Int Arch Occup Environ Health (1999) 72: 451–461 © Springer-Verlag 1999

ORIGINAL ARTICLE

G. Wieslander · D. Norbäck · K. Nordström
R. Wålinder · P. Venge

Nasal and ocular symptoms, tear film stability and biomarkers in nasal lavage, in relation to building-dampness and building design in hospitals

Received: 5 February 1999 / Accepted: 25 May 1999

Abstract ***Objectives:*** To study the relationships between dampness in concrete floors and building design on the one hand, and symptoms and medical signs of the eyes and nose in hospital workers, on the other. ***Methods:*** Four hospitals for geriatrics were selected to represent buildings with different ages and design, irrespective of symptom prevalence. The first building was built in 1925.The second, built in 1985, was known to have dampness in the floor. Conventional building techniques were used in the third building, built in 1993, and the last building was built in 1994, and was specially designed to include high ceilings, and minimal use of fluorescent lighting and interior plastic materials. The interior surfaces were painted with water-based beeswax glazing. All staff ($n = 95$) working day shifts were invited to take part in a medical examination of the eyes and nose including acoustic rhinometry and nasal lavage, and a medical questionnaire, and 93% participated. Measurements of temperature, relative air humidity, air flow, illumination, volatile organic compounds (VOCs), molds, and bacteria were carried out in all buildings, together with measurements of formaldehyde, respirable dust, carbon monoxide (CO), carbon dioxide (CO_2), nitrogen dioxide (NO_2) and ozone. Statistical analyses were performed by bivariate analysis, and linear, ordinal, and logistic multiple regressions, adjusting for age, gender, tobacco smoking, atopy, and the perceived psychosocial work environment. ***Results:*** Dampness in the upper concrete floor surface (75–84%), ammonia under the floor [3 parts per million (ppm)], and 2-ethyl-1-hexanol in the air were detected in the two buildings built in 1985 and 1993. Increased occurrences of ocular and nasal symptoms, an increased concentration of lysozyme in nasal lavage, and decreased tear film stability were found in the subjects working in the damp buildings. Those in the specially designed building had fewer ocular and nasal symptoms, and increased tear film stability. All buildings had low levels of formaldehyde, molds, bacteria, ozone, and NO_2. The lowest total concentration of VOCs, and the highest concentration of specific VOCs of microbial origin, were found in the building with special design. ***Conclusion:*** The study provides new evidence of the role of dampness-related alkaline degradation of di-(2-ethylhexyl) phthalate (DEHP) in polyvinyl chloride (PVC) building material. Emissions related to degradation of DEHP due to dampness in the floor, indicated by increased 2-ethyl-1-hexanol in the air, seem to increase both the secretion of lysozyme from the nasal mucosa and the occurrence of ocular and nasal symptoms. The indoor environment of the specially designed building with high ceilings and no fluorescent lighting or interior plastics seemed to have a positive influence on the nasal and ocular mucous membranes.

Key words Acoustic rhinometry · Building-dampness · Di-(2-ethylhexyl) phthalate · Indoor air pollution · 2-Ethyl-1-hexanol · Hospital workers · Lysozyme · Nasal lavage · Sick Building Syndrome

G. Wieslander (✉) · D. Norbäck · K. Nordström · R. Wålinder
Department of Medical Sciences,
Department of Occupational and Environmental Medicine,
University Hospital, Uppsala University,
S-751 85, Uppsala, Sweden
e-mail: gunilla.wieslander@occmed.uu.se
Tel.: +46-18-663655; Fax: +46-18-519978

P. Venge
Department of Clinical Chemistry and Asthma Research Centre,
Uppsala University Hospital, S-751 85 Uppsala, Sweden

Introduction

Disorders that have been associated with indoor air pollution include asthma, allergies, and non-specific symptoms from the eyes, upper airways and facial skin (Kreiss 1989; Norbäck 1997). These non-specific symptoms are sometimes referred to as the sick building syndrome (SBS). The SBS concept was established from observations that the occurrence of a certain type of symptom was increased in problem buildings (Apter

et al. 1994). Several epidemiological questionnaire studies on SBS have been published, relating SBS to both personal factors and the indoor environment (Apter et al. 1994; Hodgson 1995a, b; Mendell 1993). Recently, the concept of SBS has been criticized as unspecific (Järvholm 1993; Hodgson 1995a), and a subclassification of SBS depending on the type of symptoms has been suggested (Mølhave 1989; Järvholm 1993; Hodgson 1995a). Objective evaluations, aiming to study the relationship between SBS-symptoms and clinically diagnosed bronchial hyperresponsiveness and skin prick tests have been applied, with conflicting results (Björnsson et al. 1998; Muzi et al. 1998).

Recently, objective methods to study environmental effects on the eyes and upper airway have been developed. The application of these methods in epidemiological studies may increase the understanding of the etiology and cellular mechanisms behind symptoms observed in SBS. Measurement of tear film break up time (BUT), as well as self-reported break-up time [BUT(s)] have been made in studies in offices and hospitals, and experimentally (Franck et al. 1993; Wyon 1992; Wyon and Wyon 1987). Stability of the tear film measured by BUT was reduced in office workers in a sick building (Muzi et al. 1998). Acoustic rhinometry has been used to measure patency (Jessen and Malm 1997; Wålinder et al. 1998, 1999). Nasal lavage is a well-documented technique used to study inflammatory effects in the nasal mucosa related to inhalatory exposure (Wilcosky 1993; Wålinder et al. 1998, 1999). Experimental studies using nasal lavage have shown that there are many possible biomarkers, including tryptase, albumin, lysozyme, eosinophilic cationic protein (ECP) emitted from the granula of activated eosinophil granulocytes, and myeloperoxidase (MPO) from activated neutrophil granulocytes (Pipkorn et al. 1989; Raphael et al. 1989). A relationship between poor cleaning routines (Wålinder et al. 1999), low air exchange rate (Wålinder et al. 1997; Wålinder et al.1998), mechanical ventilation (Wålinder et al. 1998) and increased concentrations of ECP and lysozyme in nasal lavage has recently been demonstrated.

Earlier questionnaire studies have demonstrated a relationship between damp housing conditions and both SBS and asthma symptoms (Flannigan and Miller 1994; Husman 1996). There are various types of exposure related to building-dampness, including house dust mites, molds and bacteria. Building-dampness may also increase the emission of volatile organic compounds (VOCs) from the building, due to degradation of building material or to microbial activity. Dampness in concrete floors is known to cause chemical degradation of plasticizers in polyvinyl chloride (PVC) floor coatings and glues, with the emission of ammonia and 2-ethyl-1-hexanol (Gustavsson and Lundgren 1997). Other VOCs, such as 1-octen-3-ol and 3-methylfuran can be produced by microorganisms in damp buildings (Ström et al. 1993). To our knowledge, there is sparse information on clinical signs from the eyes or nose in relation to objectively verified building-dampness.

