



Frequency of positive allergy tests in children, adults and seniors

Benjamin Heindl · Tobias Braunsteiner · Livia Klug · Felix Wantke · Wolfgang Hemmer · Stefan Wöhr

Received: 1 September 2021 / Accepted: 31 October 2021
 © The Author(s) 2022

Summary

Background Among allergists, it is often assumed that allergies primarily affect children and young adults and are “lost” during life.

Methods To challenge this assumption, we analysed skin prick tests and patch tests from a large patient cohort of 5857 consecutive patients seen by the same physician in 2018 in a large allergy outpatient clinic in Vienna.

Results We observed a clustering of patients suffering from inhalant allergy between the ages of 5 and 59 years (44.6% = 2155/4828), although inhalant allergies were still frequent beyond the age of 60 years with 20.2% (167/826). Food allergies were most relevant in infants under 5 years of age, at 16.3% (33/203). The proportion of contact allergies was low in childhood, but steadily increased over the age and affected more often women (women: 5.28% = 187/3544, men: 1.99% = 46/2313).

Conclusion Inhalant allergies play a relevant role until old age. Food allergies are mainly a disease of infancy, and contact allergies predominantly affect adult women.

Keywords Skin prick test · Patch test · Epidemiology · Age · Gender distribution · Austria

Abbreviations

AA Allergic bronchial asthma
 AR Allergic rhinoconjunctivitis

DGAKI Deutsche Gesellschaft für Allergologie und klinische Immunologie (German Society for Allergology and Clinical Immunology)
 ESCD European Society of Contact Dermatitis
 FAZ Floridsdorf Allergy Center („Floridsdorfer Allergiezentrum“)
 INCI International Nomenclature of Cosmetic Ingredients
 LTP Lipid-transfer-proteins
 SPT Skin prick test

Introduction

Allergies to different allergens play different roles depending on age. Food allergies are a disease of childhood and get typically lost by school age [1–3]. Somewhat later in life, these are then replaced by inhalant allergies [4]. The observation that early childhood food allergies, often accompanied by atopic eczema, are later followed by allergic rhinitis and asthma was for many years circumscribed by the recently controversial catchphrase “allergy/atopic march” [5, 6]. This hypothesis generated the image of an allergic maximum in young adulthood, which often led to the false assumption that inhalant allergens could become irrelevant in the elderly. However, individual studies had shown clinically relevant sensitization even in older adults and seniors (>60 years) [7–9]. There seems to be a gender-specific effect coupled to age as in childhood, boys suffer more often from allergies compared to girls, from puberty onwards the gender ratio is reversed [10, 11].

This retrospective analysis covering all ages (0–93 years) aims to re-evaluate these observations in a large patient collective from a Viennese allergy outpatient clinic (FAZ—“Floridsdorfer Allergiezentrum”). In contrast to most other publications on allergies in old age, this study not only includes IgE-mediated im-

B. Heindl · T. Braunsteiner · L. Klug · F. Wantke · W. Hemmer · S. Wöhr (✉)
 Floridsdorf Allergy Center (FAZ), Pius Parsch Square
 1/3, 1210 Vienna, Austria
 office@faz.at

S. Wöhr
 Medical University of Vienna, Vienna, Austria

Table 1 Study population and overall rate of positive allergy tests in absolute numbers (*n*) and percent of total collective (%) or mean (M) ± standard deviation (SD)

Patients	Female	Male	Total
Age, M ± SD	38.00 ± 19.92	32.76 ± 20.44	35.93 ± 20.29
Food allergy [type I], <i>n</i> (%)	130 (2.2%)	103 (1.8%)	233 (4.0%)
Inhalant allergy [type I], <i>n</i> (%)	1270 (21.7%)	1093 (18.7%)	2363 (40.3%)
Contact Allergy [type IV], <i>n</i> (%)	187 (3.2%)	46 (0.8%)	233 (4.0%)
Total, <i>n</i> (%)	3544 (60.5%)	2313 (39.5%)	5857 (100.0%)

mediate-type allergy (type I) but also T-cell-mediated contact allergy (type IV).

Methodology and patients

Patients

As part of their diploma thesis, three students of human medicine created a retrospective database including all patients who had presented to a single physician (SW) at the Floridsdorf Allergy Center (FAZ) in 2018. Up to 352 possible individual parameters were recorded per case. All individuals from whom at least one physician's letter was available were included into the database. Exclusion criteria were incomplete data sets and contradictory test results. In case of multiple presentations with the same patient's history within the same year, only the data concerning the first presentation were included to avoid duplicate entries. This resulted in a study population of 5857 subjects (60.5% = 3544/5857 female, mean age: 35.9 ± 20.3 years). The patient population spanned across all age groups (Table 1). The study was conducted as part of the BH/TB/LK medical diploma theses, and the analysis was approved under the Ethics' Committee vote of the Medical University of Vienna (Ethics' Committee number 2212/2018).

