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Asthma and Sensitization Pattern in Children

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1. Introduction

The prevalence of specific sensitization and its clinical relevance for the development of allergic diseases and asthma is one of the subjects currently being in the focus of scientific studies. In the field of asthma we find additionally several studies of occupational asthma with specific sensitization and of treatment efficacy and duration of omalizumab in asthma patients with high IgE levels, which will not be discussed in this chapter. Several other studies focus on general aspects of sensitization pattern or classification of specific sensitization corresponding to type or severity of asthma or globally the development of asthma in different populations. Based on a short literature review of such studies we will finally present own representative data of our German Health Interview and Examination Survey for Children and Adolescents (KiGGS).

In this presentation we will describe specific IgE levels to several common aeroallergens in asthmatic and nonasthmatic children, search for a possible correlation between the number of sensitizations and the development of asthma and correlations between age, gender, social and migration status and rural or urban residency of the children and their sensitization status. Finally we will try to identify high risk mono- and polysensitization for asthma and will compare typical combinations of sensitizations in children with and without asthma.

2. Asthma and specific sensitization in the literature

During the last years the scientific community seemed to feel more and more that asthma is a disease showing very different phenotypes with different courses of the disease and therapeutic outcomes and a different prognosis. So the disease has been described not only – as in former times – as eosinophilic or neutrophilic type asthma or intrinsic, extrinsic and mix type asthma but increasingly also as early onset and late onset asthma, childhood and adult onset asthma and several special asthma forms are subject of clinical studies as exercise induced asthma, seasonal asthma, variant asthma and so on. Together with this history also dependencies between specific allergic sensitization and asthma became a target of several studies.

The fact that asthma without any signs of allergy may occur is well known. Additionally, it has become clear that being measurably sensitized does not automatically mean to suffer from any allergic disease. Ten years ago in a population of nearly 800 school children in Italy, using a skin prick test, it was monitored (Crimi et al., 2001) that “about one third of the

sensitized children were without symptoms” – meaning symptoms of asthma and/or rhinitis. So the question arose, how sensitization or special sensitization patterns may influence the development of allergic and atopic diseases like asthma.

Beforehand endeavour has been made to describe frequency and patterns of sensitization itself, for example in a population of more than 700 school children in Germany (Hader et al., 1990). 34.4 % of the studied children had been sensitized to one or more of the tested aeroallergens, 39.6 % of these monosensitized. The most common sensitization was that to grasspollen, followed by birch, than house-dust mite, cat and hazelpollen. Several patterns of mono- and polysensitization have been described.

Nowadays we have a wide overview of demographic distribution of sensitizations and its correlation to asthma. As one could expect, “residence of rural area is associated with a significant lower prevalence of allergic sensitization” seen in more than 400 school children 12-16 years old (Majkowska-Wojciechowska et al., 2007) and boys are significantly more often than girls sensitized to a wide range of allergens (Soto-Quiros et al., 1998) as they are more often affected by asthma. However, in Italy, polysensitization of children living in a rural area especially against pollen and mould led to comparable asthma prevalence as house dust mite sensitization in those living in urban regions (Verini et al., 2005). We will report about the special role of dust mite sensitization in asthma in the course of this review. Reviewing studies using skin tests for defining sensitization, it has been clearly shown that “aeroallergen sensitization occurs in most patients with asthma” (Craig, 2010). It was concluded that in mild to moderate asthma about 95 % of patients show sensitization and in severe asthma still up to 90 %. Remembering the fact that up to 5 % of asthma patients show a neutrophilic asthma and nearly all of those patients develop a severe form of asthma and subtracting those patients from the selected patient groups this may mean that with the exception of neutrophilic asthma forms all other patients show a similar high percentage of sensitization independent from asthma severity grade. This review also showed that sensitization “pattern varies with ethnicity, location of residence, and onset of asthma, but not age”.

The same author described two years earlier in a population of mild-to-moderate asthma patients 14 % of these showing a sensitization only to 1 or 2 aeroallergens but 81 % showing a polysensitization to at least 3 aeroallergens (Craig et al., 2008). He was also able to demonstrate a correlation between sensitization and factors characterising asthma as exhaled nitric oxide measures as a sign of inflammation activity and lung function values.

Not only asthma severity grade correlates with sensitization but also the chance of asthma remission during childhood. In the data of ISAAC, the international study of asthma and allergies in childhood and one of the most important international studies in this field, a cohort comparison of 7 - 8 year versus 11 - 12 year old school children showed that the “remission of asthma was 10 % yearly and inversely related to allergic sensitization” (Bjerg-Bäcklund et al., 2006).

The number of sensitizations against aeroallergens clearly correlates with the risk for asthma, as shown in a total of more than 3000 patients aged 10 to 50 years in Spain and Portugal (Valero Santiago et al. 2009).

Very interesting in this relation is the fact that asthma prevalence in children is enhanced by very different specific sensitizations. A study in a random population of more than 6000 children in New South Wales was able to show that high sensitization to house dust mites in coastal regions as well as high sensitization to alternaria in other regions correlated significantly with higher asthma prevalence compared with regions where sensitization

levels are lower (Peat et al., 1995). Sensitization to house dust mite seems to be one of the most common sensitizations linked to asthma over the world, as for example also shown in children living in Florida, where 89.6 % of the asthmatic children showed a positive RAST result to *Dermatophagoides pteronyssinus* (Nelson et al., 1996). A similar prevalence was seen in Chinese asthmatic children by skin prick testing. 81.9 % showed a positive test to house dust mite (Leung et al., 2001). And also in Zimbabwe sensitization in RAST test to dust mites was the most common sensitization in atopic children (Kambarami et al., 1999).

Astonishingly another study in children living in high altitude (7200 feet) "in a mite-free environment with low levels of outdoor air pollution" saw a comparably high asthma prevalence rate of 6.3 % and high total IgE levels in asthmatic children (Sporik et al. 1995). The explanation of this finding was that 77 % of the studied households had a pet (cat or dog) and the predominant sensitization in children therefore was a sensitization to cat. That sensitization to cat allergen generally is a risk for childhood asthma was confirmed in a prospective birth cohort study in Germany (MAS 90), the German Multicenter Allergy Study (Lau et al., 2005).

In summary, indoor allergen sensitization seems to be closer connected to asthma than outdoor allergen sensitization. This was confirmed for two different ethnic groups living in the same environment of New York City (Rastogi et al. 2006). Similar environment led in both groups to similar sensitization and only indoor allergen sensitization was significantly associated not only with asthma prevalence but also with its severity. In contrary, different environmental circumstances lead not only to different sensitization prevalences and patterns, but also to different association levels with and different attributable fractions of asthma and other atopic diseases (Rona et al. 2008).

When the close correlation between childhood asthma and sensitization had become known, also efforts had been made to define correlations between adult onset asthma and sensitization. The result of a case-control study in Finland including only cases of adult onset asthma in patients 21 - 63 years of age was that specific "IgE antibodies to house dust mite and storage mite were significantly related to an increased risk of asthma." The same correlation was found with IgE antibodies to *aspergillus fumigatus* and *cladosporium herbarum* (Jaakkola et al., 2006).

Nevertheless, one has to keep in mind sensitization being only one of several possible triggers for allergic asthma and these triggers probably showing dependencies among each other. An example was shown in children at high atopic risk, where the prevalence of asthma was higher for those children having suffered more from severe viral lower respiratory tract infections but only when they had also an early sensitization at the age 2 years or lower (Kusel et al., 2007).

