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REVIEW

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Food allergies in older people: An emerging health problem

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ABSTRACT

The prevalence of food allergy (FA) is steadily increasing worldwide. Literature about FA in older people is very scarce since this is predominantly considered as a pediatric condition. However, FA can persist and/or develop across the life course. Given the growing increase in prevalence as well as their persistence, it can be expected that FA will soon represent an important issue in older people. Several age-related factors may potentially mask FA symptoms and/or mediate them in older people. These include mechanisms related to immune senescence, inflammation, and changes in gastrointestinal function as well as micronutrient deficiencies and the use of multiple medications. A multidimensional approach, taking into account the complexity in older people, it is thus important in the evaluation and management of FA during aging. The main and safest strategy in the management of FA is the allergen avoidance since their ingestion may lead to reactions ranging from mild to life-threatening. However, food restrictions should be carefully evaluated, especially in older people, for the risk of nutritional deficiencies and undernutrition.

Keywords: Aging, Frailty, Oral allergy syndrome, Malnutrition, Food hypersensitivity

INTRODUCTION

The prevalence of food allergies (FA) is continuously growing worldwide. They are predominantly considered a pediatric condition and the problem is often neglected in older people. However, despite the onset of FA generally occur during childhood, they can also develop and persist across the life-course until older age. Several age-related factors can be potentially responsible for FA in older people. These include mechanisms related to immune senescence, inflammation, and changes in gastrointestinal function as well as micronutrient deficiencies and the use of multiple medications.[1-3] According to meta-analyses, in the last 2 decades, the presence of FA increased also in adult people, with a prevalence ranging from 3.5 to 35%.[4-6] Given the growing increase in prevalence as well as their persistence, it can be expected that FA will soon represent an important issue in older people.[7] Unfortunately, little is known about FA during older life, and the rare existing literature is mainly based on self-reported symptoms.

Adverse food reactions (Fig. 1) can be distinguished in immune mediated and non-immune mediated (primarily food intolerance). FA are immune-mediated adverse food reactions characterized by the lack of tolerance to food

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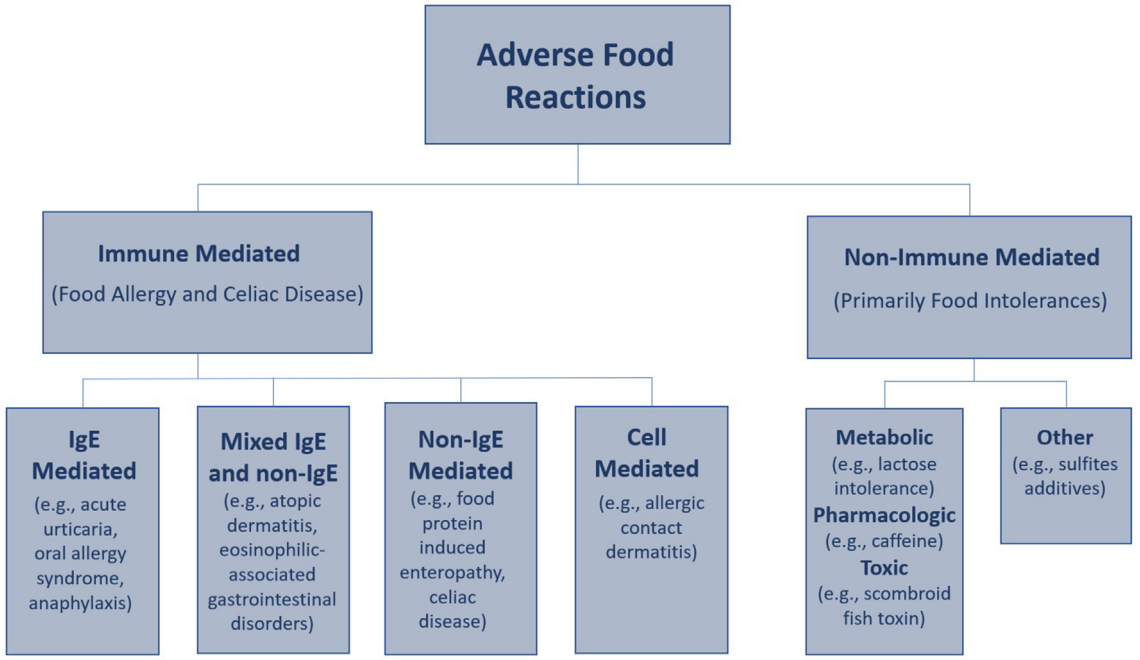

