

Patterns of Sensitization to Inhalant and Food Allergens – Findings from the German Health Interview and Examination Survey for Children and Adolescents

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Key Words

Allergic sensitization · Immunoglobulin E cross-reactivity · Children and adolescents

Abstract

Background: To assess the prevalence of allergic sensitization and to analyze patterns of sensitization to common inhalant and food allergens in a nationwide representative sample of children and adolescents in Germany. **Methods:** Data were collected from 2003 to 2006 within the KiGGS, the national Health Interview and Examination Survey covering a representative sample of 17,641 children and adolescents in Germany. Immunoglobulin E (IgE) antibodies to 20 specific allergens (11 inhalant and 9 food allergens) were quantitatively measured in a subsample of 12,988 KiGGS participants aged 3–17 years using the ImmunoCAP system. Serum concentrations ≥ 0.35 kU/l indicate sensitized participants. An exploratory factor analysis was performed in order to identify sensitization patterns. **Results:** Sensitization to at least 1 of the 20 tested allergens was detected in 40.2% [95% confidence interval (CI) 39.0–41.4] of the participants. The highest sensitization prevalences were found for pollen from Timothy grass (22.7%; 21.5–23.9) and rye (21.2%; 20.0–22.4). Sensitization was more prevalent in boys than in girls and prevalence increased generally with increasing age. We identified seven sensitization groups, namely (in descending

order of magnitude) 'Timothy grass/rye', 'house-dust mites', 'food/mugwort', 'birch/apple', 'animals', 'cow's milk/egg white' and 'moulds'. **Conclusions:** Allergic sensitization is common in German children and adolescents. The fact that sensitization potentially leads to clinically relevant allergic diseases stresses the public health relevance of this topic. Whether the grouping reflects the propensity for persons to be sensitized to multiple allergens within a group, or whether it is due to IgE cross-reactivity between different allergens of similar structure is still being discussed.

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Introduction

It is well known that sensitization to specific allergens from tree or grass pollen, animal dander, house-dust mites or food components mediated by immunoglobulin E (IgE) antibodies is able to set off inappropriate inflammatory immune responses. Allergic rhinoconjunctivitis, asthma and food allergies are counted among conditions that are clinically relevant. These diseases have the potential to become chronic, more severe, comorbid or to merge in terms of the atopic march over time. Therefore, recent epidemiological research on associations of sensitization to common inhalant or food allergens and subsequent allergic diseases is of particular interest in children

and adolescents [1–6]. Indeed, sensitization is a prerequisite, but on its own not enough to cause a subsequent allergic reaction. And the rate of clinical relevance depends, for instance, on the type of allergen. In the Global Asthma and Allergy European Network (GA²LEN) study, the overall rate of clinical relevance was at least 59%. The highest rate was observed for grass sensitization with 88.4% for all grass-sensitized patients. Furthermore, the risk of an allergic reaction significantly increased in the case of polysensitization [7].

Current epidemiological studies aiming at collecting and examining sensitization status differ in study populations, type and number of tested allergens and/or in the assessment of sensitization. For instance, the GA²LEN study was conducted among patients who were referred to one of the 17 participating centers in 14 European countries and received skin prick tests (SPT) [8]. Within the framework of the research program Obstructive Lung Disease (OLIN) in northern Sweden and in a study comparing urban and rural areas in Poland, school children were tested with SPT [9, 10]. SPT were also applied within the birth cohort study from the Isle of Wight [1]. In the German Multi-Centre Allergy Study (MAS) birth cohort, IgE-levels to airborne allergens were determined [11]. Serum allergen-specific IgE-levels were also used to define sensitized subjects in the allergy component of the American population-based National Health and Nutrition Examination Survey (NHANES) 2005–2006, which was the first nationwide assessment of IgEs among the US population [12]. In Germany, specific IgE antibodies to common inhalant and food allergens were measured at national representative level within the German Health Interview and Examination Survey for Children and Adolescents (KiGGS).

Our study aimed at estimating the prevalence of sensitization to 20 common inhalant and food allergens among German children and adolescents by using data from the KiGGS study. In order to better understand concurrent sensitizations, sensitization patterns were also investigated.