Methods

For the diagnosis of immediate type allergies (inhalant allergies, food allergies), skin prick tests (SPT ≥ 3 mm) were read after 20 min according to the criteria of the German Society of Allergology and Clinical Immunology (DGAKI) [12] and positive results were only considered as clinically relevant, in case of a concurrent, conclusive medical history. Sensitizations without clinical relevance were not considered. Standard allergen test series from the companies Bencard (Allergy Therapeutics, Worthing, United Kingdom) or ALK-Abelló (Hørsholm, Denmark) were used, depending on availability. The following inhaled allergens clinically most relevant for Eastern Austria were tested: pollen of birch, hazel, ash, timothy (grasses), rye, plantain, mugwort, ragweed, pellitory, nettle, *Atriplex*, plane tree; mold spores: *Alternaria*,

Table 2 Number of positive patch test reactions to the standard test series. The proportion of positive results in relation to all 570 patch tests performed are shown in percent (%)

Contact allergens	Positive tests [<i>n</i> (%) of all 570 patch tests]
Nickel sulphate	138 (24.21)
Fragrance mix 1	35 (6.14)
Methylchloroisothiazolinone (INCI)	27 (4.74)
Cobalt (II) chloride	26 (4.56)
Balsam of Peru (<i>Myroxylon pereirae</i> resin) (INCI)	24 (4.21)
Formaldehyde (INCI)	17 (2.98)
Methylisothiazolinone (INCI)	16 (2.81)
Fragrance mix 2	12 (2.11)
Colophonium (INCI)	12 (2.11)
Propolis Cera (INCI)	10 (1.75)
Ylang ylang oil (<i>Cananga odorata</i>) (INCI)	9 (1.58)
Potassium dichromate	8 (1.40)
Lyril 4-(4-hydroxy-4-methyl pentyl)-3-cyclohexen-1-carboxaldehyde (INCI)	8 (1.40)
Methyldibromo glutaronitrile (INCI) MDBGN/dibromdicyanobutane	7 (1.23)
Epoxy resin (bisphenol A)	7 (1.23)
Jasminum officinale extract (INCI)	6 (1.05)
Wool alcohol (lanolin)	5 (0.88)
Thiuram mix	5 (0.88)
IPPD (N-isopropyl-N'-phenyl-p-phenyldiamine)	5 (0.88)
Cetylstearylalcohol	4 (0.70)
Sesquiterpene lactone mix	4 (0.70)
Turpentine (INCI)/terpentine	2 (0.35)
Bis-(diethyldithiocarbamate)-zinc (ZBEC)	1 (0.18)
2-Mercaptobenzothiazole	1 (0.18)
Mercapto mix	0 (0.00)
Iodopropynyl butylcarbamate	0 (0.00)
Paraben mix	0 (0.00)
Total	389 (68.25)

INCI/International Nomenclature of Cosmetic Ingredients

Cladosporium, *Aspergillus*, *Penicillium*; house dust mites: *Dermatophagoides pteronyssinus* and *farinae*; storage mites: *Lepidoglyphus destructor*, *Tyrophagus putrescentiae*, *Acarus siro*, *Blomia tropicalis*; parasite: *Blatella germanica* (cockroach); pets: cat, dog, horse, rabbit, and parakeet; food allergens: hen's egg, chicken meat, pork, wheat flour, rye flour, oat flour, codfish, shrimp, peanut, walnut, peach (lipid-transfer-protein LTP), and hazelnut. Cow's milk and soy milk were performed as direct prick-to-prick tests with the native foods.

Contact allergens for the diagnosis of type IV contact allergy were acquired from SmartPracticeEurope (allergEAZE®, Greven, Germany) and tested on Curatest® (Lohmann-Rauscher, Vienna, Austria). The test results of the standard series were read according to the criteria of the European Society of Contact Dermatitis (ESCD) [13] (allergens in Table 2). Due to the

heterogeneity of >1000 additional contact allergens tested, these were not included in this study.

Results

Inhalant allergies (type I allergy), age and gender

Clinically relevant skin tests for inhaled allergens were the most common ones observed in 40.34% (2363/5857) of the patients. Female patients had more positive tests in absolute terms, but the relative proportion was higher in the male study population (female: 35.84% = 1270/3544, male: 47.25% = 1093/2313;

Table 1 and Fig. 1). As can be seen in Fig. 1, in young children (0–4 years of age), the proportion of 20.2% (41/203) patients suffering from inhalant allergies was comparatively low. Girls predominated (25.00% = 24/96, boys: 15.89% = 17/107). From preschool to school age, the proportion of inhalant allergies increased sharply and reached its peak at the age of 10–14 years. At this age, 50.77% (231/455) suffered from at least one clinically relevant inhalant allergy. Strikingly, boys had relatively and absolutely more frequent positive tests compared to girls (boys, 5–14 years: 54.71% = 267/488, girls: 40.30% = 160/397). Also in adolescence to high adulthood, the proportion

