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Asthma and the indoor environment: the significance of emission of formaldehyde and volatile organic compounds from newly painted indoor surfaces

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Abstract As a part of the worldwide European Community Respiratory Health Survey, possible relations between asthma and emissions from newly painted indoor surfaces were studied. The participants (n = 562) answered a self-administered questionnaire, with questions on symptoms and indoor exposures, including indoor painting, during the last 12 months. The participants also underwent a structured interview, spirometry, peak flow measurements at home (PEF), methacholine provocation test for bronchial hyperresponsiveness (BHR), and skin prick tests. In addition, serum concentration of eosinophilic cationic protein (S-ECP), blood eosinophil count (B-EOS), and total immunoglobulin E (S-IgE) were measured. Current asthma was defined as a combination of BHR and at least one asthma-related symptom (wheezing and attacks of breathlessness). The information gathered on indoor painting was compared with exposure measurements of formaldehyde and volatile organic compounds (VOC) performed in a selected sample of the dwellings (n = 62). Relations between exposures, asthma and clinical signs were calculated by multiple linear or logistic regression, adjusting for possible influence of age, gender and tobacco smoking. The prevalence of asthma was increased among subjects with domestic exposure to newly painted surfaces (OR = 1.5; 95% CI 1.0–2.4), particularly newly painted wood details (OR = 2.3; 95% CI 1.2–4.5) and kitchen painting (OR = 2.2; 95% CI 1.1–4.5). Moreover, blood eosinophil concentrations were significantly elevated among subjects living in newly painted dwellings. A significantly increased prevalence of symptoms related to asthma, but not BHR, was observed in relation to workplace exposure to newly painted surfaces. The indoor concentration of aliphatic compounds (C_8–C_{11}), butanols, and 2,2,4-trimethyl 1,3-pentanediol diisobutyrate (TXIB) was significantly elevated in newly painted dwellings. The total indoor VOC was about 100 $\mu g/m^3$ higher in dwellings painted in the last year. A significant increase in formaldehyde concentration was observed in dwellings with newly painted wood details. Our results indicate that exposure to chemical emissions from indoor paint is related to asthma, and that some VOCs may cause inflammatory reactions in the airways. To improve asthma management, and to counteract the increasing frequency of asthma, the significance of the indoor environment should not be neglected. Our study suggests that the contribution of emissions from paint to indoor concentrations of formaldehyde and VOCs should be as low as possible.

Key words Asthma · Indoor air quality · Formaldehyde · Paint emissions · Volatile organic compounds · Eosinophils

Introduction

Asthma is the most common lung disease associated with indoor pollutants [33, 34], with a cumulative prevalence of about 5% in the adult Swedish population [4]. There have been reports of increased morbidity and mortality in asthma and allergies in several western countries [8, 35, 41], and it has been suggested that this increase may be due to raised concentrations of pollutants in modern indoor environments [41]. It has been recognized that airway inflammation is an important component in asthma, and more information is

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needed on possible inflammatory reactions due to indoor air pollutants.

Various indoor exposures have been shown to be related to asthma, including house dust mites [36], damp housing conditions [26, 31, 38], and exposure to nitrogen dioxide (NO_2) from gas cooking [17]. Indoor air contains different types of air pollutants, including volatile organic compounds (VOC), emitted from various sources, e.g. building materials, paint, and consumer products. Formaldehyde is a reactive indoor pollutant that may induce airway irritation at low concentrations [26, 32]. In one experimental study, low level exposure to formaldehyde (0.5 mg/m^3) increased the number of eosinophils in nasal lavage [29]. Two other experimental studies have shown that VOCs may affect the airways, and induce inflammation [21] and airway obstruction [16] even at low concentrations (25 mg/m^3). Recently, a relation between nocturnal attacks of breathlessness and indoor concentrations of formaldehyde and VOC has also been reported [26]. Two recent studies demonstrated that 26–32% of the Swedish population had the interior of their dwelling painted during the last year [22, 25]. There are also some indications that emissions from fresh indoor paint may cause mucosal irritation [22] and asthma-like symptoms [25]. To our knowledge, however, there are few studies available on clinical signs of asthma and inflammation in relation to indoor exposure to emissions from newly painted surfaces.

Our primary aim was to study symptoms and clinical signs related to asthma in adults in relation to indoor exposure to emissions from fresh paint. A second aim was to study the influence of indoor painting on the indoor concentration of formaldehyde and different types of volatile organic compounds.

Materials and methods

Study population

The European Community Respiratory Health Survey (ECRHS) is a multicenter study on the prevalence of allergies and asthma. It has been performed in 48 centers in 23 countries throughout the world [7]. Each center covers a source population of approximately 150 000 inhabitants within a defined geographical and administrative area. Sweden contributes data from three such areas, one being the municipality of Uppsala [2].

The source population was all subjects living in the community of Uppsala in 1990, a mid-Swedish urban community with a total population of 160 000 inhabitants. In December 1990, a screening questionnaire was mailed to a random sample of 3600 men and women aged 20–44 years, selected from the population register of Uppsala. All symptomatic responders ($n = 216$) plus another random sample of 800 subjects were selected for further examination at the Department of Lung Medicine during the period April 1991 to February 1992 [3]. To enrich the random sample ($n = 800$), all persons from the main sample who had not been selected to the random sample, and who in the postal questionnaire reported use of asthma medication, attacks of asthma or awakening because of shortness of breath, were invited to participate ($n = 216$). The random sample therefore also included some symptomatic subjects. The classification of subjects with and without asthma-related symptoms in this investigation was, however, based on the result taken from the interview questionnaire. As the interview was conducted at the same time as the methacholine challenge test, this seems to us as the most reliable way of identifying subjects with asthma-related symptoms for this investigation. Blood samples were obtained and all participants were interviewed and examined by especially trained nurses. The participants were requested to answer a self-administered questionnaire, with additional questions on symptoms, and questions on exposures. The study was blind, to the extent that information from the exposure measurements and the questionnaire on exposure was not linked with the medical information until the data collection was completed. The protocol of the study was approved by the Ethical Committee of the Medical Faculty of Uppsala University.

