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Indoor Residential Chemical Exposures as Risk Factors for Asthma and Allergy in Infants and Children: a Review

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Summary: *Most research into effects of residential indoor air exposures on asthma and allergies has focused on exposures to biologic allergens, moisture and mold, endotoxin, or combustion byproducts. This paper briefly reviews reported findings on associations of asthma or allergy in infants or children with risk factors related to indoor chemical emissions from residential materials or surface coatings. Associations, some strong (e.g., odds ratios up to 13), were reported. The most frequently identified risk factors were formaldehyde, aromatic organic compounds such as toluene and benzene, plastic materials and plasticizers, and recent painting. Exposures and consequent effects from indoor sources may be exacerbated by decreased ventilation. Identified risk factors may be proxies for correlated exposures. Findings suggest the frequent occurrence of important but preventable effects on asthma and allergy in infants and children worldwide from modern residential building materials and coatings.*

Keywords: indoor air quality; phthalates; volatile organic compounds; formaldehyde; asthma; allergy

Category: allergy and other sensitivity reactions

1 Introduction

Concerns about recent increases in the incidence of asthma and allergies worldwide have stimulated a variety of scientific research, much focused on exposures in residences, where children spend the majority of their time. Most research into the effects of indoor residential exposures on asthma and allergies has focused on exposures to biologic allergens, moisture and mold, endotoxin, or combustion byproducts [1]. A growing body of research from outside the U.S., however, suggests that *chemical emissions* from common indoor materials and finishes have a variety of adverse effects on respiratory and immune health. The identified risk factors include specific organic compounds such as formaldehyde, benzene, and phthalates, indoor materials or finishes such as carpet, flexible flooring, paint, and plastics, and indoor activities related to these materials.

Although some recent review articles have included aspects of this larger picture [1-7], they have not considered the full range of available evidence linking indoor chemical emissions and health effects. This review summarizes current findings from studies in the peer-reviewed scientific literature on associations between indoor residential chemical emissions, or materials or activities associated with such emissions, and asthma and allergies in infants or children.

2 Methods

We searched the published biomedical literature, using the online site PubMed for relevant studies, and also searched selected conference proceedings. From the identified reports, we selected and summarized studies which met the following eligibility criteria:

publication in scientific peer-reviewed journals or scientific conference proceedings; investigation of associations between health effects related to asthma or allergy in human infants or children (up to age 16) and either indoor residential chemical exposures, or materials or activities considered to be risk factors for chemical exposures; and a cross-sectional, case-control, cohort, panel, quasi-experimental, or controlled experimental design. Findings on adult populations, on school or ambient exposures, and on risk factors related to combustion byproducts or bedding were excluded.

For the eligible findings, we first describe the health outcomes, subjects, and designs in reported studies, separately for risk factors of measured concentrations and potential sources (materials or activities). We then summarize the reported associations between risk factors and health outcomes as odds ratios (ORs). The disease process of asthma may involve inflammation, infection, and allergy. We have roughly categorized the reported associations in two broad categories of health outcomes: asthma and lower respiratory effects (e.g., diagnosed asthma, asthma symptoms, lower respiratory symptoms, obstructive or chronic bronchitis, bronchial obstruction, adverse changes in lung function assessed by spirometry, lung inflammation assessed by exhaled nitric oxide, house dust mite sensitization, or pulmonary infections) and allergic effects (e.g., atopy by skin prick tests, allergic symptoms, diagnosed rhinitis, or diagnosed eczema).

3 Results

We identified 20 studies meeting the selection criteria (Tables 1 and 2): 12 investigating effects of indoor

chemical concentrations, including formaldehyde, aromatic compounds, aliphatic compounds, and total volatile organic compounds (VOCs) as well as phthalates in dust; and 10 (with some overlap) investigating effects of indoor chemical sources, including plastics, recent painting, new furniture or particleboard, new synthetic carpets, textile wallpaper, and maternal cleaning activity.