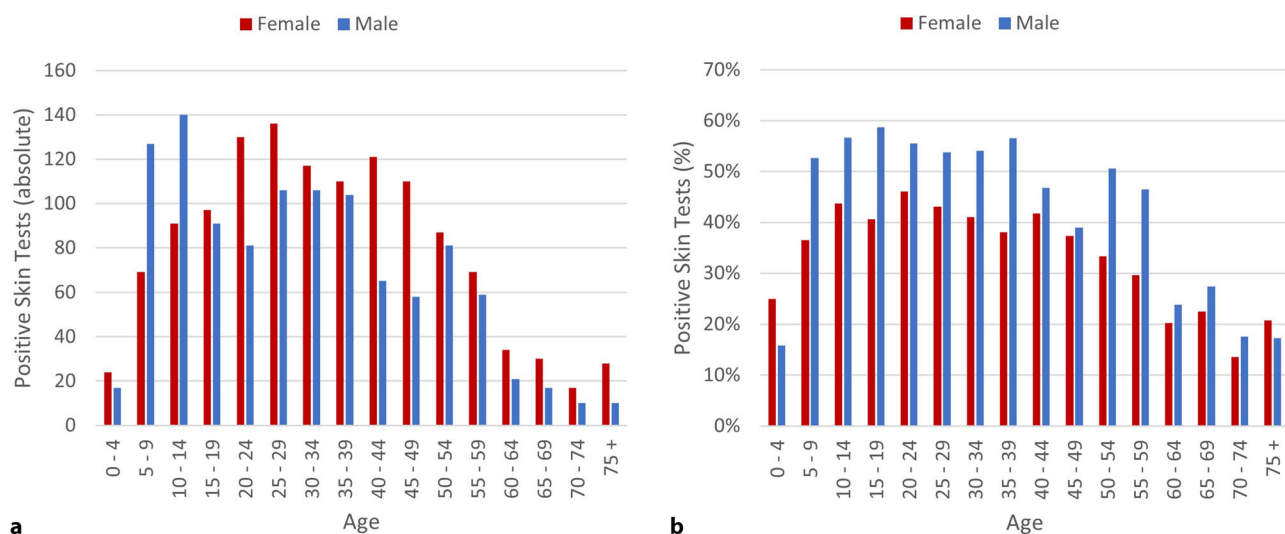


Fig. 1 Positive skin prick tests (type I allergy) to inhalant allergens, broken down by age and gender: **a** in absolute numbers, **b** relative to the total number of tests in percent (%)

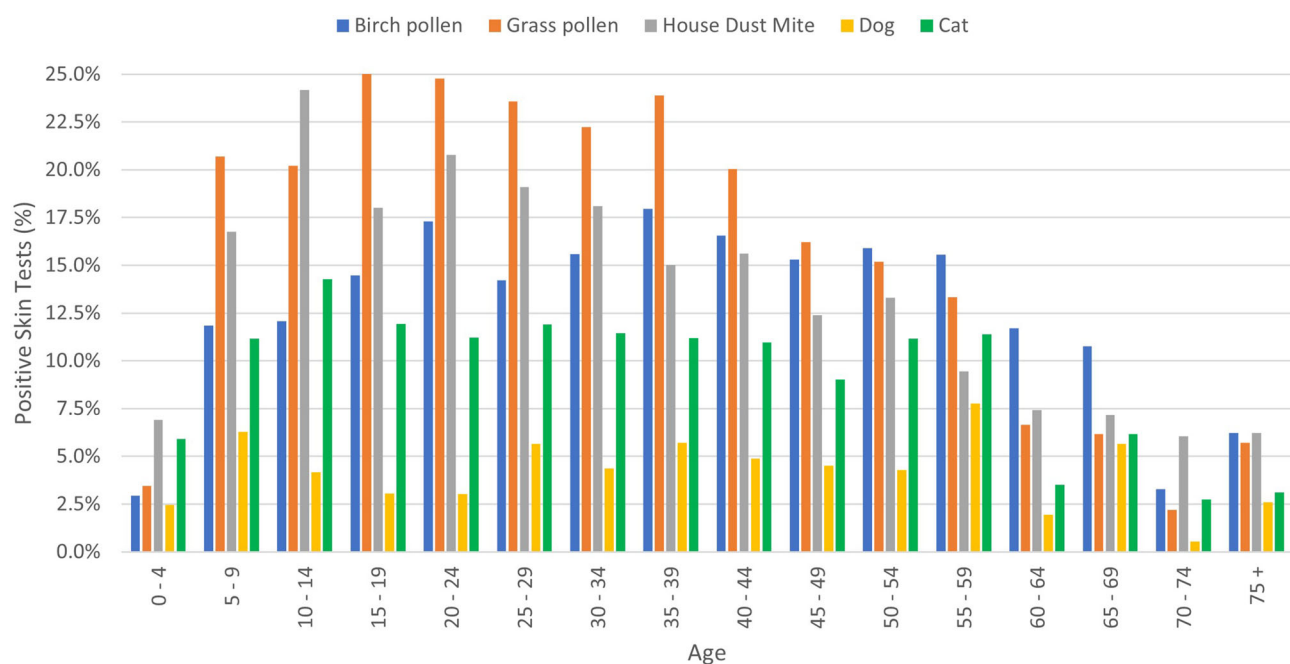
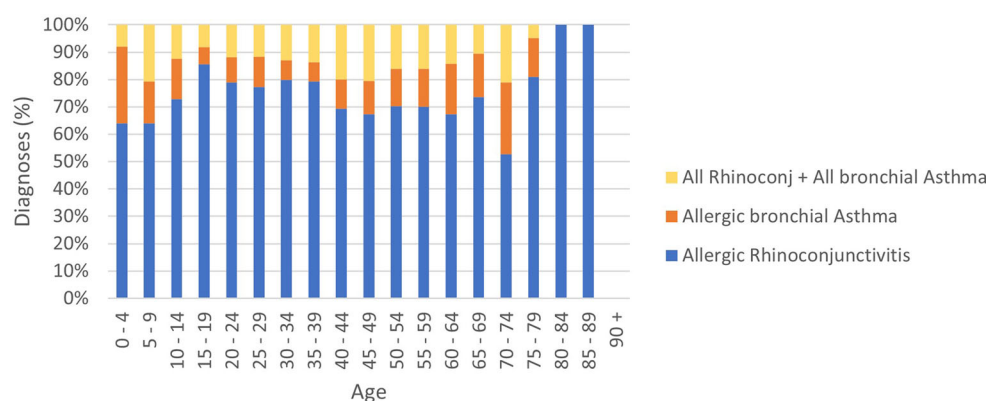


