

PVC – as flooring material – and its association with incident asthma in a Swedish child cohort study

Abstract The Dampness in Buildings and Health study (DBH) started in the year 2000 in Värmland, Sweden, with a baseline questionnaire sent to all children ($n = 14,077$) aged 1–6. Five years later, a follow-up questionnaire was sent to the children who were 1–3 years at baseline. A total of 4779 children participated in both the baseline and the follow-up studies and constitute the study population in this cohort study. The aim of this study was to examine the association between exposure to PVC-flooring in the child's and parent's bedroom in homes of children aged 1–3 and the incidence of asthma, rhinitis, and eczema during the following 5-year period. Adjusted analyses showed that the incidence of asthma among children was associated with PVC-flooring in the child's bedroom (AOR 1.52; 95% CI 0.99–2.35) and in the parent's bedroom (1.46; 0.96–2.23). The found risks were on borderline of significance and should therefore be interpreted with caution. There was further a positive relationship between the number of rooms with PVC-flooring and the cumulative incidence of asthma. PVC-flooring was found to be a stronger risk factor for incident asthma in multifamily homes when compared with single-family houses and in smoking families compared with non-smoking families and in women.

M. Larsson¹, L. Hägerhed-Engman², B. Kolarik³, P. James⁴, F. Lundin⁵, S. Janson^{1,5}, J. Sundell⁶, C. G. Bornehag^{1,2,6}

¹Karlstad University, Health and Environmental Sciences, Karlstad, ²SP, Technical Research Institute of Sweden, Borås, Sweden, ³Danish Building Research Institute (SBI), Department of Construction and Health, Horsholm, Denmark, ⁴Harvard School of Public Health, Boston, MA, USA, ⁵County Council of Värmland, Karlstad, Sweden, ⁶Technical University of Denmark, International Centre for Indoor Environment and Energy, Lyngby, Denmark

Key words: Polyvinyl chloride-flooring; Incident asthma; Children; Socioeconomic factor; Longitudinal.

M Larsson
Karlstad University
Health and Environmental Sciences
S-651 88 Karlstad
Sweden
Tel.: +46 54 700 25 34
Fax +46 54 700 22 20
e-mail: malin.larsson@kau.se

Received for review 10 June 2009. Accepted for publication 30 May 2010.

Practical Implications

These longitudinal data from the DBH study found an association between the presence of PVC-flooring in the home and incident asthma in children. However, earlier results from the DBH study have shown that PVC-flooring is one important source for phthalates in indoor dust, and exposure to such phthalates was found to be associated with asthma and allergy among children. This emphasizes the need for prospective studies that focus on the importance of prenatal and neonatal exposure to phthalates in the development of asthma and allergy in children.

Introduction

There has been an increase in asthma and allergy during the past few decades. Because of the rapid character of this phenomenon, it is believed to be caused by changes in environmental exposures rather than genetic changes (Selgrade et al., 2006). There are accumulating scientific data supporting the hypothesis that exposure to phthalates from soft polyvinyl chloride (PVC) used in building materials and in a huge

number of consumer products may be linked to asthma. Several cross-sectional studies have reported an association between PVC-flooring and asthma (Bornehag et al., 2005b; Jaakkola et al., 1999, 2000, 2004; Oie et al., 1997, 1999). PVC-flooring material has been shown to be one of the sources for phthalates in indoor dust (Bornehag et al., 2005a), and an association between phthalates in indoor dust and asthma has been reported (Bornehag et al., 2004b; Kolarik et al., 2008). However, the cross-sectional design of most of

the conducted studies leaves the potential for bias to explain the observed associations. Experimental studies present support for an adjuvant effect on basic mechanisms in allergic sensitization by high doses of several phthalates. Although some biases in the design of the experiments, a majority of published reports have identified adjuvant effects on Th2 differentiation, production of Th2 cytokines, and enhanced levels of Th2-promoted immunoglobulins (IgG1 and IgE) in mice, and a limited amount of data do also suggest phthalate-induced enhancement of mast cell degranulation and eosinophilic infiltration which are important parts in the early inflammation phase (Bornehag and Nanberg, 2010). Thus, phthalates exposure could possibly affect fundamental mechanisms in the pathophysiology responsible of allergy and asthma.

We have conducted a cohort study with the aim of examining the association between exposure to PVC-flooring – used as a proxy for indoor phthalate exposure – in the child's and parent's bedroom in homes of children aged 1–3 and the incidence of asthma, rhinitis, and eczema during the following 5-year period.