Two of the studies, published in 1989 and 1990, were from the U.S. and focused on formaldehyde. All other studies, published between 1999 and 2005, were from western Europe, Russia, or Australia. Reported study designs and analyses included five cohort or panel, eight case-control, and nine cross-sectional, with some studies including multiple approaches. Nineteen were published in peer-reviewed journals, and one in a scientific conference proceeding.

Indoor chemical concentrations

Higher concentrations of chemical compounds measured in air or dust in residences were associated in numerous studies with health effects related to asthma or allergy in infants or children. (See Table 1

Table 1. Description of studies on associations between indoor chemical concentrations in air or dust and asthma or allergy in infants and children*

Effect	Subject Age	Design	Ref
Asthma dx	6 mo–3 yr	Case-control	[8]
Asthma dx; Persistent allergic symptoms; Rhinitis dx; Eczema dx	1-6 yr	Cross-sectional	[9]
Asthma dx and respiratory symptoms in past yr; Atopy (skin prick tests)	7-14 yr	Cohort/ Cross-sectional	[10]
Asthma, emergency treatment for	6 mo–3 yr	Case-control	[11]
Asthma dx; Chronic bronchitis dx; Peak expiratory flow; Respiratory symptoms	6-15 yr	Cross-sectional	[12]
Exhaled nitric oxide; Spirometry	6-13 yr	Cross-sectional	[13]
Obstructive bronchitis; Eczema;	3 yr	Case-control	[14]
Excess variability in PEFR; Respiratory symptoms	< 16 yr	Cross-sectional	[15]
Asthma symptom severity	10-16 yr	Panel	[16]
Persistent wheezing	9-11 yr	Case-control	[17]
Pulmonary infections	6 wk	Case-control	[18]
IgE sensitization to foods; Total IgE	6 mo–3 yr	Cohort/ Cross-sectional	[19]

* see Abbreviations listed at end of paper

Table 2. Description of studies on associations between indoor chemical sources and asthma or allergy in infants and children*

Effect	Subject Age	Design	Ref
Pulmonary infections at 6 wk; Wheezing at 1 yr	6 wk and 1 yr	Case-control	[18]
Obstructive bronchitis, within first or second year	0-2 yr	Cohort	[20]
3+ wheezing episodes >3 mo of age, and either use of inhaled steroids or BHR symptoms	1-2 yrs	Case-control	[21]
Persistent wheeze; Late-onset wheeze; Transient early wheeze	0-3.5 yr	Cohort	[22]
Lower respiratory symptoms; Cough, phlegm; Asthma	1-7 yr	Cross-sectional	[23]
House dust mite sensitization	8 yr	Cohort	[24]
Bronchial obstruction	0-2 yr	Case-control	[25], [26]
Current asthma; Asthma-like symptoms; Current wheezing; Any allergy	8-12 yr	Cross-sectional	[27]
Persistent allergic symptoms	1-6 yr	Cross-sectional	[9]

* see Abbreviations listed at end of paper

for information on study designs, subjects, and health outcomes, and Table 3 for estimated associations.)

For formaldehyde, associations were reported with increases in asthma [11, 12], asthmatic symptoms [10, 17], chronic bronchitis [12], exhaled nitric oxide (an indicator of lung inflammation) [13]; adverse changes in lung function [12, 15], and atopy [10]. For aromatic organic compounds such as toluene, benzene, and dichlorobenzene, associations were reported with increases in diagnosed asthma [8], obstructive bronchitis [14], pulmonary infections (associated with asthma attacks) [18], IgE sensitization to foods and total IgE [19], and eczema [14]. Aliphatic organic compounds such as hexane and decane were associated with increased IgE sensitization to foods [19]. Total VOC concentration was associated with increased asthma diagnosis [8], but not with persistent wheezing [17].

Specific plasticizers (phthalates), which are in the class of semi-volatile organic compounds, were associated with increases in persistent allergic symptoms and diagnoses of rhinitis, eczema, and asthma, with some dose-response relations [9].

