Relationship between selected indoor volatile organic compounds, so called microbial VOC, and the prevalence of mucous membrane symptoms in single family homes

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Abstract:

Micro-organisms are known to produce a range of volatile organic compounds, so-called microbial VOC (MVOC). Chamber studies where humans were exposed to MVOC addressed the acute effects of objective and/or subjective signs of mucosal irritation. However, the effect of MVOC on inhabitants due to household exposure is still unclear. The purpose of this epidemiological study was to measure indoor MVOC levels in single family homes and to evaluate the relationship between exposure to them and sick building syndrome (SBS). All inhabitants of the dwellings were given a self-administered questionnaire with standardized questions to assess their symptoms. Air samples were collected and the concentrations of eight selected compounds in indoor air were analyzed by gas chromatography/mass spectrometry - selective ion monitoring mode (GC/MS-SIM). The most frequently detected MVOC was 1-pentanol at a detection rate of 78.6% and geometric mean of 0.60 $\mu g/m^3$. Among 620 participants, 120 (19.4%) reported one or more mucous symptoms; irritation of the eyes, nose, airway, or coughing every week (weekly symptoms), and 30 (4.8%) reported that the symptoms were home-related (home-related symptoms). Weekly symptoms were not associated with any of MVOC, whereas significant associations between home-related mucous symptoms and 1-octen-3-ol (per $\log_{10}$-unit: odds ratio (OR) 5.6, 95% confidence interval (CI): 2.1 to 14.8) and 2-pentanol (per $\log_{10}$-unit: OR 2.3, 95% CI: 1.0 to 4.9) were obtained after adjustment for gender, age, and smoking. Associations between home-related symptoms and 1-octen-3-ol remained after mutual adjustment. However, concentrations of the selected compounds in indoors were lower than the estimated safety level in animal studies. Thus, the statistically significant association between 1-octen-3-ol may be due to a direct effect of the compounds or the associations may be being associated with other offending compounds. Additional studies are needed to evaluate these possibilities.

Key words: microbial volatile organic compounds (mvoc); exposure; indoors ; home

environment; sick building syndrome; mucous membrane; symptoms; questionnaires;

1. Introduction

Previous studies have reported a relationship between increasing dampness in indoor air and health complaints (Bornehag et al., 2001; Bornehag et al., 2004; Engvall et al., 2002; Saijo et al., 2004; Takeda et al., 2009). Although it is not known which dampness-related exposures are responsible for the effect on health, suggested causative agents are dust mite allergens, microbiological exposures and chemicals emitting from degradation of building materials (Bornehag et al., 2004). Ever since Wessen and Schoeps (1996) reported that the concentrations of 26 different compounds emitted from certain micro-organisms, called microbial volatile organic compounds (MVOC), were higher in indoor air than in outdoor air, an association between MVOC levels and health problems has been sought. Wieslander (2007) reported that the MVOC concentration was higher in buildings that had problems with dampness than in control buildings. Thus, these compounds may form a link between dampness and building related symptoms. However, compounds, so-called MVOC, are also emitted from plants, furniture, furnishing, and building materials (Konig et al., 1995; Korpi et al., 1999; Pasanen et al., 1998; Schleibinger et al., 2004). Previous studies failed to find any strong association between indoor mold status and MVOC (Schleibinger et al., 2005; Schleibinger et al., 2008).

The toxicological effects of compounds regarded as MVOC has been examined in human and animal experimental studies. 3-Methylfuran and 1-octen-3-ol are commonly produced by mold (Borjesson et al., 1992; Borjesson et al., 1993; Korpi et al., 1997; Matysik et al., 2008). In human chamber studies, these compounds caused acute effects, such as objective and/or subjective signs of mild mucosal irritation of the eyes and airways due to exposure (Wålinder et al., 2005; Walinder et al., 2008). According to one animal study, 1-octen-3-ol caused a 50% decrease in respiratory rate for mice, and at the same time, a mixture of several chemicals may have some synergistic effects. Concentrations of MVOC in indoor air are actually lower than in experimental studies. Median values of measured MVOC concentrations range from 1 ng/m^3 to 5 μg/m^3 in residential indoor air (Elke et al., 1999; Keller et al., 2006; Matysik et al., 2009). However, concentrations measured in experimental human studies are 1 and 10 mg/m^3 for 1-octen-3-ol and 3-methylfran, respectively, (Wålinder et al., 2005; Wålinder et al., 2008), while in animal studies they range from 58 to more than 10,000 mg/m^3 for 1-octen-3-ol, 3-octanol and 3-octanone (Korpi et al., 1999). These are higher than levels measured indoors. In the latest review of the scientific literature regarding MVOC, the most obvious health effect of MVOC exposure was eye and upper-airway irritation (Korpi et al., 2009), but the inflammatory effects of exposure to MVOC

indoors are suspicious due to the low level. In the same review, Korpi (2009) concluded that from both theoretical calculations and actual measured MVOC levels, irritation symptoms due to MVOC should not be expected. According to mouse bioassay data, the recommended indoor air level of 1-octen-3-ol was estimated at 100 $\mu g/m^3$ even though 1-octen-3-ol is more potent than the other compounds and its effect is stronger when combined with other compounds (Korpi et al., 1999). While in the home environment, inhabitants are exposed to much lower concentrations, they are also exposed to a mixture of several compounds for longer and repeated periods. Only a few limited studies measured MVOC together with health status in the field. Kim (2007) found that exposure to several MVOC at school was associated with asthmatic symptoms such as nocturnal breathlessness in pupils. Smedje (1996) reported that 2-methyl-iso-borneol, 2-methylfuran, 2-heptanone, and 1-octen-3-ol were significantly related to a history of asthma among school employees. Due to measured MVOC concentrations indoors being several magnitudes lower than actual safety levels, Smedje (1996) concluded that the relation to asthma and MVOC is due to exposure to microorganisms. There was only one study in a household setting. Elke (1999) reported that children living in dwellings with higher MVOC levels had a higher prevalence of asthma, hay fever, wheezing, and eye irritation, although the increases

were not statistically significant. Epidemiological studies on eye and upper-airway irritation in relation to MVOC in the home environment are lacking.