Methods

With the overall aim to examine the importance of indoor-related factors for asthma and allergy in children, an epidemiologic study entitled 'Dampness in Buildings and Health' (DBH) was started in the year 2000 in Sweden (Bornehag et al., 2004a). In the first phase of the study, conducted in March–April 2000, a baseline questionnaire was distributed to the parents of all children aged 1–6 (14,077) living in the county of Värmland, Sweden. Questionnaires were collected from 10,851 children (representing 8918 families) corresponding to a response rate of 79%. An analysis of non-responders showed no indications of selection bias in this baseline investigation (Bornehag et al., 2005b). The second phase of the DBH study was a case-control study involving 198 cases (with doctor-diagnosed asthma and/or allergy) and 202 healthy controls. In this phase, physician examinations including medical tests were undertaken, and the children's homes were investigated by professional inspectors, including inspections, indoor air quality assessment, and measurements of ventilation rate, temperature, and relative humidity, as well as sampling of indoor air and dust (Bornehag et al., 2005a). In the third phase of the study, a follow-up questionnaire was sent five years after the baseline questionnaire (DBH phase I). This phase included children who were 1–3 years at baseline and consequently 6–8 years in 2005 ($n = 7509$). Questionnaires were collected from 5483 children, corresponding to a response rate of 73%. The study population in this study constitute of 4779 children, who participated in

both the baseline and the follow-up questionnaires. All children in the household between the ages of 1–3 were included in the analyses.

Questionnaire

The follow-up questionnaire consisted of 42 questions. The questions concerned the index child [(e.g. age, sex, birth weight, and length of breastfeeding), and family characteristics (number of siblings, single parenthood (number of parents living with the child; one parent vs. two or more), living with both biological parents, smoking habits in the family, and financial problems (problems with paying bills during the last 12 months)]. We have used single parenthood/divorce, smoking habits in family and financial problems as proxies for a lower socioeconomic status (Lindbaek et al., 2003). The child's and parent's health status was assessed by using the same questions as used in the International Study of Asthma and Allergies in Childhood (ISAAC) (Pearce et al., 1993).

The questionnaire included questions on building characteristics, e.g., type of building (single-family house, row house, and multifamily house), condensation on windows during the heating season (no condensation, 1–5 cm, 5–25 cm, and > 25 cm), and flooring materials in the bedrooms (PVC, plastic cork, wood, linoleum, stone, and wall-to-wall carpet). Moisture problems were assessed by using moisture indices that were established at baseline (Bornehag et al., 2005c). A 'water leakage' index was defined as flooding and/or water leakage during the previous year or earlier during the child's lifetime in the kitchen, bathroom, or child's or parent's bedroom. Earlier findings in the DBH study showed that PVC-flooring material was one of the important sources for phthalates (DEHP and BBzP) in indoor dust (Bornehag et al., 2005a) i.e., the more rooms with PVC-flooring in the home, the higher concentration of phthalates in indoor dust. However, our results showed that there are also other sources of these phthalates in indoor environments. The number of rooms with PVC-flooring was in this study used as a rough estimate of the phthalate exposure in the bedrooms.

The incidence of parent-reported doctor-diagnosed asthma during the 5-year period (2000–2005) was estimated by excluding children reported to have 'doctor-diagnosed asthma' and/or 'wheezing ever' at baseline and calculating the cumulative incidence counting those children who were reported to have 'doctor-diagnosed asthma' in the follow-up questionnaire as incident cases.

The incidence of rhinitis was estimated by excluding 'doctor-diagnosed rhinitis' at baseline and calculating the incidence based on those that were reported to have 'doctor-diagnosed rhinitis' in the follow-up questionnaire.

Finally, the incidence of eczema was calculated by excluding children with 'eczema ever' at baseline and calculating the incidence based on those that reported 'eczema ever' in the follow-up questionnaire. The inclusion/exclusion criteria for asthma, rhinitis, and eczema in this longitudinal study are further described in Larsson et al. (2008).

Statistical analyses

Associations between baseline measures of family characteristics, behaviors in the family, socioeconomic factors and environmental factors (including presence of PVC-flooring in the bedrooms), and the 5-year cumulative incidence of asthma, rhinitis, and eczema were estimated in univariate analyses by using chi-square tests. Furthermore, to control for possible confounders, multivariate logistic regression models were used. The results are expressed as crude and adjusted odds ratios with 95% confidence intervals. In multivariate analyses, adjustments were made for age (6, 7, or 8 years of age at follow-up), sex of the child, and allergies in the family (history of symptoms of asthma, rhinitis, and/or eczema in other family members; yes vs. no). Adjustments were also made for factors that were found to be associated with PVC-flooring in the home (type of building, divorce, and smoking in family). We have also investigated indications for a dose-response relationship between the number of bedrooms with PVC-flooring at baseline and the incidence of asthma by using a linear by linear analyses.

The flooring material 'plastic cork' has been grouped together with PVC material in the analyses. This was performed because an earlier validation study showed that 40 of 55 parental reports of 'plastic cork' were determined to be PVC when evaluated by professional inspectors (Engman et al., 2007). Furthermore, 'plastic cork' material has traditionally only been used in the kitchen, not in sleeping rooms, and therefore is the risk for information bias limited.

The associations were considered to be statistically significant when the *P*-value was below 0.05. Statistical analyses were carried out using SPSS for Windows (version 17.0, SPSS Inc., Chicago, IL, USA). The study was approved by the medical ethical committee in Örebro, Sweden.

Results

During the 5-year period between the baseline study and the follow-up investigation, the cumulative incidences were found to be 4.9% for asthma, 5.7% for rhinitis, and 13.4% for eczema. Further results on the cumulative incidence of asthma and allergy in this study, as well as important background factors, are included in an earlier paper (Larsson et al., 2008).