Methods

The KiGGS was a population-based cross-sectional study conducted from May 2003 to May 2006 by the Robert Koch Institute, Berlin. For the first time in Germany, a study aimed to collect nationally representative health-related data from children and adolescents aged 0–17 years. The overall response rate was 66.6%. The concept and design of the survey and the conducting of fieldwork have been described in detail elsewhere [13–15]. Briefly, a total of

Table 1. Allergens tested in serum (specific IgE antibodies) of participants aged 3–17 years

Code	Allergens
d1	<i>Dermatophagoides pteronyssinus</i> (DermPt) (house-dust mite)
d2	<i>Dermatophagoides farinae</i> (DermFa) (house-dust mite)
e1	Cat dander
e3	Horse dander
e5	Dog dander
f1	Egg white
f2	Cow's milk
f4	Wheat
f9	Rice
f13	Peanut
f14	Soya bean
f31	Carrot
f35	Potato
f49	Apple
g6	Timothy grass
g12	Cultivated rye
m2	<i>Cladosporium herbarum</i> (Clados) (mould)
m3	<i>Aspergillus fumigatus</i> (Asperg) (mould)
t3	Common silver birch
w6	Mugwort

17,641 participants (8,656 girls and 8,985 boys) were surveyed. The participants and their parents were invited to 1 of 167 local study centers, at which they filled in self-administered questionnaires followed by a standardized, computer-assisted personal interview by a trained physician with a parent attending or in the case of the adolescents (≥ 14 years of age), by themselves. In addition, the participants underwent a physical examination including physical ability tests. For these activities, study teams were thoroughly trained and were led by a physician experienced in pediatrics. The KiGGS was funded by the German Federal Ministries of Health and of Education and Research. Informed consent was obtained from all parents. The study was approved by the Charité/Universitätsmedizin Berlin ethics committee.

Upon agreement by the participants (and/or parents), blood samples were drawn. Among other laboratory tests, the samples were quantitatively analyzed for specific IgE antibodies by using the ImmunoCAP system, Phadia (now Thermo Fischer Scientific), Uppsala, Sweden. Serum concentrations of IgE antibodies were measured by UNICAP 1000, within the range $0.35 \leq \text{kU/l} \leq 100$. Concentrations $< 0.35 \text{ kU/l}$ were referred to as 'not sensitized', while concentrations $> 100 \text{ kU/l}$ were referred to as 'highly sensitized'.

Participants in the age range 3–17 years were tested for 20 allergen-specific IgE antibodies (11 inhalant and 9 food allergens; table 1). In addition, the screening test panel SX1 with 8 common inhalant allergens was performed. As less serum was available for children < 3 years of age, they were tested with SX1 and for specific IgE to cow's milk only. We report on sensitizations among 3- to 17-year-old children and adolescents.

We examined the prevalence and its 95% confidence interval (CI) of children and adolescents who were sensitized to at least 1 of the tested 20 allergens. We also examined the prevalence and its 95% CI of sensitization to each single allergen. In order to identify sensitization patterns, we performed exploratory (not confirmatory) factor analysis (principal axis factoring and subsequent oblique rotation) of the 20 allergens as a classification method, being the most suitable mathematical procedure for this kind of data [16]. Basically, we analyzed the correlations between the IgE concentrations of the 20 allergens. For this, we used factor analysis which summarized allergens with high intercorrelations to common factors. The factor analysis was performed without restriction of the number of factors and to the structure of the factor loadings. A factor was retained if its eigenvalue was >1. The resulting factor matrix was rotated by the 'oblique' method in order to differentiate between correlated and uncorrelated sensitization patterns [17–19]. Each allergen was included in the factor for which it had the highest loading, except for dog dander. Although the highest loading was on the factor 'egg white/cow's milk', it was decided to include dog dander in the factor 'animals' with the second highest load due to reasons of content. We estimated the prevalence and its 95% CI of sensitization to the identified factors.

All statistical analyses were performed using PASW statistical software (release 20.0; SPSS Inc., Chicago, Ill., USA). The design of the KiGGS study (2-stage clustered sample) was accounted for by using the PASW-18-method for complex samples. In order to assure that the derived estimates are representative at the national level, a sampling weight was applied throughout statistical analyses that corrects for age, sex, residence (East/West/Berlin) and nationality. This weighting factor was especially adopted for the presence of blood samples. All analyses were stratified by sex and, if appropriate, age group. Differences were considered statistically significant if CIs did not overlap.