Fig. 2 Positive skin prick tests (type I allergy) to selected inhalant allergens (birch pollen, grass pollen, house dust mite, cat, dog), categorized by age

Fig. 3 Symptoms recorded in association with a positive skin prick test to an inhalant allergen. Individuals without a designated symptom were omitted from this graph. All Rhinoconj + All bronchial Asthma allergic rhinoconjunctivitis and allergic bronchial asthma



of positive tests remained higher in the male gender, although more females had been tested in absolute terms (15–75+ years: males: 47.09% = 809/1718, females: 35.59% = 1086/3051). In adulthood, the proportion of inhalant allergies remained at a high but constant level above 35% (20–24 years: 49.30%, 25–29 years: 47.17%, 30–34 years: 46.36%, 35–39 years: 45.24%, 40–44 years: 43.36%, 45–49 years: 37.84%, 50–54 years: 39.90%, 55–59 years: 35.56%). Only from the age of 60–64 years was there a slight decrease to 21.48% (55/256), whereas at the high age of 75+ years still 19.69% of the patients suffered from inhalant allergies (38/193).

Fig. 2 shows the age distribution of positive skin tests of the five selected inhalant allergens birch and grass pollen, house dust mite, cat and dog. In infancy (0–4 years) the proportions were still small as in Fig. 1. The indoor allergens house dust mite and cat dominated (house dust mite: 6.90% = 14/203, cat: 5.91% = 12/203). From the age of 5 years, the allergens grass pollen, birch pollen and house dust mite played a major role. Until the age of 49 years, grass pollen remained the dominant allergen source (5–49 years: grass pollen 21.87% = 885/4047, house dust mite 17.79% = 720/4047, birch pollen 15.05% = 609/4047). Among the elderly, positive birch pollen tests were most frequent (50–75+ years: grasses 9.71% = 156/1607, house dust mite 9.09% = 146/1607, birch 11.95% = 192/1607). Positive skin tests against cats were more than twice as frequent (10.18% = 596/5857) as against dogs (4.47% = 262/5857).

Allergic rhinoconjunctivitis (AR) or AR plus allergic bronchial asthma (AA) represented the most frequent diagnosis in clinically relevant skin tests for an inhalant allergen with 75.71% (1789/2363, AR alone: 63.28% = 1500/2363, AR plus AA: 12.23% = 289/2363). AA alone occurred in a proportion of 9.82% (232/2363). No attributable clinical symptom had been recorded in 342 subjects (14.47% = 342/2363). Fig. 3 shows the distribution of the recorded diagnoses; patients without a recorded diagnosis were excluded from the figure for the sake of comprehensibility. AR clearly dominated throughout all age groups, although it became the only symptom in the most senior pa-

tients of over 80; bronchial asthma no longer played a role here (AR: 80–84 years: 100% = 8/8, 85–90 years: 100% = 1/1). The importance of single AA was highest in young children aged 0–4 years with 28% (7/25).

