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Effect of pre- and postnatal tobacco smoke exposure on specific sensitization to food and inhalant allergens during the first 3 years of life

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Key words: allergic sensitization; early childhood; food hypersensitivity; inhalant allergens; *in utero* and postnatal passive tobacco smoke exposure; parental atopy.

Background: The study aimed to assess the effect of pre- and postnatal tobacco smoke exposure on specific sensitization to food allergens and inhalant allergens during the first 3 years of life.

Methods: A total of 342 children of a prospective and observational birth cohort study on atopy (MAS) were included on the basis of a complete follow-up of specific IgE measurements at the ages of 1, 2, and 3 years with available questionnaire information about the parental smoking habit at birth, 18 months, and 3 years of age. Study children were grouped into four exposure categories representing *in utero* and postnatal environmental tobacco smoke (ETS) exposure, and according to the number of cigarettes smoked by the parents. The effect on the development of allergic sensitization to food, outdoor, and indoor allergens by 3 years of age was determined by multiple logistic regression analyses.

Results: At the age of 3, children who were pre- and postnatally exposed to tobacco smoke had a significantly higher risk of sensitization to food allergens (odds ratio: 2.3, 95% C.I.: 1.1–4.6) than unexposed children. Children who were only postnatally exposed by a smoking mother also had a 2.2 times higher risk (95% C.I.: 0.9–5.9) of sensitization than unexposed children. These two categories (pre- and/or postnatal exposure) contribute to the significant overall effect of the tobacco smoke exposure ($P \leq 0.02$). No significant association between tobacco smoke exposure and specific sensitization to inhalant allergens was observed. The determining risk factors for this type of sensitization were atopic family history and mite- and cat-allergen exposure levels.

Conclusions: During the first 3 years of life, both prenatal and

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postnatal tobacco smoke exposure has an adjuvant effect on allergic sensitization which seems to be restricted to allergens to which children are mainly exposed, in combination with the peak of the ETS exposure around the first birthday.

Studies on pre- and postnatal tobacco smoke exposure in children have mainly examined the effect on the respiratory tract including the pulmonary function, bronchial hyper-reactivity, and asthma (1–11). The American National Research Council (12) and the US Environmental Protection Agency (13) found environmental tobacco smoke (ETS) exposure to be associated with lower-respiratory-tract illnesses in young children, as well as with other adverse respiratory outcomes. But we have little knowledge about the influence on immune regulation, especially on specific sensitization. Some studies report a positive association between tobacco smoke exposure and the occurrence of allergic sensitization (14, 15), whereas others found no association (16–18), corresponding to the controversial

results in reviews by Halken et al. (19) and Strachan & Cook (20). In this recent review, the outcome of allergic sensitization in all included studies was measured by skin prick test, and not specific serum IgE as in our study. The major difference, however, is the age group examined: that review included only schoolchildren older than 6 years, whereas, in our cohort study, children were followed up from birth to investigate early sensitization. Retrospective assessment of passive smoking may introduce substantial bias in the exposure measure, especially regarding accuracy and recall of parental smoking habits.

Sensitization to food and inhalant allergens, however, must be regarded as a risk for the development of subsequent allergic airway diseases (21–23). The natural course of early sensitization in most atopic individuals is characterized by sensitization to food proteins (particularly cow's milk and hen's egg) within the first 2 years of life (24, 25). The incidence of sensitization to outdoor and indoor allergens, however, is low during infancy and increases after the second year of life (23, 26).

Table 1. Characteristics of analyzed subcohort ($n=342$) and remaining children of overall MAS cohort (due to missing information for some characteristics, number of subjects varies between 839 and 972)

	Analyzed subcohort $n=342$	Remaining subjects of MAS cohort $n=972$	P value†
Sex (male)	51%	52%	0.8
Parental education level			0.45
Middle school	56	53	
High school	14	15	
Higher education	30	32	
Duration of breast-feeding			0.29
Up to 1 month	27	32	
1–6 months	46	43	
More than 6 months	27	25	
Parental smoking habit			
Maternal smoking during pregnancy	22	26	0.12
Parental smoking after birth (1 month)	49	52	0.29
Parental atopy			
Atopic mother	35	36	0.82
Atopic father	30	30	0.94
Detectable cord-blood IgE	30	36	0.043
Prevalence of atopic disorders‡			
at 3 years of age	24	23	0.75

†Chi-square test for differences in two samples.

‡Including food allergy, atopic dermatitis, wheezy bronchitis, and allergic rhinitis.

