Health effects of flooding: changes of symptoms, tear film stability and biomarkers in nasal lavage after re-exposure to a damp office building

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ABSTRACT

The aim was to study changes of symptoms and signs in an office exposed to flooding from heavy rain. All 18 workers participated in medical investigations in January 1998. The subjects were first investigated on a Monday in a reference building and then all moved back and were reinvestigated in a damp building after 2 days of exposure. After staying two days in the damp building there was a significant increase of ocular, nasal and respiratory symptoms, decreased tear film stability ($p = 0.003$) and an increase of eosinophilic cationic protein (ECP) ($p = 0.04$) and albumin ($p = 0.01$) in nasal lavage. Both the control building and the flooded building had good general ventilation, low levels of particles and formaldehyde. The flooded building had a higher concentration of microbial volatile organic (MVOC) and the mould *Trichoderma* sp. in the air. In conclusion, exposure to building dampness may cause irritative symptoms and clinical symptoms in eyes and nasal mucosa.

INDEX TERMS

Flooding; Microbial contamination; Exposure assessment; Tear film; Biomarkers

INTRODUCTION

Building dampness is related to both sick building syndrome (SBS) and bronchial asthma (Bornehag *et al*., 2001). There are various known exposures related to building dampness, such as house dust mites, moulds and bacteria, both viable and non-viable. Microbial VOCs (volatile organic compounds) such as 1-octen-3-ol and 3-methylfuran (MVOCs) can be produced by micro-organisms in damp buildings as indicators of microbial activity (Wieslander *et al*., 1999). Water damage in the building construction due to water leakage and flooding is a common indoor environment problem and health effects have been studied previously, but there are few studies on the relationship between microbial exposure and biomarkers in airway mucosa. Increases in ECP (eosinophilic cation proteins), MPO (myeloperoxidase) and albumin in NAL were observed in buildings with pronounced microbial growth in their structure, including *Stachybotrys spp.* (Wålinder *et al*., 2001).

The aim of this investigation was to study changes of symptoms and physiological signs in subjects investigated in a reference building and then reinvestigated in a damp building after 2 days.

METHODS

The study was performed in one of the case-book archives in the main hospital in the city of Uppsala in mid-Sweden, in January 1998. The archives were situated in one main hospital building. During a heavy rainfall, for 1–2 h in the centre of Uppsala in the middle of August in 1997, water came through doors and staircases, and covered the floor with 10–15 cm of water in the archives. The floor covering in the frontal part was linoleum and in the distal part textile carpeting. All the daytime personnel employed ($n = 18$) were invited and participated

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in the investigations of the eyes and nose and airways. To achieve maximum indoor exposure, all subjects had been at their workplace at least 1 h prior to examination.

The staff was initially investigated in a reference building at the Department of Occupational and Environmental medicine on Monday, after an off-work weekend. Then, they worked in the damp building for 2 days, and were reinvestigated at the same time of the day +/– 1 h for control of diurnal variations. Two standardized questionnaires on the occurrence of symptoms used in previous investigations were distributed. One contained 23 yes/no questions on different types of symptoms, such as ocular, respiratory and dermal symptoms, as well as general symptoms, such as nausea, fatigue and headache (Wieslander *et al*., 2000). The second contained 10 rating scales on current ocular, nasal, throat symptoms, dyspnoea, malodour, and systemic symptoms (Nihlen *et al*., 1998). The tear film stability was estimated by a standardized method, previously shown to correlate with the fluoresceine method for detection of tear film break up time (BUT) (Wyon, 1992). Acoustic rhinometry (Rhin, 2000; wideband noise; continuously transmitted) was performed. The measurements were made under standardized forms (sitting), after 5 min of rest, and prior to lavage (Wålinder *et al*., 2000). Nasal lavage of the nasal mucosa was made in a standardized way, followed by analysis of biomarkers such as eosinophilic cation protein, myeloperoxidase, lysozyme, and albumin with earlier described methods (Wålinder *et al*., 2000). Lung function was measured by dynamic spirometry.