Food allergies (type I allergy), age and gender

In relation to the entire study population, food allergies played a smaller role at 4% (233/5857; Table 1). As expected, the proportion of food allergies was highest in the group of young children aged 0–4 years with 16.26% (33/203) positive tests (Fig. 4). Boys and girls roughly balanced each other (girls: 17.71% = 17/96, boys: 14.95% = 16/107). At the age of 5–9 years, there was a decrease in the proportion of elementary school students, with boys still being affected significantly more often than girls (girls: 2.12% = 4/189, boys: 7.05% = 17/241, Fisher's exact test 2-sided: $p=0.023$). Only at the age of 10–14 years did the boys converge with the girls (girls: 2.88% = 6/208, boys: 2.83% = 7/247). In the other age groups, the percentage of food allergy sufferers in the respective age categories always remained below 5% (15–19 years: 2.79%, 20–24 years: 3.27%, 25–29 years: 3.12%, 30–34 years: 4.99%, 35–39 years: 4.65%, 40–44 years: 4.66%, 45–49 years: 2.93%, 50–54 years: 4.28%, 55–59 years: 4.17%, 60–64 years: 1.56%, 65–69 years: 3.59%, 70–74 years: 0.00%, 75+ years: 1.04%). Clinically relevant food allergies remained at about the same low level in both sexes in adulthood (20–75+ years: women: 3.45% = 97/2812, men: 3.71% = 58/1563).

Dissecting the four most prominent food allergens (cow's milk, hen's egg, soy, and peanut) in Fig. 5, it was shown that food allergy tested positive in only a small proportion of patients. Hen's egg and cow's milk were rare allergens, with 15 positive skin tests each, and were more prevalent in young children aged 0–4 years (0–4: cow's milk 1.97% = 4/203, chicken egg 4.93% = 10/203). The food allergen soy bean, representing in most cases a secondary food allergy based on cross-reactivity from birch pollen (cross-reactivity through the PR-10 proteins from birch *Bet v 1* and soy *Gly m 4*), did not show a peak in infancy, but was dis-

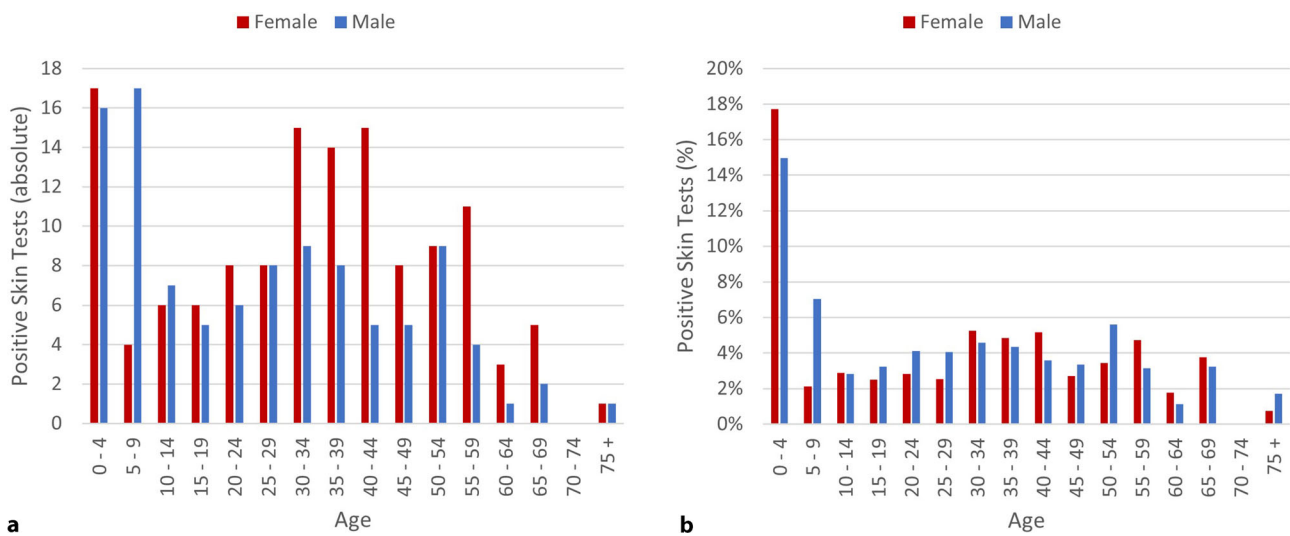


Fig. 4 Positive skin prick tests (type I allergy) to food, broken down by age and gender: **a** in absolute numbers, **b** relative to the total number of tests in percent (%)