Results

From the total of 17,641 KiGGS participants, 14,836 were ≥3 years old. Among them, 12,988, i.e. 87.5% (6,323 girls and 6,665 boys) had data for all 20 types of allergen-specific IgE (full sample sets for 20 allergen determinations). This rendered this subsample eligible for analysis.

Sensitization to at least 1 allergen was prevalent in 40.2% (95% CI 39.0–41.4) of the above-mentioned children and adolescents. The prevalence was significantly higher in boys compared to girls [44.3% (42.8–45.8) vs. 35.8% (34.3–37.3)]. For both sexes, sensitization prevalence increased considerably with increasing age (table 2).

The prevalence of sensitization to single allergens was highest for pollen from Timothy grass (22.7%; 21.5–23.9) and rye (21.2%; 20.0–22.4), followed by house-dust mites and birch pollen. We found lower sensitization preva-

Table 2. Allergic sensitization in participants aged 3–17 years according to sex and age (prevalence and 95% CI)

Age, years	Girls		Boys		Total	
	%	95% CI	%	95% CI	%	95% CI
3–6	26.8	24.4–29.3	31.7	28.8–34.7	29.3	27.4–31.3
7–10	34.2	31.8–36.8	43.7	41.0–46.4	39.1	37.3–41.0
11–13	39.5	36.3–42.7	49.3	45.8–52.9	44.5	41.9–47.2
14–17	41.7	39.3–44.2	51.1	48.7–53.6	46.5	44.8–48.3
Total	35.8	34.4–37.3	44.3	42.8–45.8	40.2	39.0–41.4

lences of 6–11% for almost all allergens from food and animals, with the highest prevalence against peanut (10.6%, 9.8–11.6) and dog dander (9.7%; 9.1–10.3), respectively. Sensitization was lowest for cow's milk, egg white, horse dander and moulds (1–6%). As expected, the prevalence of sensitization was generally higher in boys than in girls (table 3).

The order of sensitization prevalence did not differ between the sexes when analyses were stratified by age. For the youngest girls and boys (3–6 years), however, the prevalence of sensitization to egg white and cow's milk was almost as high as the prevalence of sensitization to grass pollen and house-dust mites (data not shown).

We identified the following seven groups (sensitization patterns) from factor analysis: 'Timothy grass/rye', 'house-dust mites', 'food/mugwort', 'birch/apple', 'animals', 'cow's milk/egg white' and 'moulds'. The accumulated variance reached 76.6%. The factors, the included allergens as well as the factor loadings are presented in table 4. The sensitization pattern 'Timothy grass/rye' was most prevalent, with 23.1% (21.9–24.3) of children and adolescents showing this pattern. The second highest sensitization prevalence was found for the factor 'house-dust mites' (22.4%; 21.5–23.2), while the sensitization for 'moulds' was lowest (2.8%; 2.5–3.2; table 5).

As expected, the prevalence of sensitization to all identified groups increased with increasing age, except for the factor 'cow's milk/egg white'. The sensitization prevalence for 'cow's milk/egg white' was 14.0% (11.8–16.4) in the youngest boys and 12.4% (10.6–14.4) in the youngest girls. These numbers declined to 3.7% (2.9–4.7) in adolescent boys and 4.4% (3.3–5.7) in adolescent girls. The factor 'cow's milk/egg white' was the only one for which the sensitization prevalence in girls aged 7–17 years was higher compared to boys in the same age range, although this was not statistically significant (table 5).

Table 3. Allergic sensitization against single allergens in participants aged 3–17 years (prevalence and 95% CI)