The objective of this study was to examine the concentration of selected MVOC in single family homes, and to determine if there was an association between these compounds and the prevalence of sick building syndrome (SBS) symptoms of the eye, nose, and airway irritation in the inhabitants of these homes. To distinguish between typically measured volatile organic compounds (VOC) in indoor air and so-called MVOC, selected compounds are described as MVOC in this study, whether or not these compounds are really derived from microorganisms.

2. Material and Methods

2.1. Study population

This study is based on a survey conducted in 2006; a partial second follow up study, where the measurements of MVOC were first performed. It is a cross-sectional study of 182 detached dwellings and their 624 inhabitants. The baseline questionnaire survey was conducted mainly in 2003, and the methodology has been described elsewhere (Kishi et al., 2009). Briefly, questionnaires were sent by post to 6080 single family houses, which were registered as having submitted a building plan approval

application within the past five years. The aim was to select buildings less than seven years old (construction year 1998-2003) in six regions of Japan; Sapporo, Fukushima, Osaka, Okayama and Fukuoka in 2003, and Nagoya in 2004. After excluding houses that were more than seven years post construction or questionnaires sent-back due to incorrect addresses, the number of valid questionnaires returned was 2297 (an overall response rate of 41%). In 2004, the owners of 425 houses (participation rate of 19%) agreed to home visits for environmental measurements to be taken and that all inhabitants of the home would answer health questionnaires. The association between chemical concentrations and subjective symptoms of SBS based on the 2004 survey has been reported elsewhere (Takigawa et al., 2010). The first follow-up study was conducted in 2005 and the owners of 270 houses (participation of 64%) agreed to participate. The second follow-up was conducted in 2006 and the owners of 182 houses (participation of 67%) agreed to participate.

2.2. Questionnaire

The personal questionnaire asked about the inhabitants' age, sex, number of hours spent in the house, recent allergies, current smoking history, and a set of questions for sick building symptoms. Recent allergy was defined as having taken either one or

more allergy medication(s) for bronchial asthma, atopic dermatitis, hay fever, allergic rhinitis, and / or allergic conjunctivitis at any time during the past two years. Symptoms of SBS were surveyed using the Japanese version (Mizoue et al., 2001) of standardized MM-questionnaires (Andersson, 1998). The questionnaire included symptoms in categories as follows: eye problems, nasal problems, dry throat, cough, dry/flushed skin, scaling/itching, dry hands, fatigue, heavy-headedness, headache, nausea/dizziness, and concentration problems. Each question had three alternative answers; “Yes, often (every week),” “Yes, sometimes,” and “No, never” in the three months period before answering the questionnaire. Each symptom question had a follow-up question that asked, “better when away from the dwelling” with answer choices of yes or no. In this study, when the inhabitants responded that there were experiencing symptoms frequently (every week), the result was counted as a positive “weekly symptom”. Furthermore, if the symptom was better when they were away from the dwelling, the result was defined as a positive “home-related symptoms.” To analyze the relationship between symptoms and building exposure, twelve symptoms were categorized in three groups as follows: eye problems, nasal problems, dry throat, and cough as mucous symptoms; dry/flushed skin, scaling/itching, and dry hands as skin symptoms; and fatigue, heavy-headedness, headache, nausea/dizziness, and

concentration problems as general symptoms. For inhabitants aged six to twelve years of age, the parents were asked to fill in all questions in co-operation with the child. For inhabitants aged younger than six years, the parents filled in the questions from observation, with the exception of general symptoms, which were left blank since it was not possible to assess the general symptoms by observation.

One dwelling questionnaire was distributed to each dwelling and the adult inhabitants were asked to complete it. The questionnaire included queries about environmental tobacco smoke, renovation within the past year, pets in the home, and dampness problems such as condensation on window panes and/or walls, visible mold growth within the dwelling, a moldy odor, high air humidity in the bathroom, and water leakage problems within the past five years. For building materials and the age of the building, baseline data from the 2003 survey were used.

Both personal and dwelling questionnaires were distributed and collected directly from an investigator who visited each dwelling.

2.3. Environmental Measurements

Indoor exposure measurements in each house were performed in a living room where all inhabitants commonly spent most of their time.