From another perspective, specific sensitization only enhanced the risk of being asthmatic significantly for children with "a positive parental history of asthma or atopy" (Illi et al., 2001).

Also - as another example - the socioeconomic status influences sensitization in general, indoor sensitization and together with the latter the risk of asthma in the direction that sensitization is increased with lower socioeconomic status (Lewis et al., 2001). May anyone think sensitization against cockroach and animal to be understandable by social differences in residency environment and pet ownership, the significant increase in ragweed sensitization also will stay unexplainable by such obvious status dependant circumstances.

On the other hand, as we know as another result of the ISAAC study, the correlation between asthma and sensitization seems to be closer in developed countries with higher income (Weinmayr, 2006 2007).

Looking somewhat deeper into the description of sensitization in asthmatic patients, in asthmatic children prevalence rates of sensitization to cat were 40 %, to dog 34 %, to horse 28 %, to birch 23 % and to timothy 16 % and somewhat different to sensitization shown in other atopic diseases like rhinitis or eczema (Rönmark et al., 2003).

An association between different mono-sensitizations against pollen was seen in Sweden in a birth-cohort study with more than 2500 children, where especially birch pollen sensitization was closely correlated to allergic symptoms (Ghunaim et al., 2006).

Already several years ago the knowledge of correlations between sensitization and asthma had led to establishing a new asthma classification based on specific IgE antibodies among other parameters (Kumura 1994). In our time quite ambitious efforts have been made to redefine atopic phenotype and correlate the resultant patterns of sensitization with asthma and asthma outcome parameters even in a population-based birth cohort study (Simpson et al. 2010).

3. Asthma and sensitization pattern in a population-based study in German children and adolescents

Having performed the first population-based interview and examination survey in children and adolescents in Germany, we will seize the opportunity to look for correlations between sensitization and asthma in this population. As we will continue the study, later on we will have the chance to look for changes of sensitization in individuals over time and asthma development also.

For now we want to learn something about sensitization prevalence in German children and adolescents – as well in those with asthma as in nonasthmatic children – RAST classes of indentified sensitizations, demographically based differences in sensitizations and correlations of specific sensitizations with asthma.

3.1 The German health interview and examination survey for children and adolescents (KiGGS)

A total of 17641 children and adolescents from birth up to 17 years of age have been included in this survey, being studied in 167 study points throughout Germany between May 2003 and May 2006. The survey was composed of questionnaires filled in by the parents and parallel by children aged 11 years or older, a computer assisted personal interview (CAPI) performed by study physicians and physical examination and (laboratory) test parts.

A publication describing the study design and methods, patient enrollment and randomisation, response and representativeness can be found in BMC Public Health (Kurth et al., 2008). The response rate was 66.6 % and a non-response analysis based on “key socio-demographic and health-related characteristics for children and parents” was performed for about two thirds of the non-responders. The non-response analysis did not provide an indication of relevant differences in four health related variables compared to responders. Therefore the survey will provide us with as far as possible representative information about the health status of German children and adolescents.

3.2 Methods of assessing asthma and defining specific sensitization in KiGGS

During a Computer-assisted Personal Interview (CAPI) conducted by the studyteam physician parents had been asked whether their children ever had had a positive physician diagnosis of asthma. Though the study results presented with some evidence that possibly more children suffered from asthma as being told to the parents – seen for example analysing the drug anamnesis regarding children having had specific asthma medication on prescription base without their parents having reported a physician diagnosis of asthma as already publicized (Langen & Knopf, 2007) – we think the accuracy of reported physician diagnosis to be more reliable. So we will operate in this analysis with a positive answer to the question of physician diagnosed asthma as the decisive indicator for grouping participants in asthmatic and nonasthmatic children and adolescents.

In laboratory blood tests only the blood of children more than 2 years old and adolescents, had been tested for specific IgE-antibodies to 20 common allergens including 11 frequent inhalative indoor and outdoor allergens. The test system used was the ImmunoCAP® test of Phadia. The allergens involved included food allergens and the following groups and substances of inhalative allergens:

House dust mites:	Dermatophagoides pteronyssinus and dermatophagoides farinae
Animal epithelia:	Cat, horse and dog
Pollen:	Birch, mugwort, rye and timothy grass
Mould fungi:	Cladosporium herbarum and aspergillus fumigatus

In summary we will be able to present the data of 12911 children and adolescents from 3 years to 17 years of age having had a blood test for specific IgE antibodies and having their parents had answered the CAPI.

3.3 Statistical analysis of the KiGGS data

For this analysis SPSS (Statistical Package of the Social Sciences) Version 17 was used. The data have been weighted in the intention to adjust them for deviations between the sample group and German population statistics especially regarding “age structure and disproportionately higher sample size in Eastern vs. Western Germany” (Kurth, 2008). All analyses are based on “complex samples” procedures, so that estimated variations of the results became more realistic having in mind the complex sampling procedure of the study as in detail described in the above mentioned article.

3.4 Results and interpretation

In the entire study population, 4.7 % of the participants had a positive lifetime prevalence of asthma. At least one sensitization was identified in 40.8 % of the children aged 3 years or older and the adolescents.

As asthma and sensitization prevalence rise with increasing age, asthma prevalence in our population aged 3 years and older is measurably higher as in the entire population from birth to age 17. Also the prevalence in sensitization shows differences to the complete study population while we only analyzed the above described subgroup of children and adolescents.

3.4.1 Demographic data

In Table 1 we show demographic characteristics for asthmatic and nonasthmatic participants as well as for those without sensitization, being monosensitized or polysensitized. Statistically significant differences are shown in bold numbers.

