Letter to the Editor

Current use of room disinfectants and allergic symptoms at the age of 4 years

To the Editor:

Epidemiologic studies suggest an association of occupational domestic cleaning with asthma.[1,2] More recently, a correlation of nonprofessional use of cleaning sprays with adult asthma has also been reported for private households.[3] In this study application of commonly used cleaning and air-refreshing sprays was found to be a major risk factor for asthma, but the relevance of these findings for children remains to be understood. Because of their small airway diameters, young children are particularly susceptible to respiratory symptoms. In addition, allergic diseases are frequently primed in early childhood, and potential risk factors need to be avoided. For these reasons, we wished to analyze potential associations between current use of room disinfectants in private homes and respiratory, cutaneous, and allergic symptoms in young children. To this end, we performed an observational study in 4-year-old offspring from pregnant women participating in a multicenter, randomized, double-blind, placebo-controlled clinical trial described in detail elsewhere.[4] Briefly, the effects of increased intakes of a fish oil preparation (0.5 g of docosahexaenoic acid and 0.15 g of eicosapentaenoic acid), 400 μg of 5-methyl-tetrahydrofolate, both, or placebo from the 22nd week of gestation until delivery and birth outcomes were assessed in the main trial. Thus a selection bias with respect to allergic diseases and use of room disinfectants would not be expected.

Study centers were the University Hospital of Granada (Spain), the University of Pecs (Hungary), and the University of Munich (Germany). Three hundred eleven healthy women between 18 and 40 years of age with uncomplicated singleton pregnancies completed the study until delivery. Mothers who dropped out had a higher body mass index in the 20th week of gestation ($P < .02$, Mann-Whitney U test) compared with mothers who completed the study. This difference was no longer seen in the 30th week of gestation. From 270 women completing the study, 176 offspring (all white; 43% total dropout rate) attended the clinic at the age of 4 years for a medical and neurophysiologic examination as part of the main trial. During this visit, parents completed a standardized questionnaire with the assistance of the study personnel for the present study, which included questions from the International Study of Allergy and Asthma in Childhood[5] and the Influences of Lifestyle-Related Factors on the Immune System and the Development of Allergies in Childhood study[6] on respiratory, cutaneous, and allergic symptoms, as well as physician-diagnosed allergic disease. In particular, we asked the following question: "Do you use room disinfectants or sprays (daily, at least once per week, occasionally, never)?" Written informed consent was obtained from all participating women. The local ethics committees of each participating center approved the study protocol.

Descriptive categorical data were analyzed with χ^2 analysis. The likelihood of allergic symptoms in relation to household room spray application was assessed in bivariate analyses. In multivariate analyses we controlled one by one and in a parsimonious model for the influence of potential confounders associated with exposure and outcome variables, such as center, sex, nutrient supplementation during pregnancy, maternal and paternal allergy, number of siblings, smoking, and pets. All computations were performed by using SPSS for Windows, version 15.0 (SPSS, Inc, Chicago, Ill).

TABLE I. Characteristics of the study population according to use of room disinfectants

	Current use of room disinfectants		
	No	Yes	*P* value†
Total*	75 (42.6%)	101 (57.4%)	
Sex			.76
Male	36 (40.4%)	53 (59.6%)	
Female	37 (43.5%)	48 (56.5%)	
Birth weight (g)	3348 (±442)	3257 (±458)	.13
Center			**<.0001**
Spain	22 (20.8%)	84 (79.2%)	
Hungary	11 (44%)	14 (56%)	
Germany	42 (93.3%)	3 (6.7%)	
Maternal allergy	30 (61.2%)	19 (38.8%)	**.002**
Paternal allergy	24 (57.1%)	18 (42.9%)	**.03**
Siblings with allergies	16 (35.6%)	29 (64.4%)	.30
No. of siblings‡			.30
0	19 (34.5%)	36 (65.5%)	
1	45 (48.4%)	48 (51.6%)	
2	11 (44%)	14 (56%)	
4	0 (0%)	1 (100%)	
6	0 (0%)	2 (100%)	
Furry pets	17 (45%)	21 (55%)	.85
Passive smoking	8 (22%)	28 (78%)	.60
Job training (father)			**.02**
None	20 (28.6%)	50 (71.4%)	
Apprenticeship	15 (46.9%)	17 (53.1%)	
Masters degree	7 (58.3%)	5 (41.7%)	
University degree	32 (56.1%)	25 (43.9%)	

Values shown in boldface are significant.
*Data are expressed as numbers (percentages) of subjects.
†Data refer to differences among exposure groups (Pearson χ^2 test).
‡The study population did not contain families with 3 or 5 siblings.

The population for this study consisted of 106 Spanish, 45 German, and 25 Hungarian infants (Table I). From the total of 176 children, 101 were exposed to room disinfectants. While half of the Hungarian children were exposed to disinfectants, Spanish children were exposed with significantly higher frequency and German children with significantly lower frequency, which is in line with previous publications.[3] Room disinfectants were used daily or almost daily in 14.8%, at least once per week in 33%, occasionally in 9.7%, and never in 42.6% of households of all participants. Maternal allergy, paternal allergy, and a higher socioeconomic status were associated with less frequent application of room disinfectants. Allergic asthma was present in 27 (15%) children, hay fever in 5 (2.8%) children, and atopic dermatitis (all physicians' diagnoses in the past 12 months) in 57 (32%) children, with significant differences between the centers.

