible, and they are often dose dependent. It is believed that food intolerance represents the majority of the adverse reactions to food. Food allergy refers to an abnormal immu- nologic response to a food that occurs in a susceptible host. These reactions are reproducible each time the food is ingested and they are often not dose dependent. Based on the immunological mechanism involved, food allergies may be further classified in a) IgE-mediated, which are mediated by antibodies belonging to the Immunoglobulin E (IgE) and are the best-characterized food allergy reactions; b) cell mediated when the cell component of the immune system is responsible of the food allergy and mostly involve the gastrointestinal tract; c) mixed IgE

mediated-cell mediated when both IgE and immune cells are involved in the reaction [11-12-13-14].

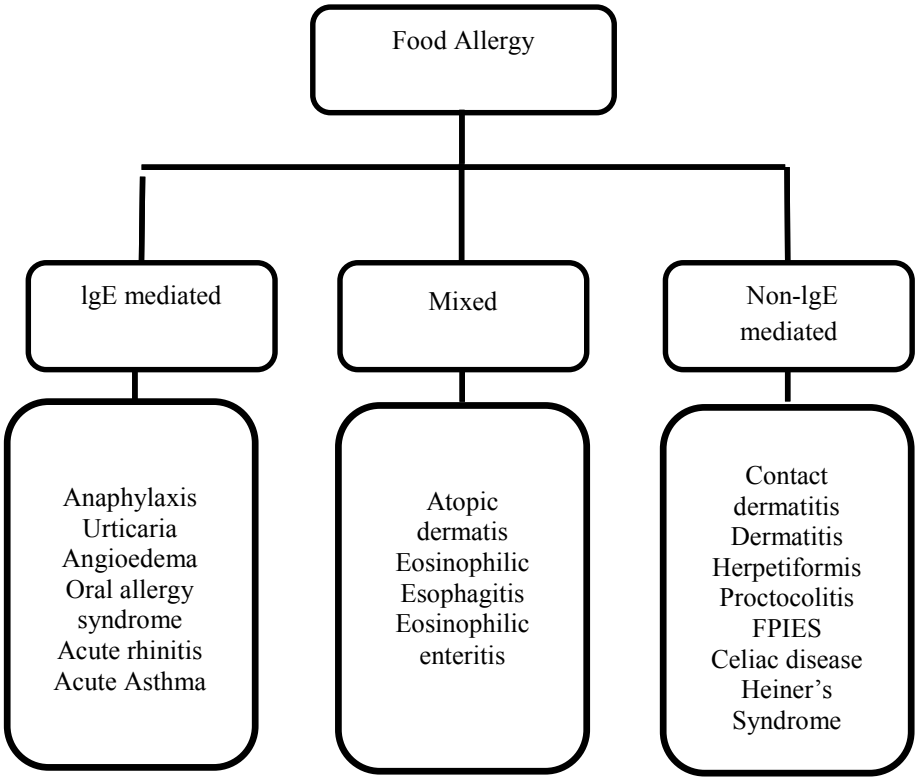

Fig. 1 Classification of food allergy [15].

Table:1 Classification of food allergic reactions [16].

IgE-mediated	Mixed IgE- & non-IgE-mediated	Non-IgE mediated (cellular)
Skin Urticaria Angioedema Erythematous morbilliform rash Flushing	Atopic dermatitis	Dermatitis herpetiformis Contact dermatitis
Respiratory Allergic rhinoconjunctivitis Acute bronchospasm	Asthma	Food-induced pulmonary hemosiderosis (Heiner's Syndrome)
Gastrointestinal Oral Allergy Syndrome Acute gastrointestinal spasm	Eosinophilic esophagitis (EOE) Eosinophilic gastritis Eosinophilic gastroenteritis	Food protein-induced entero-colitis syndrome (FPIES) Food protein-induced procto-colitis syndrome (FPIPS) Food protein-induced enteropathy syndrome Celiac disease
Cardiovascular Dizziness & fainting Anaphylaxis Food-associated, exercise-induced anaphylaxis		
Miscellaneous Uterine cramping & contractions Feeling of "pending doom"		