	Asthmatic	Non-asthmatic	Not sensitized	Mono-sensitized	Polysensitized
Overall n=12911	5.5 % (5.0-6.0 %)	94.5 % (94.0-95.0 %)	62.8 % (61.6-64.0 %)	4.8 % (4.4-5.2 %)	32.4 % (31.3-33.6 %)
Age group					
3-6 years n=2936	2.8 % (2.2-3.6 %)	97.2 % (96.4-97.8 %)	77.9 % (76.1-79.6 %)	3.6 % (2.9-4.5 %)	18.5 % (16.8-20.3 %)
7-10 years n=3649	4.7 % (4.0-5.6 %)	95.3 % (94.4-96.0 %)	64.8 % (62.9-66.7 %)	5.0 % (4.3-5.9 %)	30.2 % (28.5-32.0 %)
11-13 years n=2835	7.1 % (6.0-8.3%)	92.9 % (92.1-94.1 %)	57.5 % (54.8-60.2 %)	4.8 % (3.9-5.8 %)	37.7 % (35.1-40.3 %)
14-17 years n=3468	6.8 % (5.9-7.9 %)	93.2 % (92.1-94.1%)	54.9 % (53.2-56.7 %)	5.3 % (4.6-6.2 %)	39.8 % (38.0-41.6 %)
Sex					
Male n=6609	6.3 % (5.7-6.9 %)	93.7 % (93.1-94.3%)	58.5 % (57.0-60.0 %)	4.0 % (3.6-4.6 %)	37.5 % (36.1-38.9 %)
Female n=6279	4.7 % (4.1-5.3 %)	95.3 % (94.7-95.9 %)	67.4 % (66.0-68.8 %)	5.5 % (4.9-6.2 %)	27.0 % (25.7-28.5 %)
Parental allergy					
Yes n=5336	7.2 % (6.5-7.9 %)	92.8 % (92.1-93.5%)	55.3 % (53.7-56.9 %)	4.8 % (4.2-5.4 %)	39.9 % (38.3-41.5 %)
No n=6977	4.1 % (3.6-4.7 %)	95.9 % (95.3-96.4 %)	68.7 % (67.2-70.2 %)	4.7 % (4.2-5.3 %)	26.6 % (25.2-28.1 %)
Not known n=269	6.4 % (3.4-11.6 %)	93.6 % (88.4-96.6 %)	62.4 % (55.7-68.7 %)	7.0 % (4.3-11.1 %)	30.6 % (24.7-34.2 %)
Region					
North n=3276	6.2 % (5.3-7.4 %)	93.8 % (92.6-94.7 %)	64.7 % (62.6-66.9 %)	5.4 % (4.7-6.2 %)	29.8 % (27.8-32.0 %)
Middle n=5684	5.5 % (4.9-6.2 %)	94.5 % (93.8-95.1 %)	64.1 % (62.5-65.6 %)	4.3 % (3.7-5.0 %)	31.6 % (30.1-33.1 %)
South n=3920	5.0 % (4.3-5.9 %)	95.0 % (94.1-95.7 %)	60.3 % (58.1-62.5 %)	4.8 % (4.2-5.4 %)	34.9 % (32.8-37.0 %)
Migration status					
Yes n=1901	5.1 % (4.3-6.1 %)	94.9 % (93.9-95.7 %)	65.8 % (63.6-67.9 %)	5.4 % (4.3-6.7 %)	28.8 % (26.8-31.0%)
No n=10926	5.6 % (5.1-6.1 %)	94.4 % (93.9-94.9 %)	62.2 % (60.9-63.5 %)	4.6 % (4.2-5.1 %)	33.2 % (31.9-34.5 %)
Older siblings					
No n=3820	5.9 % (5.1-6.8 %)	94.1 % (93.2-94.9 %)	60.9 % (58.8-62.9 %)	4.8 % (4.1-5.5 %)	34.4 % (32.4-46.4 %)
One n=4395	5.3 % (4.6-6.1 %)	94.7 % (93.9-95.4 %)	63.7 % (61.8-65.5 %)	4.8 % (4.2-5.6 %)	31.5 % (29.8-33.3 %)
2 or more n=1461	4.2 % (3.2-5.5 %)	95.8 % (94.5-96.8 %)	66.8 % (63.7-69.7 %)	3.8 % (2.9-5.0 %)	29.4 % (26.6-32.4 %)

Table 1. Demographic characteristics of study population

We also analysed the population for differences regarding eastern or western region of Germany, rural or urban region, prematurity or underweight at birth, pets in household, preschool children's care outside the family (kindergarten etc.), sleeping behaviour, breast feeding and smoking behaviour and social status of the family. We have not been able to detect any additional statistically significant differences neither concerning asthma nor sensitization prevalence.

What we can clearly perceive is that sensitizations and asthma show a parallel continued rise from 3 years of age up to the age group of 11 - 13 years. Especially the polysensitizations make a major contribution to the increase in sensitization prevalence, whereas the rise in monosensitizations is significant between the agegroup of 3 - 6 and the agegroup of 14 - 17 years but numerically quite small.

Male children and adolescents suffer more often from asthma and sensitizations, both mono- and polysensitizations, than female. Such relationship between asthma and sex in children is described by the GINA (Global Initiative for Asthma) Report (GINA, 2009), while the causes for this difference are pictured as unknown. Nevertheless, the lung size, being smaller in male children and larger in male adults is mentioned as a possible reason for the different asthma prevalence. The importance of this argument may be supported by our data, as sensitizations to inhalative allergens remain more common in male adults than in female while asthma prevalence is decreasing. The fact that boys are more often sensitized than girls has been described in the literature - as mentioned in the review above - but the reasons for this gender based difference remain unclear.

Very well known in contrary is that children of atopic parents tend to more sensitizations and atopic diseases than those of healthy parents as is supported by our data.

Also living in the northern or southern part of Germany produces a significant difference regarding sensitizations. Significantly more study participants living in southern Germany suffer from polysensitizations. This finding may be caused by climatic differences as Germany borders in the North on the North and the Baltic Sea or by differences in the flora. Differences in asthma prevalence show descriptively the converse direction but did not reach significance.

Children belonging to a family with positive migration background show less polysensitizations than others, what may be explained by the known sensitization differences in differently developed countries with a more or less "westernized" lifestyle. Nevertheless, differences in asthma prevalence are barely detectable.

In the same way fitting into the so called hygiene hypothesis are the data showing children without older siblings suffering more from polysensitizations than children with two or more older siblings. This can be explained by the children with older siblings having had more contact with bacteria during early childhood leading in the maturing immune system to a decision more in favour of Th1 lymphocyte answer development which is needed for fighting infections than Th2 lymphocytes which contribute to allergic diseases. Nevertheless, the difference in asthma prevalence was not able to reach statistical significance although descriptively the correlation was similar.

3.4.2 Asthma and specific sensitizations to inhalative allergens

We have been able to scan the blood of nearly 13000 children and adolescents for specific IgE levels to certain common inhalative allergens. IgE is not detectable beneath a margin of 0.35 kU/l with the method used in this study and children not showing detectable IgE levels

are defined as not sensitized as it is common in sensitization analyses. Also common understanding is to value a result between 0.35 and 0.69 kU/l as marginally positive and all results 0.7 or higher as positive. A clear correlation between the level of sensitization and clinical severity of symptoms has not been described.

Table 2 presents the results for the IgE levels in nonasthmatic and asthmatic study participants. It clearly shows up that sensitization prevalence for each single inhalative allergen shows statistically significant differences between the two groups. For better readability, variation has not been presented in the table. Significantly different prevalence rates between asthmatic and nonasthmatic subjects are presented in bold letters.

Additionally detectable is the fact that with the exemption of house dust mites and rye all other allergens show significantly different prevalence also regarding the lowest class between 0.35 and 0.69 kU/l. Our interpretation is that the relevance of such “marginally” positive results may be higher than estimated up to now.

Though we already knew that sensitization does not have to present automatically with clinical symptoms it remains interesting that we found also subjects sensitized with IgE levels of the highest class of 100 kU/l and more without asthma symptoms.