Allergens	Girls		Boys		Total	
	%	95% CI	%	95% CI	%	95% CI
Timothy grass	18.5	17.2–19.8	26.7	25.3–28.2	22.7	21.5–23.9
Rye	17.0	15.8–18.3	25.1	23.6–26.6	21.2	20.0–22.4
DermPt	17.4	16.3–18.6	24.1	23.0–25.3	20.9	20.1–21.7
DermFa	17.0	16.0–18.2	24.2	23.0–25.4	20.7	19.9–21.5
Birch	11.6	10.6–12.6	16.6	15.4–17.8	14.1	13.3–15.0
Mugwort	8.9	8.1–9.8	12.8	11.6–14.0	10.9	10.0–11.8
Peanut	8.3	7.4–9.2	12.9	11.7–14.2	10.6	9.8–11.6
Wheat	7.6	6.8–8.4	12.1	10.9–13.3	9.9	9.1–10.8
Dog dander	7.6	6.9–8.3	11.6	10.7–12.6	9.7	9.1–10.3
Carrot	7.6	6.8–8.5	11.6	10.5–12.8	9.7	8.9–10.5
Apple	7.3	6.5–8.3	11.0	10.0–12.1	9.2	8.5–10.0
Potato	6.5	5.8–7.4	10.1	9.0–11.4	8.4	7.5–9.3
Cat dander	6.6	5.9–7.3	9.6	8.8–10.4	8.1	7.6–8.7
Rice	5.3	4.6–6.1	9.0	7.9–10.1	7.2	6.4–8.0
Soya bean	4.9	4.2–5.6	7.7	6.7–8.8	6.3	5.6–7.1
Cow's milk	5.6	4.9–6.4	5.9	5.1–6.7	5.7	5.2–6.3
Egg white	5.4	4.7–6.1	4.6	4.0–5.3	5.0	4.5–5.4
Horse dander	4.0	3.5–4.5	4.7	4.2–5.3	4.4	4.0–4.7
Asperg	1.4	1.1–1.8	3.2	2.7–3.7	2.3	2.0–2.7
Clados	1.3	1.0–1.7	2.2	1.8–2.6	1.8	1.5–2.1

Discussion

In the KiGGS, the prevalence of sensitization was assessed at national representative level for the first time in Germany. A high proportion of children and adolescents aged 3–17 years were sensitized to at least 1 of the 20 tested inhalant and food allergens (40.2%; 39.0–41.4). The highest sensitization prevalences were found for pollen from Timothy grass (22.7%; 21.5–23.9) and rye (21.2%; 20.0–22.4). Sensitization was more prevalent in boys compared to girls and it increased generally with increasing age group. To confirm the empiric observations of experienced allergologists, a statistical grouping of allergens was performed and did not show unexpected results. Nevertheless, these sensitization groups have never been demonstrated in such a number of children and adolescents. We identified seven sensitization groups, namely (in descending order of magnitude) ‘Timothy grass/rye’, ‘house-dust mites’, ‘food/mugwort’, ‘birch/apple’, ‘animals’, ‘cow’s milk/egg white’ and ‘moulds’.

Epidemiological studies aimed at evaluating the prevalence of allergic sensitization are characterized by heterogeneity mainly in methodological aspects like type and number of allergens tested, adopted methods in order to assess allergic sensitization, applied cut-off levels and re-

cruited study populations. A comparison of study results in this research field is, therefore, difficult. However, there are studies similar to the KiGGS. For instance, the NHANES study (n = 7,268 with a complete IgE panel) reported a sensitization prevalence of 43.7% to at least 1 of the 19 allergens tested. Of note, the US study did not only include children and adolescents, but also adults up to 70 years of age and older [6]. For Swiss 13- to 14-year old adolescents surveyed in 1999–2000 within the framework of the SCARPOL study (Swiss Study on Childhood Allergy and Respiratory Symptoms with Respect to Air Pollution, Climate and Pollen) the SX1 test for 8 common inhalative allergens was positive (cut-off: ≥ 0.69 kU/l) in 36.8% (crude prevalence, n = 587) [20]. Similar to the KiGGS, a higher prevalence of sensitization was found in boys than in girls in the Danish TOACS study (The Odense Adolescence Cohort Study on Atopic Diseases and Dermatitis) among adolescents aged 12–16 years (n = 1,501). In total, 29.6% of the participants were IgE-sensitized (cut-off: >0.35 kU/l) against at least 1 of the 19 tested inhalant allergens, food allergens or *Pityrosporum ovale*. The highest prevalences found were for Timothy grass and house-dust mite (18.0%) [21]. In the German MAS study, the analyses of IgE sensitization to airborne allergens among children from birth to 10 years of age

Table 4. Allergens, factors and factor loadings from factor analysis (principal component analysis) of sensitized participants aged 3–17 years