Today, there is concern about the health aspects of building design, and some studies have shown a higher prevalence of SBS-symptoms in newer buildings (Skov and Valbjørn 1987; Nordström et al. 1995b). Questionnaire studies have shown that higher ventilation rates can reduce symptom prevalence (Norbäck et al. 1997). In addition, a lower degree of nasal patency as measured by acoustic rhinometry (Wålinder et al. 1997), and increased levels of ECP and lysozyme in nasal lavage, was found in individuals in schools with low air exchange rates (Wålinder et al. 1998). Other studies have found that SBS is influenced by the type of ventilation system, with a low occurrence of symptoms in poorly ventilated buildings with natural ventilation, and higher prevalence of SBS in buildings with mechanical supply air systems (Wålinder et al. 1998). In addition, there is concern about the environmental aspects of buildings, with the aim of producing buildings compatible with a sustainable development. This debate has inspired architects to select specific materials or designs, aiming for low emissions of chemical pollutants and a more recyclable building. There is, however, little knowledge of the health aspects of the indoor environment in buildings with such special design.

The aim of the investigation was to study the occurrence relationship between tear film stability, nasal mucosal swelling and lavage biomarkers, nasal and ocular symptoms, and the indoor environment in hospitals of different ages and design. The following hypotheses were tested: Tear film stability, nasal mucosal swelling and lavage biomarkers, and nasal and ocular symptoms, are related to building age, building-dampness, ventilation, and special building design. The protocol of the study was approved by the Ethical Committee of the Medical Faculty of Uppsala University.

Material and methods

Study population

The study was performed in the municipality of Ystad in southern Sweden, with 25,000 inhabitants and eight separate geriatric hospital units. In Sweden nowadays, geriatric health care for people with chronic diseases, is provided in small geriatric hospital units and not in the larger hospitals with in-patient beds. Four of these were included in the study, to represent buildings with different ages and design, irrespective of the occurrence of symptoms. The first building was built in 1925, and redecorated in 1955. The second was built in 1985, and was known to have dampness problems in the floor. The third was conventionally built in 1993 with and the last building was constructed by an anthroposophic society in 1994, with special design and building materials and using hospital staff recruited from the ordinary labor market. Wood was frequently used and plastics and fluorescent lighting were avoided. The ceilings were high and special indoor paints were used.

Identification of the subjects was made from current lists of employees and the study population ($n = 95$) consisted of all daytime staff in the four buildings. They were invited to take part in a medical investigation of the eyes and nose including acoustic rhinometry and nasal lavage, and two medical questionnaires. In total, 88 out of 95 subjects (93%) participated. The investigation was performed simultaneously in all four buildings during the last

week in January and the first week in February 1997, out of the pollen season. Since some effects of the mucous membranes may be transient, all medical examinations were performed at the workplace. To achieve maximum indoor exposure all subjects had been at their workplace for at least one hour prior to examination. Those having a current infection or fever or who were on vacation during the past 7 days were asked to come to a follow-up investigation two weeks later.

Assessment of personal factors and nasal or ocular symptoms

Two medical questionnaires were used, the first being self-administered, and was developed by the Department of Occupational Health in Örebro (Andersson 1998). The current version (MM040NA) has been used in subsequent hospital studies (Nordström et al. 1994, Nordström et al. 1995a) and in the large Office Illness Study in northern Sweden (Stenberg et al. 1993; Sundell et al. 1993). It contains questions on SBS, including one question on weekly eye symptoms, and another on weekly nasal symptoms, with a recall period of 3 months. There were also four questions on psychosocial factors in the MM040NA questionnaire. The question involving "interesting/stimulating work" measured work satisfaction, while "too much work to do" covered stress. The "opportunity to influence working conditions" measured the degree of personal influence experienced by the subject, and "help from colleagues" measured social support. There were four possible answers: "yes, often", "yes, sometimes", "no, seldom" and "no, never". Each of the variables was assigned an index value, 3, 2, 1, or 0 respectively, according to the answer. In addition, a psychosocial dissatisfaction index (PSD) was calculated by forming a total sum of the four indices (0–12).

All participants were questioned by a physician about previous diseases, allergies and atopy, smoking habits, social status, medication and occupation. Atopy was defined as having a current history of allergic manifestations related to exposure to common IgE-mediated allergens in Sweden (tree or grass pollen, or furry animals) or a history of childhood eczema, reported in the medical interview. More detailed information on nasal and ocular symptoms during the week prior to the medical investigation was gathered by means of another questionnaire answered during the medical investigation (Wålinder et al. 1998). It included questions on the home environment, infections, and symptoms noticed in the 7 days prior to examination. Also included were six "yes/no" questions on ocular symptoms and four on nasal symptoms. A nasal symptom index (0–4) and an ocular symptom index (0–6) were calculated, by adding the number of "yes" answers.

Assessment of clinical signs from the eyes

Tear film stability was estimated by a standardized method, self-reported BUT [BUT(s)] measuring the length of time that the subject could keep the eyes open without pain when watching a fixed point on the wall. The method has been used previously and has been shown to correlate well with the fluorescein method for the detection of tear film BUT (Wyon 1992; Wyon and Wyon 1987).

Acoustic rhinometry

Acoustic rhinometry (Rhin 2000; wideband noise; continuously transmitted) was performed in the office, and each individual had been at the workplace for at least 1 h prior to the examination. The measurements were made under standardized conditions (sitting), after 5 min of rest, and prior to the lavage. By means of acoustic reflection the minimum cross-sectional areas (MCA) on each side of the nose were measured from 0 and 22 mm (MCA1) and from 23 and 54 mm (MCA2) from the nasal opening. The volumes of the nasal cavity on the right and left sides were also measured from 0 and 22 mm (VOL1) and from 23 to 54 mm (VOL2). The mean values were calculated from three subsequent measurements on each side of the nose. Data on nasal dimensions in the present study are presented as the sum of the values recorded for the right side and for the left.

Nasal lavage

Lavage of the nasal mucosa was done with a 20 ml plastic syringe attached to a nose olive. Each subject stood with head flexed ca. 30° forward, while the room-tempered (20–22 °C) 0.9% sterile saline solution was introduced into the nasal cavity. Each nostril was lavaged with 5 ml of the solution, which was flushed back and forth five times via the syringe at intervals of a few seconds. The fluid was transferred into a 10 ml polypropylene centrifuge tube. Samples were kept on ice and within 300 min the solution was centrifuged at 800 g for 5 min. The supernatant was recentrifuged at 1,400 *g* for 5 min and frozen immediately to −20 °C.

Lysozyme was analyzed by radioimmunoassay (Venge et al. 1979). The concentrations of ECP and MPO were measured by means of a double-antibody radioimmunoassay (Pharmacia Diagnostics AB, Uppsala, Sweden) (Peterson et al. 1991; Schmekel et al. 1990). The intra- and interassay coefficients of variation for all three tests were less than 11%. Albumin was measured by rate nephelometry on an Array protein system (Beckman Instruments).