Table 3. Summary table: odds ratios (ORs) for asthma, lower respiratory outcomes, and allergy in infants and children associated with *indoor chemical concentrations* and for *indoor source materials or activities*

Risk Factors	Health Outcomes	
	Asthma and Lower Respiratory OR	Allergy OR
<i>Indoor Chemical Concentrations</i>		
Formaldehyde	1.4* [11]; 1.8* [13]; 8.0*, 2.0*, * [12]; * [15]; 1.4 [17]	4.1 [10]
Aromatics toluene	1.3* [8]	13.0*, 16.0* [14]; 3.3*, 11.2* [19]
benzene	1.9*/8.0* [8]; 10*[14], 2.4*[18]	---
styrene	6.4* [14], 2.1* [18]	---
m-p-xylene	10.0* [14]	8.0* [19]
dichlorobenzene	1.2* [8]	---
chlorobenzene	---	5.9* [19]
4-ethyltoluene	---	3.0*, 9.3* [19]
Aliphatics decane	---	8.1* [19]
hexane	---	9.6* [19]
Total VOCs	1.3*/4.0* [8]	---
Phthalates (in dust) BBZP	1.9 [9];	2.0*, 2.6*, 3.0* [9]
DEHP	2.9* [9]	---
<i>Indoor sources or activities</i>		
Plastic materials	1.1, 1.4*, 1.4* [27]; 1.9* [26]; 1.5, 3.4* [23]; 2.9, 12.6* [25]; 2.1* [24]	1.3* [27]; 1.6* [9]
Recent painting	1.9*, 5.6* [18]; 1.1, 1.2, 1.3 [27]; 1.7*, * [21]; 4.1*, 4.1* [20]	1.2* [27]
New furniture or particleboard	1.3, 1.3, 1.6* [27]; 1.3, 1.4, 0.6 [27]	1.4*; 1.5* [27]
New synthetic carpets	1.7*, 1.8, 1.9* [27]	1.4* [27]
Textile wallpaper	1.6 [26]; 1.7, 3.7 [25]	---
Housecleaning by mother	2.0, 2.3* [22]	---

* p-value ≤ 0.05 (* with no OR indicates that p-value was reported without OR)

Effects were evident at relatively low levels of some exposures. Examples related to diagnosed asthma follow: In an Australian cross-sectional study, in categories with peak indoor formaldehyde concentrations of less than 20, 20-50, and greater than 50 $\mu\text{g}/\text{m}^3$ (study median=26 and maximum=140 $\mu\text{g}/\text{m}^3$), the proportions of diagnosed asthmatic children were 16%, 39%, and 44% [10]. In an Australian case-control study, risk of emergency

treatment for asthma rose by an estimated 3% per 10 $\mu\text{g}/\text{m}^3$ increase in indoor formaldehyde concentrations over the range measured, from below 10 to about 200 $\mu\text{g}/\text{m}^3$ (median =30 $\mu\text{g}/\text{m}^3$) [11]. In this study, categorical analysis showed that, relative to the lowest indoor formaldehyde concentrations below 10 $\mu\text{g}/\text{m}^3$, evident risk only increased at concentrations above 50 $\mu\text{g}/\text{m}^3$, with a statistically significant (39%) increased risk of asthma at concentrations over 60 $\mu\text{g}/\text{m}^3$ [11]. A cross-sectional study in the U.S. reported that asthma prevalence was more than three times higher in children with kitchen formaldehyde levels greater than 73 $\mu\text{g}/\text{m}^3$ (60 ppb), which were found in 7% of the study homes [12].

An Australian case-control study found increased risks of new asthma diagnoses in children with increased indoor concentrations of VOCs, with the following significant ORs per 10 $\mu\text{g}/\text{m}^3$ increase: benzene, 2.9; toluene, 1.8; dichlorobenzene, 1.6; and total VOCs, 1.3 [8]. Adjusted risks for newly diagnosed asthma for children living in houses with above median concentrations were, for benzene, eightfold, and for total VOCs, fourfold. Median and maximum indoor concentrations (in $\mu\text{g}/\text{m}^3$) in the study houses were: benzene, 20 and 82; toluene, 17 and 154; dichlorobenzene, 17 and 202; and total VOCs, 55 and 622 [8].