III. SYMPTOMS

The symptoms of delayed hypersensitivity reactions do not reach the level of severity involved in the more severe cases of immediate hypersensitivity reactions. However, the level of tolerance to the offending food is also very low for delayed hypersensitivity reactions. allergy can tolerate little milk, as their allergy may involve systemic and sometimes serious reactions. In contrast, lactose intolerance, which results from an enzyme deficiency in the small intestine, involves only gastrointestinal symptoms, and affected individuals can often tolerate appreciable quantities of milk in their diets[1].The best characterised food allergies involve the IgEmediated immune mechanism. A failure to develop oral tolerance to food allergens (antigens) may lead to an excessive production of IgE-antibodies to the specific food. IgE-mediated allergies present typically within minutes to hours after ingestion of the specific food. Patients typically present with the following symptoms or conditions [9]:

- Generalised: anaphylaxis, food dependent exercise-induced anaphylaxis.
- Cutaneous: urticaria, angioedema, flushing, acute contact urticarial.
- Gastrointestinal: oral allergy syndrome, gastrointestinal anaphylaxis, colic, vomiting & diarrhea.
- Respiratory: acute rhino-conjunctivitis, allergic asthma.

Recent estimates suggest that IgE-mediated food allergy affects 6% to 8% children and 3% to 4% adults imparting great clinical and social burdens [17-18-19-20]. Food allergy commonly manifests as adverse reactions of the gastrointestinal tract and the skin, including atopic dermatitis, acute urticaria and sometimes life-threatening anaphylaxis. However, the role of foods as triggers of asthma and rhinitis is less clear. Food-induced symptoms occur in approximately 2% to 29% of children and about less than 1% of adults with asthma [21]. Food sensitisation in early infancy could lead to the development of respiratory allergy and is a significant risk factor for asthma in 10% to 53% of cases [22-23-24].Allergic rhinitis has also become a frequent respiratory manifestation affecting 20% of food allergic population [24-25-26]. The epidemiology of food allergy is influenced by genetic, cultural and geographical dietary influences. Severe and fatal reactions can occur at any age but those at greatest risk are adolescents and young adults with asthma and a known food allergy to peanut, tree nut, fruits, milk, wine, vegetables and/or seafood. The foods most commonly causing breathlessness are hazelnut in Norway, Sweden, and Germany, fruits in Iceland, Belgium, Ireland, and Italy, and peanut in the USA [27].

Table 2: Symptoms associated with food allergic reactions [16].

Cutaneous	Pruritus Erythema/Flushing Urticaria Angioedema
Ocular	Pruritus Tearing Conjunctival injection Periorbital edema
Respiratory Upper	Pruritus Nasal congestion Rhinorrhea Sneezing Hoarseness Laryngeal edema
Lower	Cough Wheezing Dyspnea Chest tightness/pain
Gastrointestinal	Oral pruritus Oral angioedema (lips, tongue, or palate) Pharyngeal pruritus/tightness Colicky abdominal pain Nausea Vomiting Diarrhea
Cardiovascular	Tachycardia Dizziness Loss of consciousness/fainting Hypotension
Miscellaneous	Metallic taste in mouth Uterine cramping/contractions Sense of impending doom

IV. DIAGNOSIS

The patient's history can be a powerful tool, especially if the patient and family are objective historians. But the family's own perceptions and knowledge often influence history. Food allergy is clearly suspected more often than it is found by accurate diagnostic procedures and is confirmed by challenges in less than 20% of the time. In general, the history can be more helpful in IgE-mediated disorders, because these reactions occur so soon after food ingestion and because multiple target organs are affected. History is harder for food-protein induced enterocolitis, where symptoms occur hours later or days later in eosinophilic esophagitis. Thus a systematic review of the patient's diet is a highly useful first step. Important historical considerations include the following:

1.) Is the reaction reproducible? Does it occur each time the food is ingested? If not, it is an unlikely trigger.
2.) What is the time frame for the reaction? Immediate hypersensitivity reactions generally occur rapidly,

often within minutes and virtually always within 2½ hours.73 Mixed and T-cell mediated reactions have a characteristically delayed onset. Therefore patients with FPIEC typically begin to have symptoms later than 1 ½ hours after ingestion. Additional clinical history elements can be helpful. Timing of the first and last occurrences can reveal whether sensitivity is increasing or waning. These considerations together with the quantity necessary to trigger a reaction are helpful for planning diagnostic challenge procedures as well. Occasionally, the history can be complicated by the fact that trace amounts of foods may occur in certain products [15].