Assessment of exposure

The technical investigation was composed of a building survey and technical measurements. In the survey information was gathered on building age, types of building material, types of ventilation system, signs of dampness, and smoking restrictions in the building. The measurements included dampness in the upper layer of the concrete floor, room temperature, relative air humidity, exhaust air flow, illumination, indoor levels of carbon monoxide (CO), carbon dioxide (CO_2), nitrogen dioxide (NO_2), ozone, formaldehyde, total VOC, specific VOCs, and both viable and total concentration of molds and bacteria. Specific VOCs evaluated in this study included 2-ethyl-1-hexanol, 1-octen-3-ol, and 3-methylfuran. Ozone, and VOCs, were also measured outside the buildings. Exposure measurements with direct-reading instruments and pumped-air sampling were made on two different days in each building. Ozone, CO, CO_2 and NO_2 were measured by diffusion-sampling for 7 days. All measurements were performed in January-February 1997, 1–2 weeks after the medical investigations were completed.

The moisture content in the upper concrete floor surface was measured with a Waisala moisture instrument with probe HMP36. The instrument was calibrated with a solution of potassium aluminum silicate ($KAlSiO_4$) and sodium chloride (NaCl). Dampness in the floor was also indicated by a direct-reading dampness indicator. Measurements of room temperature and relative air humidity were performed by a thermohygrograph (CASELLA T 9420) for 2 weeks in each building. The thermohygrograph was calibrated by comparison with a sling psychrometer. The exhaust air flow was measured in fifteen hospital rooms in each building by thermoanemometer (ALNOR GGA 65P), calibrated by the Swedish National Institute of Building Research prior to being used. The illumination was measured by a Hagner instrument in ten places in each building.

Indoor CO and CO_2 were measured by direct-reading detector tubes from Draeger (50a-D and 1%/a-D). Indoor NO_2 was sampled with a diffusion sampler (Toyo Roshi Kaisha, Japan), and analyzed spectrophotometrically. An overall mass transfer coefficient of 0.10 cm/s was used in the calculations as suggested by Lee et al. 1993. Ozone was measured with another diffusion sampler from IVL, Sweden (Ferm and Svanberg 1998).

Indoor concentrations of formaldehyde were measured with glass fiber filters impregnated with 2,4-dinitrophenylhydrazine (Andersson et al. 1981), the air sampling rate being 0.2 l/min over 6 h. The filters were analyzed by liquid chromatography.

Volatile organic compounds, other than formaldehyde, were sampled in parallel on two charcoal sorbent tubes (Anasorb 747; SKC 226–81), with the same sampling time and rate as for formaldehyde. One charcoal tube was desorbed with 1 ml of carbon disulfide: It was analyzed for total VOC and specific VOCs, including 2-ethyl-1-hexanol. Specific VOCs were analyzed by means of a Hewlett Packard 5890 gas chromatograph equipped with a mass-selective detector (HP 5970) (GC-MS), using a 50 m cross-linked methyl silicone capillary column (HP-1, Hewlett Packard) with an inner diameter of 0.32 mm and a film thickness of one μm. The oven temperature was programmed for an initial hold of 5 min at 35 °C after which the temperature was increased to 200 °C at a rate of 15 °C min^{-1}. Carrier gas (helium) flow rate was 1 ml min^{-1}. A mass spectrum and the retention time were determined for each compound. The concentration of 2-ethyl-1-hexanol was determined by external standard techniques using a desorption efficiency of 76% reported for the actual desorption conditions.

Total VOC was determined on a gas chromatograph (Hewlett Packard 5880A) equipped with a packed non-polar column, and flame ionization detector (FID). The total concentration of volatile organic compounds (TVOC) below *n*-dodecane (C12) was calculated assuming the same response rate as for *n*-decane (decane-equivalents).

To detect possible hidden microbial growth in the buildings, VOCs of possible microbial origin (MVOCs) were determined by selective ion monitoring (SIM) by a previously described method (Ström et al. 1993). One additional charcoal tube (Anasorb 747) was desorbed by 2 ml of methylene chloride. The following ten compounds were measured: 3-methylfuran, 3-methyl-1-butanol, 2-pentanol, 2-pentanone, 2-hexanone, 2-heptanone, 3-octanone, 3-octanol, 1-octen-3-ol, dimethyldisulfide. The total concentration of the ten selected MVOCs (TMVOC) was also calculated, by adding the concentrations of detected MVOCs.

Airborne microorganisms were sampled on 25 mm Nucleopore filters with a pore size of 0.4 μm and a sampling rate of 1.5 l/min for 6 h. The total concentration of airborne molds and bacteria, respectively, was determined by the CAMNEA method (Palmgren et al. 1986). Viable molds and bacteria were determined by incubation on two different media. The detection limit for viable organisms was 100 colony-forming units (cfu) per m^3 of air.

Statistical analysis

Analyses of relationships between symptoms, clinical signs, and exposure were performed with both crude, bivariate analysis and multiple linear, ordinal, and logistic regression analysis. The chi-square-test, or Fisher's exact test was used, depending on the number in the cells, when analyzing the relationship between binary dependent and independent variables. Kendall's rank-correlation test (tau-beta) was used for the bivariate analysis of continuous variables, and the Mann-Whitney U-test for the dichotomized variables.

Multiple regression analysis was applied for the control of potential confounders: age, gender, smoking habits, atopy and psychosocial index, by using the SPIDA statistical package, (Statistical Laboratory, Macquarie University, Australia) (Gebski et al. 1992). Multiple logistic regression was applied when ocular and nasal symptoms during the last 3 months was the outcome variable. Multiple ordinal regression was used for the indices of ocular and nasal symptoms during the past week, while multiple linear regression was used for the rhinometric values, nasal lavage data, and BUT. Residual plots were made in the linear regression models, to ensure that the residuals were approximately normally distributed. Collinearity diagnostics available in SPIDA were applied for linear and logistic regression. As suggested, a conditioning index exceeding 30 was used as an indicator of collinearity problems in the linear regression models. For logistic regression, the program uses a method described by Belsey (Belsey 1991) in which a condition index exceeding 20 was used as an indicator of collinearity problems. Adjusted partial regression coefficients, with 95% confidence intervals (CI), were calculated. In all statistical analyses, two-tailed tests and a 5% level of significance were applied.

In the multiple logistic, ordinal or linear regression analysis, each exposure variable was introduced in the model separately, adjusting for potential confounders (age, gender, atopy, smoking habits, and PSD-index. In these models, no collinearity problems were detected, and the residuals of the linear regression models were approximately normally distributed.

Results

Personal factors, symptoms and signs

The majority of the subjects were women: 16% had hay fever, one third had a history of atopy and 8% had doctor's diagnosed asthma. The mean age was 45 years [standard deviation (SD) = 12]. If the "yes, often" and "yes, sometimes" alternatives were grouped together for the psychosocial scales, the following figures were obtained (Table 1). The average PSD index was 4.4; 3.8; 3.9 and 3.0 in buildings A; B; C and D respectively. These differences were not statistically significant.

