Indoor exposure associated risk for eczema in early childhood

O. Herbarth^{1,2}, G. J. Fritz², M. Rehwagen¹, M. Richter¹, S. Röder¹ & U. Schlink¹ ¹Department of Human Exposure Research and Epidemiology, Helmholtz-Centre for Environmental Research – UFZ, Germany ²Environmental Medicine and Environmental Hygiene, Faculty of Medicine, University of Leipzig, Germany

Abstract

In the development of allergic disorders other factors besides a genetic disposition seem to play a role. Exposure to risk factors such as indoor air pollution is becoming increasingly interesting, especially during early childhood.

Within an epidemiological study involving 2536 children the effect of indoor exposure on allergic symptoms and physician-confirmed eczema has been investigated. The exposure situation has been characterised on hand of the redecoration activities before birth and in the first years of life.

Highly exposed children showed a significant effect on allergic disorders. The lifetime prevalences without any vs. of all three redecoration activities (painting, floor covering and new furniture) were for allergic symptoms 9.3 vs. 17.2% and for eczema 11.5 vs. 20.4%. Adjusted for confounders, the redecoration associated burden led to odds ratios of 1.8 (95%CI: 1.3-2.6) for allergic symptoms and 1.9 (95%CI: 1.4-2.7) for eczema.

Exposure emissions due to redecoration activities seem to be associated with the risk of eczema and allergic symptoms. Thus, prevention of allergic disorders should include the avoidance of such activities around birth and in the first year

Keywords: indoor exposure, allergic disorders, children.

Introduction 1

Besides a genetic predisposition and the controversially-discussed hygiene hypothesis (Strachan [1, 2]), other factors influence the development of allergies



in early childhood: food, pollens, etc. and as lately described also indoor chemical pollutants, particularly volatile organic compounds (VOC) (Herbarth and Rehwagen [3], Wolkoff and Nielsen [4]). Important VOC sources are, e.g., smoking and emissions from building materials and furnishings (Samet et al. [5, 6], Cooke [7]). During and following home renovation activities, e.g., painting and/or floor covering, indoor exposure levels can be high. These exposure situations have been found to affect inflammatory processes as well as allergic disorders (Harving et al. [8], Koren et al. [9], Ware et al. [10], Norback et al. [11], Wieslander et al. [12] Diez et al. [13]). Moreover, it remains largely unclear whether a time window exists within which the organism may be especially sensitive to these specific environmental influences. Several studies have investigated the existence of a time period and whether varying factors of influence early in a child's life does lead to an increased incidence of sensitization later in life, including whether prenatal exposure via the mother may have an impact on the offspring. Until now these investigations have been restricted to environmental factors which are able to cause allergies directly above all to allergen exposure (Warner [14] Warner et al. [15, 16]). The effect of possibly indirectly affecting factors - trigger factors - is to a great extent unknown except for smoking. First attempts to clear up the role of indoor chemicals were given by Diez et al. [13] but restricted to risk groups.

The present study is intended not only to contribute to the debate of the extent of chemical noxes being involved in triggering allergen-induced processes but also address the question of timing by examining the influences of pre- and postnatal exposure due to renovation activities.

2 Material and methods

2.1 Study population

The presented investigation is based on the data of an epidemiologic cross-sectional study (LISS study - Leipzig infection, allergy and airway diseases study among school starters). The LISS study was carried out during the fall and winter 1997-1998 (birth cohort 1991/92) and included all children of the City of Leipzig and its surrounding county (n=3919) eligible to enter first grade in the fall of 1998 (Table 1). Participation was on a voluntary basis, requiring an informed written consent by both parents/guardian of the children. The study was approved by the ethics committee of the University of Leipzig.

The parents completed a detailed self-administered questionnaire on indoor exposure as well as their family medical history (e.g., physician-diagnosed diseases and symptoms of allergic disease). 2950 parents agreed to fill out this questionnaire. For this investigation, 2536 complete data sets were available (86% of self administered questionnaires).

