

Mini-Symposium - International Food Allergy Symposium

Food allergies in the elderly Collecting the evidence

Erika Jensen-Jarolim, MD^{*,†}; Sebastian A.F. Jensen[‡]^{*} Institute of Pathophysiology and Allergy Research, Center of Pathophysiology, Infectiology and Immunology, Medical University Vienna, Vienna, Austria[†] The Interuniversity Messerli Research Institute, University of Veterinary Medicine Vienna, Medical University Vienna, University of Vienna, Vienna, Austria[‡] AllergyCare, Allergy Diagnosis and Study Center, Vienna, Austria

ARTICLE INFO

Article history:

Received for publication April 29, 2016.

Received in revised form August 12, 2016.

Accepted for publication August 22, 2016.

Introduction: Population Getting Older Than Ever

The population of elderly people in the European Union currently ranges from 12.2% (Ireland) to 20.6% (Germany).¹ Germany, with 17 million elderly people, thus currently represents the European country with the oldest population, and this cohort will increase to approximately 23.4 million by 2050.¹ According to the US Census Bureau,² in the United States approximately 47 million (15%) of the population are currently older than 65 years. It is moreover expected that the US population will become significantly older and reach 83.7 million people older than 65 years in 2050 (ie, 20% of the population). Notably, similar trends are expected in this report for all industrial countries. In all instances, the proportion of people older than 85 years will also significantly increase. From this, it can be expected that the new situation will challenge policymakers and health care professionals. In parallel with these changes, we may expect that the occurrence of allergies will also increase in the elderly cohort, especially considering environmental challenges.

Prevalence of Food Allergies in the Elderly Population

Most studies indicate that the prevalence of atopic diseases, in terms of numbers of positive skin prick reactions and IgE test results, decreases in the elderly population (Fig 1). In continuation of the previous German Health Interview and Examination Survey for Adults³ of the Robert-Koch Institute, the 2013 survey described the prevalence ranging from 18.1% in those aged 18 to 29 years to 20.2%

in those aged 60 to 69 years and 20.7% in those aged 70 to 79 year based on positive IgE reactions in vitro to food allergens.⁴

However, studies on the prevalence of clinically approved food hypersensitivities, specifically in the elderly population, are rare. In an exceptional Korean study,⁵ the prevalence of food allergies was investigated in a longitudinal study to precisely evaluate this in each age group from infants, toddlers to adults, and those older than 65 years. The results were confirmed by skin testing, double-blind, placebo-controlled food challenge (milk, egg, wheat, soy) or food provocation (beef, pork, chicken). In the 2417 atopic patients, approximately 50% reported food hypersensitivities, among which 49% could be classified as non-IgE mediated. Only 2.2% were confirmed as clearly IgE-mediated, and this percentage decreased at older than 65 years. This number corresponds to the prevalence of food allergies in 1% to 3% of younger adults as stated in the European guidelines for food allergy and anaphylaxis, in which data from 109 studies were extracted.⁶ In this report, however, no precise numbers for the senior population are given. Considering the 17 million elderly people in Germany, 170,000 to 500,000 should theoretically need consultation, but only a few consulted allergy clinics, possibly because of a lower perception of allergic and asthmatic symptoms in elderly persons. On the other hand, considering the overwhelming number of publications on food allergies in children and younger adults, we neither expect nor watch out for elderly people with food allergies. This might prompt an underestimation of cases, resulting in underdiagnosis and missing therapeutic intervention in this group.^{7,8} Furthermore, the diagnosis of food allergy is complex because different immunologic mechanisms, IgE-mediated, cell mediated, or mixed causes, may play a role.⁶ A few studies have explicitly addressed subchapters of food allergy, such as eosinophilic esophagitis or urticaria, in the elderly population.^{9,10} To minimize the efforts and risks of food allergy testing in an elderly patient, questionnaires could be a tool that provide a first impression. However, the number of self-reported food allergies can only be confirmed in one-sixth of the suspected cases,⁶ and there seems to be a relatively lower level of

Reprints: Erika Jensen-Jarolim, MD, Institute of Pathophysiology and Allergy Research, Center of Pathophysiology, Infectiology and Immunology, Medical University Vienna, Waehringer G 18-20, 1090 Vienna, Austria; E-mail: Erika.jensen-jarolim@meduniwien.ac.at.

Disclosures: Sebastian A.F. Jensen reported being employed by AllergyCare during the study. No other disclosures were reported.

Funding Sources: Dr Jensen-Jarolim was supported by grant SFB F4606-B19 from the Austrian Science Fund.