In all subjects, the 3-months prevalence of weekly symptoms from the eyes and nose was 36% and 26% respectively. The 7-days prevalence of at least one nasal and one ocular symptom was 66% and 54% respectively (Table 2). Subjects showed great differences in symptom prevalence between buildings. Data on tear film stability, rhinometry, and biomarkers in nasal lavage in all subjects are shown in Table 3. The concentrations of biomarkers were above the detection limits in most cases except for albumin. Subjects reporting weekly ocular

Table 1 Prevalence of personal factors and self-reported psychosocial climate in the four buildings

Factor	Building				Total (n = 88)
	A (n = 15)	B (n = 32)	C (n = 18)	D (n = 23)	
Female	100	97	89	96	95
Atopy	14	33	41	30	31
Current smoking	14	34	22	22	25
Interesting/stimulating work[a]	100	100	100	100	100
Stress at work[a]	79	75	100	78	82
Influence at work[a]	64	84	89	91	84
Social support from colleagues[a]	100	100	100	100	100

[a] Often or very often

Table 2 Different types of symptoms during the previous 7 days, and three-month prevalence of weekly ocular and nasal symptoms in all subjects ($n = 88$)

Type of symptoms	Total (%)
Any symptom during previous 7 days[a]	
Sore eyes	44
Itching in the eyes	32
Dry eyes	56
Gritty eyes	36
Eye redness	16
Swollen eyelids	14
At least one eye symptom	66
Nasal catarrh	23
Nasal itch	20
Sneezing	31
Nasal obstruction	41
At least one nasal symptom	54
Weekly symptoms during previous 3 months[b]	
Itching, burning or irritated eyes	36
Irritated, stuffy or runny nose	26

[a] From a detailed symptom questionnaire (Wålinder et al. 1998)
[b] From the MM040NA questionnaire

symptoms in the last 3 months had significantly lower BUT(s) (median 12; interquartile range 8–21), compared with those without eye symptoms (median 35; interquartile range 18–55) ($P < 0.001$). Moreover, there was a significant inverse relationship between BUT(s) and the number of ocular symptoms in the last week (Kendall's tau = 0.41; $P < 0.001$). There was a positive relationship between the number of nasal symptoms during the last week and the concentration of MPO in nasal lavage (Kendall's tau = 0.23; $P = 0.006$). There were no significant relationships between nasal symptoms, or nasal symptom index, and ECP, lysozyme, albumin, or any rhinometric data.

Building characteristics

All buildings were of concrete or bricks with sloping tiled roofs, and all had windows that could be opened. According to information from the constructors, conventional concrete with high water content had been used in all buildings. There were no air humidification or air cooling devices in operation in any of the buildings. The first building (A) was erected in 1925, and had not been renovated since 1955. It was an old-fashioned single-storied building with a basement. The second, (B) from 1985 was known to have damp in the floor. It was also a single-storied, partly with a basement and partly with concrete slabs on the ground. The third building (C) was conventionally built in 1993 and was a two-storied building with a basement. The last building (D) was built in 1994, by an anthroposophic Society. It was one-storied with concrete slabs on the ground and was specially designed, with no plastic material on the interior walls, floors or ceilings and was painted inside with water-based beeswax glazing. The rooms in building D had high ceilings, and the lighting, except in the corridors, was by electric bulbs, with a lot of daylight.

Building B was equipped with mechanical ventilation with both supply and exhaust air (mixed system) in the hospital rooms. The three others had only mechanical exhaust air ventilation in the hospital rooms. The floor coatings were of PVC material in all buildings except building D, which had linoleum and clinker.

Table 3 Rhinometric measurements and lavage biomarkers in all subjects ($n = 88$)

Parameter	Median	Interquartile range
BUT(s)	17	10–33
MCA1 (cm^2)	1.00	0.85–1.15
MCA2 (cm^2)	1.34	1.00–1.59
VOL1 (cm^3)	3.61	3.18–4.00
VOL2 (cm^3)	8.74	6.82–10.4
ECP (μg/l)	< 1	< 1–1.2
MPO (μg/l)	< 2	< 2–8.0
Lysozyme (mg/l)	1.00	0.57–1.59
Albumin (mg/l)	< 2	< 2–< 2

Table 4 Building characteristics of the four buildings

Factor	Building			
	A	B	C	D
Building date	1925	1985	1993	1995
Special building design	no	no	no	yes
Average ventilation rate (m^3/h)	16	59	68	45
Average illumination (lux)	95	195	85	185
Damp building[a]	no	yes	yes	no
Measured dampness in the floor (RH%)	58	84	75	69
Measured ammonia under the floor (ppm)	0	3	3	0.5

[a] According to observation

Measured indoor climate

The average room temperature was similar in all buildings, ranging from 22.0 to 23.0° C. Average relative air humidity was 30–37%, with 37% in the oldest building and 30–33% in the others. Because of the small variation between buildings, of room temperature and air humidity, the influence of these variables was not evaluated. The average exhaust air flow in the hospital rooms was between 16 and 68 m^3/h in the different buildings. The two conventional buildings from the 1980s and 1990s with verified building-dampness (B and C) had the highest ventilation flow (Table 4).

Measurement of building-dampness and air pollutants

Dampness in the upper concrete floor surface [75–84% Relative Humidity (RH)], ammonia in the floor [3 parts per million (ppm)], and 2-ethyl-1-hexanol in the air was detected in building B and C (Tables 4, 5). The two other buildings had less dampness in the floor (< 70%

Table 5 Mean concentration of dampness-related indoor pollutants in the four buildings

Compound	Building			
	A	B	C	D
Indoor VOCs				
Sum of MVOC ($\mu g/m^3$)[a]	0.19	0.13	0.32	0.78
3-methylfuran ($\mu g/m^3$)	0.01	0.01	0.03	0.02
1-octen-3-ol ($\mu g/m^3$)	0.03	0.01	0.05	0.11
Formaldehyde ($\mu g/m^3$)	6	2	7	5
2-ethyl-1-hexanol ($\mu g/m^3$)	< 1	5	20	< 1
Indoor microorganisms				
Viable bacteria (cfu/m^3)	80	80	60	< 50
Total bacteria ($10^3/m^3$)[b]	10.9	8.5	8.4	6.0
Viable molds (cfu/m^3)	120	90	160	80
Total molds ($10^3/m^3$)[b]	6.1	6.1	6.0	6.0

[a] Sum of ten specific VOCs of possible microbial origin
[b] Measured by the CAMNEA method

RH) and no detectable emission of 2-ethyl-1-hexanol. The average concentration of viable molds and bacteria as well as total molds and bacteria was low and similar in all four buildings (Table 5). Among viable molds and bacteria, *Penicillium* sp., *Dematiaceous hyphomycetes*, *Cladosporium* sp., *Streptomyces* sp., yeast, and *Aspergillus* sp. were detected in the air of the buildings. *Aspergillus* sp. including *Aspergillus fumigatus*, and yeast were found only in the damp buildings. *Dematiaceous hyphomycetes and Streptomyces* sp. were found only in the other two buildings without dampness. The lowest concentration of viable spores was found in the specially designed building. Indoor concentrations of MVOCs differed, with a factor of 3–10 between the buildings. Higher concentrations of MVOCs were found in the two newest buildings, and the lowest concentration in the best ventilated building (B) with known dampness in the floor (Table 5). The outdoor concentrations of the sum of MVOCs (0.01–0.08 $\mu g/m^3$, 3-methylfuran (< 0.01–0.01 $\mu g/m^3$), and 1-octene-3-ol (< 0.01–0.02 $\mu g/m^3$) was about one order of magnitude lower than in than that of the indoor environment. The outdoor concentration of 2-ethyl-1-hexanol was below the detection limit (< 1 $\mu g/m^3$) in all samples.