In a Swedish cross-sectional study, children at the highest quartile of dust concentrations of two phthalate plasticizers had elevated risks for asthma diagnosis: for di(2-ethylhexyl)phthalate (DEHP), a significant OR of 2.9, and for n-butyl benzyl phthalate (BBzP), an OR of 1.9 [9]. Median dust concentrations in mg/m^3 were, for DEHP, 0.770, and for BBzP, 0.135.

Indoor sources or activities

Types of indoor residential materials and coatings, as well as renovation or cleaning activities, were associated with health effects related to asthma or allergy in infants or children. (See Table 2 for information on study design, subjects, and health outcomes, and Table 3 for estimated associations.) Interior plastic surfaces such as floors or wall coverings were associated with increases in current asthma, asthma symptoms, wheezing, and allergy [27], asthma, persistent wheeze, cough, and phlegm [23], bronchial obstruction [25, 26], and persistent allergic symptoms [9], but not lower respiratory symptoms [23]. Recent painting was associated with increases in current asthma, asthma symptoms, and allergy [27], recurrent wheezing [21], pulmonary infections at 6 weeks [18], and wheezing at 1 year [18], while redecoration (painting, new carpet, or new furniture) was associated with increases in obstructive bronchitis [20]. Textile wallpaper was associated with increased bronchial obstruction [25, 26]. New furniture, new particleboard, and new synthetic carpet were each associated with increases in current asthma, asthma symptoms, wheezing, and allergy [27].

Housecleaning by the mother was associated with persistent wheeze in young children [22].

Low outdoor air ventilation

One study found that lower ventilation rates in homes were associated with increased prevalence of asthma and allergic symptoms in children, with a dose-response trend [28]. Another study found no direct association of residential ventilation on recurrent wheezing in infants [29]. A third study found that outdoor air ventilation rates were not directly associated with risk of bronchial obstruction in infants [25]; however, lower ventilation rates *synergistically increased* the risk of bronchial obstruction associated with indoor sources such as plasticizer-containing surfaces, textile wallpaper, and environmental tobacco smoke. For instance, for risk of bronchial obstruction among infants living in homes with plasticizer-containing surfaces compared to those in homes without, the OR over all study homes was 2.9, while in analyses restricted to homes with low ventilation rates, the OR was 12.6 [25].

4 Discussion

Synthesis of findings

The reviewed studies found many associations, some strong, between risk factors for indoor residential chemical emissions and asthmatic and allergic effects in infants or children. Reported statistically significant ORs ranged to high levels: for painting, from 1.2 to 5.6; for formaldehyde, from 1.4 to 8.0; for aliphatic chemicals, from 8.1 to 9.6; for plastics and plasticizers, from 1.3 to 12.6; and for aromatic chemicals, from 1.2 to 16.0. Elevated risks were also reported for renovation and cleaning activities, new furniture or particleboard, and carpets or textile wallpaper. Findings from one study suggested that low ventilation rates may exacerbate risks from indoor sources by increasing indoor exposure concentrations.

Limitations

All the studies reviewed were observational, with the potential biases and limitations inherent in such studies; however, research on these risks in humans will of necessity be largely observational. Alternate explanations for the findings reviewed here include: recall bias related to past activities reported (although not in prospective studies); errors in measurement that are systematically biased in a direction that creates spurious relationships; confounding by other risk factors, such as outdoor-produced pollutants, not involving indoor chemical emissions; and chance positive associations resulting from large numbers of statistical comparisons but no true relationships. Even if the risk factors identified in these studies were not the result of bias, they may not directly indicate true causal factors. For instance, the aliphatic chemicals may be proxies for other exposures emitted from the same sources. Also, indoor benzene, although emitted from some products and appliances, may primarily be

an indicator for indoor tobacco smoke, with its large number of toxic components.