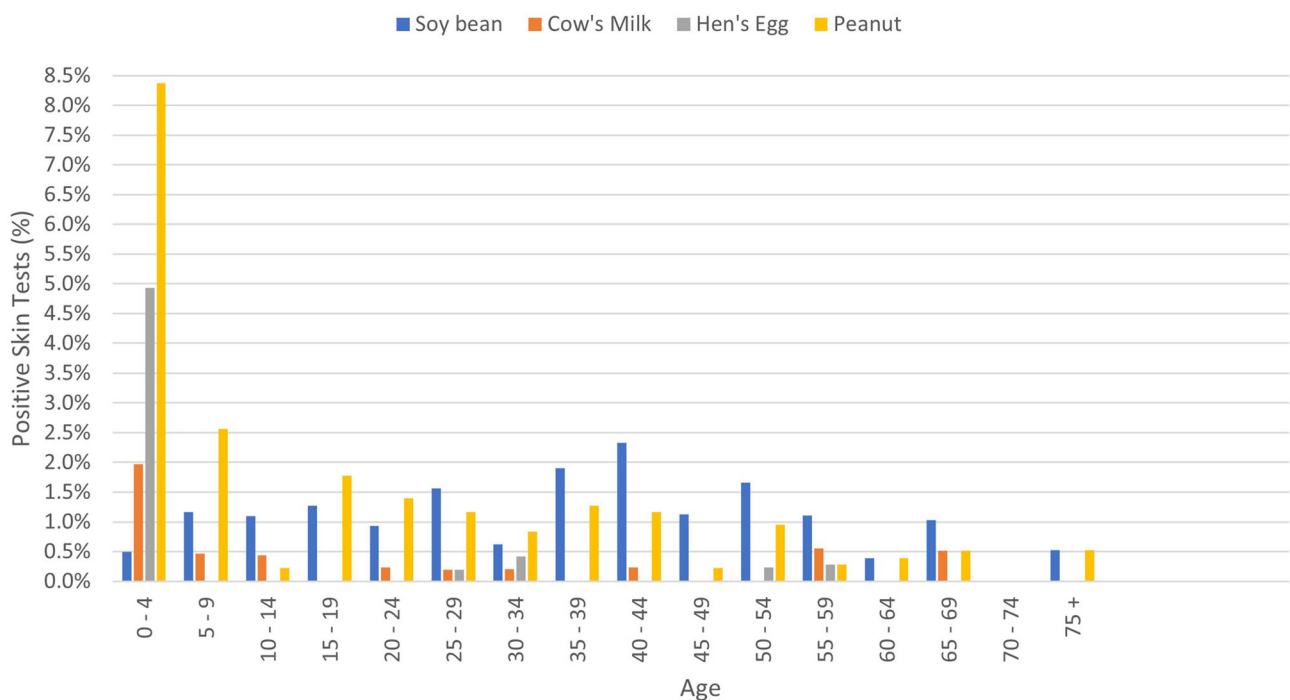


Fig. 5 Positive skin prick tests (type I allergy) to selected food allergens (soy, cow's milk, hen's egg, peanut), categorized by age

tributed equally over all age groups with a peak of 2.33% at age 40–44 (10/429). Contrary to the general belief that peanut is mainly a problem in the Anglo-Saxon region, also in Austria, a country at the heart of Central Europe, it was the most common food allergen with 72 positive skin tests and showed the highest rate at age 0–4 years with 8.37% (17/203).

Contact allergies (type IV allergy) and age

Also, 4% (233/5857) of the collective showed a positive patch test and thus a type IV contact allergy

(Table 1). Table 2 shows the number of positive reactions to the contact allergens of 570 patch tests with the European standard series. Contact allergy to nickel sulphate clearly dominated with a proportion of 24.21% (138/570). Fig. 6 shows the low relevance of contact allergies in childhood, where the proportion of all persons in the respective age category remained below 1% (0–4 years: 0.00%, 5–9 years: 0.47%, 10–14 years: 0.66%). Only from the beginning of 15 years was there a continuous increase until old age (15–19 years: 2.54%, 20–24 years: 2.57%, 25–29 years: 4.09%, 30–34 years: 3.95%, 35–39 years:

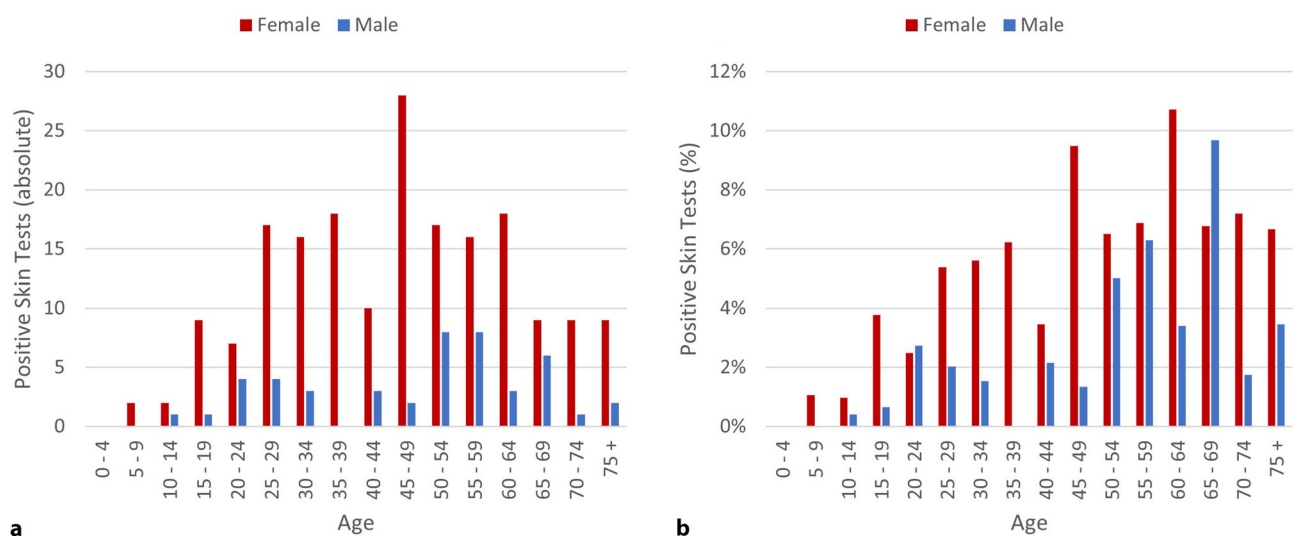


Fig. 6 Positive patch tests (type IV allergy) broken down by age category and sex: **a** in absolute numbers, **b** relative to the total number of tests in percent (%)

3.81%, 40–44 years: 3.03%, 45–49 years: 6.76%, 50–54 years: 5.94%, 55–59 years: 6.67%, 65–69 years: 7.69%, 70–74 years: 5.49%, 75–79 years: 5.15%, 80–84 years: 7.50%, 85–89 years: 6.25%, 90+ years: 0.00%). In the age group 45–49, there was the highest number of 30 positive tests in absolute terms. Overall, women were more often affected than men (total: women: 5.28% = 187/3544, men: 1.99% = 46/2313).

Discussion

As already known, our study confirmed the dominance of inhalant allergens through all age groups. The rate of positive tests decreased with age, but remained relevant even in patients well advanced in years. The results of this study are not an isolated case. A study from Burgenland (Austria) had investigated the prescription frequency of anti-allergic medication by age groups. Since the indications for antihistamine treatment are mainly inhalant allergies and urticaria/angioedema, an indirect comparability is possible with our own study [7]. Jordakieva et al. [7] found a lower proportion of prescriptions in infancy from 0–4 years of age with an increase in preschool to school age and a high proportion in working age but remaining high beyond retirement age. In contrast to our data, the proportion in the Burgenland publication did not go down more before the age of 80 years, whereas in our study it fell off as early as 60 years. Both studies indicate clinically relevant proportions of inhalant allergies or prescribed anti-allergic medication at the age of over 60 years in up to more than 10% of the collective. A Swiss study also describes that approximately 13–15% of individuals over 60 years of age suffer from allergic rhinitis [14]. A Swedish study also speaks of a sensitization rate of 15% against at least one allergen in the age group of 61–86 years [8].

In our analysis, food allergy is a disease of young age. It has its highest proportion in infancy (0–4 years), after which the proportion of positive tests drops sharply. Allergies to the primary food allergens peanut, hen's egg and cow's milk are "lost", soy bean as a probable secondary food allergen in birch pollen allergy is not. Surprisingly, the proportion of boys falls off more slowly and they seem to "lose" their food allergy later. From the age of 10 years, this difference evened out again. In an Australian study, 11% of infants younger than 1 year were found to have a food allergy to hen's egg, peanut, cow's milk or sesame. At the age of 4 years, the frequency there also dropped to 3.8%; girls and boys had not been analyzed separately [15]. Also, in the "European Anaphylaxis Registry", severe allergic reactions to food were mainly found in children under 6 years of age [1].

In our analysis, contact allergies were rare in childhood. A strong increase occurred in adulthood up to high retirement age. Women were more frequently affected. A meta-analysis of 28 studies had also described an increase in contact allergies in adulthood (<18 years: 16.5%, adults: 21.4%) [16]. Our study also confirmed another observation of the meta-analysis: women were twice as likely as men to have positive patch tests: 27.9% vs. 13.2%. In both our analysis and the meta-analysis, nickel ranked first, with fragrance mix second most frequently in each case. The higher proportion in women could be explained by more frequent exposure to contact allergens. The increased use of costume jewellery, cosmetics, and perfume in women may be the determining factor here. In two older studies from 1996 and 2003, which were also conducted at the FAZ, nickel and the preservative thiomersal/thimerosal, which is now hardly used, were also found to be the most frequent contact allergens [17, 18].