The study design and methodology have been described in detail elsewhere (Krumbiegel et al. [17], Herbarth et al. [18]).



2.2 Disorders (target variables)

The target variables were lifetime prevalences of physician-diagnosed eczema and physician-diagnosed allergy-associated symptoms. Eczema was selected separately from the allergic symptoms since this manifestation is the earliest sign of an allergic disorder in children's life. The following questions were entered into the analyses: "Has a physician ever diagnosed eczema / endogenous eczema / atopic dermatitis / neurodermatitis in your child? and "At what age was this diagnosis made for the first time?" In addition to these eczema questions, a question pertaining to physician-diagnosed allergic diseases was included: "Has a physician ever diagnosed an allergy in your child?" This question corresponds with questions about the kind of allergy and allergic symptoms and the age at what these symptoms occur at the first time.

2.3 Predisposition

A predisposition was positive when either mother or father suffered from at least one of the following disorders: hay fever, eczema and/or asthma.

2.4 Exposure

To avoid a misclassification of the total exposure the outdoor pollution had been included in the statistical analysis. The main source of outdoor pollution in the investigated area is traffic. Considering earlier experience from epidemiological studies in the same city (Herbarth et al. [19], Fritz and Herbarth [20]) the traffic related exposure in the area of residence was estimated for each participant.

Indoor exposure was assessed based on questionnaire-based information focusing on type of home renovations, time of redecoration, i.e., prenatal (during pregnancy) as well as postnatal (during the first six years of the child's life), with special emphasis on the timing of renovations and the onset of the first overt of allergic symptoms. Exposure maxima are of special interest. Such maximum of indoor exposure is marked by a high emission of potential sources. Temporary sources originate from renovating activities. These activities are associated with high emissions of volatile organic compounds (VOCs). To assess the exposure maximum, three main types of renovations [painting, new floor covering, new furniture] were summed up in a variable called "reno max". This means that all 3 activities have to be carried out at the same time, then the "reno max" variable get "yes" otherwise "no".

The time of renovation was given by the parents in the questionnaire. With all this information it was possible to realize whether the activities took place before or after the first onset of the described diseases or symptoms.

2.5 Statistical analysis

The data analysis was performed using Statistica (Statsoft, Inc. 2004, STATISTICA for Windows Vers. 6 [26]). The χ^2 -test was used to determine the statistical significance of the exposure-associated differences in prevalences.



Logistic regression analyses were applied to calculate the odds ratios (OR) for the association between target variables and indoor exposure linked activities. Odds ratios were adjusted for the following confounders: family history of atopy (FHA defined above), gender, contact to cats, number of older siblings, mother's smoking during pregnancy, smoking in the presence of the child, outdoor exposure (characterised by traffic density in the area of residence) (Fritz and Herbarth [20, 21]).

3 Results

At time of investigation (mean age of children 6.3 ± 0.6 years) (Table 1), the lifetime prevalences were 16.9% for eczema and 12.7% for allergic symptoms manifestations. They are shown in Table 2 together with the frequencies of pertinent study parameters.

The control group has been selected considering all families who have not carried out any redecoration activities neither around the birth nor afterwards in the later life time. This concerns 537 study participants (21.2% of the study population). Table 3 shows the frequencies of redecoration activities and the link between different activities, divided in painting, floor covering and new furniture. The reno_max group comprises 936 study participants (36.9% of the study population).

% Ν study area 656.878 population total no of 6 to 7 years old children 3,919 in the area (one birth year) number of involved schools 119 response 75.3 2,950 (A) questionnaire related to 3,919 (B) complete data set concerning all 85.9 2,536 questions relevant for analysis related to (A) study participants 6.3 mean age [a] female / male 1,257 / 1,279 49.6 / 50.4 participants with older siblings 414 1.051

Table 1: Study parameter description.

Table 4 shows significantly higher prevalences of both allergic symptoms and diagnosed eczema associated with "reno_max" activities at any time. All cases are counted which take place after reno_max within the first 6 years of life and compared with the control group. The association between "reno_max" and allergic symptoms after adjustment for other possible allergy risk factors are shown in Table 5.