<http://dx.doi.org/10.1016/j.anai.2016.08.036>

1081-1206/© 2016 American College of Allergy, Asthma & Immunology. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

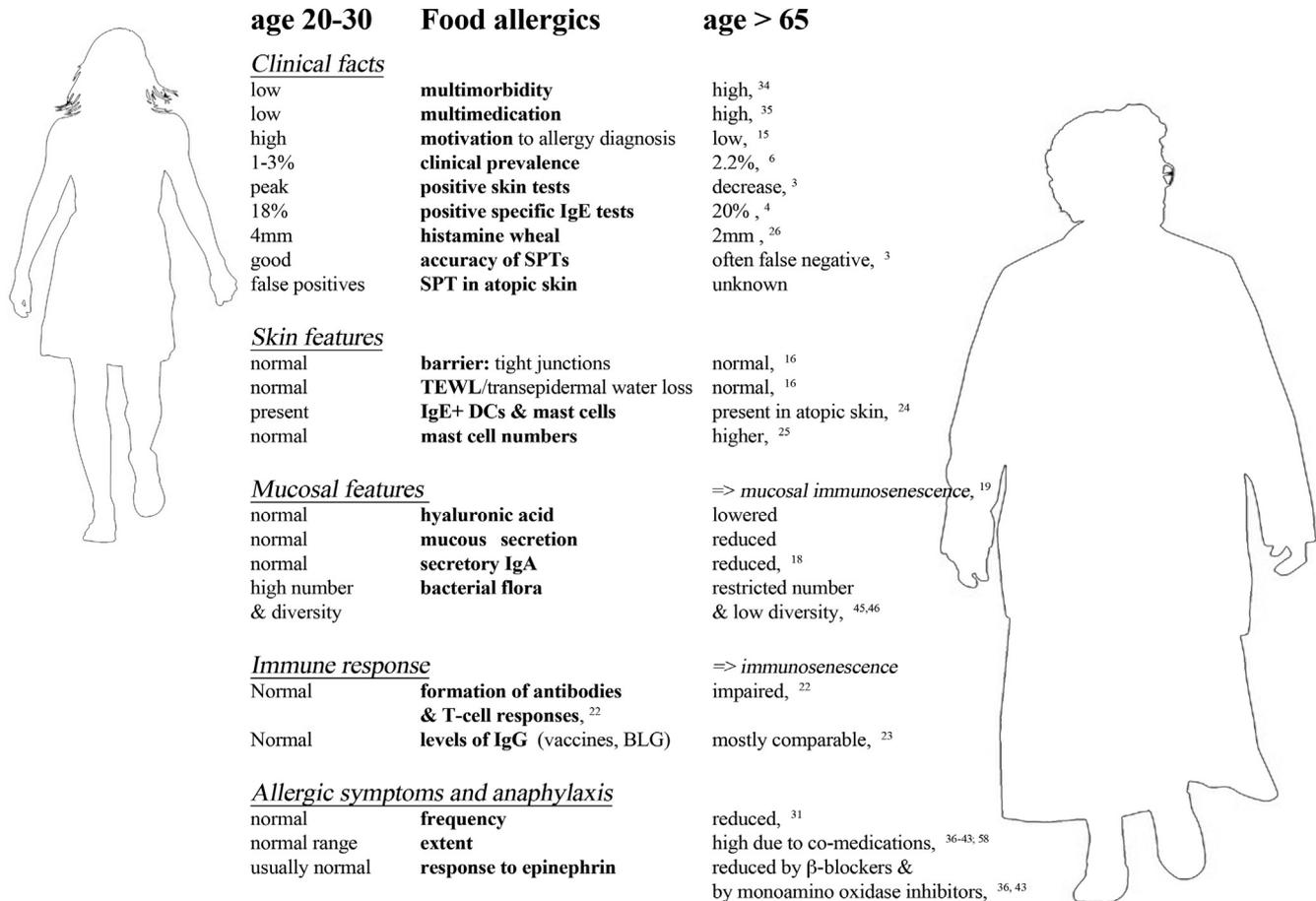


Figure 1. Comparing the preconditions and risks in young adults vs elderly people. (Photos reprinted with permission from Fotolia.com©PrintingSociety).

motivation to be diagnosed in elderly study participants. Reasons for neglecting participation in studies were, for instance too little time, tiredness, no interest in science, or too old to contribute.¹¹

Concerning Barrier and Immune Function in the Elderly Population

One would expect a reduced skin barrier function in aged skin because of thinning of the skin. However, recent data propose that transepidermal water loss is not enhanced in aged skin, which has been explained by compensation via tight junctions connecting the keratinocytes.¹² However, dryness and hyperkeratosis attributable to reduced shedding are typical problems of aged skin. These conditions often correlate with itching and an enhanced risk of cutaneous infections, which may, on the one hand, camouflage and, on the other hand, mimic allergic dermatitis.