Allergens	Factor						
	1 Food/ mugwort	2 Animals	3 House-dust mites	4 Moulds	5 Birch/ apple	6 Timothy grass/rye	7 Cow's milk/ egg white
Rice	-0.961	-0.010	-0.012	0.040	0.092	0.052	0.022
Soya bean	-0.932	0.027	-0.013	0.013	0.019	-0.113	-0.006
Potato	-0.927	-0.017	-0.009	-0.056	0.014	0.074	0.035
Wheat	-0.895	-0.018	-0.008	-0.024	0.087	0.180	0.051
Carrot	-0.528	-0.009	0.008	-0.017	-0.523	0.076	0.034
Peanut	-0.475	0.038	0.017	0.042	-0.085	-0.053	-0.032
Mugwort	-0.360	-0.027	-0.008	0.001	0.212	0.185	0.002
Cat dander	-0.051	0.839	-0.005	-0.031	-0.050	0.019	0.052
Horse dander	0.076	0.799	0.013	0.044	0.029	-0.004	-0.114
Dog dander	-0.052	0.497	-0.065	0.036	0.003	0.073	0.582
DermPt	0.009	-0.007	-0.979	-0.003	-0.001	-0.012	-0.005
DermFa	0.010	-0.004	-0.978	-0.009	-0.011	-0.008	-0.016
Clados	0.014	0.034	0.000	0.931	0.010	0.009	0.080
Asperg	0.016	-0.014	0.011	0.908	-0.027	-0.014	0.098
Birch	-0.144	0.023	-0.011	0.006	-0.958	0.058	0.004
Apple	0.099	-0.004	-0.016	0.025	-0.917	-0.045	0.002
Timothy grass	-0.016	0.021	0.007	0.006	0.000	0.983	-0.023
Rye	0.051	0.006	0.012	-0.008	-0.012	0.958	0.014
Egg white	-0.058	-0.167	-0.017	0.138	0.032	0.038	0.848
Cow's milk	0.081	0.035	0.036	-0.078	0.033	-0.062	0.518
Eigenvalue	5.69	2.12	1.88	1.61	1.52	1.41	1.09
% of variance explained	28.43	10.59	9.39	8.07	7.60	7.06	5.46
Cumulative % of variance explained	28.43	39.02	48.41	56.48	64.08	71.14	76.60

Figures in bold represent the highest factor loading of each allergen.

showed a dominance of responses to pollen allergens from grass and birch (cut-off: >1 kU/l) and increased prevalences with increasing age ($n = 273$) [11].

SPT were applied in order to assess allergic sensitization in a study of children aged 7–8 years in northern Sweden ($n = 1,700$) [10]. A proportion of 29.9% were sensitized to at least 1 of the 10 allergens tested, and prevalence was higher in boys than in girls. In this particular study, SPT results were validated against specific IgE reactivity ≥ 0.35 kU/l resulting in an 88% agreement. A similar sensitization prevalence of 36.2%, also determined by SPT, was found in Australian schoolchildren aged 8–11 years ($n = 597$), who were tested for 6 allergens [22]. In a recent study of Korean schoolchildren ($n = 7,829$; age groups: 6–7 and 12–13 years), a prevalence of sensitization of 47.9% (the most prevalent being for house-dust mite) was determined by SPT with a total of 18 inhalant allergens [23].

A major strength of the KiGGS study is the population-based sample of German children and adolescents up to 17 years of age. The applied sampling method excluded hospitalized subjects. However, as allergies generally do not result in hospitalization, we could not assume selection bias. Furthermore, comparisons between responders and nonresponders based on the standardized nonresponder questioning show marginal differences in important basic characteristics. Therefore, the KiGGS sample can be considered as extensively unbiased. The analyses presented here were performed in a subsample of participants aged 3–17 years and with successful measurement for all 20 allergens. The applied weighting factor was especially adopted for the presence of blood samples. It also corrects for age, sex, residence (East/West/Berlin) and nationality. Use of this weighting factor enabled us to generalize the results to the German population of 3–17 year olds.