Assessment of exposure

Information on age and type of building, carpeting in the dwelling, and exposure to environmental tobacco smoke in the dwelling was obtained from the interview questionnaire of the ECRHS-study. Other information on building characteristics of the dwelling and the workplace was obtained from an additional self-administered questionnaire, using the same questions as in earlier published studies [22, 25]. It requested information on type of ventilation system, type of wall material, and signs of building dampness during the previous 12 months. The subjects were also asked whether their dwelling, or workplace, had been painted indoors during the last 12 months. Finally, the questionnaire requested information on current and previous occupations. The occupations were classified in accordance with the Nordic Classification of Occupations (NYK 82), which is based on the International Standard Classification of Occupations (ISCO) with a few modifications. Current occupational exposure to organic solvents was estimated by a previously described job-matrix procedure [22].

Exposure measurements of formaldehyde and VOCs were performed in a stratified random sample of dwellings of 62 participants, from October 1991 to April 1992. These were obtained from a larger study population of 72 randomly selected subjects who in the postal questionnaire reported use of asthma medication, attacks of asthma or awakening because of shortness of breath. Also, 80 subjects who gave negative answers to all three questions were randomly selected, without matching. Details of the selection process is described elsewhere [26]. In total, 88 of these subjects lived in the same dwelling throughout the study period and gave their approval for the measurements in their dwelling; 62 of them answered the questionnaire on building-related exposures, including indoor painting. Most of the losses of individuals were due to migration during the study period. The exposure questionnaire was answered during the same period as the measurements (October 1991 to April 1992), without knowledge of the results of the exposure measurements. Room temperature, air humidity, and VOCs were measured in each participant's living room and bedroom. Measurements of fomaldehyde were performed in the bedroom only. Measurements in the living room were performed in the center of the room, 1 m above floor level. Bedroom measurements were performed beside the pillow on the bed, at the same height from the floor as the pillow. The bedroom door was closed, and no subject stayed in the bedroom during the VOC and formaldehyde measurements.

Room temperature and air humidity were recorded with an Assman psychrometer. Indoor concentrations of formaldehyde were measured with glassfiber filters impregnated with 2,4-dinitrophenylhydrazine [1], the air sampling rate being 0.25 l/min for 2 h. The filters were analyzed by liquid chromatography. Volatile organic compounds other than formaldehyde were measured both in

the bedroom and the living room by sampling on charcoal sorbent tubes [26]. The air sampling rate was 1 l/min for 2 h. The charcoal tubes were desorbed with 1 ml of carbon disulfide before analysis, which was performed within 1 week of the sampling day with a gas-chromatograph equipped with a flame ionization detector. Sixteen common solvents were identified and quantified by external standard technique, by comparing the retention times on two different columns. For quantification of low-boiling-point uncalibrated compounds (C_3–C_{12}) the response factor of *n*-decane was used; high-boiling-point unknown compounds utilized the response factor of a mixture of high-boiling-point hydrocarbons (dodecylbenzenes). The total concentration of the identified and unidentified volatile organic compounds (total VOC expressed as $\mu g/m^3$) was calculated [23].

Assessment of symptoms and personal factors

The screening and interview questionnaire used in the European Community respiratory health survey was a modified version of the IUATLD questionnaire [5,6]. All questions were translated into Swedish and then back into English, to minimize translation bias. The recall period for airway symptoms was 12 months. Symptoms related to asthma were recorded when subjects reported in the interview that they had, in the previous 12 months: (1) wheezing or whistling in the chest or (2) at least one daytime attack of shortness of breath during exercise or while resting; (3) at least one nighttime awakening because of breathlessness or tightness in the chest. Current asthma was defined in our study as a combination of bronchial hyperresponsiveness (BHR) and at least one symptom related to asthma. In addition, information on age, sex, and smoking habits was collected from the screening and interview questionnaire. A current smoker was defined as a subject reporting actual smoking in the interview, or ceasing smoking less than a year before.

Assessment of atopy

Skin prick tests were carried out in a standardized way, by means of allergen-coated lancets (PhazetsR, Pharmacia Diagnostics, Uppsala, Sweden) [7]. The following allergens were tested: cat, birch, dog, olive, ragweed, mugwort, timothy, *D. pteronyssinus* (house dust mite), *Cladosporium* and *Alternaria*. Histamine was used as a positive control. As proposed by Dreborg [10], atopy was defined as a prick test reaction to at least one of the allergens, with a mean diameter of 3 mm or greater. A negative control was used, and its mean diameter was subtracted from the allergens diameter.

Lung function tests

Forced expiratory volume in 1 s (FEV_1) was measured by using the Spiro Medics computerized dry-rolling seal spirometer system 2130 (Sensor Medics, Anaheim, Calif.). The predicted value for each subject was calculated [11]. Peak expiratory flow (PEF) rate (best of three measurements) was recorded twice daily for 1 week with a Mini-Wright Peak Flow Meter (Clement Clark, London, UK). Peak expiratory flow (best of three measurements) was recorded twice daily: in the morning on waking up and in the evening immediately before going to bed. Peak flow variability was calculated by dividing the difference between the highest and the lowest daily PEF reading by the daily mean PEF value. The index used is the one suggested by Higgins et al., who found this way of measuring peak flow to be the most sensitive when comparing asthmatic and non asthmatic subjects [18].

Bronchial hyperresponsiveness

Methacholine challenge was performed by using a MEFAR inhalation dosimeter (MEFAR, Brescia, Italy) [20]; BHR was defined as a positive methacholine test-that is, a reduction in FEV_1 by at least 20% with an accumulated dose of 2 mg or less of methacholine (PD_{20}).