Fig. 1 Classification of adverse food reactions. Adapted from Anvari et al.[11] under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/).

proteins (eg, those found in milk, wheat, eggs, fish, peanuts, tree nuts, and soy). The main FA are those immunoglobulin E-mediated (IgE-mediated).[8] However, also other conditions like food protein-induced enterocolitis syndrome, a non–IgE-mediated allergy (Fig. 1), seem to affect a growing number of adults both in Europe and in the United States.[7] In adults, food protein-induced enterocolitis syndrome has been reported to be most often related to crustacean shellfish ingestion.[8] Another commonly comorbid condition, among adults with IgE-mediated FA, is represented by eosinophilic esophagitis, in which both IgE- and non-IgE-mediated mechanisms seem to be involved (Fig. 1).[7,8] Eosinophilic esophagitis impacts people of all ages including older people and since it is a chronic condition it is expected to be more frequently encountered in the older population that may have had the disease longer before the diagnosis.[9] Furthermore, alpha-gal syndrome, which is characterized by IgE sensitization directed to the alpha galactose epitope and commonly found in red meat after being bitten by a tick, represents another kind of allergic reaction affecting a growing number of adults and older adults worldwide.[7,10] Other adverse food reactions include those mixed IgE and non-IgE mediated (eg, atopic dermatitis, eosinophilic-associated gastrointestinal disorders) and those cell mediated (ie, allergic contact dermatitis). Finally, non-immune mediated adverse food reactions include those metabolic (eg, lactose intolerance), pharmacologic (eg, caffeine), toxic (eg, scombroid fish toxin) and those idiopathic/undefined (eg, sulfites additives)[8,11] (Fig. 1). Non-IgE mediated or mixed IgE should be also considered as part of the differential diagnosis of IgE-mediated FA even in older people.[12]

Symptoms of FA generally manifest within minutes but may take up to few hours after ingestion.[13–15] They include oral and perioral itching and burning, gastrointestinal symptoms like nausea, vomiting, diarrhea and severe abdominal pain, respiratory symptoms of wheeze and asthma, urticari.a and angioedema.[8,16,17] Among the different adverse food reactions, it is important to clearly distinguish the main typical symptoms of FA (ie, urticaria/angioedema, anaphylaxis, oral allergy syndrome, vomiting) versus food intolerance (ie, abdominal bloating, digestive problems, diarrhea; Fig. 2).

Recent evidence suggests the existence of phenotypic differences between pediatric-onset vs adult-onset FA. Overall, the most common FA

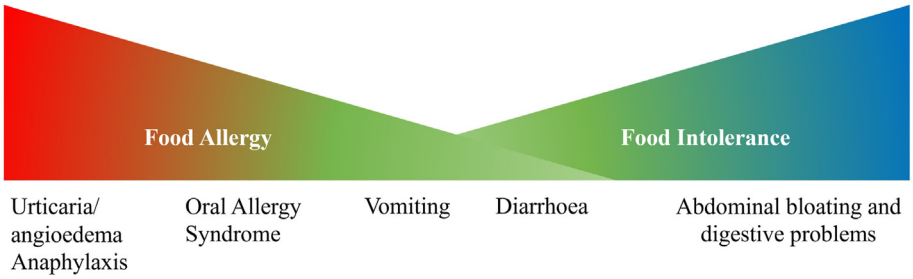

Fig. 2 Common clinical features suggestive of food allergy vs food intolerance in adults.

among adults with pediatric-onset FA include egg, peanut, and milk allergies. On the other hand, the most prevalent adult-onset FA include fish, shellfish, peanut, tree nut, and cow's milk allergies (Table 1).[18–20] In older people, despite the limited literature, the most prevalent FA seem to be shellfish and cow's milk allergies (Table 1). Recently, it has been outlined that there can be some differences in the diagnostic performances of specific tests for FA according to age.[12] Generally, it has been reported that serum levels of total IgE progressively decrease with age probably because of immune senescence processes starting from around 50 years of age. In fact, advancing age is accompanied by a natural involution of the thymus resulting in a declined output of thymic T-cells required for IgE production.[1] However, it has been pointed out that it varies widely depending on the allergen considered.[12] Both egg and cow's milk allergies have been formerly considered as very frequent conditions in early childhood but frequently disappearing over time. However, recent data reported milk allergy as a prevalent condition in older adults, in line with other age groups.[19] Other FA that have an onset in late childhood-young adulthood (eg, peanut allergy) tend to persist also during adult and older life (ie, till 70 years and over).[21] In fact, as age increases the probability of resolution of late-onset FA decreases.[12]