There were some changes in the characteristics of the studied families and their homes during the 5-year period (Table 1). There was a decreased tendency for smoking in the family, living in multifamily houses, and the use of PVC-flooring in the child's and parent's bedroom. The proportion of single-parent households had increased from 7% at baseline to 20% at follow-up.

Indoor environmental factors in the child's home and their crude associations with incident asthma, rhinitis, and eczema are presented in Table 2. PVC as flooring material in the child's or in the parent's bedroom at baseline was statistically significantly associated with

Table 1 Description of 4779 children, their families, and the homes

Factor	Frequency <i>n</i> (%)		<i>P</i> -value ^a
	Questionnaire 2000 (baseline)	Questionnaire 2005 (follow up)	
Year			
Sex			
Girls	2388	2388	
Boys	2391	2391	
Age			
1–2 years	1557	1557	
2–3 years	1568	1568	
3–4 years	1654	1654	
No. of children less than 7 years in the family			
1	2163	–	
2	2262	–	
3 or more	291	–	
Allergic symptoms in the family			
No	2167 (45.3)	–	
Yes	2563 (53.6)	–	
Current smoking in the family			
Any smoker ^b	1044 (21.8)	909 (19.0)	0.000
Smoking mother	673 (14.1)	605 (12.7)	0.001
Smoking father	497 (10.4)	398 (8.3)	0.000
Divorce ^c			
Yes	324 (6.8)	960 (20.1)	^d
Economical problems in the family ^e			
No	–	4174 (87.3)	
Yes	–	537 (11.2)	
No reply	–	68 (1.4)	
Type of building			
Single-family house	3871 (81)	4090 (85.6)	0.000
Multifamily house	793 (16.6)	546 (11.4)	0.000
Flooring material in the child's bedroom			
PVC	2360 (51.9)	1858 (40.3)	0.000
Wood	1565 (34.4)	2155 (46.8)	0.000
Linoleum	364 (8.0)	341 (7.4)	0.20
Flooring material in the parent's bedroom			
PVC	2067 (44.8)	1584 (33.6)	0.000
Wood	1922 (41.7)	2497 (54.4)	0.000
Linoleum	326 (7.1)	285 (6.2)	0.09

^a*P*-value for McNemar's test.

^bCurrent smoking in family in mother, father, sibling, or other person in the home year 2000.

^cIn 2000, there was no question on divorce but one on how many adults normally living in the home (1, 2, 3 or more). In 2005, there was a question on if the child lived with both biological parents (Yes vs. No).

^dAn estimation of *P*-value could not be performed because this variable contains of two different questions.

^eIn 2005, families were asked whether they had problems with paying bills during the last 12 months. In 2000, there was no question on economical problems.

Table 2 Crude associations between socioeconomic factors and environmental exposures at baseline 2000 and incident of asthma, rhinitis, and eczema during the 5-year follow-up period

Factors at baseline	n (%)	Asthma OR (95% CI)	Rhinitis OR (95% CI)	Eczema OR (95% CI)
Type of building ^a				
SH	3871 (83)	1.0	1.0	1.00
MH	793 (17)	1.29 (0.79–2.13)	1.16 (0.84–1.59)	1.37 (1.08–1.75)
Divorce ^b				
Yes	960 (20.2)	1.31 (0.63–2.74)	1.03 (0.63–1.69)	1.70 (1.20–2.39)
Smoking in family				
Any smoker in family vs no smoking in family	1044 (21.8)	1.21 (0.77–1.90)	0.85 (0.62–1.16)	1.28 (1.03–1.59)
Smoking mother vs no smoking mother	673 (14.1)	1.16 (0.68–1.99)	0.96 (0.67–1.37)	1.21 (0.93–1.57)
Smoking father vs no smoking father	497 (10.4)	1.32 (0.74–2.34)	0.88 (0.58–1.35)	1.32 (0.99–1.75)
Flooring material – Child's room				
All other	2052 (46)	1.0	1.0	1.0
PVC	2405 (54)	1.62 (1.07–2.46)	1.19 (0.92–1.54)	1.06 (0.87–1.29)
Flooring material – Parent's room				
All other	2389 (53.2)	1.0	1.0	1.0
PVC	2098 (46.8)	1.59 (1.06–2.39)	1.31 (1.01–1.68)	1.14 (0.94–1.38)
Number of bedrooms with PVC				
No room	1048 (42)	1.0	1.0	1.0
One room	867 (18.7)	1.51 (0.85–2.70)	1.28 (0.90–1.84)	0.79 (0.58–1.07)
Two rooms	1825 (39.3)	1.77 (1.13–2.79)	1.29 (0.97–1.72)	1.09 (0.88–1.36)
Type of flooring in the child's bedroom at baseline and at follow-up				
No PVC in 2000 and 2005	1597 (39.1)	1.0	1.0	1.0
PVC only in 2000	888 (21.7)	2.10 (1.24–3.55)	1.36 (0.96–1.92)	0.87 (0.66–1.16)
PVC only in 2005	83 (2.0)	1.74 (0.40–7.52)	2.10 (0.93–4.73)	0.70 (0.27–1.79)
PVC both in 2000 and 2005	1517 (37.1)	1.39 (0.83–2.32)	1.17 (0.85–1.60)	1.11 (0.88–1.39)
Type of flooring in the parent's bedroom at baseline and at follow-up				
No PVC in 2000 and 2005	1944 (46.1)	1.0	1.0	1.0
PVC only in 2000	786 (18.7)	1.22 (0.69–2.16)	1.13 (0.79–1.63)	1.00 (0.76–1.32)
PVC only in 2005	324 (7.7)	0.65 (0.23–1.84)	0.90 (0.52–1.57)	0.75 (0.49–1.16)
PVC both in 2000 and 2005	1159 (27.5)	1.65 (1.03–2.65)	1.46 (1.08–1.98)	1.12 (0.88–1.42)
Water leakage ^c	842 (19.7)	0.97 (0.58–1.64)	1.20 (0.88–1.65)	1.13 (0.88–1.45)
Condensation on windows				
Child's bedroom				
No	3197 (71.8)	1.0	1.0	1.0
1–5 cm	811 (18.2)	0.91 (0.52–1.57)	0.75 (0.52–1.08)	1.24 (0.96–1.59)
> 5 cm	446 (10.0)	0.71 (0.33–1.56)	1.05 (0.69–1.60)	1.48 (1.09–2.00)
Parent's bedroom				
No	2970 (65.6)	1.0	1.0	1.0
1–5 cm	941 (20.8)	1.05 (0.64–1.71)	0.73 (0.52–1.03)	1.30 (1.03–1.65)
> 5 cm	616 (13.6)	0.43 (0.18–0.99)	0.86 (0.58–1.27)	1.36 (1.03–1.79)

