

Indoor factors and IgE levels in children

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The objective of the study was to determine indoor characteristics of households in relation to total serum IgE. In a population-based cross-sectional study, 1096 6–12-year-old children were examined in three East German towns (Eisleben, Hettstedt, and Zerbst). Of the questionnaires, 772 (70.4%) were returned by the parents. Serum IgE of 703 children and urinary cotinine in a random subsample of 224 children were analyzed. Linear regression on log(IgE) adjusted for the main covariates was used to assess indoor risk factors such as room size, and the presence of curtains, carpet, and plants in the child's room. Open-heating facilities indoors, passive smoking, and furniture made of chipboard had the most important effect. A higher urinary cotinine/creatinine ratio was associated with higher total IgE level. Total IgE increased also with the number of persons living in the household, independently of indoor smoking. We conclude that indoor air pollution from smoking and open-heating facilities may increase the IgE levels of children. The role of other factors such as chipboard, which could reflect the emission of formaldehyde, or the number of persons per household, which could reflect viral or helminthic infection, remains to be analyzed.

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There is increasing concern about indoor air pollution as a risk factor for allergic diseases (28). IgE has been regarded as one of the most prominent features of atopic disease (19) since its discovery in 1967 (32). However, IgE is also influenced by various environmental factors (14, 30); virus (27, 35), parasitic (10, 11), and bacterial infection (29); outdoor air pollution (3); genetic background (22); diet (12); and smoking habits (4, 26).

Several studies have investigated the relation of total IgE to outdoor as well as indoor pollutants. Respiratory particles and gases (tobacco smoke, stoves, heaters), formaldehyde (foam insulation, chipboard, fabrics), volatile organic compounds (paints, sprays, combustion), and biologic material (dust mites, dander, bacteria, fungi, pollen) are the main indoor pollutants. Because most people spend 75–90% of their time indoors (18), there is increasing concern about potential negative effects. The energy crisis of the 1970s led to improved insulation of

houses and reduction of air-exchange rates. Therefore it would be interesting to examine people in a geographic region where these changes are now occurring.

The indoor factors that received the most attention in the past were environmental tobacco smoke (ETS) (28) and nitrogen dioxide (23) from indoor heating or cooking sources. In the present study, we analyzed these and other risk factors in relation to total IgE levels among children. Therefore the objective of the study was to identify risk factors for high IgE levels and to establish a study protocol for a later cohort study.

Material and methods

The study was conducted from April 1992 until July 1992. The two-stage sampling included all children aged 6–7 years and a random sample of 8–12-year-old children in Eisleben, Hettstedt, and Zerbst in the

former East Germany. Eisleben and Hettstedt are highly polluted areas. The main sources of the pollution are the chemical and mining industry of the former German Democratic Republic. Zerbst served as control region. The study was designed as a pilot phase for a later cohort study, and a limited number of 1000 children was estimated to be suitable for this purpose. All study methods were approved by the ethics committee of the University of Rostock, Germany, and informed, written consent was obtained from all parents.

The questionnaire had been developed according to the international recommendations (9), and it included questions concerning sociodemographic characteristics, physicians' diagnoses, and typical symptoms of respiratory and allergic disorders in relation to possible pathogenetic factors. As previously reported, the repeatability of the answers to the main questions was found to be high in a comparable setting (24). The questionnaire was distributed by the teachers to the children and included a brief explanatory letter and a return envelope.

Blood samples were taken from 8 a.m. to 1 p.m. and immediately frozen and stored at -80°C until they could be analyzed together in the last month of the study. Total serum IgE and specific IgE were determined by a commercial enzyme immunoassay (Pharmacia Diagnostics AB, Uppsala, Sweden). Values were expressed as kU/ml.

Spontaneous urine was collected in clean plastic containers and immediately stored at -18°C until analyzed during the last month of the study. Cotinine was measured after extraction and reextraction by HPLC, as described earlier (21). The intra- and interassay variations were 5.4% and 4.0%, respectively. The detection limit was 4 ng/ml urine. To adjust for urine dilution, urine cotinine concentrations were standardized to creatinine concentrations and expressed as cotinine/creatinine ratio (ng/mg). One 6-year-old child with a cotinine level of 1690 ng/ml urine was excluded from further analysis.

As IgE levels were highly skewed, 1 kU was added, and all values were transformed logarithmically to achieve a normal distribution. A multivariate linear regression analysis (20) was used to determine the effect of different factors on $\log(\text{IgE})$. Factors included in the model were sex, age, study site, season of examination, and history of the parents for either asthma or allergic rhinitis. The variable coding is shown in Table 1. All calculations were done by SAS 6.07 (SAS Institute, Inc, Cary, NC, USA).