Biochemical markers of inflammation and allergy

From each volunteer, 35 ml of venous blood was collected just prior to the methacholine provocation test. The same investigation sequence was applied to all participants. Blood eosinophil counts were analysed on a Hemalog 2R (Technicon Chemicals Company, Tournai, Belgium) in 5 ml blood supplemented with EDTA (0.34 mol/l). The concentration of eosinophilic cationic protein (S-ECP) was measured by means of a double antibody radioimmunoassay (Pharmacia Diagnostics, Uppsala, Sweden) [30]. The serum was kept frozen at $-70\,^{\circ}C$ until analysis. In addition, serum was analysed for total serum immunoglobulin E (S-IgE) by the Pharmacia CAP system (Pharmacia Diagnostics, Uppsala, Sweden).

Statistical methods

The Chi-square test was used when analysing the relation between binary dependent and independent variables. Unpaired *t*-tests were used to study relations between indoor painting and clinical signs that were approximately normal distributed (FEV_1%, PEF variability, blood eosinophils). The Mann-Whitney U-test was applied to study relations between indoor painting and clinical signs that were not normal distributed (total IgE, serum ECP). The Mann-Whitney U-test was also applied for the crude analysis of relations between indoor painting and indoor concentrations of formaldehyde and VOCs. Multivariate statistical analysis was performed by multiple linear or logistic regression, using the SPIDA statistical package (The Statistical Laboratory, Macquarie University, Australia). The collinearity diagnostics described in the SPIDA manual [13] were applied, and adjusted odds ratios with a 95% confidence interval (CI) were calculated. Adjustments were made for potential confounders: age, gender, and current smoking. In all statistical analyses, two-tailed tests were used and a 5% level of significance was applied.

Results

The total response rate in the initial self-administered questionnaire survey was 87%. The response rate in the clinical investigation was 68% among the random sample of 800 subjects, and 83% among the additional 216 symptomatic subjects, selected from the total material (Fig. 1). The self-administered questionnaire on building characteristics was answered by 562 subjects, 429 from the random sample and 133 subjects from the additional symptomatic subjects. Information on serum ECP was obtained from 462 subjects, blood eosinophils from 531 subjects, total IgE from 460 subjects, lung function test from 546 subjects, peak expiratory flow values from 530 subjects, skin prick test from 541 subjects, and methacholine challenge test from 513 subjects. The nonparticipants ($n = 454$) did not differ from the participants ($n = 562$) in age, gender, or smoking habits.

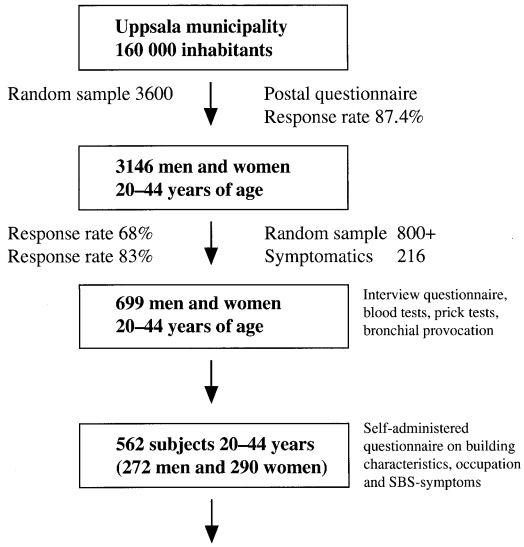

Fig. 1 The study population and response rates

Personal characteristics

Mean age of all participants was 32 years (SD = 7), and the average time spent in the present dwelling was 6 years, ranging from 0.5 to 38 years. The average FEV_1 value was 107% of predicted value (SD = 13), and the average PEF variability was $6 \pm 4\%$ (mean $\pm$ SD). Subjects with symptoms related to asthma had a higher prevalence of BHR and atopy and were more often current smokers (Table 1). In total, 99 subjects had current asthma, almost half (42%) of the subjects with symptoms related to asthma had BHR, and only 7% of subjects without such symptoms had a positive methacholine challenge test. Out of the 464 occupationally active subjects, 10 had current occupational exposure to organic solvents, according to our job-matrix classification. No significant relations were observed between occupational exposure to organic solvent and being an occupant of a newly painted dwelling or workplace building.

Characteristics of the dwelling

About half the building considered (48%) were built after 1970 (Table 2). More than half of the dwellings were apartments (56%), and 21% were single-family houses. Most of the buildings were heated by a waterborne central heating system (84%), but some buildings had a combination of different heating systems. The main source of the heat was hot water distributed by the local authority through underground ducts (69%), followed by electric radiators (25%). In a minority of the buildings, heat was produced by combustion of organic materials, mainly wood (22%), and rarely by oil central heating (6%). No kerosene heaters were used. All buildings were equipped with electric stoves only, and none had a gas stove or any other type of gas heater. Indoor tobacco smoking was reported to occur in 15% of the homes. Most of the houses had mechanical exhaust air ventilation, mainly in the kitchen and in

Table 1 Prevalence of demographic and medical data for subjects with and without symptoms related to asthma

Characteristics	Symptoms[a] ($n = 252$) (%)	No Symptoms ($n = 310$) (%)
Women	54	49
Asthma medication	21	0.3***
Current tobacco smoker	29	17***
Ex-smokers	24	25
Atopy	53	35***
Bronchial hyperresponsiveness (BHR)	42	7***

*** $P < 0.001$

[a] Subjects reported whistling in the chest, daytime attacks of shortness of breath during exercise or rest, or wakening because of breathlessness or tightness in the chest

Table 2 Selected characteristics of the dwelling of subjects with and without symptoms related to asthma ($n = 562$)

Characteristics	Symptoms[a] ($n = 252$) (%)	No Symptoms ($n = 310$) (%)
Age of the dwelling[a]		
< 1960	31	29
1961–70	24	17
1971–80	18	26
> 1980	25	25
Type of house		
Detatched	29	29
Terrace	13	13
Apartment	56	56
Other	2	2
Wooden house	36	40
Mechanical ventilation system	70	75
Indoor painting during last 12 months		
Wall or ceiling	27	26
Wood painting	14	8*
Kitchen	12	6*
Bedroom	4	6
Bathroom	9	9
Any type of painting	37	29*
Degree of indoor painting last 12 months**		
No painting indoors	63	71
Details only	9	2
One room painted	8	11
More than one room painted	20	16

* $P < 0.05$ by chi-square test for 2×2 table; ** $P < 0.01$ by chi-square test for 2×4 table

[a] 2% of symptomatic subjects and 3% of non-symptomatic subjects did not know the age of their dwellings

the bathroom, but 26% had natural ventilation only. Presence of wall-to-wall carpets was reported in 16% of the dwellings, and 16% had visible signs of building dampness or microbial growth. The relation between building dampness and current asthma will be dealt with in a separate paper and is not further analyzed here.