The aim of our study was to investigate whether prenatal and postnatal tobacco smoke exposure has an adjuvant effect on the development of allergic sensitization during infancy and early childhood. We evaluated a possible effect on the sensitization to food allergens because infants and young children are initially sensitized to food. Furthermore, we evaluated a possible effect on the sensitization to inhalant allergens because of the considerable discussion about the harmful effects of tobacco smoke on the respiratory tract.

Material and methods

Subjects

Subjects of the present study were participants of the German Multicenter Allergy Study (MAS). For this prospective and observational birth cohort study, 1314 neonates were enrolled in five German cities during 1990. A detailed description of study subjects and methods is presented elsewhere (27). The children were followed up at the ages of 1, 3, 6, 12, and 18 months and 2 and 3 years. At each visit, parents filled in questionnaires and underwent structured interviews about the atopic symptoms and diseases of their children. Study participation rate at the third birthday was 80% ($n=1050$). The study was approved by the local ethics committee. Informed consent was given by all parents before entering the study. Inclusion criteria for the present study were a complete follow-up of annual specific IgE measurements at the age of 1, 2, and 3 years and available information about parental smoking habits. The 360 children with a complete follow-up until the third birthday did not differ substantially from the overall MAS cohort in sex, parental education, parental atopy status, maternal smoking during pregnancy, and parental smoking habits after birth (Table 1).

Assessment of pre- and postnatal tobacco smoke exposure

Pre- and postnatal tobacco smoke exposure was assessed by a standard questionnaire at birth of the children and at 18 months and 3 years of age. Additional data about the number of cigarettes smoked by parents were available at 18 months. Both parents were asked about their smoking habits at home and whether they exposed their child or took special care to reduce the child's ETS exposure. Prenatal tobacco smoke exposure was defined as maternal smoking during pregnancy and postnatal ETS exposure as maternal and/or

paternal smoking at home after birth. For determination of the effect of pre- and postnatal tobacco smoke exposure, the children were assigned to four distinct exposure groups. In group 1, the children were neither prenatally nor postnatally exposed. In the second category, the children were postnatally ETS exposed only by a smoking father. It can be assumed that fathers are absent during the day and that their contribution to the ETS exposure is less than that of the mothers who care for the child. In the third group, the children were postnatally exposed by a smoking mother who began smoking after birth (and also exposed by the father if both parents [57% of this group] had been smoking). Children in the last category were prenatally and postnatally exposed by mothers who had been smoking during pregnancy and after birth (in 61% of cases in this category, a smoking father also lived in the household). Eighteen of the 360 families were excluded from the analysis because mothers and/or fathers ceased smoking during the observation period.

In summary, the exposure categories were as follows:

- 1) pre-post- (neither prenatally nor postnatally exposed; $n=178$)
- 2) pre-post+_{father} (postnatally exposed by a smoking father; $n=62$)
- 3) pre-post+_{mother} (postnatally exposed by a smoking mother and possibly a smoking father; $n=28$)
- 4) pre+post+_{mother} (prenatally and postnatally exposed by a smoking mother and possibly a smoking father; $n=74$).

In a further study, we assessed the validity of the questionnaire data by urine cotinine measurements and studied the course of the cotinine levels in our study children during early childhood (28). Urinary cotinine concentrations reached a peak around the first birthday, before decreasing with age, probably reflecting the gradually less intense contact with the parents.

Definition of sensitization

The outcome of interest was sensitization to food allergens and inhalant allergens. The children were regarded as sensitized if specific IgE antibodies were detectable at least once during the first 3 years. As described previously (29), the CAP-RAST-FEIA system (Pharmacia, Germany) was used with a detection limit of 0.35 kU/l. We analyzed three separate allergen groups:

- 1) sensitization to at least one of four tested food allergens (cow's milk, hen's egg, soybean, and wheat)

- 2) sensitization to at least one of two tested outdoor allergens (birch and grass pollen)
- 3) sensitization to at least one of two tested indoor allergens (mite and cat).

In an earlier study (30), we showed that the allergen exposure is a significant risk factor for subsequent sensitization to indoor allergens. Since the exposure levels of mite and cat allergens were available in our study, we analyzed the risk of sensitization for each indoor allergen separately.

As a marker of whether the passive smoke exposure is related to the severity of atopic sensitization, we assessed the number of positive reactions to the eight tested allergens during the first 3 years of life by categorizing the number of positive reactions in four groups (0, 1, 2 or 3, and ≥ 4 years).