Table 2: Lifetime prevalences of allergic disorders and frequencies of some covariates (data referred to the age of 6.3 years).

| ALLERGIC SYMP | prevalence [%] | n/2536 | |
|---|----------------------|--------|------|
| allergic symptoms (pl | 12.7 | 321 | |
| eczema | 16.9 | 428 | |
| EXPOSURE | frequency [%] | | |
| OUTDOOR traffic | influenced area | 35.7 | 903 |
| INDOOR renova | ation activities | | |
| | painting | 49.4 | 1252 |
| | 68.8 | 1775 | |
| | 60.1 | 1524 | |
| no renovation activity of any sort | | 21.2 | 537 |
| "reno-max" only: just before birth | | 22.0 | 557 |
| during the 1st year of life | | 6.5 | 164 |
| during the 2 nd and 3 rd year of life | | 5.2 | 131 |
| from the 4 th year of life | | 3.3 | 84 |
| PREDISPOSITION | family atopy history | 33.8 | 857 |

Table 3: Frequencies of redecoration activities.

| painting | floor covering | new furniture | | |
|----------|----------------|---------------|----------------|--|
| | | No | Yes | |
| No | No | 21.2 (537) | 4.7 (119) | |
| | | control group | | |
| No | Yes | 10.2 (258) | 14.6 (370) | |
| Yes | No | 3.4 (86) | 3.2 (82) | |
| Yes | Yes | 5.8 (148) | 36.9 (936) | |
| | | | reno_max group | |

^{% (}N); % refer to the total number of participants (N=2536).

As far as 'timing' of renovations was concerned, the data suggest that the strongest effect was observed when renovations took place just around birth (Figure 1). Only "reno max" data have been considered in these logistic models adjusted for those variables called in Table 5. Included were 1473 cases (see Table 3, control group and reno max group). All cases with one or two redecoration activities have been excluded. Apart from the adjusting variables in each of both models 4 variables were included to characterize the redecoration time (before birth, in the first, in the second / third year, in the fourth year of life and later). Both models, for allergic symptoms as well as for eczema, are significant with p<0.0001. It should be mentioned again that starting with birth only those cases have been considered for which the exposure takes place before first health effects were seen. In fact, timing showed a definite trend, the earlier in a child's life the renovations were carried out, the greater is the risk to develop allergic disorders later on (Figure 1).

Table 4: Prevalences of allergic disorders depending on extent of renovations (reno_max = wall painting + new floor covering + new furniture).

| | prevalence [%] | | |
|-------------------|--------------------------------|----------|-------------|
| | never redecorated ¹ | reno_max | $p(\chi^2)$ |
| allergic symptoms | 9.3 | 16.8 | < 0.0001 |
| eczema | 11.5 | 20.3 | < 0.0001 |

¹never redecorated means not any activity, neither painting nor floor covering nor new furniture; this group of participants is used to be the control group

Table 5: Adjusted Odds Ratios (OR) for allergic disorders depending on at most renovation activities (only cases included without any redecoration activity – internal control group - and with reno_max" activity, not included cases with one or two activities out of painting, floor covering and new furniture; total remaining cases n = 1473 included in the models).

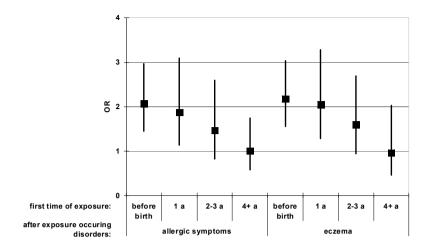
| | | allergic | allergic symptoms | | Eczema | |
|----------------------------|------------------|----------|-------------------|------|----------|--|
| | | OR | p | OR | p | |
| parental pr | edisposition | 2.53 | < 0.0001 | 1.30 | 0.0705 | |
| sex | | 0.71 | 0.0251 | 0.74 | 0.0360 | |
| older sibli | ngs | 1.13 | 0.4218 | 0.76 | 0.0594 | |
| smoking | during pregnancy | 0.93 | 0.7861 | 1.28 | 0.2501 | |
| | ETS | 1.23 | 0.2050 | 1.49 | 0.0073 | |
| pets (cat) | | 1.33 | 0.0590 | 1.21 | 0.1784 | |
| outdoor exposure (traffic) | | 1.15 | 0.3915 | 0.92 | 0.9169 | |
| indoor exposure (reno max) | | 1.85 | 0.0004 | 1.95 | < 0.0001 | |