Among the participants, 32% reported that their dwelling had been painted during the last 12 months. No relation between indoor painting and building dampness was observed. Wall or ceiling painting, wood painting, and kitchen painting were the most common types of indoor painting. The floor had been painted in one dwelling only (0.2%), and the basement had been painted in three dwellings (0.5%).

Characteristics of the workplace building

In the total population of 562 subjects, 215 women (74%) and 249 men (92%) were occupationally active. Indoor painting of the workplace was less common than indoor painting of the dwelling, only 23% of occupationally active subjects reporting and type of indoor painting during the last year at the workplace (Table 3). Wall or ceiling painting was the most common type of painting. Painting of the floor (1%) and the basement (1%) was also rare in the workplaces.

Table 3 Workplace exposure to carpeting and indoor painting among occupationally active subjects with and without symptoms related to asthma ($n = 464$)

Characteristics	Symptoms ($n = 204$) (%)	No symptoms ($n = 260$) (%)
Carpeting	11	16
Indoor painting during last 12 months		
Wall or ceiling	25	18
Wood painting	7	4
Lunch room	8	6
Toilets	4	4
Any type of painting	28	19*
Degree of indoor painting last 12 months[a]*		
No indoor painting	72	81
Details only	3	0
One room painted	8	5
Several rooms painted	17	14

* $P < 0.05$ by chi-square test for 2×2 table;
[a]* $P < 0.05$ by chi-square test for 2×4 table

Asthma and clinical signs in relation to indoor painting

In the crude analysis, subjects with symptoms related to asthma had a significantly higher prevalence of any type of indoor painting ($P < 0.05$), wood painting ($P < 0.05$) and kitchen painting ($P < 0.05$) and a significant difference ($P < 0.01$) in the degree of indoor painting (Table 2). Symptoms related to asthma were significantly increased among subjects with domestic exposure to newly painted surfaces: crude OR = 1.43; 95% CI 1.01–2.06). The relation was significant even after adjustment for possible influence of age, sex, and current smoking (Table 4). The logistic regression analysis could also demonstrate a significantly increased prevalence of nocturnal breathlessness, and a borderline significance ($P = 0.05$) for current asthma and indoor painting (Table 4). Wood painting and kitchen painting were related significantly to both asthma symptoms, BHR, and current asthma (Table 5). These relations were significant even after adjustment for possible influence of age, sex, and current smoking (Table 5). Moreover, the relation between wood painting, kitchen painting and current asthma was significant even when the ten subjects with occupational exposure to organic solvent were excluded from the regression analysis.

With regard to workplace painting, the crude analyses showed the following. Subjects with symptoms related to asthma had a significantly higher prevalence of indoor painting ($P < 0.05$) and a significant difference in the degree of indoor painting $P < 0.05$ (Table 3). The logistic regression analysis also demonstrated a significantly increased prevalence of newly painted workplace and to symptoms related to asthma, particularly wheezing, but not related to attacks of breathlessness, BHR or current asthma (Table 4).

To evaluate whether the reclassification of the symptomatic subjects had affected the results, the prevalence of indoor painting was compared between the participants in the random sample ($n = 429$) and those respondents to the postal screening questionnaire who reported use of asthma medication, attacks of asthma, or awakening because of shortness of breath ($n = 133$). Similar results to those yielded by the reclassified analysis were obtained. There was a significantly increased prevalence of wood painting (crude OR = 1.79; 95% CI 1.01–3.18) and kitchen painting (crude OR = 2.02; 95% CI 1.09–3.78) in the dwellings of symptomatic subjects, and a borderline significance for indoor painting of and type in the dwelling (crude OR = 1.46; 95% CI 0.97–2.19). In contrast, no significant relation between being a symptomatic subject according to the initial screening questionnaire and indoor painting of the workplace building, was observed.

Finally, relations between other clinical signs and exposure to indoor paint were investigated. Blood eosinophil concentration (B-Eos) was significantly increased among subjects living in newly painted dwellings ($P < 0.05$), and also significantly related to the degree of indoor painting ($P < 0.05$). In contrast, no relation was observed between indoor painting of the workplace and B-Eos. Moreover, no relation was found between exposure to newly painted surfaces at

Table 4 Relationship between indoor painting and asthma symptoms, bronchial hyperresponsiveness (*BHR*) and asthma

Type of symptom/sign	Newly painted dwelling ($n = 562$) OR(95%CI)[a]	Newly painted workplace ($n = 464$) OR(95%CI)[a]
Wheezing	1.21 (0.83–1.76)	1.60 (1.02–2.52)*
Daytime breathlessness	1.16 (0.75–1.79)	1.60 (0.96–2.67)
Nocturnal breathlessness	1.57 (1.05–2.36)*	1.35 (0.82–2.22)
At least one symptom related to asthma	1.43 (1.01–2.06)*	1.63 (1.05–2.54)*
BHR	1.37 (0.88–2.13)	1.25 (0.73–2.14)
Asthma (BHR + symptoms)	1.56 (0.98–2.48)	1.13 (0.63–2.02)

* $P < 0.05$
[a] Calculated by multiple logistic regression, adjusting for possible influence of age, gender and tobacco smoking