Since age-related immune senescence can lead to a formal decreased sensitization (eg, below the cut-off of 0.35 kU/l for what concerns specific IgE), it has been also suggested that the application of diagnostic cut-offs from literature into clinical practice should be evaluated with caution in older people.[1,12] In particular, Gupta et al[19] reported a FA estimated prevalence of 8.8% in the segment of the US population aged 60 and older, of which 5.5% developed FA during adulthood. Among the most prevalent FA, allergy to shellfish seems to highly persist through the life course (ie, 2.8% in the segment aged 18–29 years and of 2.6% in those aged 60 and older).[19] Interestingly, Gupta et al[19] also reported a prevalence of milk allergy of 1.9% in those people aged 60 and older, which is not far from the other age group considered. More recently, Hultquist et al.[18] reported that among adults with FA, older adults were more likely to have developed FA during adulthood. This is in line with previous reports suggesting that 1) FA can develop for the first time during adulthood and 2) FA tends to persist once developed.[8,22,23]

Childhood	Adults		Older adults*
-	Childhood onset	Adult onset	-
Eggs Cow's milk Peanut	Eggs Peanut Cow's milk	Fish Shellfish Peanut Tree nut Cow's milk	Shellfish Cow's milk

Table 1. The most prevalent FA by age group and time of onset.[18–20]

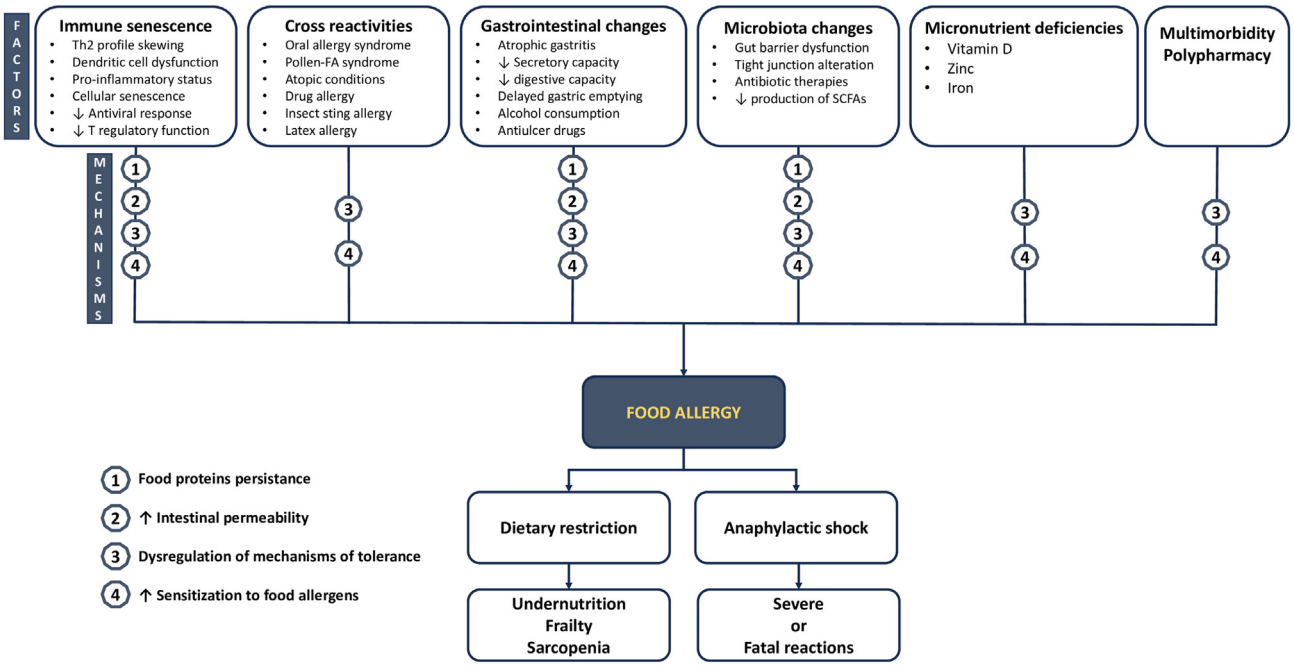

Fig. 3 Age-related factors, physiopathologycal mechanisms and consequences of food allergy in older people. Th2: T helper type 2; FA: Food allergy; ROS: Reacrive Oxygen Species; SCFAs: Short Chain Fatty Acids.