Symptoms or diagnoses suggestive of food allergy were assessed by questionnaire or structured interviews. Clinical symptoms such as repeated vomiting, diarrhea, and colic, not caused by an infectious disease, after consumption of milk, eggs, fish, or nuts, were regarded as symptoms and signs of food intolerance. The diagnosis was made by a pediatric allergist. However, according to the study protocol, a food challenge test was not performed.

Covariates

Data of the following covariates were gathered by questionnaire: sex, atopic family history (mothers and fathers were separately considered and defined as atopic if at least one of the following conditions was present: asthma, hay fever, atopic eczema, or food allergy), season of birth, duration of breast-feeding (up to 1 month, 1–6 months, or more than 6 months), and parental educational level (middle school, high school, or higher education). Cord-blood IgE (detection limit: 0.35 kU/l) was determined by the CAP-RAST-FEIA system (Pharmacia, Germany). Urine specimens were available for 74% of the children at 1 year of age. Urinary cotinine concentrations (standardized to creatinine concentrations) were measured with the detection limit of 1 ng/ml (31). Mite- (Der p 1 plus Der f 1) and cat- (Fel d 1) allergen-exposure levels were obtained from carpet dust samples at 6 and/or 18 months of age. The allergen extraction and analysis were performed, as previously described, by a sandwich ELISA from ALK (Copenhagen, Denmark [32]). When two dust samples were available, arithmetic mean values were used in the analysis.

Statistics

Statistical analysis was done with SPSS. Pearson's chi-square test was used for comparison of categorical data and the Mann-Whitney U or Kruskal-Wallis test for continuous nonparametric data analysis (allergen concentrations and cotinine levels). Multiple logistic regression with the BMDPDYN statistical software package was used to determine the effect of tobacco smoke exposure on specific sensitization (separate models for the effect of parental smoking pattern and number of cigarettes smoked). Parsimonious models were derived with stepwise logistic regression, adjusting for confounding (parental educational level and study center), as described by Hosmer & Lemeshow (33). Potential effect modifiers were examined by adding interaction terms in the logistic regression analysis. Allergen-exposure levels were log-transformed since they were skewed to the right. The statistical significance of a potential risk factor is given as *P* value of the likelihood-ratio test statistic relative to the model without the factor in question.

Results

The parental smoking habits and the characteristics of the study children and their families are shown in Table 2. Approximately half the children lived in nonsmoking households. In 18% of the families, both parents were smokers and 22% of the children had been exposed *in utero*. Heavily smoking mothers, i.e., mothers who already smoked during pregnancy, had mainly a low educational level and breast-fed their infants for a shorter period than nonsmoking mothers. In 21% of the households, 1–10 cigarettes were smoked; in 17%, 11–20 cigarettes; and in 10%, more than one pack. Cats were found more often in families with at least the mother smoking, corresponding to higher cat-allergen exposure levels. The sensitization rates for the three allergen groups stratified according to the parental smoking habits are listed in Table 3. The sensitization rates to food allergens were significantly higher in children who had been exposed to a smoking mother than in unexposed children or children exposed only by a smoking father. Sensitization rates to indoor and outdoor allergens did not differ significantly with ETS exposure. In concordance with the nonsignificantly different cotinine levels in the ETS-exposure groups (Table 2), we did not observe significant differences in cotinine levels

Table 2. Characteristics of 342 analyzed children and their families stratified by parental smoking habits (expressed as percentages in total group and in four exposure groups; prenatal: exposed during pregnancy, post(natal): exposed after birth)

	Parental smoking habits				P value†
	Prenatal– Postnatal– n=178	Prenatal– Post†father n=62	Prenatal– Post†mother n=28	Prenatal+ Post†mother n=74	
Sex (51% boys of 342 analyzed children)	55%	42%	53%	50%	0.22
Parental education level					0.001
Middle school (56%)	46	68	57	70	
High school (14%)	14	17	10	12	
Higher education (30%)	40	15	33	18	
Duration of breast-feeding					<0.001
Up to 1 month (27%)	16	32	36	47	
1–6 months (46%)	50	38	46	43	
More than 6 months (27%)	34	30	18	10	
Season of birth					0.23
Spring/autumn (Mar–May, Sep–Oct; 32%)	33	26	36	37	
Summer (May–Aug; 40%)	38	47	42	39	
Winter (Nov–Feb; 28%)	29	27	22	24	
Parental atopy					
Atopic mother (35%)	38	31	32	35	0.68
Atopic father (30%)	37	21	29	23	0.051
Detectable cord-blood IgE (30%)	29	25	31	36	0.53
Urinary cotinine excretion at 1 year of age (median (25–75th percentile); n _{total} =253)	0 (0–68)	45 (0–144)	18 (0–109)	82 (0–173)	0.18‡
Cats in household at 18 months (11%)	6	10	18	19	0.03
Cat-allergen exposure by 18 months (median)	50 ng/g	60 ng/g	71 ng/g	108 ng/g	0.008
Mite-allergen exposure by 18 months (median)	257 ng/g	620 ng/g	224 ng/g	144 ng/g	0.1
Missing information for each characteristic in 0–14 subjects.					
†Chi-square test for differences in four exposure groups.					
‡Kruskal-Wallis test for differences among three ETS-exposed groups.					