Results

The questionnaire was distributed to a total of 1096 households and was returned by 772 (70.4%). Because study methods were identical in all three

towns, the data of the different towns were pooled. After exclusion of missing or "unknown" answers, a final total of 703 blood samples (64.1%) and a random subset of 224 (20.5%) urinary probes were analyzed.

The distribution of IgE levels is shown in Fig. 1. Mean IgE in Hettstedt was 181 kU/ml (median 65 kU/ml), in Eisleben 114 kU/ml (median 38 kU/ml), and in Zerbst 173 kU/ml (median 61 kU/ml). Most (73.3%) of the children were 6–7 years old.

The prevalences of the risk factors are shown in Table 1. A multivariate linear regression analysis estimated the effect of indoor risk factors on $\log(\text{IgE})$ adjusted for sex, age, heredity, town, and month of examination. For better comparison, the risk factors were classified into six subgroups and sorted in each group for the adjusted effect size. Only a few factors showed significant influence; these were town of residence, family history of allergy, number of persons in the household, chipboard in the child's room, and open indoor heating facilities.

For a further characterization of the effect of passive smoking, urinary cotinine level was evaluated in a randomly selected subgroup of 224 children. In 70% of the examined children, no cotinine was found. In children with no exposure to ETS ($n = 134$), the mean cotinine level in urine was 10 ng/ml (median 0.00 ng/ml), and in the children with ETS exposure it was 73 ng/ml (median 31 ng/ml; $n = 88$). The distribution of the cotinine values is shown in Fig. 2. Total IgE increased in the highest cotinine group (Fig. 3).

The number of persons in the household also had an effect on total IgE (Fig. 4). This effect was also consistent in subgroups defined by smoking and social class. However, there was no effect on the number of children positive for specific IgE against grass pollen either by passive smoking (10.6%, 5.6%, 13.6%, and 17.4%, respectively, for the same categories as shown in Fig. 3, or by high number of persons in the household (9.7%, 15.7%, 12.0%, and 8.1%, respectively, for the same categories as in Fig. 4).

Discussion

Indoor heating facilities have a promoting effect on total IgE. The same effect is observed in the presence of chipboard in the household. There was also a relationship between increasing ETS exposure and total IgE level. Furthermore, with the number of persons in the household, IgE also increases independently of smoking habits.

A bias by differential selection of subjects is unlikely because of the unknown status of the subjects before the study and a high response ratio. A recall bias whereby persons with high IgE tend to report

Table 1. Prevalence of indoor risk factors determined by questionnaire answers of parents of 703 children. Multivariate linear regression analysis estimated effect on total log(IgE) of children. Results were determined for each indoor factor separately as difference Δ of log(IgE) adjusted for sex, age, history of atopy, town of residence, and month of examination. Results are shown together with lower and upper 95% confidence intervals (CI). Risk factors are sorted within subgroups for effect size

Categories		Prevalence % (mean)	Δ Log (IgE)	Lower CI	Upper CI
<i>Characteristics of study population</i>					
Exam. June to April	Vs. other months	24.5	-0.11	-0.37	0.14
Age	+ 1 year	(7.2)	0.04	-0.02	0.10
Sex	Male vs. female	50.9	0.13	-0.09	0.35
Residence Zerbst	Vs. Eisleben	32.8/28.9	0.18	-0.05	0.42
Residence Hettstedt	Vs. Eisleben	38.9/28.9	0.29	0.06	0.52
Father or mother atopic	Yes vs. no	27.5	0.30	0.04	0.55
<i>House characteristics</i>					
Construction year	< 1950/ < 1960/ 1960+	37.1/9.1/53.8	-0.06	0.25	-0.13
Rooms per household	+ 1 room	(4.4)	-0.02	-0.12	0.08
Area of home	+ 1 m ²	(77.2)	0.00	-0.05	0.05
Families per house	1 / 2-3 / 4+	26.1/17.8/56.2	0.02	0.12	-0.12
Persons per home	+ 1 person	(3.9)	0.24	0.11	0.37
<i>Child's room</i>					
Animal pelt floor	Yes vs. no	3.0	-0.50	-1.15	0.15
Quilt on child's bed	Yes vs. no	83.6	-0.06	-0.38	0.25
Wall-to-wall carpet	Yes vs. no	65.9	-0.02	-0.27	0.22
One or more plants	Yes vs. no	41.5	-0.01	-0.24	0.23
Single carpet	Yes vs. no	33.3	0.07	-0.18	0.32
Mattress of horsehair	Yes vs. no	17.6	0.10	-0.21	0.40
Curtains	Yes vs. no	66.3	0.11	-0.13	0.36
Upholstered furniture	Yes vs. no	38.4	0.13	-0.11	0.37
Chipboard	Yes vs. no	74.3	0.28	0.01	0.55
<i>Cooking, heating, dampness</i>					
Dampness of home	Yes vs. no	7.6	-0.08	-0.54	0.38
Mold in home	Yes vs. no	30.2	-0.01	-0.34	0.31
Heating coal	Vs. central heating	54.2/33.6	0.14	-0.11	0.39
Heating gas	Vs. central heating	6.8/33.6	-0.06	-0.59	0.47
Heating oil	Vs. central heating	4.0/33.6	-0.05	-0.72	0.62
Open heating indoors	Yes vs. no	51.5	0.23	0.00	0.47
<i>Smoking habits</i>					
Smoking during pregnancy	Yes vs. no	6.4	0.00	-0.52	0.51
Actual smoking	Yes vs. no	45.7	0.14	-0.09	0.38
Previous smoking	Yes vs. no	49.0	0.16	-0.07	0.40
<i>Pet kept</i>					
Hamster	Yes vs. no	1.7	-0.29	-1.20	0.62
Bird	Yes vs. no	17.2	-0.21	-0.51	0.08
Guinea pig	Yes vs. no	7.5	0.02	-0.44	0.48
Cat	Yes vs. no	27.7	0.02	-0.25	0.28
Dog	Yes vs. no	22.5	0.05	-0.24	0.33