However, it should not be overlooked that these prevalence data are mostly from population-based surveys, frequently based on self-reported symptoms, and thus they could be influenced by individual perceptions. This occurs especially for milk allergy which can be confused with lactose intolerance by some people. Therefore, it is difficult to ascertain the exact prevalence of FA during adult and older life. Interestingly, Bakos et al[24] investigated the prevalence and risk factors for sensitization in older people living in nursing home (NH) in a small rural town in Hungary. The authors found a skin prick test (SPT) positivity to food allergens in 40 (41.7%) and specific IgE to food allergens in 27 (25%) NH residents. Regarding the most common food allergens, they found specific IgE sensitization to hazelnut in 9%, to milk in 5%, to casein in 8%, to carrot in 7% and to celery in 9% of NH residents. They also reported alcohol consumption being a risk factor for sensitization to food allergens in the study population. Huang et al,[25] reported a prevalence of specific IgE sensitization to food allergens of 10.89% in those people aged 61–70 years and of 13.36% in those people aged 71–90 years living in Western China. They also reported that people older than 70 years had significantly increased sensitization against cow's milk, mutton and sea-fish mix.

The high prevalence of specific IgE sensitization to food in older people found by these latter studies needs some considerations since, as above mentioned, it has been generally reported that specific IgE levels tend to decrease with age.[1,12] First, Bakos et al[24] hypothesized that the high prevalence of sIgE sensitization found in their population could have been due to the high use of antiulcer drugs (ie, proton pump inhibitors) in NH residents. As will be discussed in detail below, food proteins could remain undigested in hypoacidic conditions caused by these medications, then transiting to the intestine conformationally intact and eliciting the production of IgE antibodies by crossing the intestinal mucosa. Second, Huang et al[25] attributed the high prevalence of specific IgE sensitization to food they found in older subjects to the age-related changes in microbiota immune function. Third, it should be not overlooked the role of an age-related increased inflammatory status (ie, inflammaging) especially in older people with an increased frailty status like NH residents. As will be discussed in detail below, the abnormal release of pro-inflammatory cytokines may lead to a dysregulation of mechanisms of tolerance by altering intestinal permeability.[26,27] Finally, the diagnostic performance of specific IgE tests may be influenced by some cross-reactions in older

people.[12] Indeed, the results of diagnostic tests may be supportive in the identification of FA but should be evaluated with caution in older people.[12]

In some areas of the world where the consumption of raw or raw-marinated fish is very common, like Sicily (Italy) and Apulia (Italy), a high prevalence of Anisakis simplex sensitization has been reported in older people.[2,28] In particular, Anisakis is a nematode parasite found in the stomach of marine mammals which is involved in IgE-mediated reactions (eg, urticaria, angioedema, asthma, and, rarely, anaphylaxis), after exposure to the parasite.[29,30] Ventura et al.[2] reported a high percentage of positivity to SPT for Anisakis among older people in the Apulia region (Italy), with the majority of them presenting with urticaria. The high prevalence of Anisakis Simplex sensitization found by Ventura et al. could be probably explained by their inhabitant's habits to consume raw fish since late childhood and thus maintaining a great immune reactivity to this allergen.[2] Furthermore, it should be considered that a high SPT positivity to Anisakis in older people may be also explained as a cross-reactivity to other invertebrates including shrimps, worms, insects such as cockroaches or mites and airborne allergens.[28]

MECHANISMS UNDERLYING FOOD ALLERGIES ONSET IN ADULT AND OLDER LIFE

Aging is accompanied by a series of physiological and pathological changes that can potentially mask FA symptoms and/or mediate them (Fig. 3). Older people frequently experience gastrointestinal alterations, comorbidities, immune senescence, increased inflammation, leading to clinical manifestations that can be often difficult to frame and define. All these age-related changes may potentially be involved in the so-called "anorexia of aging" (ie, the loss of appetite and/or decreased food intake in late life),[31] and may thus be related to FA by overlapping with their symptoms. In other words, frequent and often overlooked conditions (eg, gastrointestinal symptoms, digestive problems, nausea, abdominal pain, and malabsorption syndromes) in older people may potentially be, at least partly, explained by an underlying FA. To date, in adults, eosinophilic esophagitis, which involves localized eosinophilic inflammation of the esophagus, most often presents with dysphagia,[8] which is in turn a condition commonly encountered in older people.[32]