between sensitized and nonsensitized children for each type of sensitization ($P>0.11$).

Concerning the question of whether passive smoke exposure is related to the severity of atopic sensitization, we found a slight, nonsignificant association between passive smoke exposure and the number of positive reactions to the eight tested allergens. In those groups in which the mother was smoking either pre- and postnatally, or postnatally only, we observed more positive reactions than in the unexposed or paternally exposed children ($P=0.12$; Table 3).

By multiple logistic regression analysis, we calculated the odds ratios for the risk of sensitization to the respective allergen groups adjusting for confounding factors (Table 4).

At the age of 3 years, children who were pre- and postnatally exposed to tobacco smoke had a significantly higher risk of sensitization to food allergens (odds ratio: 2.3, 95% C.I.: 1.1–4.6) than unexposed children. Children who were only postnatally exposed by a smoking mother also had a 2.2 times higher risk (95% C.I.: 0.9–5.9) of sensitization than unexposed children. This odds ratio was not significant at the 0.05 level, but these two categories (pre- and postnatal exposure and only postnatal exposure) contributed to the significant overall effect of the tobacco smoke exposure ($P\leq 0.02$). For increasing number of cigarettes smoked in the household, we observed increasing but statistically nonsignificant risks ($P=0.15$; Table 4). Detectable cord-blood IgE was determined as an additional significant risk factor.

Table 3. Sensitization rates to food and inhalant allergens and symptoms of food allergy by 3 years of age according to pre- and postnatal tobacco smoke exposure throughout first 3 years of life (n=342)

3 years of age: sensitization to	Parental smoking habits				P value†
	Prenatally – Postnatally – n=178	Prenatally – Postnatally + father n=62	Prenatally – Postnatally + mother n=28	Prenatally + Postnatally + mother n=74	
At least one of four food allergens	28%	15%	43%	40%	0.005
At least one of two outdoor allergens	18%	13%	18%	16%	0.8
At least one of two indoor allergens	9%	5%	11%	15%	0.2
Number of positive reactions to eight allergens					
No reaction	66%		54%		0.12
≥4 reactions	10%		14%		
Symptoms of food allergy	7%	5%		9%	0.59

†Chi-square test for differences in rates.

Passive smoke exposure, however, was not related to cord-blood IgE levels, either with the detection limit (Table 2) or with 0.9 kU/l as the chosen cutoff point ($P=0.58$).

There was no significant association between pre- and postnatal tobacco smoke exposure and specific sensitization to inhalant allergens. The determining risk factors for this type of sensitization were atopic family history, especially an atopic mother (odds ratios ≥ 2.1 , $P \leq 0.03$), and exposure to mite allergen (odds ratio: 2.2, 95% C.I.: 1.1–4.6) and cat allergen (odds ratio: 1.8, 95% C.I.: 1.1–2.8). As for food sensitization, we found rising but statistically nonsignificant risks of sensitization to inhalant allergens if children were exposed to an increasing number of cigarettes smoked in the household ($P > 0.2$; Table 4).