There may be a more significant effect of age on the *mucosal* barrier, which is similarly relevant for allergen penetration and uptake. It is well known that less hyaluronic acid and mucus are produced, resulting in reduced mechanical protection. Mucus is also relevant for the transport of antibacterial and defensive proteins to the mucosal surface, including IgA. Therefore, IgA levels are significantly reduced in the aged mucosa¹³ in accordance with the concept of mucosal immunosenescence. Interestingly, no studies are available that systematically investigate the potential correlation of the reduced mucosal IgA with food hypersensitivities in the elderly population, even though IgA deficiency in general has been linked with a number of diseases associated with food intolerances, such as celiac disease, irritable bowel disease, and food allergies.

Immunologic memory is a phenomenon that has been extensively studied, mostly to provide rationale for vaccinations. Most studies indicate that elderly people have a lower response to vaccines because of more qualitative than quantitative restrictions and because immunosenescence rather affects the cellular branch of the immune system, including changes in CD62L.¹⁴

Furthermore, the IgE isotype seems to be less affected by the aging process. It has recently been identified to be fixed via Fc ϵ RI to tryptase-positive mast cells in aged atopic skin and to CD11c-positive dendritic cells in the papillary and upper dermis, pointing toward an allergic pathogenesis of the inflammation.¹⁵ However, despite increasing mast cell counts in the aged skin,¹⁶ elderly people have less reliable skin responses and a smaller wheal reaction to the histamine control but not to the allergen pricks in a longitudinal study in 854 patients.¹⁷ In other studies, skin test result sizes, either of wheal or flare reactions, were described to be reduced, with a risk of false-negative results in aged persons.¹⁸ Therefore, IgE testing may be advantageous in elderly patients, especially for risk evaluation of the causative food allergen.

Higher Risk Attributable to Physical Insufficiencies and Multimorbidity

The decrease of the incidence of adult-onset food allergy was reported to be paralleled by reduced frequency of systemic reactions continuing into old age based on an evaluation on epinephrine prescriptions and treatments in emergency departments.¹⁹ However, systemic reactions in elderly people are more hazardous because of insufficient compensation mechanisms

and a higher risk of cardiac and pulmonary failure. In this cohort, epinephrine should preferentially be given intramuscularly rather than by bolus.²⁰ Moreover, precise diagnosis of food allergy in the elderly population is especially important. The studies cited above indicate that food sensitization exists and may currently be underestimated because of decreased or unreliable skin test results and because food allergy diagnosis may be rejected for several reasons.

Studies on the prevalence of anaphylaxis rarely contain evidence for allergic seniors. In this context, in elderly patients with multimorbidities,²¹ multidrug prescriptions play an important role,²² but drugs have been recognized as important cofactors that complicate anaphylactic events.²³ Basically, all drugs that interfere with the allergic effector cells may be relevant in food allergies as well. However, some may be more potent. This fact requires a thorough risk-benefit analysis, as in the example of β -blockers for treating congestive heart failure in a patients with peanut anaphylaxis.²⁴ β -Blockers and angiotensin-converting enzyme inhibitors,²⁵ as well as nonsteroidal anti-inflammatory drugs,²⁶ are relevant cofactors in urticaria and anaphylaxis, especially in the elderly population.²⁷ In the elderly population, because of drug consumption, the treatment of anaphylaxis is also different. Whereas β -blockers decrease the response to epinephrine in an anaphylactic emergency, tricyclic antidepressants and monoamine oxidase inhibitors may increase the cardiac risk of epinephrine attributable to a potentiation of its effects.²³

Furthermore, antibiotics interfere with the microbiome and its function in immune homeostasis. In the elderly population, Bacteroidetes especially contribute to the microbiota, but their numbers decrease and the phylogenetic diversity is reduced.²⁸ In a geriatric study, 50% of antibiotic prescriptions were found to be inappropriate²⁹ but they may severely disturb the flora composition. The good news is that, even in geriatric patients, the gut flora can be reconstituted effectively by probiotics.³⁰ Whether these interventions will also be useful for preventing allergy and food hypersensitivities awaits further studies. Long-term alcohol consumption was also correlated explicitly with food allergy in the elderly population.³¹