^aType of building was defined as SH = single-family house and MH = multifamily house.^bIn 2000, there was no question on divorce but on how many adults that normally lived in the home (1, 2, 3, or more).^cFlooding and/or water leakage.

doctor-diagnosed asthma during the following 5-year period. When calculating the association between the number of bedrooms with PVC-flooring and incident asthma, we could in crude analysis find a significant linear-by-linear association ($P = 0.01$), where the 5-year incidence of asthma was 2.2% in homes with no PVC-flooring in the bedrooms at baseline, 3.3% in homes with one bedroom with PVC, and 3.8% in homes with two bedrooms with PVC. There was also an association between incident rhinitis and PVC-flooring in the parent's bedroom.

Having a PVC floor in the child's bedroom at baseline but not at follow-up was associated with incident asthma (Table 2), while having PVC-flooring in the parent's bedroom both at baseline and follow-up was associated with incident asthma and incident rhinitis. In the adjusted model, the combination of water leakage in the floor structure and the presence of

PVC-flooring in the bedroom did not show a higher association with incident asthma (AOR 1.53; 95% CI 0.72–3.24) when compared with PVC without water leakage (AOR 1.53; 95% CI 0.92–2.54) or water leakage without PVC (AOR 0.98; 95% CI 0.40–2.43), when compared to the reference category of no water leakage and no PVC.

Condensation on the inside of the window pane (more than 5 cm) in the child's or the parent's bedroom at baseline was statistically significantly associated with higher risk of incident eczema in crude analysis (Table 2); however, reports of condensation were negatively associated with asthma incidence. Incident eczema was also shown to associate with socioeconomic factors, e.g. living in multifamily house and divorce (Table 2). In adjusted analysis, the association between multifamily house and eczema disappeared (AOR 1.11; 95% CI 0.83–1.49), indicating that this

association may be a result of confounding. Regarding divorce, the association with eczema remained.

To identify potential confounders, we analyzed factors that were associated with PVC-flooring materials in the bedrooms at baseline. We found significantly more PVC-flooring in multifamily houses when compared with single-family houses (70.2% vs. 51.1%, $P = 0.001$), more PVC-flooring in single-parent families when compared with two parents (70.4% vs. 52.6%, $P = 0.001$) and more PVC-flooring in homes with a current smoking parent when compared with non-smoking families (59.1% vs. 52.3, $P = 0.001$). The associations between single parenthood or smoking in the family and PVC-flooring were not confounded by type of housing. These factors were included in the adjusted analyses.

In adjusted models, associations between PVC-flooring at baseline and incident asthma were similar to those in the crude analyses (Table 3). The adjusted analyses also showed that two bedrooms with PVC-flooring increased the risk for incident asthma when compared with no PVC-flooring. The associations between incident rhinitis and PVC-flooring disappeared in the adjusted analyses (AOR 1.11; 95% CI 0.85–1.46).

Furthermore, allergic symptoms in the family and male sex were risk factors for incident asthma, while smoking among parents, single parenthood, and age of the child were not associated with incident asthma. When adjusting separately for the water leakage index in the multivariate model, the association between asthma and PVC-flooring did not change (AOR 1.63; 95% CI 1.06–2.53).