Many of the same diagnostic tools used today to diagnose food allergy were utilized 30 years ago, but these tools have been refined. Patient history and skin testing remain the cornerstone for diagnosing food allergy. However, the characteristics of food allergic disorders and food allergic symptoms.have been more precisely defined, which has improved the diagnostic accuracy of the medical history and its utility in guiding appropriate laboratory studies [28].

V. Prevention of Food Allergy

For prevention strategies to be effective, we need to understand the causative factors underpinning this rise. Genetic factors are clearly important in the development of FA, but given the dramatic increase in prevalence over a short period of human evolution, it is unlikely that FA arises through germline genetic changes alone. Strategies for the prevention of FA might include primary prevention, which seeks to prevent the onset of IgE sensitization; secondary prevention, which seeks to interrupt the development of FA in IgE-sensitized children; and tertiary prevention, which seeks to reduce the expression of end-organ allergic disease in children with established FA [29]. In the first years of the 21st century new immunological and epidemiological considerations were added to the allergy prevention argument. Among these was the concept that acquiring tolerance to foreign (food) proteins was an active rather than a passive process and the epidemiological observations that early introduction to allergenic foods did not necessarily lead to sensitisation or allergic disease. From 2004, a plethora of publications from birth cohort studies added to the evidence base that delaying the introduction of solids into the infants' diet did not reduce the risk of developing allergic disease [30].

Until relatively recently, it was believed that the best strategy to promote "outgrowing" food allergies was strict allergen avoidance, which would prevent "boosting" and sustaining the IgE response, and the concept of patients with different allergic phenotypes, i.e. those with different ratios of IgE directed at conformational and sequential epitopes, was not known [28].Over 80 years ago Grulee and Sanford reported that exclusive breast feeding in newborn infants reduced the development of atopic dermatitis 7-fold compared to infants receiving cow's milk . This led to a series of studies in the late 1980's and 1990's demonstrating the benefit of exclusive breast feeding, use of extensively hydrolyzed infant formulas and/or avoidance of major allergenic foods from the mothers' and infants' diets in the prevention of atopic dermatitis and milk allergy. These studies supported the hypothesis that delaying the exposure to major food allergens (milk, egg, peanut and fish) would allow the infant's immune system to mature, respond appropriately to food antigens, and decrease the likelihood of the child developing food allergies. Murine studies had shown that very early introduction of antigen to immature mouse pups could lead to sensitization and that by delaying allergen exposure, their immune system would not generate antibodies against foreign substances [16-31].

Food allergy has grown in rapidly in prevalence, currently affecting 5% of adults and 8% of children. Management strategy is currently limited to 1) food avoidance and 2) carrying and using rescue intramuscular epinephrine/adrenaline and oral antihistamines in the case of accidental ingestion; there is no FDA approved treatment. Recently, oral, sublingual and epicutaneous immunotherapy have been developed as active treatment of food allergy, though none have completed phase 3 study. Efficacy and safety studies of immunotherapy have been variable, though there is clearly signal that immunotherapy will be a viable option to desensitize patients. The use of bacterial adjuvants, anti-IgE monoclonal antibodies, and Chinese herbal formulations either alone or in addition to immunotherapy may hold promise as future options for active treatment. Active prevention of food allergy through early introduction of potentially offending foods in high-risk infants will be an important means to slow the rising incidence of sensitization. and then, oral, sublingual, and epicutaneous immunotherapy, have been described in a number of trials, as have recombinant vaccines, immunobiologics, bacterial adjuvants and herbal therapeutics [32].

Primary prevention may play a role in reducing from Food allergy, especially in high-risk infants. Recommendations as follows: Avoidance diets during pregnancy and lactation are not recommended at this time, but more research is necessary for peanut. Exclusive breast-feeding for at least 4 and up to 6 months is endorsed. Complementary foods can be introduced between 4 and 6 months of age. Because no formal recommendations have been previously provided about how and when to introduce the main allergenic foods (cow's milk, egg, soy, wheat, peanut, tree nuts, fish, shellfish) [33].