Application of room disinfectants was not associated with higher effect estimates for asthma but significantly increased effect estimates for atopic dermatitis and itchy rash (Table II). Correspondingly, the likelihood for treatment of atopic eczema was increased in children exposed to room disinfectants (unadjusted odds ratio [OR], 4.2; 95% CI, 1.9-9.5; $P < .001$). The number of children with hay fever was too low to allow meaningful

TABLE II. Prevalence (%) and likelihood of respiratory symptoms and allergic diseases in 176 4-year old children

	Current use of room disinfectants	
	No (n = 75)	Yes (n = 101)
Asthma ever*		
No	66 (44)	83 (56)
Yes	9 (33)	18 (67)
OR (95% CI)	1	1.6 (0.7-3.8)
aOR (95% CI)	1	1.1 (0.4-2.8)
Asthma (past 12 months diagnosed)		
No	74 (44)	94 (56)
Yes	1 (13)	7 (88)
OR (95% CI)	1	5.5 (0.6-45.8)
aOR (95% CI)	1	4.3 (0.5-40.3)
Wheezing ever		
No	51 (45)	62 (55)
Yes	24 (38)	39 (62)
OR (95% CI)	1	1.3 (0.7-2.5)
aOR (95% CI)	1	0.9 (0.5-2.1)
Atopic eczema ever		
No	59 (50)	60 (50)
Yes	16 (28)	41 (72)
OR (95% CI)	**1**	**2.5 (1.3-5.0)**
aOR (95% CI)	**1**	**2.6 (1.2-5.6)**
Atopic eczema (past 12 months diagnosed)		
No	71 (48)	78 (52)
Yes	4 (15)	23 (85)
OR (95% CI)	**1**	**5.2 (1.7-15.9)**
aOR (95% CI)	**1**	**7.0 (1.8-27.1)**
Rash ever		
No	63 (49)	65 (51)
Yes	12 (25)	36 (75)
OR (95% CI)	**1**	**2.9 (1.4-6.1)**
aOR (95% CI)	**1**	**2.5 (1.1-6.0)**
Rash (past year for $\geq$ 6 months)		
No	65 (46)	76 (54)
Yes	10 (39)	25 (71)
OR (95% CI)	**1**	**2.1 (1.0-4.8)**
aOR (95% CI)	1	1.8 (0.7-4.7)
Sneezing attacks		
No	66 (42)	91 (58)
Yes	9 (47)	10 (53)
OR (95% CI)	1	0.8 (0.3-2.1)
aOR (95% CI)	1	1.2 (0.4-3.3)

Values shown in boldface are significant.
*Data are expressed as numbers of subjects (percentage) and unadjusted odds ratio (OR) with (95% CI) and adjusted (aOR) for center, gender, parental allergy and social status.

analyses. Adjustment for potential confounders did not change the results, except for rash in the past year lasting longer than 6 months (Table II). A causal relationship between room disinfectants and skin symptoms has not been reported previously. This association is probably a result of reverse causation because mothers of children with skin symptoms might be prone to more stringent cleaning procedures to avoid exposure to house dust mite or skin superinfections. However, this is unlikely to be the case for respiratory symptoms because one would rather expect an avoidance of room disinfectants, which could irritate airways, in such subjects.

Stratified analyses by country showed heterogeneous effect estimates. This might be due to uncertainties that arise from small case numbers, potentially different intensities of uses, or contents of chemicals in the room disinfectants among the 3 countries.

Maternal allergies are known to be more relevant for the infants' risk of allergic disease than paternal allergies. When we stratified the children for the presence or absence of maternal allergies, increased effect estimates were observed for self-reported asthma ever (adjusted OR, 4.7; 95% CI, 1.0-22.4; adjusted for center only because of limited case numbers) in offspring from allergic mothers. In contrast, an increased likelihood was observed for self-reported atopic eczema ever (adjusted OR, 3.9; 95% CI, 1.4-11.2), diagnosed atopic dermatitis (adjusted OR, 8.1; 95% CI, 1.0-77.9), and rash ever (adjusted OR, 4.7; 95% CI, 1.4-15.8) or rash in the past year (adjusted OR, 3.6; 95% CI, 1.0-15.1) in offspring from nonallergic mothers. This indicates that children at risk for allergies respond differently to room disinfectants compared with children with average risk for allergies. The presence of allergic disease in a family member might also influence cleaning strategies. Therefore we stratified also for parental allergies. Similar to stratification only for maternal allergies, skin symptoms and atopic eczema were increased in offspring from nonallergic parents, whereas no difference was observed for asthma in both strata. At present, we do not have an explanation of why atopic eczema or skin symptoms were not observed in children from allergic parents.

Thus far, a potential influence of exposure to household chemicals on pediatric lung function and wheezing was investigated in a large cohort within the Avon Longitudinal Study of Parents and Children study.[7,8] Interestingly, an association of higher exposures with increased risk for persistent wheeze was restricted to the nonatopic children.

Apart from our study, which also investigates cutaneous outcomes, no further investigations exist for children, although the present study has some limitations. The case number is low, and we do not have data on atopic sensitization or a specification of the cleaning products used. However, it was shown previously that a single product is unlikely to account for the observed effects.[8]

There is a potential risk for a selection bias because we lost 43% of the participants to follow-up, but we could not identify major differences between mothers who dropped out and mothers who completed the study. Furthermore, we do not know for how long room disinfectants were used in the households. Nevertheless, our study further supports the contention that exposure to conventional household cleaning products represents a risk factor for obstructive airway disease in children with pre-existing risk for allergic disease. Future preventive strategies might aim to restrict use of common room disinfectants.

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