Immune senescence can be envisioned as one of the potential mechanisms mediating FA in older people. Advancing age is characterized by a progressive decline in both innate and adaptive immune system often accompanied by an augmented inflammatory status (ie, the so-called "inflammaging").[26] Senescent cells are able to secrete proinflammatory cytokines with a shift from T helper type 1 (Th1) to T helper type 2 (Th2)-like cytokines which further contribute to inflammaging processes.[33] The transition towards a Th2 profile during aging can be thus potentially responsible for allergen sensitization as commonly occurring during childhood in which Th2 weighted imbalance is evoked as the major determinant of allergic response.[34] Inflammaging can also be responsible for the progressive alteration of intestinal permeability (ie, tight junctions) with the consequent dysregulation of mechanisms of tolerance. Furthermore, antibiotic therapies can disrupt gut microbiota composition causing dysbiosis and increasing intestinal permeability with a consequent enhanced sensitization to food allergens.[27]

Age-related gut microbiota alterations can promote host inflammation and consequently mitochondrial dysfunction with the release of mitochondrial damage-associated molecular patterns (DAMPs). The alteration in the mitochondrial function can further stimulate the production of pro-inflammatory molecules, thus creating a vicious circle, further increasing intestinal permeability by altering the epithelial tight junctions[35,36] and potentially promoting sensitization to food allergens.[37] Additionally, short-chain fatty acids (SCFAs) produced by gut microbiota have immunomodulatory properties and suppress the production of pro-inflammatory cytokines promoting a more tolerogenic phenotype.[38] Age-related alterations in gut microbiota have been also associated with a decreased production of SCFAs[35] thus potentially altering mechanisms of tolerance.

Oral tolerance is mainly established during childhood and is generally retained until older life. However, the ingestion of novel dietary proteins may lead to *de novo* sensitization in older people. Furthermore, adult people with seasonal allergic rhinitis may exhibit allergic (cross)reactions to plant-derived food antigens with a structural similarity to certain pollen proteins, constituting the so-called Pollen-FA Syndrome (PFAS),[7] including the mild form termed Oral Allergy Syndrome (OAS),[39] which are among the most common cases of adult-onset FA.[40] It has been recently outlined that PFAS and OAS show some differences in their manifestations.[7] In the OAS the allergens are usually labile to heat and stomach acids, thus resulting in lower rates of multiple-organ reactions or resulting in potentially life-threatening anaphylaxis. In fact, in the OAS symptoms are usually limited to oropharyngeal mild reactions. On the other hand, PFAS may take various forms ranging in severity despite limited data are available.[7]

As mentioned above, advancing age is also associated with physiological changes in gastrointestinal function like delayed gastric emptying which can prolong the period during which nutrients are absorbed.[41] The secretory capacity of the stomach also physiologically changes with aging, resulting in a decreased acid secretion which influences gastric protein digestion.[42] Additionally, atrophic gastritis commonly seen with aging can negatively affect the secretory capacity of the stomach thus leading to decreased digestive ability.[24] Atrophic gastritis can also result from chronic alcohol abuse and chronic use of antiulcer medications which also reduce the secretory capacity of the stomach and further enhances gastrointestinal permeability augmenting sensitization against food allergens.[24,43] Indeed, in the context of delayed gastric emptying and/or reduced gastric acid secretion, some proteins can persist the gastric transit conformationally intact potentially acting as food allergens.[24]

Little is known about the relationship between multimorbidity and FA in relation to age.[8] Hultquist et al[18] recently reported that adults with both childhood- and adult-onset FA showed highest rates of comorbidities including atopic conditions (ie, environmental allergies, atopic dermatitis/eczema, medication allergy, insect sting allergy, and latex allergy). Additionally, the presence of multiple clinical conditions may also negatively influence both symptom severity and response to treatment in case of food-induced anaphylaxis.[8] Chronic lung disease (ie, chronic obstructive pulmonary disease and recurrent pneumonia) may increase the risk of anaphylaxis and cardiovascular disease and has been reported to be a risk factor for death from anaphylaxis, especially in middle-aged and older people.[8,44] The concomitant use of multiple medications (ie, polypharmacy), which is generally more common in older people and frequently directly related to the management of multiple chronic conditions, has been also associated with increased rates of FA.[45]

Micronutrient deficiencies, frequently seen during aging, have been also identified as potential factors mediating sensitization to food allergens in older people.[46] Vitamin D, zinc and iron are acknowledged to have both immunomodulatory and antioxidant properties.[30] First, calcitriol (ie, the active form of vitamin D) modulates both innate and adaptive immune responses. In particular, calcitriol through T cells and antigen presenting cells seems to promote both tolerance by inhibiting inflammatory processes and the maturation of regulatory T cell subpopulations.[47] Second, zinc deficiency can promote a decrease of Th1 cytokines towards Th2 responses, potentially favoring sensitization to food allergens in older people.[48,49] Finally, iron deficiency has been associated with a diminished antibody response, predominantly in the Immunoglobulin G4 (IgG4) subclass, by inhibiting the activation of effector cells through incorporating allergens before binding to the IgE.[50]