Table 5. Sensitization patterns in participants aged 3–17 years, according to sex and age (prevalence and 95% CI)

Age, years		Timothy grass/rye		House-dust mites		Food/mugwort		Birch/apple		Animals		Cow's milk/egg white		Moulds	
		%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Girls															
3–6	1,443	10.1	8.4–12.1	10.2	8.6–12.2	6.5	5.2–8.2	5.4	4.2–7.0	4.5	3.6–5.7	12.4	10.6–14.4	0.7	0.4–1.3
7–10	1,769	18.6	16.4–21.0	14.8	13.1–16.8	12.3	10.5–14.3	11.3	9.6–13.2	8.7	7.4–10.2	9.3	7.8–10.9	1.9	1.3–2.8
11–13	1,395	23.1	20.4–26.1	23.6	21.1–26.4	15.1	13.1–17.3	14.7	12.3–17.5	12.5	10.4–14.9	8.2	6.5–10.2	1.6	1.0–2.4
14–17	1,716	23.0	20.9–25.1	25.7	23.4–28.2	16.4	14.8–18.3	15.7	13.8–17.7	14.7	13.2–16.3	4.4	3.3–5.7	3.5	2.6–4.6
Total	6,323	18.8	17.6–20.2	18.9	17.7–20.1	12.8	11.8–13.8	11.9	10.9–13.0	10.3	9.5–11.2	8.3	7.4–9.2	2.0	1.7–2.4
Boys															
3–6	1,510	13.1	11.1–15.4	13.8	11.8–16.2	8.5	7.0–10.2	7.7	6.3–9.5	6.7	5.4–8.5	14.0	11.8–16.4	1.9	1.2–2.9
7–10	1,898	26.9	24.6–29.4	23.1	20.9–25.4	19.3	17.2–21.6	16.3	14.4–18.4	14.2	12.4–16.1	8.8	7.5–10.3	3.0	2.3–3.9
11–13	1,470	33.2	29.9–36.7	29.5	26.9–32.1	22.4	19.4–25.7	21.1	18.4–24.1	17.5	15.3–20.0	6.1	4.7–7.7	4.5	3.6–5.7
14–17	1,787	33.8	31.3–36.3	34.3	31.9–36.7	22.7	20.5–25.0	21.7	19.5–24.2	19.5	17.7–21.5	3.7	2.9–4.7	4.9	3.9–6.1
Total	6,665	27.1	25.6–28.6	25.7	24.5–26.9	18.4	17.1–19.9	16.9	15.7–18.2	14.7	13.8–15.7	7.9	7.1–8.8	3.6	3.1–4.2
Total															
3–6	2,953	11.6	10.2–13.2	12.1	10.7–13.6	7.5	6.5–8.7	6.6	5.6–7.7	5.7	4.8–6.7	13.2	11.7–14.8	1.3	0.9–1.8
7–10	3,667	22.9	21.3–24.7	19.1	17.6–20.7	15.9	14.4–17.5	13.8	12.6–15.2	11.5	10.4–12.7	9.0	8.0–10.2	2.4	1.9–3.1
11–13	2,865	28.3	25.9–30.8	26.6	24.6–28.7	18.8	16.9–20.9	18.0	16.0–20.1	15.0	13.4–16.9	7.1	6.0–8.4	3.1	2.5–3.8
14–17	3,503	28.5	26.8–30.4	30.1	28.5–31.8	19.6	18.1–21.3	18.8	17.3–20.4	17.2	16.0–18.4	4.0	3.4–4.8	4.2	3.5–5.1
Total	12,988	23.1	21.9–24.3	22.4	21.5–23.2	15.7	14.7–16.7	14.5	13.6–15.4	12.6	12.0–13.2	8.1	7.5–8.7	2.8	2.5–3.2

A further strength of the KiGGS study is the objective measurement of allergic status via specific serum IgE levels. Measurement of IgE levels is a well-established and standardized method for assessing sensitization in vitro. It has several advantages over SPT (especially in the setting of an epidemiological study) which include (1) the quantification of the results, (2) many allergens can be assayed with a limited amount of serum which can be stored easily, (3) it is not influenced by antihistamine treatment of the patient and (4) it is independent of the condition of the skin which can interfere with SPT [24].