Unit: kU/l Nonasthmatic Asthmatic children	Not detectable <0.35	Low 0.35-0.69	Medium 0.70-3.49	High 3.50-17.49	Very high 17.5-49.99	Very high 50.0-99.99	Very high ≥100
Derm. pteronysinus	80.7 % 44.0 %	3.3 % 3.7 %	5.2 % 9.5 %	4.4 % 11.8 %	3.8 % 12.4 %	1.6 % 10.9 %	1.0 % 7.8 %
Derm. farinae	80.7 % 45.8 %	3.4 % 3.1 %	5.1 % 9.3 %	4.5 % 11.5 %	3.9 % 12.9 %	1.7 % 11.7 %	0.7 % 5.8 %
Cat	93.1 % 67.0 %	1.8 % 4.6 %	3.2 % 13.2 %	1.5 % 7.1 %	0.3 % 5.6 %	0.1 % 2.0 %	0.0 % 0.6 %
Horse	96.7 % 75.6 %	1.1 % 4.7 %	1.6 % 10.7 %	0.4 % 6.4 %	0.1 % 2.0 %	0.0 % 0.3 %	0.0 % 0.3 %
Dog	91.9 % 58.9 %	3.4 % 12.4 %	4.0 % 18.4 %	0.6 % 7.5 %	0.1 % 1.5 %	0.0 % 0.7 %	0.0 % 0.6 %
Birch	87.1 % 58.7 %	2.3 % 4.8 %	4.6 % 10.3 %	3.4 % 12.6 %	1.6 % 7.6 %	0.6 % 3.2 %	0.5 % 2.9 %
Mugwort	89.9 % 70.4 %	3.3 % 8.9 %	5.0 % 11.7 %	1.5 % 7.5 %	0.3 % 1.5 %	0.0 % 0.0 %	0.0 % 0.0 %
Rye	80.1 % 47.2 %	3.4 % 5.4 %	5.8 % 15.6 %	4.7 % 12.1 %	3.1 % 11.0 %	1.8 % 5.2 %	1.1 % 3.3 %
Timothy	78.6 % 43.7 %	3.4 % 5.5 %	5.9 % 13.5 %	5.0 % 13.5 %	2.9 % 10.5 %	2.0 % 6.9 %	2.2 % 6.6 %
Cladosporium herbarum	98.7 % 89.8 %	0.5 % 1.7 %	0.6 % 4.7 %	0.1 % 2.8 %	0.0 % 0.7 %	0.0 % 0.3 %	0.0 % 0.0 %
Aspergillus fumigatus	98.3 % 86.8 %	0.8 % 3.7 %	0.8 % 6.6 %	0.1 % 2.2 %	0.0 % 0.4 %	0.0 % 0.3 %	0.0 % 0.0 %

Table 2. Specific IgE to several inhalative allergens in asthmatic and nonasthmatic subjects

Nevertheless, the most subjects showing very high IgE levels equal or higher than 50 kU/l also suffered from asthma. Nearly 20 % of the asthmatic children and adolescents showed sensitizations to house dust mite in these both classes.

3.4.3 Number of sensitizations and asthma

When we saw the clear correlation between sensitizations to each of the tested inhalative allergens and asthma, the question arose, whether the development of asthma may also show a correlation with the number of sensitizations persons have developed during their life.

Figure 1 presents the correlation between asthma and the number of sensitizations we found in our study. We see that there seems to be a quite clear exponential relationship between the mentioned circumstances.

Only 2.1 % of the study participants without any sensitization suffered from asthma whereas 49.8 % of the participants showing sensitizations to each of the tested 11 inhalative allergens also have had an asthma anamnesis.

For those children and adolescents suffering from asthma but not showing sensitization to any of the inhalative allergens we made an additional analyses with the intention to identify possible sensitizations to food allergens (egg white, milk protein, rice flour, peanut, soybean, carrot, potato, wheat flour or green apple) but were not able to find any correlation. Only a few single cases showed sensitizations to egg, milk or peanut, all other test results were negative.

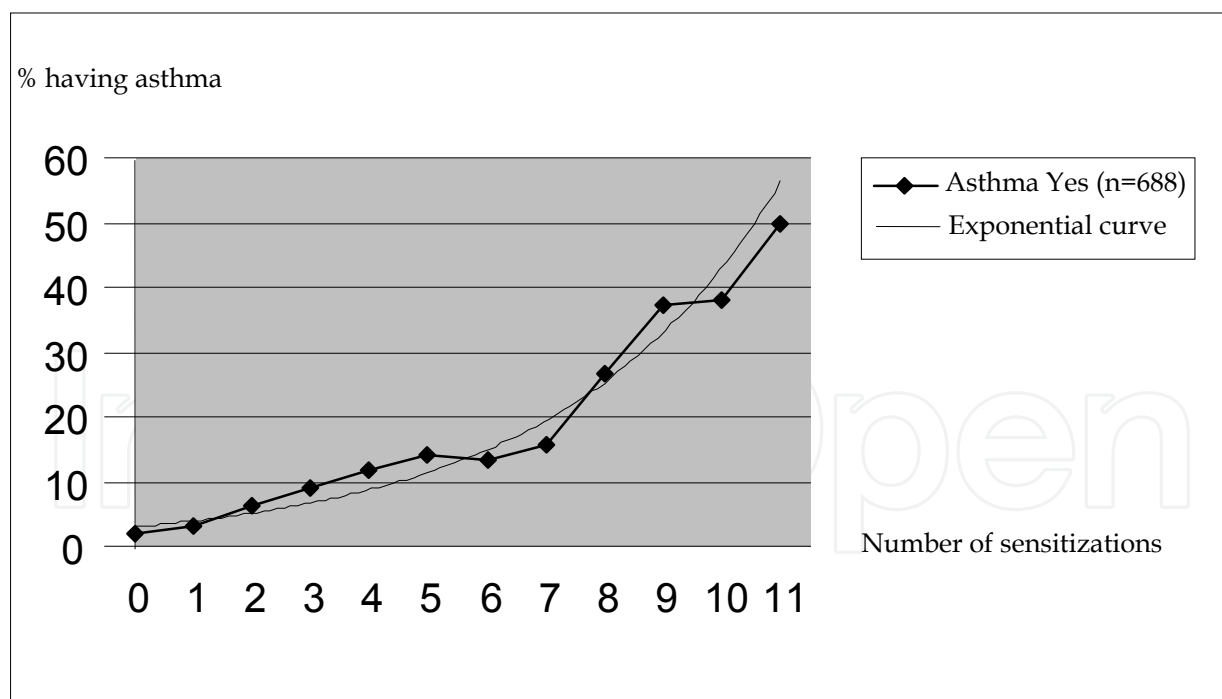


Fig. 1. Number of sensitizations to inhalative allergens and asthma

We also performed the same analyses for different age groups, sex, migration and social status as well as groups living in rural or urban regions of Germany. In each case we have been able to repeatedly find the same relationship – an exponentially sloping curve showing

a positive correlation between the number of sensitizations and asthma. Additionally those curves are located very closely together so that the shown relationship seems to be somewhat like a constitutional or natural correlation.

3.4.4 Course of sensitizations with increasing age

With increasing age the prevalence of sensitizations is rising as well in children with as in those without asthma but in the former the rise starts on much higher values.

Table 3 shows in bold numbers statistically significant increases (those will be marked in all other tables in the same manner) of specific sensitizations with age in comparison with the youngest group or the last group having displayed significant differences already. Variations are presented, those in asthmatic children being much wider than the others as this group is much smaller as that of nonasthmatic children.

The first fact to detect is that in each case with only one exemption sensitization prevalence in asthmatic participants is statistically significant higher than that in nonasthmatic participants. Only in the age group 3 - 6 years sensitization to cladosporium herbarum does not reach significance between those two groups and this circumstance is explainable by the comparatively low prevalence of such sensitization in this age group.