Technical Measurements

The technical investigation was composed of a building survey and technical measurements. The measurements included room temperature, relative air humidity, carbon dioxide, ozone, formaldehyde, respirable dust, total VOC, specific VOCs, both viable and total concentration of moulds and bacteria. Specific VOCs evaluated in this study included 2-ethyl-1-hexanol, 1-octen-3-ol, and 3-methylfuran. Exposure measurements with direct reading instruments and pumped air sampling were made in the reference building, as well as in the damp building during investigations. Indoor concentrations of formaldehyde were measured with glass fibre filters impregnated with 2,4-dinitro-phenylhydrazine, the air sampling rate being 0.2 l/min during 6 h. The filters were analysed 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 analysed for total VOC and specific VOCs, including 2-ethyl-1-hexanol, by GC-MS (Norbäck *et al*., 1995). 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). VOCs of possible microbial origin 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. Airborne micro-organisms 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 moulds and bacteria, respectively, was determined by the CAMNEA method (Palmgren *et al*., 1986). Viable moulds and bacteria were determined by incubation on two different media.

Statistical Methods

Differences in VAS scales, nasal patency and lung function before and after exposure to damp buildings were analysed by Student's test for paired comparisons. Statistical analysis was performed by multiple logistic regression and adjusted odds ratios with 95% confidence, and were analysed by Student's *t*-test for paired comparisons. As the tear film stability was not

normally distributed, change in tear film stability was analysed by Wilcoxon matched pairs signed rank test. Changes in symptoms, measured as a dichotomous outcome variable, were measured by the McNemars test.

RESULTS

Room temperature and relative air humidity was similar in the reference building, and the damp workplace building. Both buildings were well ventilated, with CO_2 levels well below the current ventilation standard of 1000 ppm. The indoor level of respirable particles was low in both buildings (8–10 μg/m^3), and similar to that in the outdoor air (11 μg/m^3). Moreover, the indoor concentration of formaldehyde was also low in both buildings (5–7 μg/m^3) (Table 1). When comparing the concentration of specific VOC of possible microbial origin (MVOC), numerical differences could be noted. For all types of compounds, except iso-butanol, 2-heptanone and 2-pentylfuran, the concentrations were higher in the damp building despite the fact that the ventilation was better in this building. The highest total concentrations of MVOC (140 ng/m^3) was measured in the frontal part of the case book archive, where the floor material was made of linoleum. The concentration of total and viable moulds and bacteria were very low in all samples. Among viable species, *Penicillium sp.* was detected both in the control building and the flooded case-book archive. In contrast, the mould species, *Trichoderma sp.,* could only be detected in the damp building.

Table 1 Indoor and outdoor exposures

Type of exposure factor	Control building *M* (min–max)	Damp building *M* (min–max)	Outdoor air
Temp (°C)	21.9 (21.5–22.5)	22.0 (21.0–23.0)	4.5
Relative air humidity (%)	39 (32–47)	40 (33–46)	100
Carbon dioxide (ppm)	490 (450–600)	400 (380–500)	380
Respirable particles (μg/m^3)	9 (8–10)	9 (8–10)	11
Formaldehyde (μg/m^3)	6 (5–7)	5(5–6)	NA
Sum of MVOC (ng/m^3)[a]	97 (54–71)	152 (70–140)	10
Viable bacteria (cfu/m^3)	140 (<70–220)	<70 (<70–<70)	NA
Total bacteria (10^3/m^3)	7.3 (<7–7.6)	<7 (<7–<7)	NA
Viable moulds (cfu/m^3)	71 (<70–72)	<70 (<70–<70)	NA
Total moulds (10^3/m^3)	7.3 (<7–7.6)	<7 (<7–<7)	NA

[a]Sum of identified MVOC, excluding iso-butanol and *n*-butanol.