From previously reports (Elke et al., 1999; Schleibinger et al., 2005; Wessen and Schoeps, 1996), five major alcohols and three ketones were selected as the target compounds of MVOC to define the sampling rates. A MVOC measurement was conducted using the diffusive sampling method which was validated in advance (Araki et al., 2009). Briefly, air samples were continuously collected with carbon molecular sieves (ca. 300mg of Carboxen 564) -containing tube-type diffusive samplers, SUPELCO VOC-SD (Sigma-Aldrich, St. Louise, MO, USA) at 100 cm from the wall and 100-150 cm above the floor for 48 hours. Samplers were sealed in a container and sent at a temperature maintained at 4 ºC to Osaka Occupational Health Service Center, Japan Industrial Safety and Health Association (Osaka, Japan) for analysis. Samplers were prepared with 5% propan-2-ol /Carbon disulfide (CS_2), and then eight compounds (3-methyl-1-butanol, 1-pentanol, 2-pentanol, 2-hexanone, 2-heptanone, 3-octanol, 3-octanone, and 1-octen-3-ol) were identified and quantified using gas chromatography/mass spectrometry (GC/MS) (Hewlett Packard 630N/MSD) (Hewlett Packard Co., CA, USA). For MS analysis, the compounds were analyzed by the selected ion monitoring (SIM) mode. The sampling rate of each compound was 31 ml/min for 3-methyl-1-butanol and 3-octanol, 32 ml/min for 2-heptanone, 1-octen-3-ol, and 3-octanone, 33 ml/min for 2-penaton, and 35 ml/min for 1-pentanol and 2-hexanone.

The limit of detection (LOD) was 0.25 μg/m^3, and if concentrations were lower than LOD, they were considered half the LOD, which was 0.125 μg/m^3. The concentrations of the eight compounds were determined and summed are described as the "sum of 8 MVOCs" hereafter.

Formaldehyde and VOCs measurement was conducted using the method described by Takigawa (2004). Briefly, formaldehyde was collected with a 2,4-dinitrophenylhydrazine (DNPH)-coated silica cartridge, SUPELCO DSD-DNPH (Sigma-Aldrich, St. Louise, MO, USA). The VOCs were collected with SUPELCO VOC-SD (Sigma-Aldrich, St. Louise, MO, USA). Both samplers were placed in parallel with a sampler for MVOC. After 24 hours of air sampling, the sampler for formaldehyde was sent to Osaka Occupational Health Service Center, Japan Industrial Safety and Health Association (Osaka, Japan). Prepared samples with acetonitrile were analyzed using high-performance liquid chromatography equipped with a UV detector analysis (Hitachi D-7100, Hitachi Ltd., Tokyo, Japan). Samplers for VOC were sent to Kanto Occupational Health Service Center, Japan Industrial Safety and Health Association (Tokyo, Japan). Prepared samples with CS_2 were analyzed using GC/MS (Hewlett Packard 630N/MSD) (Hewlett Packard Co., CA, USA). If aldehydes and VOC concentrations were lower than the limit of detection (5 μg/m^3 and 10 μg/m^3,

respectively), they were considered half the LOD. The sum of concentrations of 29 determined VOCs (methylethylketone, ethylacetate, n-hexane, chloroform, 2,4-dimethylpentane, 1,2-dichloroethane, 1,1,1-trichloroethane, 1-butanol, benzene, carbon tetrachloride, 1,2-dichloropropane, trichloroethylene, n-heptane, methylisobuthylketone, toluene, chlorodibromomethane, buthylacetate, n-octane, tetrachloroethylene, ethyl benzene, xylene, styrene, n-nonane, α-pinene, trimethylbenzene, n-decane, p-diclorobenzene, limonene, and n-undecane) is described as the "sum of 29 VOCs" hereafter. Room temperature and relative humidity were measured with Thermo Recorder TR-72U (T & D Corporation, Nagano, Japan) in each house for 48 hours.

Fungal spore collection and analysis was performed as previously described by Takahashi (1997). Nine centimeter petri dish containing dichloran-18% agar (DG-18) with 100 μg/L chloramphenicol was attached to an AINEX BIO-SAS sampler (International PBI S.p.A., Milano, Italy) and airborne mold sampling was performed for a flow amount of 100 L/min for 1 minute, at a height of 150 cm above the floor. One sample was collected per house and determination and count of fungal species was conducted at Mitsubishi Chemical Medience Corporation (Tokyo, Japan). The number of all determined fungal colonies was described as "total fungi" and expressed as colony

forming units per cubic meter of air (CFU/m^3). To transform data to their logarithmic values, 0 CFU/m^3 for fungus was changed to 0.5 CFU/m^3.

To evaluate mite allergens, floor dust was collected from 1–4 m^3 area in each house with a paper filter attached vacuum cleaner (198 Watt, 0.60 m^3/min airflow rates) (HC-V15; National, Osaka, Japan) for 1 m^3/min. Samples were stored at –20 ºC in a plastic bag and sent to Nichinichi Pharmaceutical Co., Ltd. (Mie, Japan) where 5 mg of fine house dust sieved with 300 μm mesh was measured and *Dermatophagoides pteronyssinus* 1 allergen (Der p1) and *Dermatophagoides farinae* 1 allergen (Der f1) levels were determined using commercially available monoclonal antibody-based colorimetric enzyme-linked immunosorbent assays (ELISA) (Der p1 and Der f1 ELISA kits; Nichinichi Pharmaceutical Co., Ltd, Mie, Japan). The treatment of dust and the measurement of dust mite allergens was carried out using the method described by Ogino (2002). If allergen levels were lower than the limit of detection (0.1 g/g fine dust), they were considered 0.05 g/g fine dust. The sum of Der p1 and Der f1 determined is described as “mite allergen Der1” hereafter.