Table 3 Associations between incident asthma and background factors and home environmental factors (2000) expressed as adjusted odds ratio

Factor at baseline	Incident Asthma aOR (95% CI) ^a		
	Model I ^b	Model II ^c	Model III ^d
Flooring material			
PVC vs. other material	1.52 (0.99–2.35)	1.46 (0.96–2.23)	–
Number of bedrooms with PVC			
No room	–	–	1.0
One room	–	–	1.55 (0.85–2.82)
Two rooms	–	–	1.71 (1.06–2.75)
Smoking in family ^e	0.95 (0.56–1.59)	1.15 (0.71–1.86)	0.86 (0.50–1.47)
Age			
1–2	1.0	1.0	1.0
2–3	0.86 (0.52–1.42)	0.84 (0.51–1.38)	0.81 (0.49–1.33)
3–4	0.80 (0.48–1.32)	0.85 (0.51–1.39)	0.79 (0.48–1.30)
Sex (male)	1.80 (1.18–2.74)	1.96 (1.28–3.00)	1.98 (1.30–3.04)
Allergy in family	2.00 (1.30–3.09)	2.22 (1.43–3.45)	2.19 (1.41–3.41)
Single-parent hood	1.02 (0.42–2.49)	0.63 (0.22–1.82)	0.67 (0.23–1.91)
Multifamily house	1.51 (0.88–2.58)	1.44 (0.83–2.49)	1.48 (0.86–2.57)

^aAdjusted for all variables in each model.

^bModel I – Flooring material in the child's bedroom.

^cModel II – Flooring material in the parent's bedroom.

^dModel III – Number of bedroom with PVC flooring.

^eCurrent smoking in mother, father, siblings, or other person in the home vs. no smoking in family.

To investigate potential effect modification, we stratified by type of building and smoking habits in the family. The crude association between asthma and PVC-flooring in the bedrooms was stronger for families living in multifamily houses (PVC in the child's bedroom: OR 4.19; 95% CI 0.96–18.28; PVC in the parent's bedroom OR 2.64; 95% CI 0.76–9.20) compared to families living in single-family houses (child's bedroom OR 1.32; 95% CI 0.83–2.11, parent's bedroom OR 1.32; 95% CI 0.84–2.09). When stratifying for smoking (mother, father, sibling or another person is smoking in the home at baseline), a stronger association between PVC-flooring in the child's bedroom and incident asthma was found in smoking families (OR 3.02; 95% CI 1.12–8.14) when compared with non-smoking families (OR 1.36; 95% CI 0.85–2.18). There was also a stronger association between PVC-flooring in the parent's bedroom and asthma in smoking families (OR 2.07; 95% CI 0.84–5.08) compared with non-smoking families (OR 1.47; 95% CI 0.93–2.33). There were also indications that the association between PVC exposure and incident asthma was stronger for girls compared with boys.

Discussion

In this cohort study, children living in homes with PVC-flooring in the bedroom when they were 1–3 years of age were more likely to develop doctor-diagnosed asthma during the following 5-year period when compared with children living in homes without PVC-flooring in the bedroom (AOR 1.52; 95% CI 0.99–2.35), and there was a positive relationship between the number of rooms in a home with PVC-flooring and the incidence of asthma (no room 1.0 (ref); one room OR 1.51; 95% CI 0.85–2.79; two rooms OR 1.77; 95% CI 1.13–2.79).

Such finding that PVC-flooring can be a risk for asthma and airway problems in children is in agreement with several other studies. In a Finnish cross-sectional study of children aged 1–7, the risk of lower respiratory tract symptoms was strongly related to the presence of plastic wall materials (Jaakkola et al., 2000). A Norwegian case-control study showed that the risk of bronchial obstruction was related to the presence of PVC-flooring as well as to a plasticizer exposure index (Jaakkola et al., 1999; Oie et al., 1999). Moreover, a population-based incident case-control study among adults showed an association between the risk of asthma and the presence of plastic wall materials at work (Jaakkola et al., 2006). A review on the relationship between exposure to phthalates and the occurrence of asthma and allergies presents further evidence from epidemiological studies focusing on non-industrial environments, as well as occupational investigations and case studies (Jaakkola and Knight, 2008).

In the second phase (a case-control study in 390 homes) of the DBH study, we demonstrated that PVC-flooring is a strong source of phthalates such as di(2-ethylhexyl)phthalate (DEHP) and butyl benzyl phthalate (BBzP) in settled indoor dust (Bornehag et al., 2005a) i.e., the more rooms with PVC as flooring material, the higher concentration of phthalates in indoor dust. The study showed that the median concentration of BBzP in indoor dust was significantly higher in rooms with PVC when compared with rooms without such flooring material (0.192 vs. 0.089 mg/g dust, $P < 0.001$) and for DEHP (0.868 vs. 0.700 mg/g dust, $P = 0.001$), (Bornehag et al., 2005a). Moreover, exposure to phthalates was associated with case status among the children. There was a dose-response relationship found between DEHP concentration in the dust and doctor-diagnosed asthma and between BBzP concentration and rhinitis and eczema (Bornehag et al., 2004b). More indications for a relationship between DEHP in house dust and the risk of airway symptoms were later shown in a study with the same design as this DBH study, a case-control study conducted among Bulgarian children (Kolarik et al., 2008). Finally, an experimental study from Denmark showed that exposure to phthalate esters in climate chamber exposure experiments was associated with a small increase in exhaled nitric oxide (NO) – a marker of subclinical inflammation (Kolarik et al., 2009).