Table 5 Asthma-related symptoms, bronchial hyperresponsiveness, and asthma in relation to selected types of painting in the dwelling ($n = 562$)

	Wood painted OR(95%CI)[a]	Kitchen painted OR(95%CI)[a]
Wheezing	1.60 (0.92–2.78)	1.70 (0.92–3.16)
Daytime breathlessness	1.94 (1.07–3.50)*	1.66 (0.84–3.30)
Nocturnal breathlessness	1.75 (0.98–3.14)	2.67 (1.42–5.04)**
At least one asthma symptom	1.80 (1.04–3.12)*	2.24 (1.20–4.21)*
BHR	2.00 (1.06–3.76) *	2.14 (1.08–4.23)*
Asthma (BHR + symptoms)	2.33 (1.22–4.46)*	2.21 (1.09–4.51)*

* $P < 0.05$; ** $P < 0.01$
[a] Calculated by multiple logistic regression, adjusting for possible influence of age, gender and tobacco smoking

home or at work, and atopy, serum ECP, serum IgE, PEF variability, or lung function (FEV_1%).

Relations between indoor painting, formaldehyde, and measured VOCs

Relations between measured indoor concentration of formaldehyde, VOCs and different types of indoor painting were studied in 11% of the dwellings. These 62 buildings did not differ significantly from those 500 buildings in which no measurements were taken with respect to the prevalence of indoor painting, building dampness, mechanical ventilation, building age, or type of building. The most common compounds detected in the indoor air were aromatic compounds (toluene, xylene, ethylbensen), aliphatic compounds (C_8–C_{11}), and 2,2,4-trimethyl 1,3-pentanediol diisobutyrate (TXIB). TXIB was detected in 57% of the living rooms and 60% of the bedrooms. The maximum concentration of TXIB (373 $\mu g/m^3$) was measured in an apartment with all rooms painted and with a 1-year-old polyvinyl chloride (PVC) floor covering. Texanol (2,2,4-trimethyl 1,3-pentanediol monobutyrate), another compound used in water-based paints, was detected in 8% of the buildings (two living rooms and four bedrooms). The highest concentration of Texanol (50 $\mu g/m^3$) was measured in a dwelling in which walls, ceilings and the kitchen had been painted.

The concentrations of total volatile organic compounds (TVOC), which were measured by charcoal sampling, were higher in buildings with newly painted surfaces. In living rooms, the average TVOC was 413 $\mu g/m^3$ in painted and 302 $\mu g/m^3$ in non-painted dwellings ($P < 0.05$). In bedrooms, the average TVOC was 387 $\mu g/m^3$ in painted and 286 $\mu g/m^3$ in non-painted dwellings, a non-significant difference. Significantly increased concentrations of aliphatic compounds (C_8–C_{11}) ($P < 0.05$), TXIB ($P < 0.05$), and butanols ($P < 0.05$) were also observed in newly painted dwellings. Formaldehyde concentrations were significantly increased in dwellings where wood paint had been used, but were not related to other types of painting or indoor smoking. Aliphatic compounds (C_8–C_{11}) were related to wall or ceiling painting ($P < 0.05$), and TXIB was related to various types of indoor painting ($P < 0.05$; Table 6).

Finally, the contribution of both indoor painting and building characteristics to indoor VOCs was estimated by multiple linear regression (Table 7). Wall-to-wall carpeting and wood painting made approximately equal contributions of 13 $\mu g/m^3$ and 16 $\mu g/m^3$ of formaldehyde, respectively. Significantly higher levels of formaldehyde in wooden houses than in stone or brick

Table 6 Mean indoor concentration of formaldehyde and selected volatile organic compounds (VOCs) ($\mu g/m^3$) in a subsample of 62 dwellings with and without different types of recent painting

Type of compounds	Wall/ceiling painted		Wood painted		Kitchen painted		Bedroom painted		Bathroom painted	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Formaldehyde, bedroom	16	21	32	17**	18	20	24	19	19	20
TXIB[a], bedroom	38	12	51	13**	70	11**	68	15	73	13
TXIB[a], livingroom	36	10*	53	10**	65	10**	71	12	68	12*
Butanols[b], bedroom	15	12	20	11	18	12	24	12*	16	13
Butanols[b], livingroom	16	12	20	11	18	12	26	11**	16	12
Alifatics[c], bedroom	36	16	28	19	27	20	46	19	17	22
Alifatics[c], livingroom	39	17*	35	20	30	22	42	20	19	23

* $P < 0.05$; ** $P < 0.01$ by Mann-Whitney U test.
[a] 2,2,4-trimethyl 1,3-pentanediol diisobutyrate (CAS No. 6846-50-0)
[b] Sum of n-butanol and iso-butanol
[c] Sum of n-octane, n-nonane, n-decane, and n-undecane
Note: In total 24 buildings were painted indoors; walls or ceiling were painted in 10 dwellings, 10 had wood details painted, 8 had the kitchen painted, 5 had the bedroom painted, and 6 had the bathroom painted.

Table 7 Regression model for average indoor concentration of selected compounds as a function of significant building characteristics, and indoor painting

	Wooden house S (95%CI)[a]	Wall-to-wall carpeting S (95%CI)[a]	Wood painted S (95%CI)[a]	Kitchen painted S (95%CI)[a]	Bedroom painted S (95%CI)[a]	Degree of painting S (95%CI)[a]
Formaldehyde	7 (1–3)*	13 (4–22)**	16 (7–25)***	− 4 (− 14–6)	3 (− 9–15)	− 7 (− 16–2)
TXIB[b]	− 4 (− 26–18)	1 (− 27–29)	38 (10–66) *	56 (24–88)***	40 (1–79)*	− 20 (− 59–19)
Butanols[c]	− 8 (− 1– − 15)*					
		− 6 (− 16–4)	10 (1–19)*	6 (− 4–16)	10 (− 3–23)	2 (− 7–11)
Alifatics[d]	− 13 (− 27–1)	3 (− 17–23)	6 (− 14–26)	− 17 (− 43–9)	10 (− 19–39)	25 (7–43)[e]*