VI. Conclusion

Food allergy can be a significant impact on one's daily life and can even affect the 'lifestyle' of an entire family. Adverse reactions to food allergy may or may not be immune-mediated. The immune-mediated adverse reaction to food is defined as the food allergy (FA) which is roughly divided into IgE-mediated and non-IgE-mediated FA (NFA). As opposed to IgE-mediated FA, NFA primarily affects the GI mucosa. In

addition, there is far less of an understanding of NFA than IgE-mediated FA and its clinical relevance is likely underestimated in most cases. This is partly due to delayed onset of symptoms and subsequent difficulty in making the clinical association between offending food and clinical symptoms. The lack of easily accessible diagnostic measures also contributes to the problem.

REFERENCES

[1] Taylor, S.L., Emerging problems with food allergens. Food Nutrition and Agriculture, (26), 2000, pp.14-23.
[2] Urisu, A., Ebisawa, M., Mukoyama, T., Morikawa, A. and Kondo, N., Japanese guideline for food allergy. Allergology International, 60(2), 2011,pp.221-236
[3] Eriksson, N.E., Moller, C., Werner, S., Magnusson, J., Bengtsson, U. and Zolubas, M., Self-reported food hypersensitivity in Sweden, Denmark, Estonia, Lithuania and Russia. Journal of investigational allergology and clinical immunology, 14(1), 2004, pp.70-79.
[4] Sampson, H.A. Food allergy. Part 1: immunopathogenesis and clinical disorders. Journal of Allergy and Clinical Immunology, 103(5), 1999, pp.717-728.
[5] Muraro, A., Werfel, T., Hoffmann-Sommergruber, K., Roberts, G., Beyer, K., Bindslev-Jensen, C., Cardona, V., Dubois, A., Dutoit, G., Eigenmann, P. and Fernandez Rivas, M. EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. Allergy, 69(8), 2014, pp.1008-1025.
[6] Radauer, C., Bublin, M., Wagner, S., Mari, A. and Breiteneder, H. Allergens are distributed into few protein families and possess a restricted number of biochemical functions. Journal of Allergy and Clinical Immunology, 121(4), 2008, pp.847-852.
[7] Hoffmann-Sommergruber, K. and Mills, E.C.Food allergen protein families and their structural characteristics and application in component-resolved diagnosis: new data from the EuroPrevall project. Analytical and bioanalytical chemistry, 395(1), 2009, pp.25-35.
[8] Hoffmann-Sommergruber, K. Proteomics and its impact on food allergy diagnosis. EuPA Open Proteomics, (12), 2016, pp.10 -12.
[9] Levin, M.E., Gray, C.L., Goddard, E., Karabus, S., Kriel, M., Lang, A.C., Manjra, A.I., Risenga, S.M., Terblanche, A.J. and Van der Spuy, D.A. South African food allergy consensus document 2014. SAMJ: South African Medical Journal, 105(1),2015, pp.62-65.
[10] Gray, C.L., Goddard, E., Karabus, S., Kriel, M., Lang, A.C., Manjra, A.I., Risenga, S.M., Terblanche, A.J., Van der Spuy, D.A. and Levin, M.E. Epidemiology of IgE-mediated food allergy. SAMJ: South African Medical Journal, 105(1), 2015, pp.68-69.
[11] Sampson, H.A. Food allergy. Part 2: diagnosis and management.Journal of Allergy and Clinical Immunology, 103(6), 1999, pp.981-989.
[12] Sicherer, S.H. and Sampson, H.A. Food allergy: recent advances in pathophysiology and treatment. Annual review of medicine, (60), 2009, pp.261-277.
[13] Nowak-Wegrzyn, A. and Sampson, H.A.Adverse reactions to foods.Medical Clinics of North America, 90(1), 2006, pp.97-127.
[14] Lee, L.A. and Burks, A.W. Food allergies: prevalence, molecular characterization, and treatment/prevention strategies. Annu. Rev. Nutr., (26), 2006, pp.539-565.
[15] Cianferoni, A. and Spergel, J.M. Food allergy: review, classification and diagnosis. Allergology International, 58(4), 2009, pp.457-466.