In a recently published review, Chalubinski and Kowalski (2006) discuss suspected endocrine disrupting chemicals (EDCs) – such as phthalates – as potential modulators of the immune system in humans, presenting data on both epidemiological and experimental data from *in vitro* and animal studies. Evidence regarding EDCs and their importance in the synthesis of cytokines, immunoglobulins, and cell mediators as well as immune cell activation and survival is presented, and the authors conclude that such exposure may impact the immune system with allergic responses as a possible result.

The association between PVC-flooring at baseline and incident asthma was less pronounced for the youngest children (1–2 year at baseline) when compared to the older children (2–3 and 3–4 years) (data not shown). A possible explanation for this could be that the older children in general have been exposed for PVC for a longer period of time than the younger children. However, one of the weaknesses of this study is that asthma that developed during the early life period (the first year of life for the youngest children and the first three years for the oldest children) has not been considered because the diseased children were excluded at baseline. This means that we have not investigated the importance of PVC exposure for development of asthma during infancy.

Our study confirmed that, as many studies have earlier showed, boys are at greater risk to develop

asthma (Anderson et al., 1992; Pearce et al., 1993; Roel et al., 1999; Rönmark, 2002). Review studies have stated that PVC or phthalates are associated with asthma in the child (Bornehag and Nanberg, 2010; Bornehag et al., 2001; Jaakkola and Knight, 2008). One study from Germany has shown that boys have a higher phthalate concentration in urine compared with girls (Becker et al., 2004). However, in our study there were indications that the association between PVC exposure and incident asthma was stronger for girls compared with boys.

An interesting finding was that PVC-flooring in the child's bedroom at baseline in combination with no PVC-flooring at follow-up was associated with incident asthma. Families with PVC-flooring at baseline but not at follow-up ($n = 860$) have either changed flooring material ($n = 371$) during this time or moved to another building without PVC-flooring ($n = 489$). Within these groups, we found that there was a higher risk with PVC-flooring for developing asthma in the group that had moved (OR 3.02; 95% CI 1.36–6.67) when compared with the group that had changed flooring in the current dwelling (OR 1.37; 95% CI 0.63–3.01). Within the group that has moved, almost two-thirds of families that lived in multifamily houses at baseline had moved to single-family houses. We also found a stronger association between PVC-flooring and incident asthma among families living in multifamily houses at baseline compared with those living in single-family houses. One possible explanation for these findings could be attributed to the fact that most multifamily houses in Sweden are built with a concrete floor structure, while the single-family houses most often have a wooden structure. If a PVC-flooring material is glued on a concrete structure with high moisture and high alkalinity content, there is a risk for chemical degradation of the PVC material and adhesives followed by increased emissions of degradation products, e.g., phthalates (Gustafsson and Lundgren, 1997; Sjöberg and Ramnas, 2007; Wengholt Johnsson, 1995). The cross-sectional data in the DBH-I study found that the combination of PVC-flooring and water leakage was a risk factor for asthma in children (Bornehag et al., 2005b). However, in the current longitudinal data such an association was not found. This could indicate that it might be bias problems in cross-sectional studies where parents report health effect and moisture-related problems such as water leakage at the same time. Another possible explanation for these different findings could be that moisture in concrete, as described previously, is something else than moisture problems related to water leakage and flooding. Water leakage and flooding is visible for parents and can be reported in questionnaire studies; however, moisture in concrete is mostly hidden in the construction and not visible. Our data do not allow us to go any further in these speculations.

Asthma has been shown to be more common in lower socioeconomic groups (Almqvist et al., 2005; Bråbäck et al., 2005; Lindbaek et al., 2003). As shown in this study, PVC-flooring was associated with incident asthma, but PVC-flooring was also correlated with proxies for lower socioeconomic status (SES) such as living in multifamily houses, divorce in the family (Lindbaek et al., 2003), and smoking among parents. It is therefore possible that the reported associations between PVC-flooring and asthma in this study are confounded by socioeconomic factors. We made adjustments and stratifications for SES factors and could not find any substantial reduction in the estimated ORs between PVC-flooring and incident asthma in the children. There was also a strong association between divorce and eczema in the child, which could be an indication of a stress-related mechanism. Studies have shown that stress could influence the immune system and even increase the risk of asthma and allergy in the child (Bockelbrink et al., 2006). However, as the most efficient proxies of SES, such as parental education, family income, or parental occupation (Lindbaek et al., 2003), were not measured in this study, there is still the possibility of residual confounding.

A validation of the questionnaire used in this study has been reported earlier (Engman et al., 2007), where parental reports on building characteristics were compared with professional inspectors' observations. There was a good agreement between parental reports and inspectors' observations regarding wooden flooring ($\kappa = 0.77$), but lower agreement for PVC and plastic cork as used in this paper (kappa value 0.50 and 0.48 respectively). The agreement for linoleum was even lower ($\kappa = 0.22$). The disagreement was mainly attributed to misclassification of PVC and linoleum among questionnaire respondents. The same misclassification was observed in a Bulgarian study (Kolarik et al., 2008). Consequently, families often misclassify types of flooring, but we have no reason to believe that such misclassification differs between healthy children and children with asthma, especially because the type of flooring was assessed before the onset of asthma. Therefore, we do not believe that reporting bias is the reason for the observed associations between PVC-flooring and incident asthma in children. In this study, we have only parental reported data on the health

outcome of the children, and no diagnoses by physicians and no test of lung function etc. However, parent-reported doctor-diagnosed asthma has been shown to be valid and in concordance with diagnoses by physicians owing to earlier findings in the DBH study (Hederos et al., 2007).