Unit: kU/l Nonasthmatic Asthmatic children	3-6 years n=2936	7-10 years n=3649	11-13 years n=2835	14-17 years n=3468
Derm. pteronysinus	10.7 % (9.3-12.2) 32.3 % (22.5-44.2)	15.8 % (14.4-17.4) 46.7 % (38.1-55.3)	22.3 % (20.3-24.5) 59.0 % (50.2-67.3)	26.2 % (24.4-28.0) 65.4 % (58.5-71.7)
Derm. farinae	10.7 % (9.4-12.1) 30.7 % (21.0-42.3)	16.7 % (15.2-18.3) 45.5 % (37.1-54.1)	21.8 % (19.8-23.9) 56.3 % (47.7-64.6)	25.5 % (23.8-27.3) 64.0 % (56.8-70.5)
Cat	3.1 % (2.5-3.8) 16.9 % (9.6-28.1)	6.7 % (5.8-7.6) 30.7 % (24.0-38.2)	7.3 % (6.0-8.8) 38.8 % (31.4-46.7)	9.4 % (8.4-10.5) 34.6 % (28.0-41.9)
Horse	1.4 % (1.0-1.9) 15.4 % (8.5-26.1)	3.1 % (2.5-3.8) 20.8 % (14.4-29.0)	4.1 % (3.1-5.4) 24.4 % (18.1-32.0)	4.3 % (3.7-5.1) 28.9 % (22.9-35.7)
Dog	3.1 % (2.5-3.9) 23.5 % (15.2-34.6)	7.5 % (6.6-8.6) 31.1 % (23.4-40.0)	9.2 % (7.8-10.8) 45.4 % (37.4-53.6)	11.3 % (10.2-12.4) 48.4 % (41.1-55.7)
Birch	6.2 % (5.3-7.2) 21.1 % (12.8-32.7)	12.3 % (11.1-13.6) 37.4 % (30.2-45.2)	15.2 % (13.2-17.4) 45.7 % (37.8-53.9)	16.5 % (14.9-18.1) 46.0 % (39.2-52.9)
Mugwort	3.4 % (2.7-4.3) 12.6 % (6.4-23.4)	10.7 % (9.5-12.1) 21.2 % (15.2-28.7)	11.7 % (10.1-13.5) 32.7 % (25.8-40.4)	13.1 % (11.7-14.7) 36.6 % (30.5-43.1)
Rye	9.5 % (8.2-11.0) 34.1 % (23.5-46.7)	20.0 % (18.4-21.7) 40.4 % (33.0-48.3)	24.2 % (21.8-26.8) 56.5 % (47.7-64.9)	24.0 % (22.1-26.1) 62.2 % (54.5-69.3)
Timothy	11.3 % (9.9-12.9) 42.5 % (30.3-55.6)	21.6 % (19.9-23.3) 42.5 % (34.6-50.8)	25.1 % (22.6-27.1) 60.2 % (51.8-68.0)	25.5 % (23.7-27.6) 65.0 % (57.4-72.0)
Cladosporium herbarum	0.7 % (0.4-1.1) 2.4 % (0.7-7.8)	1.3 % (1.0-1.8) 6.3 % (3.3-12.0)	1.2 % (0.8-1.7) 11.9 % (7.7-18.0)	1.8 % (1.3-2.4) 13.1 % (9.1-18.7)
Aspergillus fumigatus	0.8 % (0.6-1.3) 6.3 % (2.5-15.1)	1.6 % (1.2-2.1) 9.0 % (5.3-14.9)	1.8 % (1.4-2.4) 17.3 % (12.0-24.3)	2.4 % (1.9-3.1) 14.6 % (10.5-20.0)

Table 3. Percentage of nonasthmatic and asthmatic participants of different age being specifically sensitized

Another fact we have to notice is the high prevalence of sensitizations in asthmatic children of very young age (3 - 6 years) to dermatophagoides pteronyssinus, dermatophagoides farinae, rye and timothy. The prevalence lies between more than 30 up to nearly 43 %. For the same allergens we see in the highest age group nearly two thirds of the asthmatic adolescents being sensitized. These findings support what was referred in the literature review - the most important role of house dust mite sensitization in asthma development.

A much minor role play sensitizations to moulds as shown in sensitizations to cladosporium herbarum and aspergillus fumigatus. The prevalence of sensitizations to pets and the not already mentioned pollen varies in between those described groups.

Sensitization rates in asthmatic children and adolescents rise significantly over time for each allergen with two exemptions: sensitizations to horse epithelia do not reach statistical significance although descriptively the rise seems quite clear, probably explained by the high variation of these results and the same holds true for sensitizations to aspergillus fumigatus where numbers may have become too small for showing significance in this somewhat less steep increase of sensitizations over time.

In nonasthmatic children as well as in asthmatic children we find the highest prevalence rate of sensitizations in the highest age group to the same allergens, both house dust mites, rye and timothy. So, from this point of view the kind of sensitization does not seem to influence the development of asthma in contrary to the number of sensitizations and - to some extent - the specific IgE level.

In the group of nonasthmatic children, increase over time did reach statistical significance for each tested inhalative allergen.

3.4.5 Demographic differences in sensitizations to inhalative allergens

Having learned boys to suffer more often from asthma as girls (in our study 5.5 % of the male children and adolescents have ever had a physician diagnosed asthma versus 3.9 % of the female) and to be more often sensitized, as shown in table 1, we wanted to know whether sensitizations in boys and girls occur to different allergens.

The results are shown in table 4. All statistically significant differences between boys and girls did show up only in the group of nonasthmatic children and adolescents. Here we see differences in favour for the girls being less often sensitized for both house dust mites, cat and dog (but not horse), and all tested pollen but not to moulds.

Regarding the tested moulds, even here boys are descriptively more often sensitized but numbers all together are very small. Looking to the result for sensitization to horse epithelia girls are nearly as often sensitized as boys. This does not seem to be remarkable as horse riding in Germany has to be reckoned as a typical girl's hobby and only a small number of boys have horse contacts. So the greater sensitivity of boys for developing sensitizations seems to be counteracted by girls dealing more often with horses.

Again, the group of asthmatic children is clearly too small for differences in sensitizations between boys and girls becoming significant. With the exemption of horse epithelia sensitization, to all other allergens boys are descriptively more often sensitized than girls.

As mentioned above, with the development of polysensitization, the risk for asthma is increasing exponentially for boys and girls as well. Unfortunately not identifiable in the data is a sensitization pattern difference between boys and girls which could have explained the higher asthma prevalence in boys.

Unit: kU/l Nonasthmatic Asthmatic children	boys n=6609	girls n=6279
Derm. pteronyssinus	22.3 % (21.1-23.6) 59.5 % (54.3-64.5)	16.3 % (15.1-17.5) 51.1 % (44.5-57.6)
Derm. farinae	22.5 % (21.3-23.7) 57.7 % (52.6-62.7)	15.9 % (14.8-17.1) 49.3 % (42.6-55.9)
Cat	8.3 % (7.5-9.1) 33.7 % (28.9-38.9)	5.5 % (4.8-6.2) 32.0 % (26.6-37.9)
Horse	3.5 % (3.1-4.1) 24.0 % (19.7-29.1)	3.1 % (2.6-3.7) 24.9 % (20.0-30.5)
Dog	9.8 % (8.9-10.7) 43.8 % (38.7-49.0)	6.4 % (5.7-7.2) 37.2 % (31.7-43.1)
Birch	15.0 % (13.8-16.3) 45.9 % (40.8-51.0)	10.7 % (9.7-11.9) 34.9 % (29.4-40.9)
Mugwort	11.9 % (10.7-13.6) 31.8 % (27.4-36.4)	8.2 % (7.4-9.2) 26.4 % (21.2-32.4)
Rye	23.7 % (22.2-25.4) 55.1 % (49.9-60.2)	15.9 % (14.6-17.3) 49.6 % (42.9-56.3)
Timothy	25.2 % (23.7-26.8) 60.0 % (54.7-65.1)	17.4 % (16.0-18.8) 51.2 % (44.5-57.8)
Cladosporium herbarum	1.6 % (1.3-2.0) 11.3 % (8.1-15.5)	1.0 % (0.7-1.3) 8.5 % (5.4-13.3)
Aspergillus fumigatus	2.4 % (2.0-3.0) 15.4 % (11.8-19.9)	1.0 % (0.8-1.4) 10.2 % (6.7-15.1)

Table 4. Percentage of participants sensitized to inhalative allergens by sex

Regarding the social status of the families our participants live with, not many significant differences in sensitization status can be observed, as shown in table 5.