exposures differently may be possible. This may have worked especially for the weak "protective" effect of pets in the household. Children with higher IgE levels are more likely to develop allergic symptoms, and this will lead to the physician's advising the avoidance of pets. The problem of confounding was addressed by including age, sex, town of residence, allergic family history, and month of examination (1) in the analysis. Residual confounding may be possible, especially for unknown factors. There may also be type I errors. For this reason, only risk factors with a high strength should be considered for further

evaluation, especially if they are consistent with other studies and existing biologic knowledge.

Tobacco smoke is one of the most important indoor air pollutants. Exposure misclassification may be one reason for the inconsistency among studies about the effects on IgE level. A more precise determination of cotinine, which is the major metabolite of nicotine, has been used (7) to overcome the fallacy of questionnaires. As compared with questionnaire answers in our study, other studies have found only a few unexposed children with measurable cotinine levels. This may be caused by more

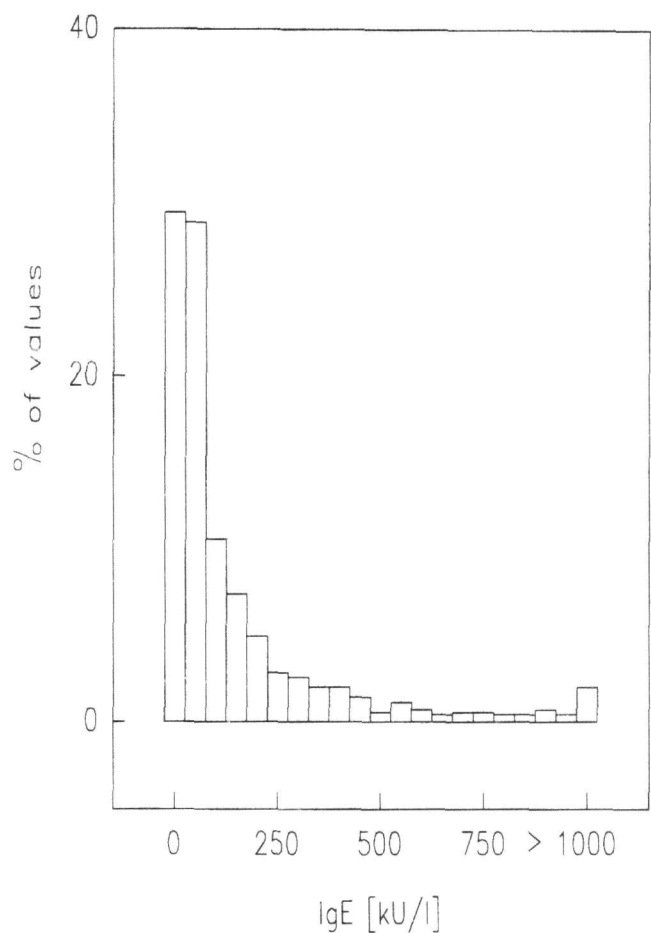


Fig. 1. Distribution of IgE levels in 703 children.

food intake of other vegetables which contain nicotine (16) or other sources outside the home. One major problem seems to be the intersubject variability