2.4. Data analysis

Each environmental valuable was $\log_{10}$-transformed before the analysis, since the distributions of the measured values were right-skewed. Possible associations between room characteristics as the independent variables and the transformed concentrations of MVOC were calculated using the t-test. The influence of dichotomous factors on the prevalence of symptoms was calculated from four-fold tables, and the probability (p) value was calculated by X^2 test for 2x2 contingency tables. Age was categorized as 15-year strata and the p value was calculated by Pearson's X^2 test. Relationships between environmental variables and symptoms were first calculated using the t-test, and then analyzed by the logistic regression method. For the logistic regression method, each $\log_{10}$-transformed environmental variable was introduced into the model separately, adjusted for sex (categorical variable, male as a reference), age strata (categorical variable, 0–14 year-old as a reference), and current smoking (categorical variables, not smoking as a reference). Finally, all environmental variables ($p<0.1$) were introduced into the model together and adjusted for sex, age strata and current smoking.

In all statistical analyses, two-tailed tests and a 5% level of significance were used. Calculations were performed using the Statistical Program for Social Sciences (SPSS Inc., Chicago, IL, USA) for Windows, version 14.0 J.

2.5. Ethics

The study protocol was approved by the ethical board for epidemiological studies at Hokkaido University Graduate School of Medicine and at all the regional universities involved in the study. This study was conducted with written informed consent from all subjects and parents.

3. Results

The original study protocol was prospective and the subjects in this study agreed to the environmental measurements being conducted over three years. To examine the potential selection bias, the characteristics of the building and inhabitants were compared to those who did not participate in the study. By using data from 2003, building characteristics, such as building structure, number of inhabitants, or the presence of condensation or visible mold growth, did not differ between those houses who participated in the study and those who did not, with the exception of building age, which was slightly lower, on average 0.54 years, for the houses in this study. Characteristics of the inhabitants in this study were also compared to those who did not participate by using data from 2004 and there were no significant differences with

regards to gender, age, or symptom prevalence (data not shown). Air and dust samples were collected at 182 single family houses. All homes were built in the previous three to eight years, and mean age±standard deviation of the buildings in 2006 was 5.3±1.4. The mean number of inhabitants was 3.5±1.2, and the mean population density (number of inhabitants / number of rooms) was 0.7±0.3. Table 1 shows the detection rate, GM, GSD, and maximum levels of the indoor concentrations of selected MVOC, and other environmental measurements. Although the sum of the 8 MVOCs or 29 VOCs is not values for assessment of biological effects, they are described as very crude measures of exposure levels. Dominant fungi detected in the houses were *Cladosporium genera*, *Aspergillus genera*, and *Penicillium sp.*, and the average indoor room temperature and relative humidity was 21.9±3.0 ^{o}C and 54.1±9.2%, respectively (data not shown).

Table 2 shows the differences in GM and GSD of MVOC and housing characteristics. Levels of 3-methyl-1-butanol, and sum of 8 MVOCs in houses with condensation on both the walls and window panes were higher than those without, and levels of 1-pentanol, 2-hexanone, 2-heptanone and sum of 8MVOCs in wooden structure houses were higher than other structure houses. However, visible mold growth and moldy odor were not related with the level of MVOC.

Six hundred and twenty four inhabitants living in the 182 dwellings answered the personal questionnaire. Six hundred and twenty participants completed the SBS questions and were included in the result. The prevalence of symptoms reported is shown in Table 3. Nasal problems were the most frequently reported with a weekly prevalence rate of 14.5%, and 3.9% when restricted to home-related symptoms. For categorized symptoms, the weekly prevalence rate of mucous symptom was 19.4%, whereas only 4.8% reported it as home-related.

The relationship between weekly and home-related mucous symptoms and personal and housing characteristics is shown in Table 4. Because weekly general symptoms and skin symptoms were not related to any of the environmental variables, and the prevalence of home-related general symptoms and skin symptoms was low, no further statistical examination was performed for skin or general symptoms. Relationships between mucous symptoms and environmental variable(s) are shown in Table 5,6, and 7. No further analysis was conducted for 3-octanol and 3-octanone, since the percentage below the detection limit was >90% for these two compounds. In a crude analysis, weekly mucous symptoms were significantly associated with 1-octen-3-ol positively and total fungi negatively. However, only the relationship with total fungi remained after being adjusted for multiple environmental variables. With

home-related symptoms, 1-Octen-3-ol showed a significant and 2-pentanol a borderline association after being adjusted for multiple environmental variables, and mite allergen Der1 also showed a significant relationship.

4. Discussion

This is the first study reporting the relationship between levels of MVOC in single dwellings and the prevalence of mucous symptoms of inhabitants of a wide range of ages. The result showed statistically significant associations between home-related mucous symptoms and 1-octen-3-ol, and these associations remained after mutual adjustment. Allergies were a strong predictor of mucosal symptoms in this study as has been previously reported (Skyberg et al. 2003). Our analysis included adjustment for allergies and the same trend was obtained (data not shown). For correlated factors, previously reported environmental factors related with SBS, such as formaldehyde, VOCs, fungi or dust might allergen (Cooley et al., 1998; Franchi et al., 2006; Garrett et al., 1998; Meyer et al., 2004; Takeda et al., 2009; Takigawa et al., 2009) were examined.

Total fungi showed negative relation with weekly symptoms and dust mite allergen showed a positive relation with home-related symptoms. In Kim's study

(2007), viable fungi was also negatively associated with symptoms and the author suggested the effect have come from window opening. As seen in Table 1, the few subjects were exposed to high level of Der1, and more than 10 μg/g of fine dust of Der p1 in infancy increased the relative risk of asthma (Sporik et al., 1990). However, associations between home-related symptoms and 1-octen-3-ol did not vary after mutual adjustment with Der1. Previous studies reporting associations between MVOC and health are compared with the results of this study in Table 8. MVOC exposure at school was associated with asthmatic symptoms including nocturnal breathlessness in pupils (Kim et al., 2007), or a history of asthma among school employees (Smedje et al., 1996). The range of MVOC concentrations in school studies were lower than those found in our study. Previous studies measuring MVOC level in houses by the diffusing sampling method were those by Elke (1999) and Matsysik (2009), and the range of MVOC concentrations was within a similar range to this study. The only study that looked into household exposure to MVOC and health outcome was that of Elke (1999). In Elke's study, children living in dwellings with higher MVOC levels had a higher prevalence of asthma, hay fever, wheezing, and irritation of the eyes, although none of these relationships were statistically significant.