The concentration of formaldehyde was low in all four buildings, ranging from 2 to 7 $\mu g/m^3$. Indoor concentration of NO_2 and CO, which are traffic exhaust-related pollutants, was low in all four buildings. The 7-day mean indoor concentration of NO_2 was 8–11 $\mu g/m^3$ in the four buildings, and the CO concentration ranged from 0.16 to 0.24 ppm. The average indoor concentration of ozone, another outdoor air pollutant, ranged from 1.2 to 8.5 parts per billion (ppb), with the lowest concentration in the newest, specially designed building, and the highest concentration in the oldest building. The average 7-day level of CO_2 was 610–960 ppm. Values above the recommended limit of 1,000 ppm (National Swedish Board of Occupational Safety and Health 1993) were measured in the oldest building only.

Signs, symptoms, and building-dampness

In the two buildings (B and C) with observed dampness and emission of 2-ethyl-1-hexanol, the bivariate analysis showed an increased occurrence of ocular and nasal symptoms during the previous 3 months (Table 6). In addition, hospital staff in the buildings with observed dampness had increased ocular ($P < 0.001$) and nasal symptom indices ($P < 0.001$). Finally, BUT(s) was significantly decreased, and lysozyme in nasal lavage was increased (Table 8). All these findings remained significant in the multiple regression analysis, controlling for age, gender, atopy, smoking, and PSD-index.

In the bivariate analysis, measured dampness in the upper concrete floor surfaces was related to increased occurrence of ocular ($P = 0.002$) and nasal symptoms during the past 3 months ($P = 0.004$) (Table 7). In addition, there was a relationship between measured dampness and the ocular symptom index (Kendall's tau = 0.43; $P < 0.001$), and nasal symptom index (Kendall's tau = 0.24; $P = 0.04$). There was also a decreased BUT(s), decreased VOL2, and increased concentrations of lysozyme (Table 9). All these relationships remained significant when multiple regression analysis was applied, except for VOL2 in relation to measured dampness ($P = 0.07$).

In the bivariate analysis, the concentration of ammonia under the floor surface was related to ocular ($P = 0.002$) and nasal symptoms in the previous

Table 6 Three-month prevalence of weekly ocular and nasal symptoms, in relation to observed building-dampness and special building design

Type of symptoms	Observed building-dampness			Special building design		
	Yes ($n = 50$) (%)	No ($n = 38$) (%)	2-tailed P-value[a]	Yes ($n = 23$) (%)	No ($n = 65$) (%)	2-tailed P-value[a]
Weekly symptoms during the previous 3 months[b]						
Itching, burning or irritated eyes	60	3	< 0.001	5	47	< 0.001
Irritated, stuffy or runny nose	42	6	< 0.001	0	36	< 0.01

[a] By chi-square test or Fisher's exact test for four-fold tables
[b] From the MM040NA questionnaire

Table 7 Odds ratio (OR) adjusted for possible influence of age, gender, atopy, current smoking and psychosocial dissatisfaction index, with 95% confidence interval (95% CI) of relationships between weekly ocular and nasal symptoms and measured building-dampness, exhaust air flow and building age

Type of symptom	Dampness in the upper concrete floor OR(95%CI)[b]	Ammonia in the floor OR(95%CI)[c]	Exhaust air flow OR(95%CI)[d]	Building age OR(95%CI)[e]
Weekly symptoms during previous 3 months[a]				
Itching, burning or irritated eyes	1.29(1.15–1.45)***	4.77(2.08–10.9)***	1.11(1.05–1.18)**	0.70(0.52–0.96)*
Irritated, stuffy or runny nose	1.10(1.02–1.18)*	2.36(1.33–4.18)**	1.05(1.01–1.10)*	0.94(0.73–1.21)

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

[a] From the MM040NA questionnaire

[b] Odds ratio expressed as change of coefficient per % relative humidity in the upper concrete floor

[c] Odds ratio expressed as change of coefficient per ppm of ammonia under the floor carpets

[d] Odds ratio expressed as change of coefficient per m^3/h of exhaust air flow

[e] Odds ratio expressed as change of coefficient per 10 y of building age

3 months ($P = 0.004$), ocular symptom index (Kendall's tau = 0.42; $P < 0.001$), nasal symptom index during the past week (Kendall's tau = 0.25; $P = 0.004$), decreased BUT(s), decreased VOL2, and increase of lysozyme in nasal lavage (Table 9). All relationships between symptoms (Table 7) and signs of dampness, ammonia, exhaust air flow, and building age remained significant in the multiple regression model, except for VOL2 in relation to ammonia ($P = 0.30$).

Signs and symptoms in the specially designed building

In the bivariate analysis, subjects in the building with special design and materials had significantly fewer ocular and nasal symptoms during the previous 3 months (Table 6). Moreover, the subjects in that building had a decreased ocular symptom index ($P = 0.01$) and decreased nasal symptom index ($P = 0.02$). Finally, they had increased BUT(s) (Table 8). For nasal and ocular symptoms and symptom indices, the results remained significant in the multiple regression analysis, controlling for age, gender, atopy, smoking and PSD-index. Self-reported BUT became non-significant ($P = 0.27$).

Signs and symptoms in relation to other building characteristics

No relationships between illumination and ocular symptoms during the past 3 months, ocular symptom index during the last week, or BUT(s) was observed. Significant relationships between a high exhaust ventilation flow and higher prevalence of ocular ($P = 0.006$) and nasal symptoms in the previous 3 months ($P = 0.004$) was observed in the bivariate analysis. Moreover, relationships between ventilation flow and ocular symptom index (Kendall's tau = 0.33; $P < 0.001$), nasal symptom index (Kendall's tau = 0.20; $P = 0.01$), and increased lysozyme in nasal lavage (Table 9) were also found. The relationship between high ventilation flow and symptoms remained significant in the multiple regression analysis.