Discussion

Our results indicate an increased risk of early sensitization to food allergens for children who were pre- and postnatally exposed to tobacco smoke. The effect seemed to be restricted to food allergens, whereas the risk of developing sensitization to inhalant allergens was not increased. This may be explained by the fact that allergic sensitization in infancy generally occurs first to food allergens (24, 25) and that tobacco smoke exposure seems to act very early, starting already during pregnancy (3–5, 34). Furthermore, we have shown in another investigation that ETS exposure reaches a peak around the first birthday (28). The early and simultaneous exposure to tobacco smoke and food allergens may interfere with the normal development of immunologic tolerance, facilitating sensitization to food. The risk

estimates for the effect of pre- and postnatal tobacco smoke exposure are relatively small. Since allergic sensitization to food is a common sign in early childhood and is regarded as a risk factor for subsequent development of allergic diseases (21–23), the overall impact of tobacco smoke exposure may be quite large. Moreover, it can be assumed that parents tend to underreport active smoking, classifying themselves as nonsmokers rather than as smokers because of possible social stigmatization. Such nondifferential misclassification would result in a too conservative risk estimation. Our risk estimates are comparable in magnitude to other findings regarding the association between ETS exposure and the development of diseases such as asthma and bronchial hyperreactivity in childhood (5, 9, 10, 35, 36). However, we found no studies examining the effect of pre- and postnatal exposure on sensitization which were comparable with regard to adequate control of potential confounders and/or sample size and age of study children. One birth cohort study assessed the effect of tobacco smoke exposure on 2-year-old children (37), but did not distinguish between smoking in pregnancy and current maternal smoking. In most studies, sensitization was determined not in early childhood but in school-age children by measuring skin prick reactivity (38–40). In questioning years after the exposure period in question, a substantial recall bias in assessing pre- and postnatal parental smoking habits has to be considered.

In other studies, control for confounding factors was often insufficient, and parents of children at risk may have changed their smoking behavior to reduce exposure. Beyond inadequate recall, other sources of potential misclassification of exposure status must be considered, especially

Table 4. Multiple logistic regression analysis of risk factors for sensitization to food, outdoor, and indoor allergens in 328 children to 3 years of age. Odds ratios (with 95% confidence interval) and *P* value, adjusted for parental educational level and study center. Effects of parental smoking pattern and number of cigarettes smoked were determined by separate models (Pre: exposed during pregnancy; Post: exposed after birth)

	Sensitization			
	Food allergens	Outdoor allergens	Cat allergens	Mite allergens
Parental smoking habits				
Pre-/Post-†	1	1	1	1
Pre-/Post+ _{father}	0.7 (0.3–1.6)	0.9 (0.4–2.1)	0.5 (0.1–2.6)	0.3 (0.1–2.6)
Pre-/Post+ _{mother}	2.2 (0.9–5.9)	1.4 (0.5–4.3)	0.5 (0.1–3.6)	0.6 (0.1–6.3)
Pre+/Post+ _{mother}	2.3 (1.1–4.6)	1.2 (0.5–2.2)	1.4 (0.4–4.9)	1.0 (0.2–5.3)
	<i>P</i> =0.02	<i>P</i> =0.9	<i>P</i> =0.48	<i>P</i> =0.62
Cord-blood IgE				
Not detectable†	1	1	1	1
Detectable (≥ 0.35 kU/l)	3.1 (1.7–5.4)	1.0 (0.5–2.1)	0.9 (0.4–2.8)	1.3 (0.4–4.9)
	<i>P</i> <0.001	<i>P</i> =0.9	<i>P</i> =0.9	<i>P</i> =0.7
Atopic family history				
Nonatopic mother†	1	1	1	1
Atopic mother	1.5 (0.9–2.7)	2.1 (1.1–3.9)	4.6 (1.6–13.3)	3.5 (1.1–12.1)
	<i>P</i> =0.16	<i>P</i> =0.02	<i>P</i> =0.003	<i>P</i> =0.03
Nonatopic father†	1	1	1	1
Atopic father	1.6 (0.9–2.9)	1.1 (0.6–2.1)	1.8 (0.6–4.9)	2.4 (0.7–8.5)
	<i>P</i> =0.14	<i>P</i> =0.8	<i>P</i> =0.3	<i>P</i> =0.17
Allergen exposure* (ng/g dust)				
			1.8 (1.1–2.8)	2.2 (1.1–4.6)
			<i>P</i> =0.01	<i>P</i> =0.02
Sex				
Male†	1	1	1	1
Female	0.7 (0.4–1.1)	0.9 (0.5–1.7)	1.6 (0.6–4.5)	1.9 (0.6–6.8)
	<i>P</i> =0.07	<i>P</i> =0.7	<i>P</i> =0.3	<i>P</i> =0.2
Season of birth	<i>P</i> =0.28	<i>P</i> =0.55	<i>P</i> =0.53	<i>P</i> =0.83
Breast-feeding	<i>P</i> =0.63	<i>P</i> =0.52	<i>P</i> =0.9	<i>P</i> =0.49
Number of cigarettes smoked by parents (<i>N</i> _{total} =294)				
None	1		1	1
1–10/day	1.5 (0.7–3.5)	0.5 (0.2–3.9)	0.3 (0.1–1.8)	0.4 (0.1–3.4)
11–20/day	2.1 (1.1–4.1)	1.5 (0.7–3.4)	1.9 (0.5–8.4)	1.4 (0.2–13)
More than 20/day	2.0 (0.6–7.2)	2.2 (0.9–5.5)	2.4 (0.4–17)	2.5 (0.2–38)
	<i>P</i> =0.15	<i>P</i> =0.25	<i>P</i> =0.21	<i>P</i> =0.71
<i>n</i> =328 children were analyzed since information was missing for each characteristic in 0–14 subjects.				
†Reference category.				
*Allergen exposure levels were log-transformed.				