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$
[a] Increase of indoor concentration (S) ($\mu g/m^3$) with 95% confidence interval (95% CI), calculated by multiple linear regression, adjusting for the influence of other significant building characterisitics. No significant influence of building age, mechanical ventilation, environmental tobacco smoke, wall or ceiling painting, or bathroom painting was observed for any of the selected compounds.
[b] 2,2,4-trimethyl 1,3-pentanediol diisobutyrate (CAS No. 6846-50-0)
[c] Sum of n-butanol and iso-butanol
[d] Sum of n-octane, n-nonane, n-decane, and n-undecane
[e] Increase of indoor concentration ($\mu g/m^3$) when more than one room is painted, as compared to no indoor painting.

houses were also observed. Wood painting, kitchen painting and bedroom painting were related to an average increase of TXIB by 38, 56 and 40 $\mu g/m^3$, respectively. Butanol concentration was higher in buildings made of stone or brick than in wooden houses, and also increased by 10 $\mu g/m^3$ if wood had been painted. The indoor concentration of aliphatic compounds (C_8–C_{11}) was not related to any particular type of painting, but was significantly increased by 25 $\mu g/m^3$ if more than one room had been painted (Table 7).

Discussion

We found a relation between exposure to recent indoor painting and current asthma and BHR. The design was cross-sectional, and in such studies selection bias may affect the results. This could be of particular significance for asthma, which is a severe condition. Moreover, the cross-sectional design does not enable us to differentiate between exacerbation of symptoms in subjects who already have asthma and induction of new asthma.

Selection bias due to low response rate is less likely, since the participation rate in the initial postal questionnaire was high (87%) and the participants and non-participants in the clinical study did not differ in age, sex, and smoking habits. A number of statistical tests were carried out, but many of the relations were significant below the 1% level and similar results were obtained both in the crude data analysis and in the logistic multiple regression analysis. Moreover, similar results were obtained when the classification of symptomatic subjects was based on the initial

screening questionnaire and when symptomatic subjects were classified on the basis of the medical interview and the methacholine challenge tests. Thus, we do not believe that our conclusions are seriously biased by selection or response errors or because of chance findings. The true adverse health effect of indoor painting could, however, have been underestimated if there were a health-based selection. In addition, the limited number of exposure measurements could have underestimated some relations between indoor VOCs and indoor painting.

We found a relation between asthma and exposure to emissions from recently applied paint, particularly wood paint and kitchen painting. Other factors affecting the personal exposure to VOCs could be occupational exposure to organic solvents, and do-it-yourself painting in dwellings. Ten subjects were classified as being occupationally exposed to organic solvents, but we found no significant relations between such occupational exposure and being an occupant of a painted dwelling or workplace building. Moreover, relations between wood painting and kitchen painting and current asthma were significant even when these ten subjects were excluded from the statistical analysis. Thus, we do not believe that occupational exposure to organic solvents was a confounder in this study. Another potential source of exposure could be do-it-yourself painting in the dwelling. According to information from the largest paint producer in Sweden, 80% of indoor painting in Swedish dwellings is performed by professional painters, and only 20% is performed by the inhabitants of the dwelling, mainly the man of the family (M. Winell, personal communication). This indicates that exposure from do-it-yourself painting in dwellings affected only a minority of our study population.

To our knowledge, relations between clinically verified asthma and indoor painting have not been reported earlier. There are, however, some earlier studies supporting the hypothesis that asthmatic symptoms may be related to indoor levels of VOCs. In one population study, presence of newly painted surfaces indoors was related to an increased prevalence of symptoms related to asthma [25]. In addition, two experimental studies have shown that even moderate levels of VOCs (25 mg/m^3) may cause inflammation [21] and obstructive reactions [16] in the airways. Finally, a relation between indoor VOC concentrations and nocturnal attacks of breathlessness was demonstrated in a subsample of the Uppsala part of the ECRHS-study [26]. Our results are also in agreement with earlier studies showing an excessive risk of obstructive airway illness among house painters exposed to higher exposure levels of emissions from indoor paint [39, 40]. Surprisingly, we found no significant relation between the type of ventilation system and current asthma or asthma-like symptoms. Presence or absence of mechanical ventilation is, however, only a crude measure of the ventilation of dwellings. Most mechanical ventilation in dwellings is in the kitchen or in the bathroom, and may not influence the air exchange rate in the bedroom where people spend a large proportion of their life. In another study, we used carbon dioxide concentration in the bedroom as a better indicator of the ventilation and demonstrated a relation between carbon dioxide and nocturnal asthma-like symptoms [26].

We have demonstrated that indoor painting is related to an increased indoor concentration of formaldehyde and VOCs. For practical reasons, our exposure measurements were performed in a limited number of dwellings. The total indoor VOC was about 100 $\mu g/m^3$ higher in dwellings painted during the last year. Moreover, significantly increased indoor levels was observed for specific compounds, such as formaldehyde, aliphatic compounds (C_8–C_{11}), butanols and TXIB. The exposure measurements were performed from October 1991 to April 1992, and the questions on indoor painting were answered during the same period. We have no exact information on the month of the painting, but as far as we know indoor painting is performed during all parts of the year in Sweden. This suggests that our measurements are representative of the average exposure during the colder part of the year in dwellings that have been painted during the last 12 months. Since there were no significant differences in indoor painting or building characteristics between buildings with and without exposure measurements, we do not believe that observed relationships between indoor VOCs and indoor painting is due to selection bias. The exposure causing the observed increased prevalence of asthma may, however, have been underestimated; the peak exposure in close connection to the painting occasions were not measured.