In general, a detection of specific IgE antibodies does not principally indicate a clinically evident allergic disease. The probability of allergic symptoms merely increases with increasing sensitization level. The level of sensitization at which symptoms occur might also differ between allergens. If a study aims to distinguish symptomatic individuals (i.e. 'better' patients) from asymptomatic ones in terms of clinical relevance, then a test of sensitivity and specificity is obligatory. Our study, however, was intended to show the prevalence of a population at risk from an epidemiological point of view. Therefore, the cut-off value of 0.35 kU/l was applied for the detection

of allergic sensitization, which corresponds to the lowest detection level of the CAP system.

Due to the cross-sectional nature of the data, it remains unclear whether the pattern seen in the younger children will develop into the pattern seen in the older children; this could be considered a limitation of the study. Longitudinal studies, for instance Matricardi et al. [11], provided sensitization data in the same group of participants at different ages. It was shown that IgE-sensitization to airborne allergens developed dynamically throughout childhood, i.e. the prevalence of sensitization increased steadily, mono-sensitization developed rapidly into polysensitization and new sensitization or remission were highly prevalent. The authors concluded that the intensity of IgE sensitization affects long-term persistence and clinical impact.

In NHANES, the 19 allergen-specific IgEs were shown to cluster into five groups that correspond to reported biological classifications, i.e. pollens, mammals, dust mite, cockroach/shrimp and egg/milk [12]. Our results indicate similar sensitization patterns for German children and adolescents. It is not clear what plays the predominant role in allergic sensitization; is it whether grouping reflects the propensity for people to be sensitized to multiple allergens within a group, or whether it is

due to IgE cross-reactivity between different allergens of similar structure? Indeed, multiple allergen reactivity might result from consecutive sensitization to different allergens. However, polysensitization is also mediated by evolutionary conserved protein structures, so-called pan-allergens [25]. Soeria-Atmadja et al. [26] recently analyzed IgE reactivity read-outs from 1,011 deidentified patient blood samples. Read-outs for 89 separate extracts were available for each sample. Twelve clusters of related allergens (fungi, weed pollen, mites, tree and weed pollen, tree pollen/apple, epithelium/dander, animal food, fish, seafood/insect, grass pollen, plant food general, nuts/legumes) were identified. Cluster analyses, based on IgE reactivity or on amino-acid-sequence similarity, gave a relatively high degree of correspondence. Thus, the authors suggested that there is a substantial participation of IgE cross-reactivity in polysensitization.

Today, allergens are characterized in great detail right down to their molecular structure. This knowledge expands the classification of allergens beyond their sources of plant or animal origin to their similar biochemical characteristics. Component-resolved diagnostics (CRD) via molecule-based microarray technology provides information about the nature of the molecules involved in the immunological recognition. This method is capable of differentiating between primary sensitization (species-specific) and immunological cross-reactivity. Mostly, there is a clear identification of sensitizations to specific allergen components such as profilins, tropomyosins, Bet v 1-homologue pathogenesis-related-10 proteins, or nonspecific lipid transfer proteins. As their clinical relevance varies

widely, from oral allergy syndrome to anaphylaxis, CRD therefore facilitates the risk assessment of reaction on exposure to different allergen sources [27]. Scala et al. [28] evaluated IgE reactivity to allergenic molecules in serum samples from a cohort of 23,077 Italian patients. The authors observed IgE recognition of either homologous allergens from different biological sources or nonhomologous allergens from the same source. The reported high prevalence of sensitization to Timothy grass pollen allergen Phl p 1 in the cohort and the highest prevalence being to cow's milk and hen's egg allergens in patients <5 years of age is also, for instance, comparable to our KiGGS results. Another study assessing the IgE repertoire at component level among allergic patients confirmed that components of milk and egg were most commonly recognized in the youngest age groups compared to IgE specific to plant allergens. The authors also reported that IgE cross-reactivity tended to appear only after the age of 6 years [29].

In the near future, molecular allergology for clinical and scientific purposes will hopefully answer the question whether allergen grouping reflects the propensity for persons to be sensitized to multiple allergens within a group or whether it is due to IgE cross-reactivity between different allergens of similar structure. Apart from this, the grouping of specific IgE-antibodies implies the efficient use of selected tests in order to classify individual sensitivity. The research of IgE reactivity in population-based cross-sectional studies enhances our knowledge of diagnostic procedures. It supports the assessment of therapeutic needs and quality and therefore has the capacity to improve the prognosis of therapeutic regimens.

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