DIAGNOSIS OF FA

The diagnosis of FA is a complex pathway, especially in older people in which concomitant conditions may overlap with FA complaints. The first step is represented by a comprehensive medical history and a focused physical examination. Medical history is pivotal to investigate the signs and symptoms probably involved in the sensitization to food allergens. It is thus important to explore the type of

symptoms and manifestation, their time of onset after food ingestion, the kind and quantity of food ingested, preparation method (ie, extensively cooked or not), as well as if the adverse reactions have been experienced more than once and only after food ingestion or also at other times.[8] A detailed evaluation is thus particularly important in older people since they are frequently characterized by multiple (often chronic) conditions, as well as signs and symptoms which can mutually interact in the definition of geriatric syndromes. In this context, the comprehensive geriatric assessment (CGA) can be envisioned as the instrument allowing the in-depth evaluation.

The United States National Institute of Allergy and Infectious Diseases (NIAID) expert panel, in its guidelines for the diagnosis and management of FA,[8] also suggests considering some complementary factors like exercise, alcohol consumption, and use of aspirin or nonsteroidal anti-inflammatory drugs when evaluating older adults. In fact, allergic reactions may be experienced in some cases only by those individuals ingesting specific foods in association with these factors. Obtaining information about the culprit food responsible for allergic reactions is extremely important since mainly eight types of food (ie, milk, eggs, fish, crustacean shellfish, nuts, peanuts, wheat and soy) account for approximately 90% of FA.[51] However, despite medical history and physical examination are useful to help the evaluation of FA, they are not sufficient to definitively make a diagnosis of FA.[8]

The subsequent step includes first-level tests like the SPT, in which a lancet is used to prick the skin under a drop of allergen. However, also in this case, SPTs as stand-alone are not enough to make a definitive diagnosis of FA since these tests are characterized by low specificity and low positive predictive value.[8] In the aging context, age-related changes in the skin (ie, atrophy, photoaging, decreased mast cells) may render challenging the execution of SPTs. As outlined by a position paper of the World Allergy Organization (WAO) on IgE allergy diagnostics and other relevant tests in allergy,[52] skin reactivity is decreased in older people and thus positive reactions tend to be smaller in this population. Additionally, the use of certain medications like antihistamines, tricyclic antidepressants or selective serotonin reuptake inhibitors, can further impact the results of the SPT (ie, decreased response).[38,39] Indeed, a non-damaged suitable skin area should be preferred, or alternatively *in vitro* testing should be considered.[53] Subsequently, second-level tests include blood tests measuring total IgE levels or allergen-specific serum IgE which can be used as supportive measures in case of FA suspicion but are not considered enough sensitive and specific for FA definitive diagnosis. Finally, the double-blind placebo-controlled food challenge (DBPCFC) is the *in vivo* test considered the "gold standard" for the diagnosis of IgE-mediated FA. The DBPCFC permits the identification of the causative allergen, the quantity of food needed to elicit a reaction, as well as the existence of other co-factors (ie, exercise-induced anaphylaxis).[54] However, DBPCFC is expensive and time-consuming, requires highly trained personnel and exposes the patient to potential severe allergic reactions (ie, anaphylaxis). Therefore, given the risk of severe reactions, DBPCFC must be performed in a medical setting with trained staff able to respond to anaphylactic reactions.[8,54] Single-blind and open-food challenges have been thus proposed as valid diagnostic alternatives to DBPCFC in the clinical setting but, in case of positivity, they need to be supported by both medical history and laboratory data.[8]

Unfortunately, in the FA scenario, there are a lot of non-standardized and unproven methods (ie, hair analysis, applied kinesiology, allergen-specific IgG4, cytotoxicity assays, electrodermal, or vega test) that are not recommended by the scientific community. These methods, being not validated for the diagnosis of FA, may in fact result in false positive or false negative diagnoses.[8,55] The implementation of these methods may thus lead to unnecessary dietary restrictions with adverse effects on nutritional status as well as the delay of the appropriate diagnostic process.