Rem: ETS – environmental tobacco smoking (passive smoking); smoking in presence of the child, sex: 0 = male; 1 = female, both models high significant: $p_{\text{model}} < 0.0001$, trend in italics.

To derive a kind of dose-response relationship the number of activities has been included in the model. The variable "indoor exposure (reno_max)" (Table 5) has been replaced by the number of renovation activities: no activity (control group), 1 or 2 activities and 3 activities (reno_max group). The risk increases per additional activity about 1.27 (95%CI: 1.14 ... 1.41; p<0.0001) in the case of allergic symptoms and about 1.21 (95%CI: 1.10 ... 1.33; p<0.0001) in the case of eczema. Both models are significant with p<0.0001 and base on n=2536 included cases.

A siblings and birth order effect as reported by Strachan and colleagues [22] was not observed in association with renovation activity among these study participants. Only a trend is visible for eczema and the number of older siblings within the logistic model. It can be suspected that with increasing birth number the renovation activity goes down. This is not the case. The ratio "number of no renovation activities/number of reno_max activities" within the group without older siblings (n=875) is 0.59 and within the group with older siblings (n=598) 0.55.





Odds Ratios (OR +/- 95%CI) for allergic disorders depending on Figure 1: the timing of the renovations - reno max - (in years) and subsequent occurring disorders and symptoms (adjusted for parental predisposition, sex, older siblings, smoking in presence of the child in the first years of life (ETS), smoking during pregnancy, exposure characterised by outdoor (Rem: redecoration activities in the 1st, 2nd and 3rd, 4th year and later - 1a, 2-3a, 4+a; in both models (p<0.0001) considered only reno max and control group, not considered cases with one or two redecoration activities (see Table 2, N_{total}=1473)).

Conclusion

This study suggests an influence of residential renovations on allergic disorders. The chemical indoor exposure levels seem to play an important role because of the frequency of renovations which were carried out in the investigated households. 78.8% of all parents in this study redecorate their apartment before birth and in early life of the children, 36.9% carry out all three activities, painting, floor covering and new furniture (Table 3), 28.5% of them before birth and in the first year of life (Table 2). Compared to other lifestyle behaviours, such as smoking (e.g., ETS - environmental tobacco smoking), renovation activities associated indoor exposure leads to the same or to a higher risk in terms of the increase of the odds ratio (Table 5).

The early manifestation of eczema and its role as predictor of respiratory allergic disorders later in life (Bergmann et al. [25]) allocates a special importance on this disorder in defining the timing of any adverse exposure effects, one reason to avoid redecoration associated exposure as well as their level of concentration during pregnancy and the first year of life (Figure 1 and Table 5).



The results of this study confirm the results of the LARS study (Diez et al. [13]). Whereas high risk children were involved in the LARS study the LISS study is population based on 75.3% of all children of one birth year living in the area (Table 1).

Considering the "hygiene-hypothesis" (Strachan [1, 2]) a strong sibling effect was not observed. A birth order effect on the frequency of the renovation activity was not observed as well.

Several limitations need to be considered. First, the presented results base on questionnaire data. The questions have been answered by the parents when the children were 6 years old. Secondly, regarding the symptoms and/or diseases the parents were asked to put down on the questionnaire physician diagnosed symptoms and/or diseases only. Results of newborn cohort studies which are carried out in the same area come to similar results concerning the frequency of redecoration activities and prevalence's (Herbarth et al. [23], Diez et al [13], Zutavern et al [24]). In these studies the information of redecoration activities and of health effects has been collected immediately.