In this study, the prevalence of not only home-related symptoms but also weekly symptom was analyzed since the effect of inflammatory response is slower to occur. However, only home-related symptoms were related with 1-octen-3-ol and 2-pentanol and the result suggested that the effect would be mainly sensory irritation. In a human experimental study (Walinder et al., 2008), the nasal lavage biomarkers were significantly increased after exposure, together with subjective symptoms of nasal irritation, throat irritation, eye irritation, headache, or nausea when volunteers were exposed to 10 mg/m^3 1-octen-3-ol. However, the concentrations of selected compounds measured in this study were far below the level considered to cause sensory irritation in experimental studies. Based on the mouse bioassay data, 100 $\mu g/m^3$ for 1-octen-3-ol was determined as the recommended indoor level (Korpi et al., 1999; Korpi et al., 2009; Pasanen et al., 1998). This is more than 100 to 1000 times higher than the level measured in this study. Therefore, additional studies to confirm the result are needed.

In this study, the concentration of MVOC was not related to visible mold or moldy odor, but related to wooden housing structure and condensation on walls and window panes. In the previous study, 1-octen-3-ol associated with inspected mold status; however, in only a small portion (Schleibinger et al., 2008) and there must be

other sources such as hidden mold growth due to condensation on walls (Small, 2003). The other possible emitting sources of selected compounds in indoor were the building materials themselves (Korpi et al., 1998; Pasanen et al., 1998). Levels of MVOC in wooden housing structure were higher than other structures, and all houses in this study had been constructed within eight years. The newest school building had the highest levels of total MVOC (Kim et al., 2007). If the selected compounds were emitted from building materials, it is not proper to call them microbial VOC (Korpi et al., 1998). Unfortunately, it was not possible to determine the exact emitting source of the selected compounds in the dwelling.

There are several limitations in this study. Firstly, the prevalence of mucous symptoms was not high. As described in the study population, the baseline selection of the subjects was population based. Consequently, the subjects of the study were basically healthy and the prevalence of symptoms was relatively low. A low prevalence may affect the results, especially when performing logistic regression with several covariates. However, the results obtained by crude data and adjusted data did not vary. Thus, despite the fact that the range of the 95% confidence interval for 1-octen-3-ol and home-related symptoms is relatively wide in Table 6, this was probably due to the small sample size, and thus the result is acceptable. Secondly, the original study protocol

was prospective and the subjects in this study agreed to conduct the environmental measurements for three years. Families who are willing to be involved in a study and open to extensive inspection tend to be those with more severe symptoms (Bornehag et al., 2006). The characteristics of the buildings and inhabitants in the present study were compared to those who did participate by using data from 2003 and 2004 and there were no significant differences. In addition, self-reported symptoms may change every year (Takigawa et al., 2009), so we used symptoms reported at the same time exposure measurements were collected. Therefore, any bias in the association between MVOC and symptoms is probably negligible. Thirdly, it had been suggested that to answer the questionnaire by observation can be difficult for small children. An analysis excluding preschool age children was also carried out and the same trend for all subjects was obtained. Therefore, all given results include small children. Another concern was that parents with health problems may also “give” their children health problems, and this could have led to an overestimate of the exposure risk. Only three children had problems similar to their parents, and therefore, the risk of over estimation in the prevalence of symptoms in children due to problem parents is small. Fourthly, the buildings studied were between three and eight years old. If these chemicals are emitted from microbes in the building, the affect of MVOC may be more severe in older

homes, which are more likely to have problems with dampness or mold (Kishi et al., 2009). Lastly, only eight MVOC were measured in this study. Indoor levels of MVOC were weakly correlated with each other (data not shown). It may be better to use more compounds to find houses with problems or associations to health. Therefore, compounds other than the selected eight may have been present and may have affected the inhabitants. One such example, 3-methylfuran, was reported to cause acute effects in mucous membranes in a human experimental study (Wålinder et al., 2005). Another such example, 2-ethylhexanol, is used as a solvent but is also derived from microorganisms (Nalli et al., 2006) and shares some chemosensory features with other long chain alcohols, such as 1-octanol. It caused irritation in one human experimental study (van Thriel et al., 2007).

In conclusion, this is a field study measuring indoor exposure levels of MVOC and mucous symptoms. The results of this study show that exposure to 1-octen-3-ol is associated with the self-reported prevalence of home-related mucous symptoms. Thus the existence of these compounds indoors was related to sensory irritation of nose, eyes, or throat mucous membrane and lowering the quality of life of the inhabitants. However, the concentration levels of the selected compounds were lower than estimated safety levels, and the prevalence was low. The statistically significant association

between 1-octen-3-ol may be due to a direct effect of the compounds or the associations may be due to these compounds being associated with other offending compounds. Additional studies are needed to evaluate these possibilities, which are important for establishing cause-effect relationships and the introduction of evidence based preventions.