Formaldehyde is a well-known irritant, and indoor formaldehyde may be emitted from different sources, including tobacco smoke, polyurethane foams, wood chip boards, and paint. We found a relation between formaldehyde and both carpeting and wooden houses, but no relation between formaldehyde and indoor smoking. The increased level of formaldehyde in wooden houses could be due to emissions from woodchip boards. One explanation to the observed relationship between carpeting and formaldehyde could be that fleecy textile materials may accumulate and re-emit water-soluble pollutants, such as formaldehyde. We also found an increased formaldehyde concentration related to wood painting. Acid curing paint is a well-known source of formaldehyde, and such paints are commonly used for spray painting of kitchen wood details in Scandinavia [19]. During industrial spray painting with such paints, average concentrations of 480 $\mu g/m^3$ and peak exposures up to 3000 $\mu g/m^3$ of formaldehyde have been measured [19]. Another possible source of indoor formaldehyde could be water-based paints. During indoor painting, 30–400 $\mu g/m^3$ of formaldehyde has been measured in the breathing zone

of house painters [15, 28, 39]. There is one experimental study available showing that emissions from acid curing paint cause airway irritation on mice [12]. There is also some epidemiological evidence suggesting that low levels of indoor formaldehyde are related to airway symptoms. One study from USA reported that dwellings with more than 30 $\mu g/m^3$ of formaldehyde had a higher proportion of children with abnormal variability in PEF [32]. We have also reported on a relation between indoor concentration of formaldehyde and attacks of nocturnal breathlessness [26]. Thus, we suspect that emissions of formaldehyde, or other particular VOCs from wood paint, can be a contributing cause of BHR and symptoms related to asthma. There is also a possibility that paint chemicals bound to dust could explain some of the observed effects. A relation between the dust-bound chemicals in settled dust in offices and mucosal irritation has been demonstrated previously [14].

The chemical composition of indoor paints used in Scandinavia has changed drastically during the last few decades. Nowadays, water-based paints account for 95% of the indoor paints sold in Sweden [39]. Earlier, indoor painting was performed mainly with solvent-based paints, which have rapid and high emission of well-known non-polar organic solvents. The water-based paints now in common use have a complex chemical composition, including biocides, plastic monomer, and polar and high-boiling polar compounds like Texanol and TXIB [9, 15, 27, 28, 37, 39]. High-boiling-point compounds, e.g., TXIB, may bind to dust and thus give a higher local exposure on mucous membranes [24]. Emissions from paint may affect both house painters and inhabitants in newly painted buildings. Recently, an increased prevalence of asthmatic symptoms and BHR has been demonstrated in Swedish house painters occupationally exposed to mainly water-based paints [39, 40].

We demonstrated that the indoor concentration of VOCs, particularly butanols, *n*-alkanes, and TXIB, were increased in newly painted dwellings. Butanols and *n*-alkanes are emitted from both solvent-based paints and water-based paints, but VOC emissions are about 100 times higher with solvent-based paints [28]. TXIB, but not Texanol, is also used as a plasticizer in PVC floor coatings [24]. TXIB was found in more than half of our dwellings, but Texanol was less common. In conclusion, water-based paints may be a contributing source of indoor VOCs in our study, but a contribution from solvent-based paints and TXIB emissions from PVC materials, cannot be excluded.

In conclusion, our results indicate that indoor exposure to emissions from paint could be related to current asthma and asthma-related symptoms. To improve asthma management, and to counteract the increasing prevalence of asthma, the significance of the indoor environment should not be neglected. One way to improve the indoor environment could be to minimize paint emissions. Indoor painting with solvent-based paints or paints with a high emission of formaldehyde could be restricted to a minimum. When painting is done in the summer, open windows can ensure a sufficient air exchange rate during the initial emission of chemicals. Finally, painting of slowly drying porous surfaces consuming large amounts of paint could be avoided, and paints with low emissions could be developed.

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References

1. Andersson K, Hallgren C, Levin J-O, Nilsson C-A (1981) Chemosorbtion sampling and analysis of formaldehyde in air: influence of recovery during the simultaneous sampling of formaldehyde, phenol, furfural and furfuryl alcohol. Scand J Work Environ Health 7:282–289
2. Björnsson E, Plaschke P, Norrman E, Janson C, Lundbäck B, Rosenhall A, Lindholm N, Rosenhall L, Berglund E, Boman G (1994) A population-based study of symptoms related to asthma and chronic bronchitis in three areas of Sweden. Eur Respir J 7:2146–2153
3. Björnsson E, Janson C, Håkansson L, Enander I, Venge P (1994) Serum eosinophilic cationic protein in relation to bronchial asthma in a young Swedish population. Allergy 49:730–736
4. Boman G (1991) Epidemiology of obstructive lung diseases in the Nordic countries. Eur Respir Rev 1:316–320
5. Burney PGJ, Chinn S (1987) Developing a new questionnaire for measuring the prevalence and distribution of asthma. Chest 19 [Suppl]:79–92
6. Burney PGJ, Laitinen LA, Perdrizet, et al (1989) Validity and repeatability of the IUATLD (1984) bronchial symptoms questionnaire: an international comparison. Eur Respir J 2:940–945
7. Burney PGJ, Luczynska CM, Chinn S, Jarvis D (1994) The European Community respiratory health survey. Eur Respir J 7:954–960
8. Burr ML, Butland BK, King S, Vaughan-Williams E (1989) Changes in asthma prevalence: two surveys 15 years apart. Arch Dis Child 64:1452–1456
9. Clausen PA, Wolkoff P, Holst E, Nielsen PA (1991) Long term emission of volatile organic compounds from waterborne paints – methods of comparison. Indoor Air 1:562–576
10. Dreborg S (1989) Skin tests used for epidemiological studies. Allergy 44 [Suppl]:52–59
11. European Community for Coal and Steel (1983) Standardization of lung function tests, Clin Resp Phys 19 [Suppl 5]:22–27
12. Frimann Hansen L, Damgård Nielsen G, Tottrup J, Abildgaard A, Dahl Jensen OF, Kragh Hansen M, Nielsen O (1991) Biological determination of irritants in paint and lacquer. Indoor Air 1:95–110
13. Gebski V, Leung O, McNeil D, Lunn D (1992) SPIDA users manual, version 6. Statistical Computing Laboratory, Eastwood, Australia
14. Gyntelberg F, Suadicani P, Wohlfahrt Nielsen J, Skov P, Valbjørn O, Nielsen PA, et al. (1994) Dust and the sick building syndrome. Indoor Air 4:223–238
15. Hansen MK, Larsen M, Cohr KH (1987) Waterborne paints: a review of their chemistry and toxicology and the results of determinations during their use. Scand J Work Environ Health 13:473–485