Considering the classification of food allergens, structurally stable proteins usually harbor a higher risk of eliciting systemic reactions. However, labile proteins may persist in gastrointestinal transit when digestion is hampered and become food allergens.³² In the elderly population, there are several conditions that regularly impair gastric pH: (1) atrophic gastritis or (2) intake of anti-ulcer drugs for the treatment of gastritis, gastric ulcer, or as comedication to pain killers and corticosteroids. This is a problem for protein digestion because pepsin, the gastric protease, is only activated below pH 3.0. Furthermore, only acidic chymus entering the duodenum leads to a release of pancreatic enzymes. Impairment of the gastric acidity in the elderly population therefore has a double effect by transforming harmless proteins into potentially hazardous allergens.⁷ Whereas in existing food allergy, these mechanisms lower the thresholds for allergic reactions, the same mechanism may lead in 15% of cases to de novo sensitization during proton pump inhibitor therapy, as demonstrated in a typically elderly, gastroenterologic cohort.³²

Conclusion

The geriatric population is still a fringe group in allergy research, and only a few longitudinal studies are available to truly determine the prevalence of food allergies in the elderly population. This may also be hampered by lower skin reactivity to histamine. Conversely, IgE stays reactive in aged persons and can be exploited in serum testing. Importantly, IgE resides on mast cells and dendritic cells in the atopic elderly skin. Because of their general multimorbidity,

including lowered cardiac and pulmonary function, as well as comedications, anaphylaxis represents a relatively higher risk (Fig 1). Therefore, allergy diagnosis in elderly patients may be especially important for risk evaluations in food allergies. It therefore needs to be emphasized that for risk evaluation the advanced biological age has to be specifically considered in the diagnosis and management of food allergies in elderly patients.

Acknowledgment

We express our thanks to Amelia Wein for proofreading.

References

- [1] Hausteil T, Mischke J. *In the Spotlight: Older People in Germany and the EU, 2011*. Wiesbaden, Germany: Statistisches Bundesamt (Federal Statistical Office); 2011.
- [2] Ortman J, Velkoff V, Hogan H. *An Aging Nation: The Older Population in the United States*. Washington, DC: US Census Bureau; 2014.
- [3] Langen U, Schmitz R, Steppuhn H. Prevalence of allergic diseases in Germany: results of the German Health Interview and Examination Survey for Adults (DEGS1) [in German]. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz*. 2013;56:698–706.
- [4] Haftenberger M, Laussmann D, Ellert U, et al. Prevalence of sensitization to aeroallergens and food allergens: results of the German Health Interview and Examination Survey for Adults (DEGS1) [in German]. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz*. 2013;56:687–697.
- [5] Kwon J, Kim J, Cho S, Noh G, Lee SS. Characterization of food allergies in patients with atopic dermatitis. *Nutr Res Pract*. 2013;7:115–121.
- [6] Muraro A, Hoffmann-Sommergruber K, Holzhauser T, et al. EAACI Food Allergy and Anaphylaxis Guidelines. Protecting consumers with food allergies: understanding food consumption, meeting regulations and identifying unmet needs. *Allergy*. 2014;69:1464–1472.
- [7] Diesner SC, Untersmayr E, Pietschmann P, Jensen-Jarolim E. Food allergy: only a pediatric disease? *Gerontology*. 2011;57:28–32.
- [8] Montanaro A. Allergic disease management in the elderly: a wakeup call for the allergy community. *Ann Allergy Asthma Immunol*. 2000;85:85–86.
- [9] Maradey-Romero C, Prakash R, Lewis S, Perzynski A, Fass R. The 2011–2014 prevalence of eosinophilic oesophagitis in the elderly amongst 10 million patients in the United States. *Aliment Pharmacol Ther*. 2015;41:1016–1022.
- [10] Ventura MT, Napolitano S, Buquicchio R, Cecere R, Arsiene A. An approach to urticaria in the elderly patients. *Immunopharmacol Immunotoxicol*. 2012;34:530–533.
- [11] Sidenvall B, Fjellstrom C, Andersson J, Gustafsson K, Nygren U, Nydahl M. Reasons among older Swedish women of not participating in a food survey. *Eur J Clin Nutr*. 2002;56:561–567.
- [12] Svoboda M, Bilkova Z, Muthny T. Could tight junctions regulate the barrier function of the aged skin? *J Dermatol Sci*. 2016;81:147–152.
- [13] Miletic ID, Schiffman SS, Miletic VD, Sattely-Miller EA. Salivary IgA secretion rate in young and elderly persons. *Physiol Behav*. 1996;60:243–248.
- [14] Rosenberg C, Bovin NV, Bram LV, et al. Age is an important determinant in humoral and T cell responses to immunization with hepatitis B surface antigen. *Hum Vaccin Immunother*. 2013;9:1466–1476.
- [15] Tanei R, Hasegawa Y, Sawabe M. Abundant immunoglobulin E-positive cells in skin lesions support an allergic etiology of atopic dermatitis in the elderly. *J Eur Acad Dermatol Venereol*. 2013;27:952–960.
- [16] Gunin AG, Kornilova NK, Vasilieva OV, Petrov VV. Age-related changes in proliferation, the numbers of mast cells, eosinophils, and cd45-positive cells in human dermis. *J Gerontol A Biol Sci Med Sci*. 2011;66:385–392.
- [17] Song WJ, Lee SM, Kim MH, et al. Histamine and allergen skin reactivity in the elderly population: results from the Korean Longitudinal Study on Health and Aging. *Ann Allergy Asthma Immunol*. 2011;107:344–352.
- [18] Scichilone N, Callari A, Augugliaro G, Marchese M, Trogias A, Bellia V. The impact of age on prevalence of positive skin prick tests and specific IgE tests. *Respir Med*. 2011;105:651–658.
- [19] Kamdar TA, Peterson S, Lau CH, Saltoun CA, Gupta RS, Bryce PJ. Prevalence and characteristics of adult-onset food allergy. *J Allergy Clin Immunol Pract*. 2015;3:114–115.e111.
- [20] Campbell RL, Bellolio MF, Knutson BD, et al. Epinephrine in anaphylaxis: higher risk of cardiovascular complications and overdose after administration of intravenous bolus epinephrine compared with intramuscular epinephrine. *J Allergy Clin Immunol Pract*. 2015;3:76–80.
- [21] Vetrano DL, Foebel AD, Marengoni A, et al. Chronic diseases and geriatric syndromes: the different weight of comorbidity. *Eur J Intern Med*. 2016;27:62–67.
- [22] Collerton J, Jagger C, Yadegarfar ME, et al. Deconstructing complex multimorbidity in the very old: findings from the Newcastle 85+ study. *Biomed Res Int*. 2016;2016:8745670.
- [23] Simons FE, Arduoso LR, Bilo MB, et al. World allergy organization guidelines for the assessment and management of anaphylaxis. *World Allergy Organ J*. 2011;4:13–37.