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Tables

Table 1: Concentrations of indoor MVOC and other environmental variables (N=182)

	Detection rate[a] (%)	GM[b]	GSD[c]	Max
MVOC ($\mu g/m^3$)				
3-methyl-1-butanol	68.7	0.47	2.97	10.64
1-pentanol	78.6	0.60	3.01	12.15
2-pentanol	48.4	0.30	2.83	4.17
2-hexanone	70.9	0.32	2.06	2.56
2-heptanone	35.2	0.19	1.87	1.52
3-octanone	7.7	0.14	1.60	1.88
1-octen-3-ol	29.1	0.19	2.01	8.58
3-octanol	0			
Sum of 8 MVOCs	91.8	2.95	1.97	16.85
Formaldehyde ($\mu g/m^3$)	99.5	32.6	1.8	120.1
Sum of 29 VOCs ($\mu g/m^3$)	85.2	217.2	1.7	2821.3
Total fungi (CFU/m^3)	98.9	289.0	3.0	3490.0
Mite allergen Der1 (µg/g fine dust)	91.2	2.4	7.1	502.3

[a]Detection Rate is >LOD/total number of analyzed (%)

[b]GM is Geometric Mean, [c]GSD is Geometric Standard Deviation

Table 2: Differences in GM and GSD of MVOC and housing characteristics

		3-Methyl-1-butanol			1-Pentanol			2-Pentanol			2-Hexanone			2-Heptanone			3-Octanone			1-Octene-3-ol			Sum of 8 MVOCs		
	n	GM[a]	GSD[b]		GM[a]	GSD[b]		GM[a]	GSD[b]		GM[a]	GSD[b]		GM[a]	GSD[b]		GM[a]	GSD[b]		GM[a]	GSD[b]		GM[a]	GSD[b]	
Housing structure																									
wooden	144	0.49	2.95		**0.69**	3.03	**	0.31	2.82		**0.35**	2.05	**	**0.20**	1.93	**	0.14	1.65		0.20	2.06		**3.21**	1.95	**
others	35	0.38	2.96		**0.34**	2.43		0.24	2.84		**0.21**	1.83		**0.14**	1.46		0.13	1.39		0.16	1.75		**2.12**	1.84	
Building Age																									
3-5 years	128	0.47	2.94		0.58	3.07		0.30	2.89		0.32	2.10		0.18	1.87		0.14	1.56		0.19	1.92		2.93	2.00	
6-8 years	24	0.55	2.97		0.51	2.78		0.41	2.78		0.29	2.02		0.20	1.92		0.15	1.72		0.21	2.00		3.04	1.82	
Environmental tobacco smoke																									
yes	36	0.51	2.91		0.47	2.64		0.31	2.60		0.29	2.15		0.17	1.80		0.15	1.58		0.18	1.97		2.68	1.91	
no	146	0.45	2.99		0.64	3.08		0.29	2.90		0.33	2.04		0.20	1.89		0.14	1.60		0.19	2.02		3.01	1.99	
Renovation																									
yes	7	0.69	2.74		0.53	3.72		0.30	2.35		0.29	1.96		0.20	2.29		0.14	1.32		0.20	1.82		2.92	2.01	
no	175	0.46	2.98		0.60	2.99		0.30	2.86		0.32	2.07		0.19	1.86		0.14	1.61		0.19	2.02		2.95	1.97	
Condensation on walls and window panes																									
yes	6	**1.15**	2.20	*	1.44	5.17		0.60	3.88		0.49	1.88		0.34	3.14		0.18	2.35		0.31	2.22		**6.89**	1.83	**
no	175	**0.45**	2.96		0.59	2.93		0.29	2.79		0.32	2.06		0.19	1.82		0.14	1.57		0.18	1.99		**2.87**	1.94	
Visible mold growth																									
yes	140	0.48	3.03		0.64	2.89		0.30	2.81		0.32	2.02		0.19	1.84		0.14	1.57		0.19	2.05		3.01	1.96	
no	42	0.43	2.78		0.48	3.35		0.29	2.96		0.31	2.24		0.19	2.00		0.15	1.70		0.18	1.88		2.75	2.01	
Moldy odor																									
yes	37	0.53	3.02		0.60	3.13		0.25	2.57		0.33	2.00		0.19	2.03		0.13	1.13		0.17	1.70		2.83	2.07	
no	144	0.45	2.96		0.60	3.00		0.31	2.90		0.32	2.08		0.19	1.84		0.15	1.68		0.19	2.08		2.99	1.95	
High humidity in the bathroom																									
yes	35	0.46	2.97		0.58	2.65		0.34	2.90		0.30	2.08		0.17	1.66		0.15	1.82		0.18	1.87		2.77	1.99	
no	146	0.46	2.98		0.61	3.12		0.29	2.83		0.32	2.07		0.19	1.92		0.14	1.54		0.19	2.04		2.99	1.97	
Water leakage																									
yes	20	0.41	3.04		0.79	3.45		0.25	2.48		0.32	2.14		0.21	2.21		0.13	1.18		0.18	1.97		3.05	2.19	
no	161	0.48	2.96		0.58	2.96		0.30	2.89		0.32	2.06		0.19	1.83		0.14	1.64		0.19	2.02		2.95	1.95	
Housing pet																									
yes	60	0.45	3.23		0.52	2.74		0.29	2.60		0.29	1.92		0.17	1.74		0.15	1.66		0.17	1.82		2.69	1.96	
no	121	0.47	2.86		0.65	3.15		0.29	2.92		0.34	2.13		0.20	1.93		0.14	1.57		0.19	2.10		3.07	1.98	