While the reviewed studies contained very few reports of lack of association between the studied risks and outcomes, it is well recognized that negative results, or entirely negative studies, are less likely to be reported or published [30].

This brief summary does not provide details on the design of studies, or on their measurement methods for risk factors and health outcomes. Nor does it critique the findings or synthesize them by specific risk factor or outcome. For instance, this paper does not distinguish health outcomes of causation and exacerbation of asthma, and the specific findings for each. This important distinction and others will be made, to the extent possible, in a future more detailed review paper.

Although this review includes many single, unreplicated findings, it also includes repeated findings for some risk factors and similar health outcomes. The most frequently identified risk factors include formaldehyde, aromatic compounds such as toluene and benzene, plastic materials or plasticizers, and recent painting. The finding in one study that lower ventilation rate increased the risks associated with indoor chemical sources is consistent with the well-understood process by which both sources and removal processes determine indoor concentrations.

Related findings

Associations have been reported between indoor chemical emissions in homes and altered immune parameters in children, which may be related to development of asthma or allergy [19, 31]. After homes, children spend most time in schools, but little research is available on the effects of chemical exposures in schools on children's health. One study reported an OR of 2.9* for asthma and exposure to formaldehyde in schools [32]. Numerous studies have reported associations of indoor chemical emissions and emission sources with respiratory and allergic effects in adults [33-39]. Studies have found that, for some chemicals identified as risk factors in indoor air, higher concentrations in *outdoor* air are health risks for asthma severity in children: ORs were, for formaldehyde, 1.4 [40]; for benzene, 5.9, for toluene, 5.0, and for m-p-xylene, 3.6 [16]. A substantial body of research shows increased risk of various asthma and respiratory outcomes associated with synthetic bedding materials, although this increased risk, also found for sheepskin bedding, currently seems likely to be due to enhanced growth of dust mites [41] rather than to chemical emissions.

Interpretation and implications

At this time, it is not clear through what mechanisms inhalation of relatively low levels of chemicals such as formaldehyde, aromatic and aliphatic compounds, other components of paint, and plasticizers could increase asthma or allergies. Animal models and other evidence suggest that either inflammation, or

increased sensitization without inflammation, may be involved [42-44].

Long term indoor chemical emissions in the home, where infants and children spend most of their time, may result in substantial cumulative exposures during a period of relatively high susceptibility. There is biologic plausibility for at least some of the associations summarized here. The risk factors reviewed here are nearly ubiquitous in modern homes, and it seems likely that use of the associated source materials will increase, leading to increased emissions. Furthermore, as average ventilation rates continue to decrease in houses in the U.S. [45] and presumably in other countries in order to increase energy efficiency, concentrations of indoor pollutants will increase even if levels of indoor emissions remain unchanged.

Available findings thus suggest the possible large-scale occurrence, and future increase, of important yet preventable adverse respiratory effects in infants and children worldwide, related to modern residential building materials and coatings and exacerbated by decreased ventilation. Where necessary, research should confirm risk factors, identify specific causal exposures, and elucidate mechanisms. For risk factors with sufficient documentation, research should quantify risk/response relations, estimate the magnitude of public health impacts, and evaluate effective preventive actions.

ABBREVIATIONS

BBzP	n-butyl benzyl phthalate
BHR	bronchial hyperresponsiveness
DEHP	Di(2-ethylhexyl)phthalate
dx	diagnosis, diagnosed
HR	hyperresponsiveness
IgE	immunoglobulin E
mo	month
OR	odds ratio
PEFR	peak expiratory flow rate
PVC	polyvinyl chloride
VOC	volatile organic compound
wk	week
yr	year

REFERENCES

- [1] C.C. Johnson, et al. Environmental epidemiology of pediatric asthma and allergy. *Epidemiol Rev* 24 (2002) 154-75.
- [2] R.J. Delfino. Epidemiologic evidence for asthma and exposure to air toxics: Linkages between occupational, indoor, and community air pollution research. *Environ Health Perspect* 110 Suppl 4 (2002) 573-89.
- [3] B. Brunekreef. The great indoors. *Thorax* 59 (2004) 729-30.
- [4] R. Dales and M. Raizenne. Residential exposure to volatile organic compounds and asthma. *J Asthma* 41 (2004) 259-70.