- [24] TenBrook JA Jr, Wolf MP, Hoffman SN, et al. Should beta-blockers be given to patients with heart disease and peanut-induced anaphylaxis? a decision analysis. *J Allergy Clin Immunol*. 2004;113:977–982.
- [25] Lee S, Hess EP, Nestler DM, et al. Antihypertensive medication use is associated with increased organ system involvement and hospitalization in emergency department patients with anaphylaxis. *J Allergy Clin Immunol*. 2013;131:1103–1108.
- [26] Demir S, Olgac M, Unal D, Gelincik A, Colakoglu B, Buyukozturk S. Evaluation of hypersensitivity reactions to nonsteroidal anti-inflammatory drugs according to the latest classification. *Allergy*. 2015;70:1461–1467.
- [27] Ventura MT, D'Amato A, Giannini M, Carretta A, Tummolo RA, Buquicchio R. Incidence of allergic diseases in an elderly population. *Immunopharmacol Immunotoxicol*. 2010;32:165–170.
- [28] Claesson MJ, Cusack S, O'Sullivan O, et al. Composition, variability, and temporal stability of the intestinal microbiota of the elderly. *Proc Natl Acad Sci U S A*. 2011;108(suppl 1):4586–4591.
- [29] Afekouh H, Baune P, Abbas R, De Falvelly D, Guermah F, Haber N. Antibiotic prescription evaluation in the rehabilitation ward of a geriatric hospital. *Med Mal Infect*. 2015;45:427–435.
- [30] Senan S, Prajapati JB, Joshi CG, et al. Geriatric respondents and non-respondents to probiotic intervention can be differentiated by inherent gut microbiome composition. *Front Microbiol*. 2015;6:944.
- [31] Bakos N, Scholl I, Szalai K, Kundi M, Untersmayr E, Jensen-Jarolim E. Risk assessment in elderly for sensitization to food and respiratory allergens. *Immunol Lett*. 2006;107:15–21.
- [32] Pali-Scholl I, Jensen-Jarolim E. Anti-acid medication as a risk factor for food allergy. *Allergy*. 2011;66:469–477.