However, the study has several notable strengths. First, the study sample size is very large. No comparative study with respect to the population size is known which addressed the topic we deal with especially concerning indoor air quality. Second, the study participants have been recruited from one birth year.

It can be concluded that extensive renovations during pregnancy, especially around the time of birth, and during the first year of life seem to affect the development of allergic disorders. These findings should be considered like active and passive smoking by general practitioners or specialists when they advice prospective parents, especially expectant mothers, on the "dos and don'ts" during and after pregnancy. Avoidance of such activities particularly by parents themselves affected by atopy would be an effective measure of prevention. In fact, in contrast to smoking (active and passive smoking), this prevention measure may be more effective, since the risk is greater, it is easier to achieve and avoidance of such activities (renovation, floor covering or painting) involve no personal consequences (e.g., habit and withdrawal symptoms).

The complexity of the problem will gain in importance since legislative measures to conserve energy will continue which indirectly will affect the air indoors. The reduction in air exchange between in- and outdoor will lead to elevated concentrations of noxious substances and an increasing indoor air problem.

Acknowledgements

The study was supported by the BMBF - Federal Ministry of Education and Research of Germany, the UFZ - Centre for Environmental Research Leipzig-Halle and the State Ministry of Family and Health of Saxony.

The authors wish to thank the children and their parents as well as the staff of the local public health departments for their excellent cooperation in carrying out the field study. We are also indebted to our co-workers of the LISS Study Team for the field work in the schools.

Parts of this paper have been published in Int J Hyg Environ Health 209 (2006) 241-247. The authors thank the publisher Elsevier for the possibility to republish parts of the published article.

References

- Strachan, D.P.: Hay fever, hygiene, and household size. B.M.J. 299, 1259-[1] 60 (1989).
- [2] Strachan, D.P.: Family size, infection and atopy: the first decade of the "hygiene hypothesis". Thorax 55(Suppl 1), 2-10 (2000).
- Herbarth, O., Rehwagen, M.: VOCs Investigation into Outdoor and [3] Indoor Exposure: Initial results. Umweltmed. Forsch. Prax. 3:281-286 (1998).
- [4] Wolkoff, P., Nielsen, G.D.: Organic compounds in indoor air - their relevance for perceived indoor air quality. Atmos. Environ. 4407-4417 (2001).
- Samet, J.M., Marbury, M.C., Spengler, J.D.: Health effects and sources of [5] indoor air pollution. Part I. Am. Rev. Respir. Dis. 136, 1486-1508 (1987).
- [6] Samet, J.M., Marbury, M.C., Spengler, J.D.: Health effects and sources of indoor air pollution. Part II. Am. Rev. Respir. Dis. 137, 221-242 (1988).
- Cooke, T.F.: Indoor air pollutants. A literature review. Rev. Environ. [7] Health 9, 137-160 (1991).
- Harving, H., Dahl, R., Mølhave, L.: Lung function and bronchial [8] reactivity in asthmatics during exposure to volatile organic compounds. Am. Rev. Respir. Dis. 143, 751-754 (1991).
- Koren, H.S., Graham, D.E., Devlin, R.B.: Exposure of humans to volatile [9] organic mixture. III. Inflammatory response. Arch. Environ. Health 47: 39-44 (1992).
- Ware, J.H., Spengler, J.D., Neas, L.M., Samet, J.M., Wagner, G.R., [10] Coultas, D., Ozkaynak, H., Schwab, M.: Respiratory and irritant health effects of ambient volatile organic compounds. The Kanawaha County Health Study. Am. J. Epidemiol. 137, 1287-1301 (1993).
- Norbäck, D., Björnsson, E., Janson, C., Widström, J., Boman, G.: [11] Asthmatic symptoms and volatile organic compounds, formaldehyde, and carbon dioxide in dwellings. Occup. Environ. Med. 52, 388-395 (1995).
- Wieslander, G., Norback, D., Bjornsson, E., Janson, C., Boman, G.: [12] Asthma and the indoor environment: the significance of emission of formaldehyde and volatile organic compounds from newly painted indoor surfaces. Int. Arch. Occup. Environ. Health 69, 115-124 (1997).
- Diez, U., Kroessner, T., Rehwagen, M., Richter, M., Wetzig, H., Schulz, [13] R., Borte, M., Metzner, G., Krumbiegel, P., Herbarth, O.: Effects of indoor painting and smoking on airway symptoms in atopy risk children in the first year of life: results of the LARS-study. Leipzig Allergy High-Risk Children Study. Int. J. Hyg. Environ. Health 203:23-28 (2000).
- Warner, J.A.: Primary sensitization in infants. Ann. Allergy Asthma [14] Immunol. 83(5), 426-30 (1999).