In nonasthmatic children with medium social status sensitizations to both house dust mites are significantly more common than in those with low social status. This may possibly be explainable by hygiene measures as vacuum cleaning, which may be – as other hygiene measures – more often practised in families with higher social status. In the literature, it has been shown that vacuum cleaning can enhance air levels of specific house dust allergens (Kalra et al., 1990, online 2003). In contrary, in asthmatic children that difference should not be able to play a major role as parents of those children should have been taught to use vacuum cleaners with small particle filters and especially parents with high social status are thought to follow those instructions closely.

Nonasthmatic children with medium social status are more often sensitized to horse epithelia than both, children with lower as well as those with higher social status, significantly more often compared to the children living in families with high social status. The reason of this difference seems to remain unclear. Horse riding may be a somewhat more expensive hobby so that children with low social status may not have as often contact to horses as other children, but this does not explain why children with high social status show significantly less often sensitizations to horse epithelia than those with medium social status.

Unit: kU/l Nonasthmatic Asthmatic children	Low social status n=3373	Medium social status n=5957	High social status n=3241
Dermatophagoides pteronyssinus	17.5 % (15.9-19.2) 54.3 % (46.9-61.6)	20.5 % (19.4-21.8) 55.9 % (49.6-62.0)	19.0 % (17.3-20.9) 57.7 % (49.6-65.3)
Dermatophagoides farinae	16.8 % (15.3-18.4) 51.4 % (43.5-59.2)	20.2 % (19.0-21.5) 53.8 % (47.7-59.8)	20.0 % (18.2-21.9) 57.7 % (49.5-65.5)
Cat	6.3 % (5.3-7.4) 25.9 % (20.1-32.8)	7.6 % (6.9-8.4) 36.0 % (30.2-42.3)	6.6 % (5.6-7.6) 34.7 % (28.2-41.9)
Horse	2.8 % (2.2-3.5) 19.5 % (14.3-26.0)	4.1 % (3.5-4.8) 25.6 % (20.4-31.7)	2.6 % (2.0-3.4) 28.7 % (22.2-36.3)
Dog	7.6 % (6.6-8.7) 35.4 % (28.7-42.8)	9.0 % (8.1-9.9) 39.3 % (32.7-46.2)	7.3 % (6.3-8.4) 50.8 % (43.8-57.7)
Birch	11.1 % (9.8-12.6) 31.7 % (24.7-39.6)	13.6 % (12.3-15.0) 44.2 % (38.1-50.4)	14.0 % (12.3-15.8) 47.4 % (38.8-56.1)
Mugwort	8.7 % (7.5-10.1) 25.0 % (18.6-32.7)	10.8 % (9.7-12.0) 29.8 % (24.9-35.3)	10.7 % (9.3-12.3) 34.4 % (27.1-42.4)
Rye	17.8 % (16.1-19.7) 46.2 % (37.8-54.9)	20.9 % (19.3-22.6) 55.4 % (49.2-61.5)	20.8 % (18.8-22.9) 56.4 % (48.4-64.2)
Timothy	19.6 % (17.8-21.5) 47.5 % (38.8-56.4)	22.3 % (20.7-24.1) 59.6 % (53.7-65.2)	22.0 % (20.1-24.2) 60.3 % (52.1-67.9)
Cladosporium herbarum	1.0 % (0.7-1.5) 14.1 % (9.3-20.9)	1.6 % (1.3-2.0) 8.3 % (5.2-12.9)	1.0 % (0.7-1.4) 8.9 % (5.4-14.2)
Aspergillus fumigatus	1.8 % (1.4-2.3) 12.9 % (8.3-19.5)	1.8 % (1.4-2.4) 13.8 % (9.9-19.0)	1.5 % (1.1-2.0) 12.5 % (8.4-18.2)

Table 5. Percentage of participants sensitized to inhalative allergens by social status

The only significant difference we can observe in asthmatic children is the very high degree of sensitizations to dog epithelia in children with high social status compared to those with low social status. Pet ownership and the development of asthma and other atopic diseases are very controversially discussed. Time point of pet contact, cat / dog ownership and other circumstances may be puzzle pieces of a picture not yet completely visible. Some studies seem to direct to early dog contacts being protective regarding a development of atopy (Gern et al., 2004). Having in mind, that dog ownership in Germany is more common in families with high social status (high income and house owner), as was shown in a situation bulletin to dog ownership in Germany by the German University of Göttingen (Ohr & Zeddies, 2006), we have to query a protective effect of dog ownership on asthma development. Cross-sectional studies showing a protective effect of dog ownership could be biased by atopic parents avoiding dog ownership leading to children more in danger of atopy development more often growing up in a household without dogs.

Descriptively but not statistically significant for all tested pollen sensitizations numbers rise from low over medium to high social status, what, if confirmed by other studies, could be explained by different free time behaviour. Children with lower social status are known to spend more time indoor than others, as confirmed by other analyses of the KiGGS study (Robert Koch Institut, 2008).

Independent of social status, in all three groups, again, number of asthma cases rises with rising number of sensitizations in an exponential manner.

Looking for children with or without migration background (table 6), we can observe more significant differences in sensitizations than in the above mentioned groups with different social status but only in nonasthmatic children.

To cat and horse but not dog children without migration background show more sensitizations. Unfortunately, we did not find data showing pet ownership behaviour in people living in Germany with migration background. Therefore we can not discuss pet ownership in relation to sensitization status. Sensitizations to horse epithelia nevertheless could be higher in children without migration background more due to income differences than cultural disparity.

Children without migration background are more often sensitized to all tested pollen than the other group of children. As it was previously shown in the KiGGS data, children with migration background spend much more time with indoor activities than children without such a background. Sensitization to pollen may be a consequence of outdoor activities.

No differences were seen regarding house dust mite and mould allergies. In children with migration background as in all other groups asthma prevalence rises with rising number of sensitizations.

Unit: kU/l Nonasthmatic Asthmatic children	With Migration background n=1906	Without Migration background n=10928
Dermatophagoides pteronyssinus	19,1 % (17.2-21.0) 67,2 % (56.6-76.2)	19,4 % (18.5-20.4) 54,0 % (49.3-58.6)
Dermatophagoides farinae	17,9 % (16.0-20.0) 64,7 % (54.5-73.6)	19,5 % (18.6-20.5) 52,4 % (47.8-56.9)
Cat	5,0 % (4.0-6.3) 30,6 % (22.0-40.8)	7,3 % (6.7-7.9) 33,5 % (29.6-37.6)
Horse	2,0 % (1.4-2.7) 16,2 % (9.9-25.0)	3,6 % (3.2-4.1) 26,0 % (22.1-30.3)
Dog	6,4 % (5.1-8.0) 38,8 % (28.9-49.6)	8,5 % (7.8-9.1) 41,6 % (37.4-45.9)
Birch	8,7 % (7.2-10.3) 36,0 % (27.2-46.0)	13,8 % (12.7-14.9) 42,4 % (38.3-46.6)
Mugwort	7,5 % (6.0-9.2) 22,5 % (15.0-32.4)	10,7 % (9.8-11.7) 30,9 % (27.1-35.0)
Rye	15,9 % (13.9-18.0) 57,8 % (47.4-67.5)	20,8 % (19.4-22.2) 52,0 % (47.2-56.7)
Timothy	17,9 % (15.9-20.0) 60,2 % (50.6-69.2)	22,1 % (20.8-23.5) 55,7 % (50.7-60.5)
Cladosporium herbarum	1,0 % (0.6-1.7) 7,3 % (2.9-17.3)	1,3 % (1.1-1.6) 10,7 % (8.1-14.0)
Aspergillus fumigatus	1,9 % (1.3-2.7) 13,6 % (6.9-24.9)	1,7 % (1.4-2.1) 13,2 % (10.4-16.4)

Table 6. Percentage of participants sensitized to inhalative allergens by migration status

Additionally we searched for differences in sensitizations between children living in more rural or urban regions of Germany. We have been able to identify only one single significant difference: in rural regions 12.7 % of the children without asthma were sensitized to mugwort, in small towns 10.4 % in medium towns 9.6 % and in large cities 8.5 %. The difference between the smallest and the biggest region class reaches significance. As, according to the hygiene hypothesis, sensitization occurs more easy in urban regions, these data in our view back up the hypothesis of outdoor activities leading to more sensitizations to outdoor allergens – independent of residence.