Our hypothesis was based on findings from epidemiologic studies reporting an association between PVC as flooring material in the home and asthma in children described in a review by Bornehag and Nanberg (2010). In this study, multiple statistical comparisons might have contributed to the association between PVC-flooring and asthma. However, even if our finding of an indication for a dose-response relationship between the number of rooms with PVC-flooring and the incidence of asthma not necessarily means that multiple comparisons are excluded as an explanation for our findings, we believe that indications for a dose-response relationship decrease the risk for mass significance.

The main findings of this cohort study were an association between PVC-flooring in the bedrooms and incident asthma as well as a relationship between the number of rooms in a home with PVC-flooring and the cumulative incidence of asthma. However, limitations with the study are as follows: only questionnaire reports on environmental factors and health outcomes, risk for confounding problems owing to misclassification of flooring materials, and limited data on socioeconomic status as well as borderline of significance for found associations. This means that our data should be interpreted with caution. The present observations warrant confirmation in a prospective cohort design including early life exposure during pregnancy and infancy period as well as measurements of the phthalate exposure.

Acknowledgements

The study was funded by grants from the Swedish Research Council for Environment, Agricultural Sciences and Spatial Planning (Formas), Swedish Asthma and Allergy Association's Research Foundation, the Swedish Foundation for Health Care Sciences and Allergy Research and the County Council of Värmland. We also thank all the participating families.

References

- Almqvist, C., Pershagen, G. and Wickman, M. (2005) Low socioeconomic status as a risk factor for asthma, rhinitis and sensitization at 4 years in a birth cohort, *Clin. Exp. Allergy*, **35**, 612–618.
- Anderson, H.R., Pottier, A.C. and Strachan, D.P. (1992) Asthma from Birth to Age 23 – Incidence and Relation to Prior and Concurrent Atopic Disease, *Thorax*, **47**, 537–542.
- Becker, K., Seiwert, M., Angerer, J., Heger, W., Koch, H.M., Nagorka, R., Rosskamp, E., Schluter, C., Seifert, B. and Ullrich, D. (2004) DEHP metabolites in urine of children and DEHP in house dust, *Int. J. Hyg. Environ. Health*, **207**, 409–417.
- Bockelbrink, A., Heinrich, J., Schafer, I., Zutavern, A., Borte, M., Herbarth, O., Schaaf, B., Von Berg, A. and Schafer, T. (2006) Atopic eczema in children: another