16. Harving H, Dahl R, Mølhave L (1991) Lung function and bronchial reactivity in asthmatics during exposure to volatile organic compounds. Am Rev Respir Dis 143:751–754
17. Hasselblad V, Eddy DM, Kotchmar DJ (1992) Synthesis of environmental evidence: nitrogen dioxide epidemiology studies. J Air Waste Manage Assoc 42:662–671
18. Higgins BG, Britton JR, Chinn S, Jones TD, Jenkinson D, Burney PG, Tattersfield AE (1989) The distribution of peak expiratory flow variability in a population sample. Am Rev Respir Dis 140:1368–1372
19. Hultengren M, Axelsson I, Johnsson S, Rosen G (1992) Industrial surface coating of wood and associated health hazards. Exposure to formaldehyde and solvents during surface coating of wood with acid curing paints and laquers (in Swedish with summary in English). Arbete och Hälsa 23:1–15
20. Knox AJ, Wisniewski A, Cooper S, Tattersfield AE (1991) A comparison of the Yan and a dosimeter method for methacholin challenge in experienced and inexperienced subjects. Eur Respir J 4:497–502
21. Koren HS, Graham DE, Devlin RB (1992) Exposure of humans to volatile organic mixture. III. Inflammatory response. Arch Environ Health 47:39–44
22. Norbäck D, Edling C (1991) Environmental, occupational and personal factors related to the prevalence of sick building syndrome in the general population. Br J Ind Med 48:451–462
23. Norbäck D, Torgen M, Edling C (1990) Volatile organic compounds, respirable dust, and personal factors related to prevalence and incidence of sick building syndrome in primary schools. Br J Ind Med 47:733–741
24. Norbäck D, Björnsson E, Widström J, Ström G, Palmgren U, Janson C, Boman G (1993) Asthmatic symptoms in relation to volatile organic compounds (VOC) and bacteria in dwellings. In: Leslie G, Perry R (eds) Volatile organic compounds in the environment. Indoor Air International, Rotenfluh, Switzerland, pp 377–386
25. Norbäck D, Edling C, Wieslander G (1994) Asthma symptoms and the sick building syndrome (SBS) – the significance of microorganisms in the indoor environment. In: Samson RA, Flannigan B, Flannigan ME, Verhoeff AP, Adan OCG, Hoekstra ES (eds) Health implications of fungi in indoor environments. (Air quality monographs, vol 2) Elesvier, Amsterdam, pp 229–239
26. Norbäck D, Björnsson E, Janson C, Widström J, Boman G (1995) Asthmatic symptoms and volatile organic compounds, formaldehyde, and carbon dioxide in dwellings. Occup Environ Med 52:388–395
27. Norbäck D, Wieslander G, Ström G, Edling C (1995) Exposure to volatile organic compounds of microbial origin (MVOC) during indoor application of water-based paints. Indoor Air 5:166–170
28. Norbäck D, Wieslander G, Edling C (1995) Occupational exposure to volatile organic compounds (VOC) and other air pollutants from the indoor application of water based paints. Ann Occup Hyg 39:783–794.
29. Pazdrak K, Gorski P, Krakowiak A, Ruta U (1993) Changes in nasal lavage fluid due to formaldehyde inhalation. Int Arch Occup Environ Health 64:515–519
30. Peterson CGB, Enander I, Nystrand J, Andersson AS, Nilson L, Venge P (1991) Radioimmunoassay of human eosinophilic cationic protein (ECP) by an improved method. Establishment of normal levels in serum and turnover in vivo. Clin Exp Allergy 21:561–567
31. Platt SD, Martin CJ, Hunt SM, Lewis CW (1989) Damp housing, mould growth and symptomatic health state. Br Med J 298:1673–1678
32. Quackenboss JJ, Lebowitz MD, Michaud JP, Bronniman D (1989) Formaldehyde exposure and acute health effects study. Environ Int 15:169–179
33. Samet J (1990) Environmental controls and lung disease. Am Rev Respir Dis 142:915–939
34. Samet JM, Marbury MC, Spengler JD (1989) Health effects of indoor air pollution. II. Am Rev Respir Dis 137:221–242
35. Sears MR (1991) Epidemiological trends in bronchial asthma. In: Kaliner MA, Barnes PJ, Persson CG (eds) Asthma. Its pathology and treatment. Dekker, New York, pp 1–50
36. Sporik R, Holgate ST, Platts-Mills TEA, Cogswell JJ (1990) Exposure to house-dust mite allergen (der p I) and the development of asthma in childhood. N Engl J Med 323:502–507
37. Ulfvarson U, Alexanderson R, Dahlkvist M, Ekholm U, Bergström B, Scullman J (1992) Temporary effects from exposure to water-brone paints. Scand J Work Environ Health 18:376–387
38. Waegemakers M, Van Wageningen N, Brunekreef B, Bolsei JSM (1989) Respiratory symptoms in damp houses. Allergy 44:192–198
39. Wieslander G (1995) Water-based paints–occupational exposure and some health effects. Comprehensive summaries of Uppsala dissertations from the Faculty of Medicine, thesis 519. Acta Universitatis Upsaliensis, Uppsala
40. Wieslander G, Janson C, Norbäck D, Björnsson E, Stålenheim G, Edling C (1994) Occupational exposure to water-based paints and self-reported asthma, lower airway symptoms, bronchial hyperresponsiveness, and lung function. Int Arch Environ Health 66:261–267
41. Åberg N (1989) Asthma and allergic rhinitis in Swedish conscripts. Clin Exp Allergy 19:59–63