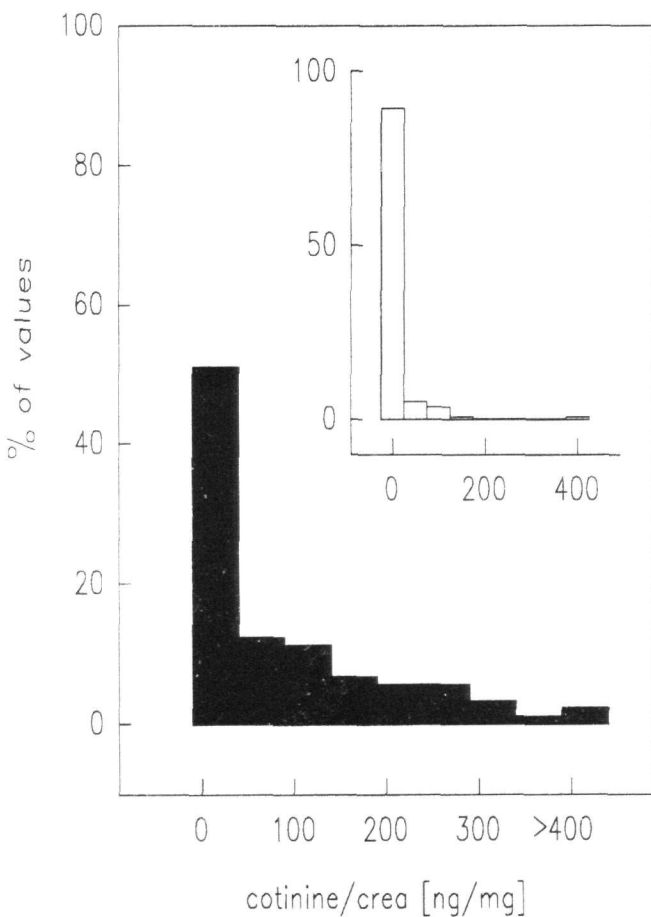


Fig. 2. Distribution of urinary cotinine level in 224 children living in homes with (filled bars) or without (open bars) environmental tobacco smoke.

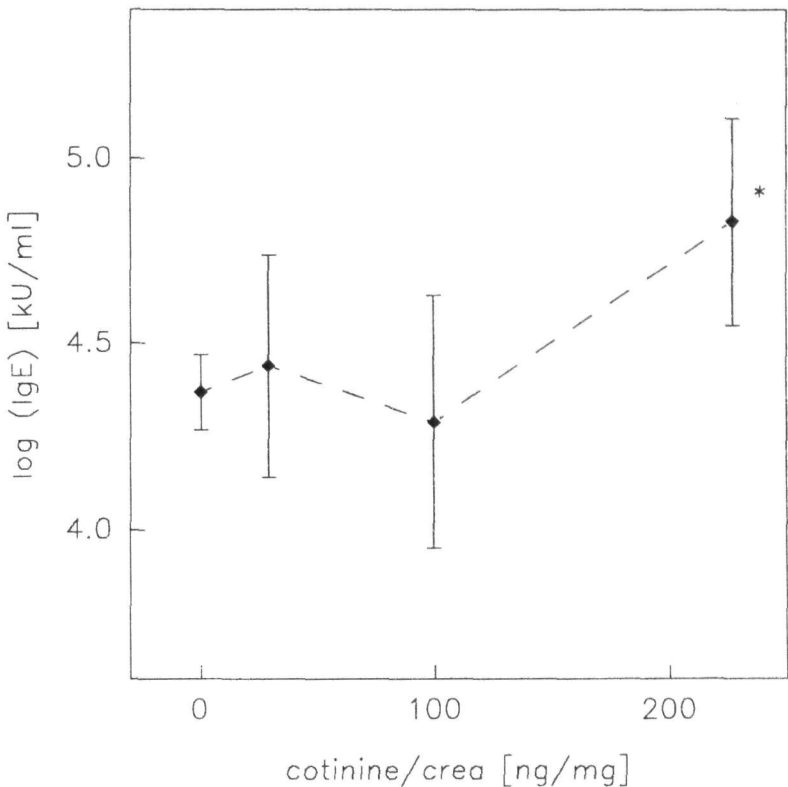


Fig. 3. Relation of urine cotinine/creatinine ratio in 224 6-12-year-old children. IgE values are shown in four groups defined by 0.0 ng/mg (70th percentile), <60 ng/mg (80th percentile), <138 ng/mg (90th percentile), and <709 ng/mg (maximum). Points indicate mean in group; error bars, SEM. * $P < 0.05$, as compared with lowest category.