- [5] K. Andersson, et al. TVOC and health in non-industrial indoor environments. *Indoor Air* 7 (1997) 78-91.
- [6] C.P. Weisel. Assessing exposure to air toxics relative to asthma. *Environ Health Perspect* 110 Suppl 4 (2002) 527-37.
- [7] G. Viegi, et al. Indoor air pollution and airway disease. *Int J Tuberc Lung Dis* 8 (2004) 1401-15.
- [8] K. Rumchev, et al. Association of domestic exposure to volatile organic compounds with asthma in young children. *Thorax* 59 (2004) 746-51.
- [9] C.G. Bornehag, et al. The association between asthma and allergic symptoms in children and phthalates in house dust: A nested case-control study. *Environ Health Perspect* 112 (2004) 1393-7.
- [10] M.H. Garrett, et al. Increased risk of allergy in children due to formaldehyde exposure in homes. *Allergy* 54 (1999) 330-7.
- [11] K.B. Rumchev, et al. Domestic exposure to formaldehyde significantly increases the risk of asthma in young children. *Eur Respir J* 20 (2002) 403-8.
- [12] M. Krzyzanowski, J.J. Quackenboss, and M.D. Lebowitz. Chronic respiratory effects of indoor formaldehyde exposure. *Environ Res* 52 (1990) 117-25.
- [13] P. Franklin, P. Dingle, and S. Stick. Raised exhaled nitric oxide in healthy children is associated with domestic formaldehyde levels. *Am J Respir Crit Care Med* 161 (2000) 1757-9.
- [14] U.E. Rolle-Kampczyk, et al. Passive smoking, excretion of metabolites, and health effects: Results of the Leipzig's Allergy Risk Study (LARS). *Arch Environ Health* 57 (2002) 326-31.
- [15] J.J. Quackenboss, et al. Formaldehyde exposure and acute health effects study. *Environment International* 15 (1989) 169-176.
- [16] R.J. Delfino, et al. Respiratory symptoms and peak expiratory flow in children with asthma in relation to volatile organic compounds in exhaled breath and ambient air. *J Expo Anal Environ Epidemiol* 13 (2003) 348-63.
- [17] A.J. Venn, et al. Effects of volatile organic compounds, damp, and other environmental exposures in the home on wheezing illness in children. *Thorax* 58 (2003) 955-60.
- [18] U. Diez, et al. 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 (2000) 23-8.
- [19] I. Lehmann, et al. Enhanced in vivo IgE production and T cell polarization toward the type 2 phenotype in association with indoor exposure to VOC: Results of the LARS study. *Int J Hyg Environ Health* 204 (2001) 211-21.
- [20] U. Diez, et al. Redecoration of apartments promotes obstructive bronchitis in atopy risk infants--results of the LARS study. *Int J Hyg Environ Health* 206 (2003) 173-9.