Descriptively, children with asthma show the same slope in sensitization prevalence to mugwort as children without asthma. Again, children in all regions show the above described exponential coherency between asthma and number of sensitizations.

3.4.6 Sensitization patterns in asthmatic children

In the intention to look for patterns of sensitizations we grouped sensitizations to house dust mites, animals, pollen and moulds respectively. In table 7 we demonstrate groups of children showing sensitizations to at least one allergen of one of the mentioned groups alone or to at least one allergen of the mentioned group and any other allergens and the prevalence of asthma in those groups compared to the overall prevalence.

If sensitizations to allergens of only one of the four groups show up, asthma prevalence is not enhanced with the exemption of sensitizations to animals. These more than double the asthma prevalence. In the underneath mentioned groups with combined sensitizations, asthma prevalence is enhanced in each group, what may result from the above described effect of multiple sensitizations exponentially leading to an increase of asthma.

Sensitization type	Asthma prevalence (%) n=690, 5.5 % (5.0-6.0)
only to house dust mites	5.9 % (4.5-7.7)
only to animals	12.5 % (7.7-19.8)
only to pollen	4.5 % (3.4-5.9)
only to moulds	5.4 % (0.7-30.4)
to house dust mites and other allergen(s)	13.6 % (12.1-15.3)
to animals and other allergen(s)	19.8 % (17.7-22.2)
to pollen and other allergen(s)	12.7 % (11.4-14.1)
to moulds an other allergen(s)	27,2 % (22.3-32.8)

Table 7. Percentage of sensitization types having asthma

Nevertheless, noticeably asthma prevalence is much higher in children with animal epithelia and other sensitizations as with house dust mite or pollen and other sensitizations and highest in the group of children and adolescents with mould and other sensitizations. So, in monosensitized children, sensitization to animals plays the major role and in polysensitizations animals and even more moulds.

After these insights we wanted to know exactly the sequence of mono- and polysensitizations regarding asthma prevalence and present the data in figure 2.

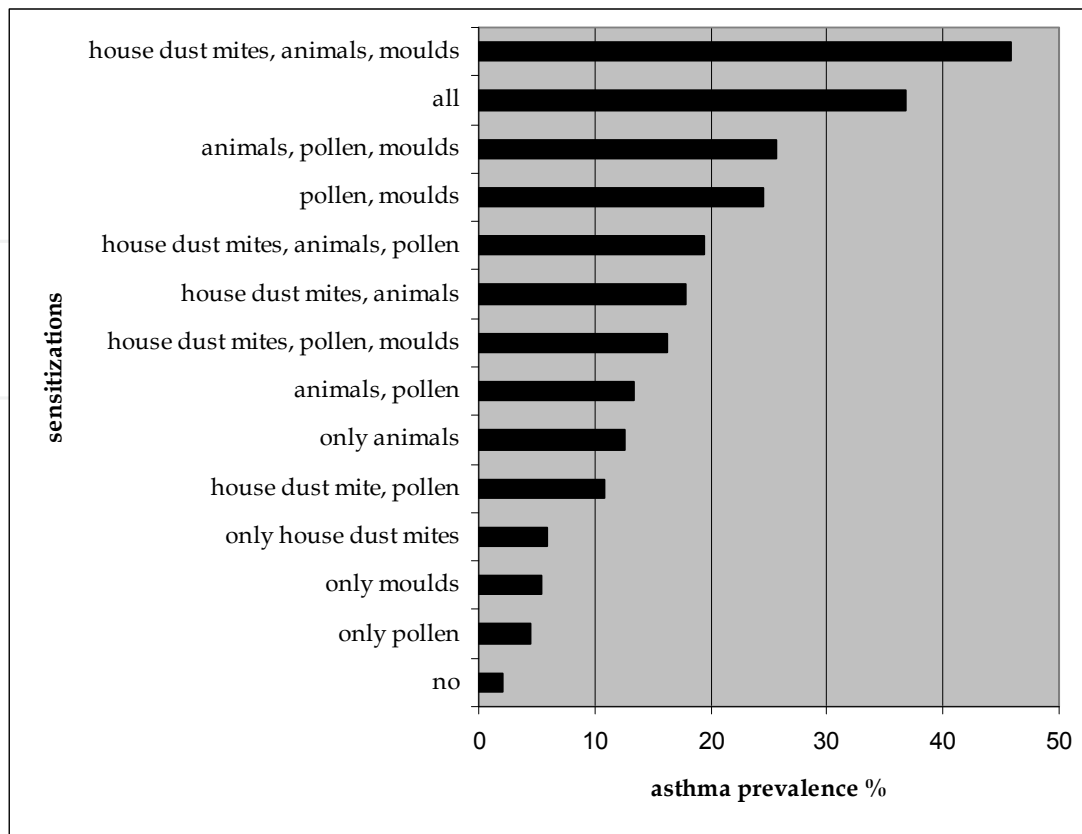


Fig. 2. Sensitization pattern and asthma prevalence

Combinations we did not find were that of animal and mould sensitizations and house dust mite and mould sensitizations.

Again, we have to keep in mind that increasing number of sensitizations lead to exponentially increasing asthma prevalence so that the shown figure must be strained by that effect. But - as an example - the combination of sensitizations to pollen and moulds seems to result in much higher asthma prevalence than the combination of sensitizations to pollen and animal epithelia, whereas the addition of a sensitization to animals to pollen and mould sensitizations does nearly not further enhance asthma prevalence.

Having a look into these data from another perspective we find that nearly a quarter of our asthmatic children and adolescents did not show any sensitization to the tested inhalative allergens (23.7 %). Never or infrequently (< 5 %) seen in the asthmatic children were sensitizations to mould only, pollen and mould, animals only, animals and mould, animals, pollen and mould, house dust mite and mould, house dust mite, pollen and mould, mould and animals as well as house dust mite, animals and mould. More frequently (5 - 10 %) we saw sensitizations to pollen only, animals and pollen and house dust mite only. Sensitizations to at least one allergen of each group were more frequent with 10.4 % of the asthmatic children concerned, sensitizations to house dust mite and pollen occurred in 10.9 % of the asthma cases and most frequent were sensitizations to house dust mites, pollen and animals in 22 % of asthmatic children.

In a cross-sectional study we are not able to detect the time sequence of acquired sensitizations. Alternatively we looked for dual combinations of sensitizations. Taking the assumption that sensitizations are lifelong conditions, a dual combination could indirectly

light the way of the beginning of multisensitizations and may show us, how sensitizations usually combine or start to build cluster.