Among fourth-level tests, the basophil activation test (BAT) is widely used for research purposes but not yet implemented as a routine diagnostic test since there is a lack of large clinical studies on its diagnostic performance.[8,56] Recently, an epitope-level characterization of allergen-associated IgE and IgG responses has demonstrated promising results for allergy research and may potentially represent a good adjunct to current methodologies for FA diagnosis.[57]

Reference	Study design, country and sample	Aim	Relevant results
Europe			
Aurich et al., 2019[66]	Cross-sectional study; Europe; n = 1123 older anaphylactic patients (aged ≥65 years).	Describe anaphylaxis in patients aged ≥65 years.	The frequency of FIA in older adults was of 11% (n = 122 out of 1123 older anaphylactic patients). The main culprit food allergens were wheat (14%) and hazelnut (13%).
El Hanache et al., 2023[65]	Cross-sectional study; France, Belgium, Luxembourg, Switzerland; older people (aged ≥60 years) with FIA.	Describe the main allergens involved in FAs in older people, and risk factors, such as medications and comorbidities.	191 cases of FIA in older people. The most frequent allergens were mammalian meat and offal (31 cases, 16.2%). Legumes were reported in 26 cases (13.6%), fruits and vegetables in 25 cases (13.1%), shellfish in 25 cases (13.1%), nuts in 20 cases (10.5%), and cereals in 18 cases (9.4%). Anaphylaxis severity was grade II in 86 cases (45%), grade III in 98 cases (52%) and grade IV in 6 cases (3%) with one death. Alcohol intake, beta-blockers or nonsteroidal anti-inflammatory drugs were present in 61% of cases. Chronic cardiomyopathy (11.5% of the population) was associated with greater, grade III or IV reaction severity (OR 3.4; 1.24–10.95).
America			
Arroyo et al., 2021[64]	Cross-sectional; USA, older adults (aged 65 and older) ED visits n = 93,795 and hospitalizations n = 72,677 for anaphylaxis	Characterize trends in ED visits and hospitalizations for acute allergic reactions and anaphylaxis among US older adults from 2006 to 2014 and examine factors associated with severe anaphylaxis.	Frequency of ED visits for FIA among older adults was 6% (n = 5920 out of 93,795 anaphylaxis ED visits), and of 4.1% (n = 2956 out of 72,677 anaphylaxis hospitalizations) for hospitalization.

(continued)

Reference	Study design, country and sample	Aim	Relevant results
Asia			
Rathnayake et al., 2015[67]	Cross-sectional study; Sri Lanka; 311 institutionalized people aged ≥60 years.	Assess nutritional status, dietary diversity and lifestyle risk factors associated with undernutrition.	FA (OR: 8.0; 95% CI 3.9–16.2) significantly increased the risk of undernutrition.
Kim et al., 2016[68]	Cross-sectional; South Korea; older patients with FIA.	Examine regional differences in serum vitamin D levels and FIA incidence.	451 cases of FIA in older people. Incidence of FIA (per 100,000 person-years) was 1.8 (95% CI: 1.5–2.1) and the RR of FIA was 1.06 (95% CI: 1.01–1.12) in people ≥60 years. The FIA incidence was higher in rural areas than in urban areas.

Table 2. (Continued) Overview of main studies that explored food allergy consequences in older people. *FIA = Food induced anaphylaxis; FA = Food allergy; ED = Emergency department; OR = Odds ratio; RR = Relative risk; CI = confidence interval*

In summary, the diagnosis of FA in the routine clinical practice is often based on a combination of clinical history and the results of specific IgE testing and/or SPT.[11] In older people, SPT results must be carefully interpreted and positive results must correlate with clinical history of exacerbation to the causative allergen.[53]

MANAGEMENT AND CONSEQUENCES OF FA

Data on the consequences of FA in older people are very scarce. Food is considered among the less common causes of anaphylaxis in older people where drugs and insect bite/stings being the more frequent causes of severe or fatal anaphylaxis.[58,59] However, risk factors for severe and fatal anaphylaxis include old age probably as a consequence of underlying cardiovascular comorbidity and compromised physiological response.[58,60] In contrast to what is seen in younger people in which risk factors for severe anaphylaxis are determined by the presence of atopy and asthma, in older people exercise, alcohol or drugs have been reported to increase the risk for severe reactions.[61] Furthermore, several studies suggested that older people have an increased risk of adverse cardiac events after epinephrine use.[58,62,63] Nevertheless, it has been recently recommended a prompt treatment of anaphylaxis with intramuscular epinephrine in older people given their risk of severe or fatal anaphylaxis.[58] Table 2 presents an overview of the main studies that explored FA consequences in older people. Arroyo et al,[64] using data from the Nationwide Emergency Department Sample and the National Inpatient Sample in 2006–2014, documented a frequency of 6% of emergency department visits and of 4% of hospitalizations for food-induced anaphylaxis (FIA) among US older adults (ie, age ≥65 years). It has been recently suggested that patterns of FIA seem to be quite different in older people compared to younger groups, with seafood, mammalian meat, legumes, fruits and vegetables but also pollen-FA syndrome being the most frequent elicitors of FIA while reactions to nuts, milk or egg (typical in younger people) have been reported to be limited[61,65] (Table 2). Aurich et al,[66] using data from the European Anaphylaxis Registry, reported a prevalence of 11% of FIA in European older adults, with wheat, hazelnut and shellfish being the most frequent elicitors. Rathnayake et al[67] reported a positive association between self-reported FA and the risk of undernutrition (OR = 8.0; 95% CI 3.9–16.2) in a population of institutionalized older people living in Sri Lanka.