Conclusion

Inhalant allergies play a major role in the Austrian population. Older people are also still affected and should therefore also be tested for allergies and treated if they are suspected of suffering from them. Food allergies are mainly a disease of infancy and are usually “lost” again. Contact allergies increase with age and mainly affect women.

Author Contribution B. Heindl, T. Braunsteiner and L. Klug collected the data from routine records. B. Hemmer wrote the manuscript. F. Wantke and W. Hemmer proofread the manuscript. S. Wöhrle supervised the patients, created the concept, supervised B. Heindl in the context of his medical diploma thesis and edited the manuscript.

Funding Open access funding provided by Medical University of Vienna.

Conflict of interest B. Heindl, T. Braunsteiner, L. Klug, F. Wantke, W. Hemmer and S. Wöhrle declare that they have no competing interests.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

References

1. Grabenhenrich LB, Dölle S, Moneret-Vautrin A, Köhli A, Lange L, Spindler T, et al. Anaphylaxis in children and adolescents: the European anaphylaxis registry. *J Allergy Clin Immunol*. 2016;137:1128–1137.e1.
2. Wood RA. The natural history of food allergy. *Pediatrics*. 2003;111(6 Pt 3):1631–7.
3. Savage J, Johns CB. Food allergy: epidemiology and natural history. *Immunol Allergy Clin North Am*. 2015;35:45–59.
4. Kulig M, Bergmann R, Klettke U, Wahn V, Tacke U, Wahn U. Natural course of sensitization to food and inhalant allergens during the first 6 years of life. *J Allergy Clin Immunol*. 1999;103(6):1173–9.
5. Bergmann RL, Wahn U, Bergmann KE. The allergy march: from food to pollen. *Environ Toxicol Pharmacol*. 1997;4:79–83.
6. Paller AS, Spergel JM, Mina-Osorio P, Irvine AD. The atopic march and atopic multimorbidity: many trajectories, many pathways. *J Allergy Clin Immunol*. 2019;143:46–55.
7. Jordakieva G, Kundi M, Untersmayr E, Pali-Scholl I, Reichardt B, Jensen-Jarolim E. Country-wide medical records infer increased allergy risk of gastric acid inhibition. *Nat Commun*. 2019;10:3298.
8. Warm K, Hedman L, Lindberg A, Lötvall J, Lundbäck B, Rönmark E. Allergic sensitization is age-dependently associated with rhinitis, but less so with asthma. *J Allergy Clin Immunol*. 2015;136(6):1559–1565.e2.
9. Calhoun KH. Allergy in the geriatric population. *Curr Opin Otolaryngol Head Neck Surg*. 2015;23:235–9.
10. De Martinis M, Sirufo MM, Suppa M, Di Silvestre D, Ginaldi L. Sex and gender aspects for patient stratification in allergy prevention and treatment. *Int J Mol Sci*. 2020;21(4):1535.
11. Leffler J, Stumbles PA, Strickland DH. Immunological processes driving IgE sensitisation and disease development in males and females. *Int J Mol Sci*. 2018;19(6):1554. <https://doi.org/10.3390/ijms19061554>.
12. Ruëff F, Bergmann K-C, Brockow K, Fuchs T, Grübl A, Jung K, et al. Hauttests zur Diagnostik von allergischen Soforttypreaktionen. *Allergo J*. 2010;19:402–15.
13. Johansen JD, Aalto-Korte K, Agner T, Andersen KE, Bircher A, Bruze M, et al. European society of contact dermatitis guideline for diagnostic patch testing—recommendations on best practice. *Contact Dermatitis*. 2015;73:195–221.
14. Wüthrich B, Schmid-Grendelmeier P, Schindler C, Imboden M, Bircher A, Zemp E, et al. Prevalence of atopy and respiratory allergic diseases in the elderly SAPALDIA population. *Int Arch Allergy Immunol*. 2013;162:143–8.
15. Peters RL, Koplin JJ, Gurrin LC, Dharmage SC, Wake M, Ponsonby AL, et al. The prevalence of food allergy and other allergic diseases in early childhood in a population-based study: HealthNuts age 4-year follow-up. *J Allergy Clin Immunol*. 2017;140:145–153.e8.
16. Alinaghi F, Bennike NH, Egeberg A, Thyssen JP, Johansen JD. Prevalence of contact allergy in the general population: a systematic review and meta-analysis. *Contact Dermatitis*. 2019;80:77–85.
17. Wantke F, Hemmer W, Jarisch R, Götz M. Patch test reactions in children, adults and the elderly. A comparative study in patients with suspected allergic contact dermatitis. *Contact Dermatitis*. 1996;34:316–9.
18. Wöhrle S, Hemmer W, Focke M, Götz M, Jarisch R. Patch testing in children, adults, and the elderly: influence of age and sex on sensitization patterns. *Pediatr Dermatol*. 2003;20:119–23.