In the bivariate analysis, VOL1 was increased with increased building age ($P = 0.002$). No significant relationship was observed in the bivariate analysis between building age and eye or nasal symptoms during the last 3 months, symptom indices in the past week, BUT, other rhinometric data or other biomarkers (Table 9). In the multiple regression analysis controlling for age, gender, atopy, current smoking, and PSD-index, the relationship between VOL1 and building age remained significant ($P = 0.002$). Moreover, lysozyme decreased

Table 8 Rhinometric measurements and lavage biomarkers in relation to observed building-dampness and special building design (*M median*, *IR interquartile range*)

Parameter	Observed building-dampness			Special building design		
	Yes ($n = 50$) M (IR)	No ($n = 38$) M (IR)	*P*-value[a]	Yes ($n = 23$) M (IR)	No ($n = 65$) M (IR)	*P*-value[a]
BUT(s)	12 (7–24)	25 (14–41)	0.002	25 (12–41)	15 (9–27)	0.049
MCA1(cm^2)	1.00 (0.85–1.10)	1.00 (0.90–1.21)	0.3	0.96 (0.87–1.10)	1.00 (0.85–1.18)	0.30
MCA2(cm^2)	1.34 (1.00–1.53)	1.36 (1.00–1.60)	0.48	1.38 (1.05–1.62)	1.38 (1.00–1.53)	0.31
VOL1 (cm^3)	3.64 (3.17–3.88)	3.60 (3.18–4.19)	0.45	3.39 (3.00–3.71)	3.74 (3.29–4.01)	0.08
VOL2 (cm^3)	8.62 (6.71–9.88)	8.90 (6.96–11.1)	0.16	8.71 (6.89–9.67)	8.74 (6.75–10.71)	0.44
ECP (μg/l)	< 1 (< 1–1.2)	< 1 (< 1–1.1)	0.22	< 1 (< 1–1.1)	1.0 (< 1–1.2)	0.07
MPO (μg/l)	< 2 (< 2–9.2)	< 2 (< 2–6.1)	0.42	< 2 (< 2–< 2)	< 2 (< 2–< 2)	0.16
Lysozyme (mg/l)	1.21 (0.82–1.66)	0.65 (0.34–1.17)	0.002	0.76 (0.47–1.21)	1.04 (0.59–1.59)	0.24
Albumin (mg/l)	< 2 (< 2–< 2)	< 2 (< 2–< 2)	0.42	< 2 (< 2–< 2)	< 2 (< 2–< 2)	0.35

[a] Calculated by Mann-Whitney U-test

Table 9 Rhinometric measurements and lavage biomarkers in relation to measured building-dampness, exhaust air flow and building age

Parameter	Dampness in the upper concrete floor (% R.H.)		Ammonia under the floor carpet (ppm)		Exhaust air flow (m^3/h)		Building age (y)	
	Tau-beta	*P*-value[a]	Tau-beta	*P*-value[a]	Tau-beta	*P*-value[a]	Tau-beta	*P*-value[a]
BUT(s)	−0.30	< 0.001	−0.29	0.001	0.21	0.007	−0.08	0.17
MCA1(cm^2)	−0.11	0.09	−0.06	0.26	0.01	0.45	0.02	0.43
MCA2(cm^2)	−0.03	0.36	0.02	0.40	0.07	0.20	−0.11	0.11
VOL1 (cm^3)	−0.11	0.10	−0.13	0.07	−0.13	0.07	0.24	0.002
VOL2 (cm^3)	−0.20	0.01	−0.15	0.047	−0.07	0.22	−0.01	0.48
ECP (μg/l	0.01	0.44	0.08	0.19	0.14	0.07	0.08	0.20
MPO (μg/l)	0.05	0.30	0.05	0.30	0.04	0.33	0.12	0.08
Lysozyme (mg/l)	0.28	< 0.001	0.29	< 0.001	0.23	0.002	−0.03	0.37
Albumin (mg/l)	−0.09	0.17	−0.06	0.27	−0.02	0.42	0.05	0.30

[a] Calculated by Kendall's tau-beta test

with building age ($P = 0.048$), and eye symptoms in the previous 3 months decreased with building age ($P = 0.03$).

Discussion

Our results suggest that dampness in concrete floors, causing emission of 2-ethyl-1-hexanol due to alkaline degradation of octyl-phthalates in floor materials, is related to ocular and nasal symptoms, decreased tear film stability and signs of inflammatory or secretory activity in the nasal mucosa. To our knowledge ours is the first epidemiological study on biological effects such as ocular and nasal effects of building-dampness. The study was small, and the number of buildings limited. Problems with impaired indoor air quality in relation to dampness in concrete floors is common in Scandinavia (Gustavsson and Lundgren 1997; Norbäck et al. 1999; Nordström et al. 1995b). Moreover, a relationship between clinically verified asthma, bronchial hyperresponsiveness and signs of dampness in the floor has been demonstrated (Norbäck et al. 1999). In addition, the results indicate that measurement of tear film stability and biomarkers in nasal lavage such as ECP and lysozyme, may be used as tools to monitor biological effects of the indoor environment.

The design was cross-sectional and in such studies selection-effects may result in an underestimation or overestimation of the true relationship. In this study, selection bias due to a low response rate is less likely since the participation rate was high (93%). There was a high prevalence of self-reported nasal and ocular symptoms, which might be due to both recall bias and attention bias. On the other hand, other studies have also shown a high prevalence for self-reported nasal and ocular symptoms (Jessen and Malm 1997). Recall bias due to awareness of exposure may affect symptom-reporting, but is unlikely to affect nasal congestion or biomarkers in nasal lavage fluid.

A time difference between examination of the nasal mucosa and exposure measurements may induce a possible bias. In this study, exposure measurement and inspections were done 1–2 weeks after the medical investigation. Thus, we do not believe that our conclusions are seriously biased by selection or response errors.

Symptoms and signs

We found some relationship between low building age and decreased nasal patency. An increased occurrence of symptoms compatible with SBS has been found in new buildings (Skov and Valbjørn 1987), or in newly-decorated buildings (Wieslander et al. 1997). It has also been found that SBS symptoms increase after moving from old to new buildings (Norbäck et al. 1990). The fact that the newest, specially designed building had a low occurrence of symptoms and low concentrations of ECP and lysozyme indicate that it is not the building age itself that is of importance.

Unexpectedly, we found an increase in symptoms, lysozyme and BUT(s) at higher air flow rates. Similar observations have been made in an earlier study in geriatric hospitals, concerning symptoms compatible with the sick building syndrome (Nordström et al. 1995b). In a recent review of available studies on SBS in relation to ventilation flow (Godish and Spengler 1996), it was concluded that increased personal outdoor air flow rate, up to 10 l/s, is related to a decreased occurrence of SBS. In contrast, available review articles on building-dampness suggest ocular and respiratory effects (Husman 1996). Thus, we conclude that our results concerning ventilation are due to the covariation between ventilation flow rate and building-dampness in our study.

Our main finding was that dampness in concrete floors with emission of 2-ethyl-1-hexanol, was related to ocular and nasal symptoms, decreased tear film stability and lysozyme in nasal lavage. Building-dampness is common and is related to an increased risk of respiratory symptoms (Dales et al. 1991; Husman 1996), including ocular (Routsalainen et al. 1995) and upper respiratory symptoms (Waegemaekers et al. 1989). In

the Uppsala part of the European Community Respiratory Health Survey (ECRHS) (Burney et al. 1994), increased concentrations of ECP in serum, and eosinophilic granulocytes in blood were found in subjects in damp buildings (Björnsson et al. 1995). A relationship between building-dampness and microbial growth in an office building, and increased concentrations of ECP, MPO, lysozyme, and albumin in nasal lavage has earlier been reported (Wålinder et al. 1993). None of the subsequent studies, however, has ascertained building-dampness by objective measurements of dampness in the construction.