ity of the cytochrome P-450 oxidation, which is involved in the metabolic conversion of nicotine (16). The average level of cotinine measured in this study

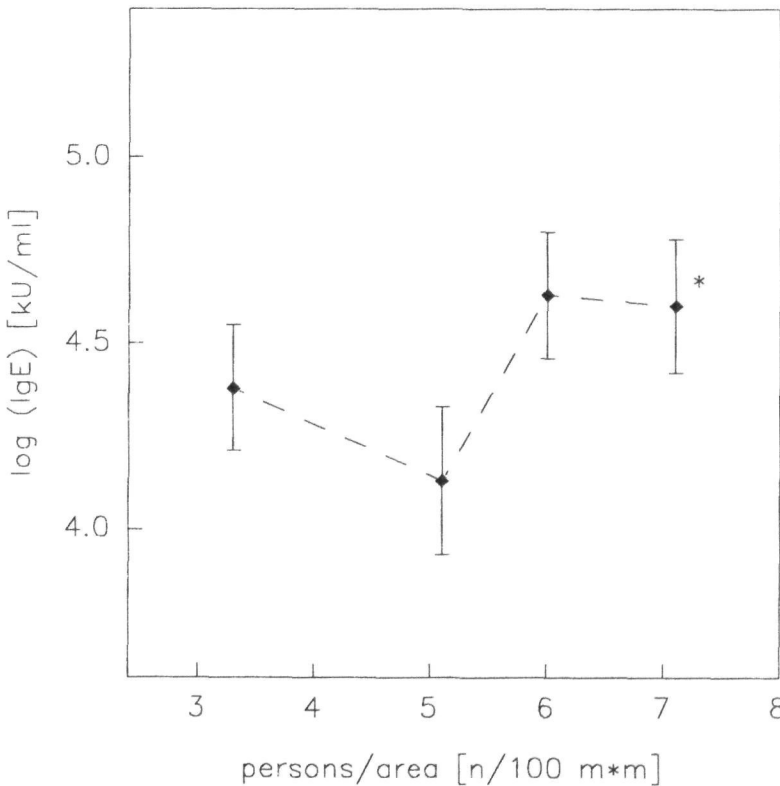


Fig. 4. Relation of person per area ratio in same subgroup as Fig. 3. IgE values are shown in four quartile groups defined by <4.4 persons/100 m² (25th percentile), <5.6 (median), <6.6 (75th percentile), and 11.9 (maximum). Points indicate mean in group; error bars, SEM. * $P < 0.05$, as compared with lowest category.

was lower than in other studies (28). This may be also explained by the fact that the examinations were done during spring and summer when ventilation may be better than during the other seasons. In general, however, the number of children with positive cotinine assays from nonsmoking households and of children with negative nicotine from smoking households was comparable with other studies (13), and the effect of passive smoking on IgE agrees with many previous studies (2, 8, 17, 26). It is assumed that ETS acts not as an allergen but as an adjuvant which facilitates sensitization (25). The mechanism is not fully understood. ETS may damage the respiratory epithelium, and this damage may itself increase the likelihood that allergens will reach immunoreactive cells (15). In the present study, there was no effect of ETS exposure on specific IgE against grass pollen. Therefore, the effect on total IgE cannot be explained by this subset of antibodies.

A further source of indoor air pollution is open heating facilities. The mechanism by which combustion products may influence IgE level is also unclear, but it may be the same as for ETS. One possible mechanism by which air pollution could enhance sensitization is offered by the observation that pollutants bound to pollen may enhance allergic sensitization (2). Nitrogen dioxide destroys cilia, as shown by exposing epithelial cells to low concentrations of this gas. If ciliated cells are killed, allergens remain longer on the cells, increasing the possibility of contact with immunoreactive cells (25). However, there was no clear evidence for this hypothesis in our study, because the ratio of children with specific antibodies against grass pollen was unaltered by passive ETS exposure. For the effect of chipboard, the high content of formaldehyde may be responsible. The effect on IgE of formaldehyde has been discussed earlier (5, 6, 34). This should be investigated in further studies.

Other investigators have also suggested an association between respiratory infections and allergic disease (35). It is possible that the number of persons in the household is associated with the number of infections in a child (33) and subsequently with elevated IgE levels. This has been hypothesized in a recent study on preschool children living in the same area of the former East Germany who also showed significantly higher IgE levels in relation to the number of persons in the household (2). Ten percent of the children were supposed to have antibodies against the *Ascaris* antigen. Further studies of stool probes or serum antibodies will be necessary (31) to clarify this issue.

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