[16] Sampson, H.A.Food allergy: Past, present and future. Allergology International, 65(4), 2016, pp.363-369.
[17] Sampson, H.A. Update on food allergy. Journal of Allergy and Clinical Immunology, 113(5), 2004, pp.805-819.
[18] Osterballe, M., Hansen, T.K., Mortz, C.G., Høst, A. and Bindslev-Jensen, C.The prevalence of food hypersensitivity in an unselected population of children and adults. Pediatric Allergy and Immunology, 16(7), 2005, pp.567-573.
[19] Zuberbier, T., Edenharter, G., Worm, M., Ehlers, I., Reimann, S., Hantke, T., Roehr, C.C., Bergmann, K.E. and Niggemann, B. Prevalence of adverse reactions to food in Germany–a population study. Allergy, 59(3), 2004, pp.338-345.
[20] Roehr, C.C., Edenharter, G., Reimann, S., Ehlers, I., Worm, M., Zuberbier, T. and Niggemann, B. Food allergy and non-allergic food hypersensitivity in children and adolescents. Clinical & Experimental Allergy, 34(10), 2004, pp.1534-1541.
[21] James, J.M. Respiratory manifestations of food allergy. Pediatrics, 111(3),2003, pp.1625-1630.
[22] Tariq, S.M., Matthews, S.M., Hakim, E.A. and Arshad, S.H. Egg allergy in infancy predicts respiratory allergic disease by 4 years of age. Pediatric Allergy and Immunology, 11(3),2000, pp.162-167.
[23] Roberts, G., Patel, N., Levi-Schaffer, F., Habibi, P. and Lack, G. Food allergy as a risk factor for life-threatening asthma in childhood: a case-controlled study. Journal of Allergy and Clinical Immunology, 112(1), 2003, pp.168-174.
[24] Pénard-Morand, C., Raherison, C., Kopferschmitt, C., Caillaud, D., Lavaud, F., Charpin, D., Bousquet, J. and Annesi-Maesano, I. Prevalence of food allergy and its relationship to asthma and allergic rhinitis in schoolchildren. Allergy, 60(9),2005, pp.1165-1171.
[25] Wang, J., Visness, C.M. and Sampson, H.A. Food allergen sensitization in inner-city children with asthma. Journal of allergy and clinical immunology, 115(5), 2005, pp.1076-1080.
[26] Bozkurt, B., Karakaya, G. and Kalyoncu, A.F. Food hypersensitivity in patients with seasonal rhinitis in Ankara. Allergologiaetimmunopathologia, 33(2), 2005, pp.86-92.
[27] Woods, R.K., Abramson, M., Bailey, M. and Walters, E.H. International prevalences of reported food allergies and intolerances.Comparisons arising from the European Community Respiratory Health Survey (ECRHS) 1991-1994. European Journal of Clinical Nutrition, 55(4), 2001, pp.298-304.
[28] Panel, N.S.E. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. Journal of Allergy and Clinical Immunology, 126(6), 2010, pp.S1-S58.
[29] du Toit, G., Tsakok, T., Lack, S. and Lack, G. Prevention of food allergy. Journal of Allergy and Clinical Immunology, 137(4),2016, pp.998-1010.
[30] Grimshaw, K.Food allergy prevention. Current Allergy & Clinical Immunology, 25(1),2012, pp.18-23.
[31] von Berg, A., Koletzko, S., Grübl, A., Filipiak-Pittroff, B., Wichmann, H.E., Bauer, C.P., Reinhardt, D. and Berdel, D.The effect of hydrolyzed cow's milk formula for allergy prevention in the first year of life: the German Infant Nutritional Intervention Study, a randomized double-blind trial. Journal of Allergy and Clinical Immunology, 111(3), 2003, pp.533-540.
[32] Kobernick, A.K. and Burks, A.W.Active treatment for food allergy..Allergology International, 65(4), 2016, pp.388-395.
[33] Fleischer, D.M., Spergel, J.M., Assa'ad, A.H. and Pongracic, J.A. Primary prevention of allergic disease through nutritional interventions. The Journal of Allergy and Clinical Immunology: In Practice, 1(1), 2013, pp.29-36.

AUTHOR'S PROFILE

First Author:
Wedad Q. AL-Bukhaiti
School of Food Science and Technology, Jiangnan University, Wuxi, Jiangsu, China. Tel: +86 15251516277