Our study suggested that emissions from dampness in the concrete floors were related to both symptoms and signs. There were no indications of water leakage, and we found no indication of microbial growth in the buildings with dampness in the concrete floors. It is well known that dampness in the floor may cause chemical degradation of building material without microbial growth. One example is the formation and emission of 2-ethyl-1-hexanol from the plasticizer di-(2-ethylhexyl) phthalate (DEHP) in PVC floor coatings or glues (Gustavsson and Lundgren 1997). DEHP is widely used in PVC plastics, and may constitute 40% of the PVC material (Doelman et al. 1990). There are some recent indications that DEHP and related compounds may cause respiratory inflammation. Preterm infants exposed to DEHP from respiratory tubing have been reported to have a higher risk of asthma (Roth et al. 1988). On alkaline hydrolysis of DEHP, 2-ethyl-1-hexanol and mono-(2-ethylhexyl) phthalate (MEHP) are formed (Øie et al. 1997). Since 2-ethyl-1-hexanol is a volatile compound, it can be detected easily by conventional VOC measurements, and the presence of 2-ethyl-1-hexanol is commonly used in Sweden as an indicator of alkaline degradation of DEHP (Gustavsson and Lundgren 1997). MEHP is a larger and less volatile compound, but has been found to induce bronchial hyperresponsiveness in rats (Doelman et al. 1990). It has been hypothesized that MEHP mimics prostaglandins and thromboxanes in the lungs and thereby increases the risk of inducing airway inflammation (Øie et al. 1997). Recently, a matched-case control study in a cohort of 3,754 newborn infants in Oslo, Norway demonstrated an increased risk of bronchial obstruction in the presence of PVC floor materials in dwellings (Odds Ratio (OR) = 1.89; 95% CI 1.14–3.14) (Jaakkola et al. 1999). In this study, it was pointed out that plasticizers have a high affinity for particles, and that the exposure to DEHP and MEHP could be mediated by respirable dust.

Possible cellular mechanisms

We found a relationship between building age and dampness, and lysozyme in nasal lavage. Moreover, we found a relationship between MPO and nasal symptoms. In cytological analyses of nasal lavage about 90% of leukocytes are neutrophil granulocytes (Pipkorn et al. 1989), and MPO has been shown to be a specific biomarker for the activity of neutrophil granulocytes (Schmekel et al. 1990). The level of ECP is a measure of the activity of eosinophil granulocytes. This protein is cytotoxic and can be destructive to the epithelium of the airways (Venge et al. 1989). Lysozyme, which is a less specific biomarker in nasal lavage fluid, might be the most sensitive end point in the lavage test-battery of biomarkers, especially since it is secreted from several sources: nasal submucosal glands via parasympathetic cholinergic effects, activated macrophages, and neutrophil granulocytes (Wålinder et al. 1998).

In conclusion, the study provides new evidence of the role of dampness-related alkaline degradation of (DEHP) in PVC building material. Emissions related to the degradation of DEHP due to dampness in the floors, indicated by increased 2-ethyl-1-hexanol in the air, may affect the mucous membranes in the eyes and nose, decrease tear film stability and increase the occurrence of ocular and nasal symptoms. The low occurrence of both symptoms and signs in the building with special materials and design illustrates that it is possible to construct a new building with a minimum of adverse effects on nasal and ocular mucous membranes.

Acknowledgements This study was supported by grants from The Swedish Building Research Institute, The Swedish Foundation for Health Care Sciences and Allergy Research and the Swedish Association against Asthma and Allergy.

References

Andersson K (1998) Epidemiological approach to indoor air problems. Indoor Air. [Suppl 4]: 27–34

Andersson K, Hallgren C, Levin JO, Nilsson CA (1981) Chemosorption sampling of formaldehyde in air: influence on recovery during the simultaneous sampling of formaldehyde, phenol, furfural and furfuryl alcohol. Scand J Work Environ Health 7: 282–289

Anonymous (1993) Ventilation and quality of air: National Swedish Board of Occupational Safety and Health (in Swedish) AFS 1993: 5

Apter A, Bracker A, Hodgson M, Sidman J, Leung WY (1994) Epidemiology of the sick building syndrome. J Allergy Clin Immunol 94: 277–288

Belsley D (1991) Conditioning diagnostics collinearity and weak data in regression, Wiley, New York

Björnsson E, Janson C, Norbäck D, Boman G (1998) Symptoms related to the Sick Building Syndrome in a general population sample: associations with atopy, bronchial hyperresponsiveness and anxiety Int J Tuberc Dis 2: 1023–1028

Björnsson E, Norbäck D, Janson C, Widström J, Palmgren U, Ström G, Boman G (1995) Asthmatic symptoms and indoor levels of micro-organisms and house dust mites. Clin Exp Allergy 25: 423–431

Brunekreef B, Dockery DW, Speizer FE, Ware JH, Spengler JD, Ferris BG (1989) Home dampness and respiratory morbidity in children. Am Rev Respir Dis 140: 1363–7

Burney PGJ, Luczynska CM, Chinn S, Jarvis D (1994) The European Community Respiratory Health Survey. Eur Respir J 7: 954–960

Dales RE, Burnett R, Zwanenburg H (1991) Adverse health effects among adults exposed to home dampness and molds. Am Rev Respir Dis 143: 505–509

Doelman CJA, Borm PJA, Bast A (1990) Plasticiser and bronchial hyperreactivity. Lancet 335: 725

Ferm M, Svanberg PA (1998) Cost-efficient techniques for urban and background measurements of SO_2 and NO_2. Atmos Environ 32: 1377–1381

Flannigan B, Miller DJ (1994) Health implications of fungi in indoor environments – an overview 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: 229–239 Amsterdam

Franck C, Bach E, Skov P (1993) Prevalence of objective eye manifestations in people working in office buildings with different prevalences of the sick building syndrome compared with the general population. Int Occup Environ Health 65: 65–69

Gebski V, Leung O, McNeil D, Lunn D (1992) SPIDA users manual, version 6. Statistical Computing Laboratory, Eastwood, Australia

Godish T, Spengler JD (1996) Relationships between ventilation and indoor air quality: a review. Indoor Air 6: 135–145

Gustavsson H and Lundgren B (1997) Off-gassing from building materials: a survey of case studies In: Brune D, Gerhardsson G, Crockford GW, Dáuria D (eds) The Workplace, Vol, 1 Fundamentals of Health, Safety and Welfare. International Labor Office, Geneva pp 533–555

Hodgson M (1995a) The sick-building syndrome. Occup Med: State of the art reviews 10: 167–175

Hodgson M (1995b) The medical evaluation. Occup Med: State of the art reviews 10: 177–194

Husman T (1996) Health effects of indoor-air microorganisms. Scand J Work Environ Health 22: 5–13

Jaakkola JJK, Øie L, Nafstad P, Botten G, Samuelsen SO, Magnus P (1999) Interior surface materials in the home and the development of bronchial obstruction in young children in Oslo, Norway. Am J Public Health 89: 188–192