- [15] Warner, J.A., Warner, J.O.: Early life events in allergic sensitization. Br .Med. Bull. 56(4), 883-893 (2000).
- [16] Warner, J.A., Jones, C.A., Jones, A.C., Warner, J.O.: Prenatal origins of allergic disease. J. Allergy Clin. Immunol. 105, 493-498 (2000).
- [17] Krumbiegel, P., Herbarth, O., Fritz, G.J., Schlink, U., Gutsmuths, F.-J., Kindler, A., Richter, T.: Helicobacter pylori prevalence in Leipzig's 1998 school entries: methodology and first results. Int. J. Hyg. Environ. Health 203:11-16 (2000).
- [18] Herbarth, O., Fritz, G.J., Krumbiegel, P., Diez, U., Franck, U., Richter, M.: Effect of sulfur dioxide and particulate pollutants on bronchitis in children -- a risk analysis. Environ .Toxicol. 16(3), 269-276 (2001).
- [19] Herbarth, O., Fritz, G.J., Diez, U., Rehwagen, M., Borte, M., Schulz, R., Richter, M., Krumbiegel, P., Müller, A.: Effect of volatile organic compounds in- and outdoors on allergies. 619-628. In Air Pollution VI. Ed. C.A. Brebbia, C.F. Ratto, H. Power. WIT Press Boston, Southampton (1998)
- [20] Fritz, G.J., Herbarth, O.: Pulmonary function and urban air pollution in preschool children. Int. J. Hyg. Environ. Health 203, 235-244 (2001).
- [21] Fritz, G.J., Herbarth, O.: Asthmatic disease among urban preschoolers: an observational study. Int. J. Hyg. Environ. Health 207, 23-30 (2004).
- [22] Strachan, D.P., Harkins, L.S., Johnston, I.D., Anderson, H.R.: Childhood antecedents of allergic sensitization in young British adults. J. Allergy Clin. Immunol. 99, 6-12 (1997).
- [23] Herbarth, O., Fritz, G.J., Behler, JC., Rehwagen, M., Puliafito, J.L., Richter, M., Schlink, U., sernaglia, J., Puliafito, E., Puliafito, C., Schilde, M., Wildführ, W.: Epidemiologic risk analysis of environmental attributed exposure on airway diseases and allergies in children. Centr. Eur. F. publ. Health 7, 2, 72-76 (1999)
- [24] Zutavern, A., Brockow, I., Schaaf, B., Bolte, G., von Berg, A., Diez, U., Borte, M., Herbarth, O., Wichmann, H.E., Heinrich, J.: Timing of solid food introduction in relation to atopic dermatitis and sensitation considering reverse causality: results from a prospective birth cohort study. Pediatrics 117(2) 401-411 (2006)
- [25] Bergmann, R.L., Edenharter, G., Bergmann, K.E., Forster, J., Bauer, C.P., Wahn, V., Zepp, F., Wahn, U.: Atopic dermatitis in early infancy predicts allergic airway disease at 5 years. Clin. Exp. Allergy 28(8), 965-970 (1998).
- [26] StatSoft, Inc. STATISTICA für Windows [Software-System für Datenanalyse] Version 6. www.statsoft.com, 2001.