The main and safest strategy in the management of FA is the allergen avoidance since their ingestion may lead to reactions ranging from mild to life-threatening (ie, from oral and perioral itching to anaphylactic shock).[8] It becomes thus evident that food restrictions should be carefully evaluated, especially in older people, for the risk of nutritional deficiencies and malnutrition (ie, undernutrition). Food restriction may be further enhanced by the anxiety of avoiding even minimal quantities of food allergens (ie, trace elements) in food preparations.[69] Advancing age is characterized by a progressive and even accelerated decline in muscle mass and function.[70] It is, therefore, widely acknowledged that older people need to ingest more protein to counteract the age-related muscle loss. The strict avoidance of those protein-rich foods (ie, milk, egg, fish), in case of sensitization to food allergens contained in them, may further result in an inadequate protein intake in older people.[69]

Additionally, the avoidance of certain food categories may also result in several micronutrient deficiencies (ie, iron, calcium, vitamin D, zinc).[69] As mentioned above, some determinants of the anorexia of aging (ie, gastrointestinal alterations, abdominal pain, vomiting) may also frequently overlap with FA symptoms thus exacerbating the risk of malnutrition and sarcopenia. It has been also reported that older people with anorexia can exhibit altered eating patterns like lower consumption of protein-rich foods (ie, meat, eggs, and fish),[71,72] thus potentially creating a vicious circle in the case of sensitization to allergens contained in these food categories. Furthermore, it could be interesting to investigate if these altered eating patterns seen in people with anorexia occur because of a sensitization to food allergens. In this case, FA could be envisioned as another potential determinant of the anorexia of aging. Indeed, nutritional counseling plays an even more pivotal role in those older people with FA in order to prevent malnutrition, sarcopenia and frailty.

CONCLUSION AND FUTURE PERSPECTIVES

The global increase in the prevalence of adult-onset FA as well as the persistence of early-onset FA across the life course need special attention, especially in older people. Unfortunately, data about FA prevalence and outcomes during older life are scarce and often based on self-reported symptoms. Little is known about FA etiology in older life but several mechanisms including immune senescence and inflammaging as well as micronutrient deficiencies may play a major role in sensitization to food allergens. Given that the mainstay of intervention towards an established FA is the avoidance of the offending food, it is important to consider and prevent the consequent risk of malnutrition, sarcopenia and frailty in older people. The large use of non-validated and unproven methods to screen for FA may inevitably lead to unnecessary dietary restrictions. It is thus pivotal to follow a correct diagnostic process taking also into account the peculiarities of the older people population characterized by a high clinical complexity. A carefully planned nutritional counseling is even more important in those older people with FA to prevent malnutrition. Future research needs to be focused on: 1) the prevalence of FA in older people with standardized and reproducible methods, 2) their underlying mechanisms and interactions with age-related conditions, and 3) their health impact.

Abbreviations

FA: Food Allergy; IgE: Immunoglobulin E; SPT: Skin Prick Test; NH: Nursing Home; Th1: T helper type 1; Th2: T helper type 2; DAMPs: Damage-Associated Molecular Patterns; SCFAs: Short-Chain Fatty Acids; OAS: Oral Allergy Syndrome; IgG4: Immunoglobulin G4; CGA: Comprehensive Geriatric Assessment; NIAID: National Institute of Allergy and Infectious Diseases; DBPCFC: Double-Blind Placebo-Controlled Food Challenge; FIA: Food-Induced Anaphylaxis; OR: Odds Ratio; ED: Emergency Department; RR: Relative Risk; CI: Confidence Interval; ROS: Reactive Oxygen Species.

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Author contributions

DA contributed to conceptualizing and writing the manuscript. LV, SP, IB, MC and TL edited and revised manuscript. DA, LV, SP, IB, MC and TL approved the final version of manuscript.

Ethics statement

Not applicable

Authors' consent for publication
I confirm that each of the authors has reviewed this paper in its submitted form and approved submission for publication of this paper to the World Allergy Organization Journal.

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