Järvholm B (1993) Is it time to change the terminology of sick building syndrome? Indoor Environ 2: 186–188

Jessen M, Malm L (1997) Definition, prevalence and development of nasal obstruction. Allergy 52: 3–6

Kreiss K (1989) The epidemiology of building-related complaints and illness. Occup Med: State of the art reviews 4: 575–592

Lee K, Yanagisawa Y, Spengler JD, Özkaynak H, Billick IH (1993) Sampling rate evaluation of NO_2 Badge: (I) In indoor environments. Indoor Air 3: 124–130

Mendell MJ (1993) Non-specific symptoms in office workers: a review and summary of the epidemiological literature. Indoor Air 3: 227–236

Mølhave L (1989) The sick building and other buildings with indoor climate problems. Environ Intl 15: 65–74

Muzi G, dellòmo M, Abbritti G, Accattoli P, Fiore MC, Gabrielli AR (1998) Objective assessment of ocular and respiratory alterations in employees in a sick building. Am J Ind Med 34: 79–88

Norbäck D (1997) Indoor air quality, sick building syndrome (SBS), and specific building related illness. In: The Workplace. Vol. 1 Fundamentals of Health, Safety and Welfare CIS-ILO and Scandinavian Science Publisher, Oslo, pp 501–532

Norbäck D, Björnsson E, Janson C, Palmgren U, Boman G (1999) Current asthma and biochemical signs of inflammation in relation to dampness and mould growth in workplace buildings Int J Tuberc Lung Dis 3: 368–376

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

Nordström K, Norbäck D, Akselsson R (1994) The effect of humidification on the Sick Building Syndrome and perceived indoor air quality in hospitals. A four month longitudinal study. Occup Environ Med 51: 683–688

Nordström K, Norbäck D, Akselsson R (1995a) Subjective indoor air quality in hospitals – the influence of building age, ventilation flow, and personal factors. Indoor Environ 4: 37–44

Nordström K, Norbäck D, Akselsson R (1995b) The influence of indoor air quality and personal factors on the Sick Building Syndrome (SBS) in Swedish Geriatric hospitals. Occup Environ Med 52: 170–176

Øie L, Hersoug L-H, Madsen JØ (1997) Residential exposure to plasticizers and its possible role in the pathogenesis of asthma. Environ Health Perspect 105: 972–978

Palmgren U, Ström G, Blomqvist G, Malmberg P (1986) Collection of airborne micro-organisms on Nucleopore filters, estimation and analysis – CAMNEA method. J Appl Bacteriol 61: 401–406

Peterson CGB, Nystrand J, Andersson AS, Nilsson L, Venge P (1991) Radioimmunoassay of human eosinophil cationic protein (ECP) by an improved method. Establishment of normal levels in serum and turnover in vivo. Clin Exp Allergy 21: 561–567

Pipkorn N, Karlsson G, Enerbäck L (1989) Nasal mucosal response to repeated challenges with pollen allergen. Am Rev Resp Dis 140: 729–736

Raphael GD, Jeney EV, Baraniuk JN, Kim I, Meredith SD, Kaliner MA (1989) Pathophysiology of rhinitis, lactoferrin and lysozyme in nasal secretions. Clin Invest 84: 1528–1535

Roth B, Herkenrath P, Lehman H-J, Ohlens H-D, Homig HJ, Benz-Bohm G (1988) Di-(2-ethylhexyl)-phthalate as plasticizer in PVC respiratory tubing systems: indication of hazardous effects on pulmonary function in mechanically ventilated, preterm infants. Eur J Pediatr 47: 41–46

Routsalainen R, Jakkola N, Jakkola JJK (1995) Dampness and moulds in day-care centres as an occupational health problem. Int Arch Occup Environ Health 66: 369–374

Schmekel B, Karlsson SE, Linden K, Sundström C, Tegner H, Venge P (1990) Myeloperoxidase in human lung lavage I. A marker of local neutrophil activity. Inflammation 14: 447–454

Skov P, Valbjørn O (1987) The ''sick'' building syndrome in the office environment: The Danish Town Hall Study. Environ Int 13: 339–349

Stenberg B, Hansson Mild K, Sandström M, Sundell J, Wall S (1993) A prevalence study of the sick building syndrome (SBS) and facial skin symptoms in office workers. Indoor Air 3: 71–81

Ström G, Norbäck D, West J, Wessen B, Palmgren U (1993) Microbial volatile organic compounds (MVOC): a causative agent to sick building problems. Sterling E, Bieva C, Collett C (eds) Building Design, Technology, and Occupant Well-being in Temperate Climates ASHRAE Special Publications 90353, Atlanta, USA, pp. 351–357

Sundell J, Andersson B, Andersson K, Lindvall T (1993) Volatile organic compounds in ventilating air in buildings at different sampling points in the buildings and their relationship with the prevalence of occupant symptoms. Indoor Air 3: 82–93

Venge P, Håkansson L, Peterson CGB (1989) Eosinophil activation in allergic disease. Int Arch Allergy Appl Immunol 2: 33–337

Venge P, Hällgren R, Stålenheim G, Olsson I (1979) Effects of serum and cations on the selective release of granular proteins from human neutrophils during phagocytosis. Scand J Haematol 22: 317–326

Waegemaekers M, van Wageningen N, Brunekreef B, Boleij SM (1989) Respiratory symptoms in damp homes. Allergy 44: 192–198

Wålinder R, Norbäck D, Carlsson E, Venge P, Wilander E (1993) Objective investigation methods for the eye and nose – a sensitive method to study environmental influence in indoor environments? [Objektiva undersökningsmetoder för näsa och ögon- en känslig metod för att studera miljöpåverkan i inomhusmiljöer?] Hygiea 102: 119 (in Swedish)

Wålinder R, Norbäck D, Wieslander G, Smedje G, Erwall C (1997) Nasal mucosal swelling in relation to low air exchange rate in schools. Indoor Air 7: 198–205

Wålinder R, Norbäck D, Wieslander G, Smedje G (1998) Nasal congestion and biomarkers in nasal lavage – the significance of air exchange rate and type of ventilation in schools. Int Arch Occup Environ Health 71: 479–486

Wålinder R, Norbäck D, Wieslander G, Smedje G, Erwall C, Venge P (1999) Nasal patency and lavage biomarkers in relation to settled dust and cleaning routines in schools. Scand J Work Environ Health 25: 137–143

Wilcosky TC (1993) Biological markers of intermediate outcomes in studies of indoor air and other complex mixtures. Environ Health Perspec [Suppl 101]: 193–197

Wieslander G, Norbäck D, Björnsson E, Janson C, Boman G (1997) Asthma and the indoor environment: the significance of emission of formaldehyde and volatile organic compounds (VOC) from newly painted indoor surfaces. Int Arch Occup Environ Health 69: 115–124

Wyon D (1992) Sick buildings and the experimental approach. Environ Technol 3: 313–322

Wyon NM, Wyon DP (1987) Measurement of acute response to draught in the eye. Acta Ophthalmol 65: 385–392