In our data we found 1420 nonasthmatic and 86 asthmatic children with exactly two sensitizations (not grouped) as shown in figures 3 and 4 in absolute numbers.

Non-asthmatic	DermPt	DermFA	Cat	Horse	Dog	Birch	Mugwort	Rye	Timothy	Clado	Asperg
DermPt											
DermFa	810										
Cat	4	2									
Horse	3		6								
Dog	1	3	24	2							
Birch	5	1	5		5						
Mugwort	3	4	1	1	2	10					
Rye	1	1				4	1				
Timothy	2	5	3	1	2	11	6	474			
Clado		1				1	1				
Asperg		4			1		1	1		7	
n=1420	829	21	39	4	10	26	9	475	0	7	

Fig. 3. Combinations of exactly two sensitizations in nonasthmatic children

Asthmatic	DermPt	DermFA	Cat	Horse	Dog	Birch	Mugwort	Rye	Timothy	Clado	Asperg
DermPt											
DermFa	53										
Cat											
Horse			1								
Dog			3	1							
Birch											
Mugwort						1					
Rye											
Timothy			1			3		21			
Clado											
Asperg								1		1	
n=86	53	0	5	1	0	4	0	22	0	1	

Fig. 4. Combinations of exactly two sensitizations in asthmatic children

In the group of the nonasthmatic children we can observe that combinations of the two house dust mites are very common and also the combination between rye and timothy, two kinds of weed, so that these combinations are likely produced by cross reactivity. The same applies to the rarer combination of cat and dog sensitizations. The pattern in asthmatic

children is exactly the same, only the numbers are too small to show a peak at cat and dog sensitizations.

As a last step we then looked into the data of exactly two sensitizations in the above described sensitization groups and the results are shown in figure 5.

Non-asthmatic	House dust mite	Animals	Pollen	Moulds	Asthmatic	House dust mite	Animals	Pollen	Moulds
House dust mite					House dust mite				
Animals	125 (11.6 %)				Animals	23 (16.3 %)			
Pollen	607 (56.4 %)	292 (27.1 %)			Pollen	66 (46.8 %)	45 (31.9 %)		
Moulds	19 (1.8 %)	2 (0.2 %)	32 (3.0 %)		Moulds	0	0	7 (5.0 %)	
n=1077					N=141				

Fig. 5. Combinations of exactly two group sensitizations in children and adolescents

Again, it becomes clearly visible, that sensitization patterns of dual group sensitizations in our study do not differ between asthmatic and nonasthmatic children. The number of sensitizations influences asthma prevalence very much but patterns of sensitization to a much lesser degree – although the most differentiated analysis of the data shown in figure 2 seems to indicate some coherence between sensitization pattern and asthma.

3.5 Discussion and perspectives

We have been able to confirm data known from the literature on the grounds of a database as far as possible representative for German children and adolescents.

There is no mandatory coherency between sensitizations to inhalative allergens and asthma looking into individual developments. While in adults non allergic asthma forms concern a high percentage of asthmatic persons, in children it was thought that a broad majority suffers from allergic asthma. We identified 23.7 % of the asthmatic children not showing a sensitization to any of the tested inhalative allergens and additionally only a few of them showing sensitizations to food allergens. Though sensitizations to allergens not being included in our test are theoretically possible (included were the most common allergens being content of standard test series), possibly non allergic asthma forms in children may still be somewhat underestimated.

We also saw that sensitizations confirmed in the range of 0.35 - 0.69 kU/l and up to now regarded only as marginally positive are already statistically significant more frequent in asthmatic children for all tested allergens with the exemption of the two house dust mites. Potentially such low sensitization results for animals, pollen and moulds should be noticed more attentively in clinical practise at least in children with a higher risk for the development of atopy.

In contrary, very high levels of sensitizations from 50.0 kU/l on have been seen nearly only in asthmatic children and only some single nonasthmatic individuals. Such high levels seem to be nearly an indicator for asthma development.

In contrast to the literatur identifying significantly less sensitizations in rural compared to urban regions, in Germany we were able to identify differences in sensitization patterns

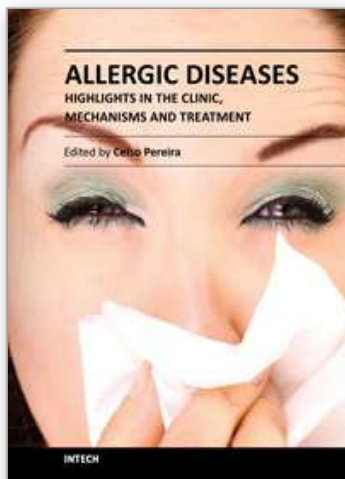
between those regions but no overall differences regarding sensitization prevalence. Possibly life style differences between rural and urban regions in Germany are very low as we are a country with a pronounced "westernized lifestyle". A higher prevalence of sensitizations to pollen in rural regions already had been described for Italian children. We identified significantly higher sensitization prevalence in rural regions only for mugwort. Sensitization prevalence being higher for boys compared to girls was already depicted. In connection with asthma it was an interesting fact that with increasing age sensitization prevalence in boys remains still higher than that in girls while asthma prevalence in boys declines. This could possibly back up the theory of lung size being an important factor in asthma prevalence differences in men and women being contrary to those in boys and girls. Living in families with a lower social status was said to enhance the chance for having sensitizations. In our study, for most tested allergens the contrary held true. Especially regarding house dust mites, one of the most important factors for the development of asthma, higher social status was a risk factor for sensitizations. As far as causes are known, disproportionate hygiene behaviour could be one of the factors, what would fit in the widely respected hygiene hypothesis. We think that social habits like the use of disinfectants and odors in the household and in public have to be questioned and that activities for prevention of allergies should be also directed to such behavioural factors. The findings of polysensitization more often to cohere with asthma than monosensitization and the number of sensitizations to correlate with the risk for asthma were substantiated by our data. We have been able to show a clear exponential correlation between the number of sensitizations and asthma. This may be considered as an impulse to reconsider hyposensitization therapy in children at high risk for atopy. Maybe those children should undergo therapy the minute a second or third sensitization occurs regardless of symptoms of hayfever to prevent asthma development. As in the literature it was also shown that asthma remission relates inversely to sensitizations, this may make hyposensitization therapy also more fundamental in asthmatic children as it already is. The special importance of house dust mite sensitizations was confirmed by our study, as was to be expected. Presumably based on cross reactivity sensitization to both tested house dust mites showed an overlap of nearly 100 % so that testing sensitizations to only one of the house dust mites would be in nearly every case able to confirm house dust mite allergy. All in all we learned that the number of sensitizations was a much stronger element in asthma development than sensitization patterns. Nevertheless, it became clear that sensitizations to only animal epithelia more than double asthma prevalence compared to house dust mite, pollen or mould sensitizations only. In combined sensitization patterns containing animal sensitizations and by far more mould sensitizations are linked with enhanced asthma prevalence. The KiGGS study will be carried forward and partly transformed into a longitudinal study. So we are looking forward to being better able to identify sensitizations or sensitization patterns really leading to asthma development. Additionally - as we will include in our study questions for hyposensitization therapy - we should be able to show whether early specific immunotherapy will be capable to prevent the development of polysensitizations and/or the development of asthma or influence asthma remission during adolescence. Also the effectiveness of social measures such as proposed for example by the ABAP (an alliance for prevention of allergies initiated by the German Ministry for Health) could be followed up by this study.

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