- harmful sequel of divorce, *Allergy*, **61**, 1397–1402.
- Bornehag, C.G. and Nanberg, E. (2010) Phthalate exposure and asthma in children, *Int. J. Androl.*, **33**, 333–345.
- Bornehag, C.G., Blomquist, G., Gyntelberg, F., Järnholm, B., Malmberg, P., Nordvall, L., Nielsen, A., Pershagen, G. and Sundell, J. (2001) Dampness in buildings and health. Nordic interdisciplinary review of the scientific evidence on associations between exposure to “dampness” in buildings and health effects (NORDDAMP), *Indoor Air*, **11**, 72–86.
- Bornehag, C.G., Sundell, J. and Sigsgaard, T. (2004a) Dampness in buildings and health (DBH): report from an ongoing epidemiological investigation on the association between indoor environmental factors and health effects among children in Sweden, *Indoor Air*, **14**(Suppl 7), 59–66.
- Bornehag, C.G., Sundell, J., Weschler, C.J., Sigsgaard, T., Lundgren, B., Hasselgren, M. and Hägerhed-Engman, L. (2004b) The association between asthma and allergic symptoms in children and phthalates in house dust: a nested case-control study, *Environ. Health Perspect.*, **112**, 1393–1397.
- Bornehag, C.G., Lundgren, B., Weschler, C.J., Sigsgaard, T., Hägerhed-Engman, L. and Sundell, J. (2005a) Phthalates in indoor dust and their association with building characteristics, *Environ. Health Perspect.*, **113**, 1399–1404.
- Bornehag, C.G., Sundell, J., Hägerhed-Engman, L., Sigsgaard, T., Janson, S. and Aberg, N. (2005b) ‘Dampness’ at home and its association with airway, nose, and skin symptoms among 10,851 preschool children in Sweden: a cross-sectional study, *Indoor Air*, **15**(Suppl 10), 48–55.
- Bornehag, C.G., Sundell, J., Weschler, C.J. and Sigsgaard, T. (2005c) Potential selection biases, *Environ. Health Perspect.*, **113**, A152–A153.
- Bråbäck, L., Hjertqvist, A. and Rasmussen, F. (2005) Social class in asthma and allergic rhinitis: a national cohort study over three decades, *Eur. Respir. J.*, **26**, 1064–1068.
- Chalubinski, M. and Kowalski, M.L. (2006) Endocrine disrupters – potential modulators of the immune system and allergic response, *Allergy*, **61**, 1326–1335.
- Engman, L.H., Bornehag, C.G. and Sundell, J. (2007) How valid are parents’ questionnaire responses regarding building characteristics, mouldy odour, and signs of moisture problems in Swedish homes? *Scand J Public Health*, **35**, 125–132.
- Gustafsson, H. and Lundgren, N. (1997) Off-gassing from building materials; a survey of case studies, In: Brune, D., Gerhardsen, G., Crockford, G.W. and D’auria, D. (eds) *The Workplace Vol. 1*, Geneva, International Labour Office, Fundamentals of Health, Safety and Welfare, 1.
- Hederos, C.A., Hasselgren, M., Hedlin, G. and Bornehag, C.G. (2007) Comparison of clinically diagnosed asthma with parental assessment of children’s asthma in a questionnaire, *Pediatr. Allergy Immunol.*, **18**, 135–141.
- Jaakkola, J.J. and Knight, T.L. (2008) The role of exposure to phthalates from polyvinyl chloride products in the development of asthma and allergies: a systematic review and meta-analysis, *Environ. Health Perspect.*, **116**, 845–853.
- Jaakkola, J.J., Oie, L., Nafstad, P., Botten, G., Samuelsen, S.O. and Magnus, P. (1999) Interior surface materials in the home and the development of bronchial obstruction in young children in Oslo, Norway, *Am J Public Health*, **89**, 188–192.
- Jaakkola, J.J., Verkasalo, P.K. and Jaakkola, N. (2000) Plastic wall materials in the home and respiratory health in young children, *Am. J. Public Health*, **90**, 797–799.
- Jaakkola, J.J., Parise, H., Kisilitsin, V., Lebedeva, N.I. and Spengler, J.D. (2004) Asthma, wheezing, and allergies in Russian schoolchildren in relation to new surface materials in the home, *Am. J. Public Health*, **94**, 560–562.
- Jaakkola, J.J., Ieromnimon, A. and Jaakkola, M.S. (2006) Interior surface materials and asthma in adults: a population-based incident case-control study, *Am. J. Epidemiol.*, **164**, 742–749.
- Kolarik, B., Naydenov, K., Larsson, M., Bornehag, C.G. and Sundell, J. (2008) The association between phthalates in dust and allergic diseases among Bulgarian children, *Environ. Health Perspect.*, **116**, 98–103.
- Kolarik, B., Lagercrantz, L. and Sundell, J. (2009) Nitric oxide in exhaled and aspirated nasal air as an objective measure of human response to indoor air pollution, *Indoor Air*, **19**, 145–152.
- Larsson, M., Hägerhed-Engman, L., Sigsgaard, T., Janson, S., Sundell, J. and Bornehag, C.G. (2008) Incidence rates of asthma, rhinitis and eczema symptoms and influential factors in young children in Sweden, *Acta Paediatr.*, **97**, 1210–1215.
- Lindbaek, M., Wehring, K.W., Grangard, E.H. and Ovsthus, K. (2003) Socioeconomic conditions as risk factors for bronchial asthma in children aged 4–5 yrs, *Eur. Respir. J.*, **21**, 105–108.
- Oie, L., Hersoug, L.G. and Madsen, J.O. (1997) Residential exposure to plasticizers and its possible role in the pathogenesis of asthma, *Environ. Health Perspect.*, **105**, 972–978.
- Oie, L., Nafstad, P., Botten, G., Magnus, P. and Jaakkola, J.K. (1999) Ventilation in homes and bronchial obstruction in young children, *Epidemiology*, **10**, 294–299.
- Pearce, N., Weiland, S., Keil, U., Langridge, P., Anderson, H.R., Strachan, D., Bauman, A., Young, L., Gluyas, P., Ruffin, D. (1993) Self-reported prevalence of asthma symptoms in children in Australia. England, Germany and New Zealand: an international comparison using the ISAAC protocol, *Eur. Respir. J.*, **6**, 1455–1461.
- Roel, E., Olsen Faresjö, Å., Kjellman, N.-I.M. and Faresjö, T. (1999) Cumulative incidence of asthma diagnosis at the age of seven in a birth cohort, *Eur J Gen Pract*, **5**, 71–74.
- Rönmark, E. (2002) Incidence rates and risk factors for asthma among school children: a 2-year follow-up. Report from the Obstructive Lung Disease in Northern Sweden (OLIN) studies, *Respir. Med.*, **96**, 1006–1013.
- Selgrade, M.K., Lemanske, R.F. Jr, Gilmore, M.I., Neas, L.M., Ward, M.D., Henneberger, P.K., Weissman, D.N., Hoppin, J.A., Dietert, R.R., Sly, P.D., Geller, A.M., Enright, P.L., Backus, G.S., Bromberg, P.A., Germolec, D.R. and Yeatts, K.B. (2006) Induction of asthma and the environment: what we know and need to know, *Environ. Health Perspect.*, **114**, 615–619.
- Sjöberg, A. and Ramnas, O. (2007) An experimental parametric study of VOC from flooring systems exposed to alkaline solutions, *Indoor Air*, **17**, 450–457.
- Wengholt Johnsson, H. (1995) Kemisk emission från golvsystem – effekt av olika betongkvalitet och fuktbelastning (in Swedish). Tekn Dr, Chalmers University of Technology, Institutionen för byggnadsmaterial.