reliance on only one parent's report of a partner's smoking status, lack of awareness of exposure of the child, or the general difficulty of accurately determining the long-term ETS-exposure history of the child. As of today, no fully satisfactory method for quantifying ETS exposure has been

found [34]. In our cohort study, we assessed ETS exposure by urinary cotinine measurements and by a standard questionnaire asking parents about their smoking habits. In the present study, our analysis relied on questionnaire information because cotinine measurements were available only at

1 year of age, and not for all children included. The main reason, however, was the problem of determining the long-term ETS exposure. Adverse health effects of ETS exposure are believed to be associated with long periods of exposure, but biomarkers such as urinary cotinine have relatively short half-times, and significant differences have been reported in uptake, metabolism, and excretion between individuals (34, 41). Urinary cotinine reflects exposure over the past day or two and can therefore indicate changes in exposure patterns, as shown in another investigation of the MAS cohort (unpublished data). But that different measure of ETS exposure may not adequately represent *chronic* exposure. Moreover, it can be difficult to interpret cotinine values. For example, in children from nonsmoking households, urine cotinine concentrations are detectable as well, and which cotinine level should be chosen as a cutoff point for passive exposure to tobacco smoke? It was shown that questionnaires assessing ETS exposure provide sufficiently accurate qualitative information on exposure, although quantitative information seems to be less reliable (34). In our cohort, both parents were questioned several times during the observation period, so that long-term exposure of the children was accurately determined.

We did not assess the relation between passive smoke exposure and atopic diseases because in early childhood prevalence of allergy is still low (7.3% for symptoms suggestive of food allergy in our sample, one possible reason for the absence of significant relation to passive smoke exposure). Moreover, it is often difficult to distinguish between atopic diseases or only related symptoms (e.g., wheezing), resulting in some uncertain diagnosis. Specific sensitization, however, must be regarded as an early sign of allergic hyperreactivity with a higher risk of developing allergic diseases in later years. Thus, our analysis was based on sensitization to food and inhalant allergens.

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For the evaluation of the effect of pre- and postnatal tobacco smoke exposure on allergic sensitization, we used exposure categories according to the smoking pattern and the number of cigarettes smoked in the household. The slightly increasing but not statistically significant odds ratios for rising numbers of cigarettes smoked in the household indicate that besides the timing of exposure, the level of exposure may also be relevant to the observed risk of allergic sensitization. For of the following reasons, the children were assigned to four distinct ETS-exposure groups according to the parental smoking status. Firstly, we distinguished between only paternal, and maternal or combined exposure because the father was usually not the primary caregiver. We found that paternal ETS exposure had no significant effect on the development of allergic sensitization. Therefore, it may be assumed that the quantitative exposure by fathers as the only smokers in the household is less than that of smoking mothers, especially during the first years of life. Secondly, we distinguished postnatal exposure from prenatal exposure due to maternal smoking during pregnancy because of the controversial discussion of the effect of prenatal factors on the development of allergic sensitization. Despite the significance of the odds ratio of the prenatal plus postnatal exposure category in comparison to only postnatal exposure, we found no conclusive evidence of a much stronger effect of prenatal exposure. As the odds ratios of both maternal-exposure categories were very similar, our results indicate that there is a combined effect of pre- and postnatal tobacco smoke exposure on the occurrence of food sensitization throughout early childhood.

In conclusion, our data indicate that during the first 3 years of life, both prenatal and postnatal tobacco smoke exposure has an adjuvant effect on allergic sensitization which seems to be restricted to allergens to which children are mainly exposed, in combination with the peak of the ETS exposure around the first birthday.

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