- [21] G. Emenius, et al. Indoor exposures and recurrent wheezing in infants: A study in the BAMSE cohort. *Acta Paediatr* 93 (2004) 899-905.
- [22] A. Sherriff, et al. Frequent use of chemical household products is associated with persistent wheezing in pre-school age children. *Thorax* 60 (2005) 45-9.
- [23] J.J. Jaakkola, P.K. Verkasalo, and N. Jaakkola. Plastic wall materials in the home and respiratory health in young children. *Am J Public Health* 90 (2000) 797-9.
- [24] L.F. Trevillian, et al. An association between plastic mattress covers and sheepskin underbedding use in infancy and house dust mite sensitization in childhood: A prospective study. *Clin Exp Allergy* 33 (2003) 483-9.
- [25] L. Oie, et al. Ventilation in homes and bronchial obstruction in young children. *Epidemiology* 10 (1999) 294-9.
- [26] J.J. Jaakkola, et al. Interior surface materials in the home and the development of bronchial obstruction in young children in Oslo, Norway. *Am J Public Health* 89 (1999) 188-92.
- [27] J.J. Jaakkola, et al. Asthma, asthma-like symptoms and allergies in Russian school children in relation to new surface materials in the home. in *Indoor Air '02: Proceedings of the 9th International Conference on Indoor Air Quality and Climate*, Monterey, CA, 2002. Indoor Air.
- [28] C.G. Bornehag, et al. Association between ventilation rates in 390 Swedish homes and allergic symptoms in children. *Indoor Air* 15 (2005) 275-80.
- [29] G. Emenius, et al. Building characteristics, indoor air quality and recurrent wheezing in very young children (BAMSE). *Indoor Air* 14 (2004) 34-42.
- [30] J. Copas and J.Q. Shi. Meta-analysis, funnel plots and sensitivity analysis. *Biostatistics* 1 (2000) 247-62.
- [31] I. Lehmann, et al. The influence of maternal exposure to volatile organic compounds on the cytokine secretion profile of neonatal T cells. *Environ Toxicol* 17 (2002) 203-10.
- [32] G. Smedje and D. Norback. Incidence of asthma diagnosis and self-reported allergy in relation to the school environment--a four-year follow-up study in schoolchildren. *Int J Tuberc Lung Dis* 5 (2001) 1059-66.
- [33] D. Norback, et al. Asthmatic symptoms and volatile organic compounds, formaldehyde, and carbon dioxide in dwellings. *Occup Environ Med* 52 (1995) 388-95.
- [34] K. Pazdrak, et al. Changes in nasal lavage fluid due to formaldehyde inhalation. *Int Arch Occup Environ Health* 64 (1993) 515-9.
- [35] D. Norback, et al. Indoor air pollutants in schools: Nasal patency and biomarkers in nasal lavage. *Allergy* 55 (2000) 163-70.
- [36] J.A. Hoppin, R. Ulmer, and S.J. London. Phthalate exposure and pulmonary function. *Environ Health Perspect* 112 (2004) 571-4.
- [37] G. Wieslander, et al. 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 (1997) 115-24.
- [38] J.J. Jaakkola, P. Tuomaala, and O. Seppanen. Textile wall materials and sick building syndrome. *Arch Environ Health* 49 (1994) 175-81.
- [39] H. Harving, R. Dahl, and L. Molhave. Lung function and bronchial reactivity in asthmatics during exposure to volatile organic compounds. *Am Rev Respir Dis* 143 (1991) 751-4.
- [40] R.J. Delfino, et al. Asthma symptoms in Hispanic children and daily ambient exposures to toxic and criteria air pollutants. *Environ Health Perspect* 111 (2003) 647-56.
- [41] A.L. Ponsonby, et al. Synthetic bedding and wheeze in childhood. *Epidemiology* 14 (2003) 37-44.
- [42] K. Sadakane, et al. Formaldehyde enhances mite allergen-induced eosinophilic inflammation in the murine airway. *J Environ Pathol Toxicol Oncol* 21 (2002) 267-76.
- [43] F. Riedel, et al. Formaldehyde exposure enhances inhalative allergic sensitization in the guinea pig. *Allergy* 51 (1996) 94-9.
- [44] L. Oie, L.G. Hersoug, and J.O. Madsen. Residential exposure to plasticizers and its possible role in the pathogenesis of asthma. *Environmental Health Perspectives* 105 (1997) 972-78.
- [45] R.C. Diamond, *An overview of the U.S. Building stock*, in *Indoor Air Quality Handbook*, J. Spengler, J.M. Samet, and J.F. McCarthy, Editors. 2000, McGraw-Hill: New York. p. 6.1-6.18.

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