Units: $\mu g/m^3$

P-values were calculated by Student t-test

**P*<0.05, **P*<0.01

[a]GM is Geometric Mean, [b]GSD is Geometric Standard Deviation

Table3: Prevalence of reported symptoms (N=620 except for general symptoms, where N=558)

	weekly symptoms		home-related symptoms	
	N	%	N	%
Mucous symptoms	120	19.4	30	4.8
itching, burning or irritation of the eyes	*27*	*4.4*	*5*	*0.8*
irritated, stuffy or runny nose	*90*	*14.5*	*24*	*3.9*
hoarse, dry throat	*27*	*4.4*	*10*	*1.6*
cough	*37*	*6.0*	*8*	*1.3*
Skin symptoms	55	8.9	8	1.3
dry or flushed facial skin	*16*	*2.6*	*3*	*0.5*
scaling/itching scalp or ears	*30*	*4.8*	*4*	*0.6*
hands dry, itching, red skin	*37*	*6.0*	*5*	*0.8*
General symptoms (only above school age)	99	16.0	6	1.1
fatigue	*81*	*13.1*	*5*	*0.9*
feeling heavy-headed	*23*	*3.7*	*2*	*0.4*
headache	*19*	*3.1*	*1*	*0.2*
nausea/dizziness	*7*	*1.1*	*0*	*0.0*
difficulties concentrating	*15*	*2.4*	*1*	*0.2*

Table 4: Association between mucous symptoms and personal and building characteristics

			weekly symptoms (n=120)		house-related symptoms(n=30)	
Predictors	denotations	n	Prevalence (%)	*P*	Prevalence (%)	*P*
Personal characteristics						
Gender	male	299	17.1	0.162	4.7	0.861
	female	321	21.5		5.0	
Age strata	0-14	159	23.9	0.073	7.5	0.057
	15-29	68	19.1		7.4	
	30-44	170	19.4		5.3	
	45-59	126	21.4		3.2	
	>60	96	9.4		0.0	
Resent allergies	yes	207	**30.9**	**<0.001**	**9.7**	**<0.001**
	no	398	**13.1**		**2.5**	
Current smoking	yes	56	23.2	0.443	5.4	0.850
	no	564	19.0		4.8	
Duration spend in the dwelling	17hour and more	219	17.8	0.481	3.7	0.297
	less than 17hours	397	20.2		5.5	
Building characteristics						
Housing Structure	Wooden	438	19.7	0.851	5.2	0.512
	others	132	18.9		3.8	
Building age	3-5 years	537	18.8	0.297	4.5	0.240
	6-8 years	80	23.8		7.5	
Environmental tobacco smoke	yes	128	22.7	0.289	5.5	0.709
	no	492	18.5		4.7	
Renovation	yes	23	**39.8**	**0.014**	13.0	0.062
	no	597	**18.6**		4.5	
Visible moulds growth	yes	499	20.4	0.165	5.4	0.178
	no	121	14.9		2.5	
Condensation on walls and window panes	yes	22	22.7	0.689	4.5	1.000
	no	596	19.3		4,9	
Moldy odor	yes	121	20.7	0.676	3.3	0.372
	no	495	19.0		5.3	
High air humidity in the bathroom	yes	124	16.1	0.319	6.5	0.357
	no	493	20.1		4.5	
Water leakage within 5 years	yes	71	15.5	0.374	1.4	0.237
	no	547	19.0		5.3	
pets in the dwelling	yes	212	18.9	0.770	4.7	1.000
	no	403	19.9		5.0	

P-values were calculated by X^2 test

Table 5: Mucous symptom prevalence and each environmental variable

		weekly symptoms				home-related symptoms			
		n	GM	GSD	*P*	n	GM	GSD	*P*
MVOC (μg/m^3)									
3-methyl-1-butanol	yes	120	0.49	2.89	0.428	30	0.60	2.43	0.101
	no	500	0.45	2.94		590	0.45	2.95	
1-pentanol	yes	120	0.59	3.20	0.734	30	0.80	3.16	0.157
	no	500	0.61	2.99		590	0.60	3.02	
2-pentanol	yes	120	0.33	2.82	0.156	30	0.41	2.72	0.062
	no	500	0.28	2.79		590	0.29	2.80	
2-hexanone	yes	120	0.34	2.17	0.388	30	0.38	2.37	0.169
	no	500	0.32	2.06		590	0.32	2.07	
2-heptanone	yes	120	0.20	1.89	0.468	30	0.21	2.17	0.522
	no	500	0.19	1.85		590	0.19	1.84	
1-Octene-3-ol	yes	120	**0.21**	**2.00**	**0.017**	30	**0.30**	**2.28**	**0.002**
	no	500	**0.18**	**1.99**		590	**0.18**	**1.96**	
Sum of 8 MVOCs	yes	120	3.03	1.99	0.519	30	3.68	1.98	0.058
	no	500	2.90	1.97		590	2.89	1.97	
Formaldehyde (μg/m3)	yes	120	33.10	1.90	0.736	30	37.10	1.90	0.237
	no	500	32.50	1.90		590	32.40	1.90	
Sum of 29 VOCs (μg/m3)	yes	120	226.50	1.90	0.269	30	219.00	1.70	0.537
	no	500	211.60	1.60		590	214.10	1.70	
Total fungi (CFU/m^3)	yes	120	**216.9**0	**3.2**0	**0.001**	30	202.20	4.50	0.157
	no	500	**320.4**0	**2.8**0		590	302.90	2.80	
Total mite allergen Der1	yes	119	2.13	6.31	0.844	30	3.11	4.73	0.227
(μg/g fine dust)	no	496	2.05	6.87		585	2.02	6.85	

Table 6: Association between mucous symptoms and each environmental variable.

	weekly symptoms			Home-related symptoms		
	OR (95%CI)		*P*	OR (95%CI)		*P*
MVOC						
3-methyl-1-butanol	1.2	(0.8-1.9)	0.354	1.9	(0.9-4.2)	0.102
1-pentanol	0.9	(0.6-1.4)	0.614	1.6	(0.7-3.6)	0.230
2-pentanol	1.5	(0.9-2.3)	0.093	**2.3**	**(1.0-4.9)**	**0.039**
2-hexanone	1.2	(0.6-2.3)	0.561	1.9	(0.6-6.1)	0.294
2-hepanone	1.3	(0.6-2.7)	0.516	1.6	(0.4-5.6)	0.493
1-octen-3-ol	**2.0**	**(1.1-3.7)**	**0.029**	**5.6**	**(2.1-14.8)**	**<0.001**
Sum of 8 MVOCs	1.3	(0.6-2.5)	0.486	3.2	(0.9-11.1)	0.061
Formaldehyde	1.1	(0.5-2.2)	0.860	2.0	(0.5-7.8)	0.333
Sum of 29 VOCs	2.1	(0.9-4.9)	0.085	1.8	(0.4-8.6)	0.455
Total fungi	**0.5**	**(0.3-0.7)**	**0.001**	0.5	(0.2-1.0)	0.066
Mite allergen Der1	1.1	(0.9-1.4)	0.379	1.6	(1.0-2.5)	0.061

Each variable was introduced separately in the logistic regression model and adjusted for sex, age category and current smoking.

Odds ratios were calculated using $\log_{10}$-transformed variables.

Table 7: Association between mucous symptoms and multiple environmental variables.

	weekly symptoms			home-related symptoms		
	OR (95%CI)		*P*	OR (95%CI)		*P*
2-Pentanol	1.3	(0.8-2.0)	0.353	2.1	(0.9-4.9)	0.087
1-Octen-3-ol	1.4	(0.7-2.8)	0.293	4.6	(1.7-12.9)	0.004
Sum of 29 VOCs	1.4	(0.6-3.5)	0.486	-		
Total Fungi	0.5	(0.3-0.8)	0.004	0.6	(0.3-1.4)	0.248
Der 1	-			1.7	(1.0-2.7)	0.042

All variables were introduced in the logistic regression modal together and adjusted for sex, age category and current smoking.

"-" was not introduced into the model because of p>0.1 in Table 6.

Table 8: Association between exposure to MVOC and symptoms

Study	Subject	Sampling method	Range of MVOC concentration	Results
Experimental studies				
Wålinder. et al., 2005 (Sweden)	20–54 years old volunteers, n=29	experimental chamber exposure	3-methylfuran 1 mg/m^3 or clean air, 2 hours	Acute effects in the eyes, nose, and airways were detected during exposure to 3-methylfuran.
Wålinder. et al., 2008 (Sweden)	20–54 years old volunteers, n=29	experimental chamber exposure	1-octen-3-ol 10 mg/m^3 or clean air, 2 hours	Objective and subjective signs of mild mucosal irritation of eyes and airways together with symptoms of headache and nausea
Field studies				
Smedje et al., 1996 (Sweden)	school employees, n=1410	active sampling at school exposure	3-methyl-1-butanol: 150 ng/m^3 (mean) 1-octen-3-ol: 48 ng/m^3 (mean) 3-methylfuran: 4 ng/m^3 (mean)	3-methylfuran, 2-heptanone, 1-octen-3-ol, 2-methyl-iso-borneol were positively associate with asthma adjustment for those who had repainted their home recently or felt that their work was stressful
Kim et al., 2006 (Sweden)	5–14 years old school children, n=1014	active sampling 0.25l/min for 4 h at school exposure	3-methyl-1-butanol: 95 ng/m^3 (mean) 1-octen-3-ol: 53 ng/m^3 (mean) 2-hexanone: 39 ng/m^3 (mean)	3-methyl-1-butanol, 2-methyl-1-butanol,1-octen 3-ol, 2-heptanone, 3-methylfuran, were positively associate with nocturnal breathlessness adjusted for age and gender
Elke et al., 1999 (Germany)	5–7 years old children n=132	diffusive sampling 4 weeks at home exposure	3-octanol: w/ mold 4.6 μg/m^3 (GM)[a)] w/o mold 1.8 μg/m^3 (GM) 3-methyl-1-butanol: w/ mold 1.3 μg/m^3 (GM) w/o mold 0.7 μg/m^3 (GM) 2-hexanone: w/ mold 0.2 μg/m^3 (GM) w/o mold 0.1μg/m^3 (GM)	higher MVOC levels had a higher prevalence of asthma, hay fever, wheezing, and irritations of eyes, (not significance) adjusted for age, gender, BMI, number of siblings, social status, passive smoking, type of heating, ventilation habits
Present study	all inhabitants (0–92 years old) n=620	diffusive sampling 48 hours at home exposure	3-methyl-1-butanol: 0.47 μg/m^3 (GM) 2-pentanol: 0.30 μg/m^3 (GM) 2-hexanone: 0.32 μg/m^3 (GM) 1-octen-3-ol: 0.19 μg/m^3 (GM)	2-pentanol and 1-octen-3-ol were positively associate with a prevalence of mucous symptoms in the house adjusted for age, gender, and allergy

[a], w/: with, w/o: without,
GM is Geometric Mean