The majority of the subjects were women (78%), the mean age was 44 years 22% were smokers, 35% had hay fever and 17% had doctor diagnosed asthma. In the questionnaire with 23 yes/no questions, increased symptoms from the ocular, nasal and respiratory system were registered in the damp building, as compared to the reference building. Seven persons (54%) without previous symptoms developed at least one eye symptom after exposure to the damp building, six (43%) developed at least one nasal symptom, 6 (43%) developed some throat symptom, 5 (33%) developed lower respiratory symptoms, 4 (44%) developed general symptoms, while none (0%) developed dermal symptoms. After moving to the damp building, the mean ratings on the analogue scales (0–100%) increased for eyes, nose and throat symptoms, as well as for dyspnoea, headache and tiredness (Table 2).

Table 2 Average VAS scale ratings for 10 questions[a] before, and after 2 days of re-exposure in a damp building (N = 18)

Type of rating	Before re-exposure M (SD)	After re-exposure M (SD)	2-tailed p-value[a]
1. Ocular irritation	10(14)	35(27)	<0.001
2. Nasal irritation	14(17)	36(27)	0.002
3. Throat irritation	10(17)	35(30)	<0.001
4. Difficulty in breathing	9(14)	24(28)	0.006
5. Odour	1(2)	13(26)	0.06
6. Headache	8(18)	30(32)	0.002
7. Fatigue	18(26)	37(34)	0.01
8. Nausea	2(3)	8(13)	0.04
9. Dizziness	2(5)	14(26)	0.07
10. Intoxication	1(4)	6(15)	0.10

[a]Calculated by Student's t-test for paired comparison.

No significant difference after re-exposure was seen for nasal patency or any lung function parameter. In contrast, there was an effect on tear film stability and inflammatory biomarkers in nasal lavage. The tear film break up time BUT(s) decreased from 17 to 10 s after re-exposure in the damp building ($p < 0.05$) (Table 3).

Table 3 Tear film break up time and biomarkers in nasal lavage, before, and after 2 days of re-exposure to a damp building (N = 18)

Physiological parameter	Before re-exposure Median (IQR)	After re-exposure Median (IQR)	2-tailed p-value[a]
BUT (s)	16 (8-18)	8 (5–10)	0.003
ECP (µg/l)	1.0 (<1–1.2)	1.2 (<1–1.4)	0.04
MPO(µg/l)	4.4 (1.5–3.4)	5.1 (2.0–14.3)	NS
Lysozyme (mg/l)	1.00 (0.66–1.98)	1.17 (0.59–2.24)	NS
Albumin (mg/l)	1.5 (1.5–3.4)	1.5 (1.5–4.4)	NS

[a]Calculated by Wilcoxon matched pairs signed rank test.

The spontaneous change of nasal biomarkers from Monday to Wednesday was investigated in a separate test, performed after the exposure experiment. In this test, nasal lavage was made twice in 13 of the previous participants, when staying in the same building from Monday to Wednesday. A non-significant decrease of the concentration of biomarkers from Monday to Wednesday was observed. The mean ratio (Wednesday values/Monday values) were 78% for ECP, 71% for MPO, 75% for lysozyme, and 64% for albumin. These differences could be interpreted as a wash-out effect, e.g. the nasal mucosa was influenced by the nasal lavage investigation. After adjustment for the wash-out effect, a relative increase of both ECP (p = 0.04) and albumin (p = 0.01) after re-exposure in the damp building was observed.

DISCUSSION

Subjects re-exposed to a well-ventilated workplace building with a history of flooding, got a pronounced increase of ocular, nasal, throat and lower respiratory symptoms, as well as headache, nausea and fatigue. In addition, the re-exposure was associated with a decreased tear film stability, and signs of eosinophilic inflammation in the nasal mucosa. The design was quasi-experimental, and all staff had previously worked in the damp building during 5 months. The exposure measurements revealed the presence of the mould species

Trichoderma sp., and numerically higher concentrations of volatile organic compounds of possible microbial origin (MVOC) in the flooded building.

The physiological methods in the acute effect test battery have been used in previous epidemiological and experimental investigations (Norbäck and Wieslander, 2002). Recall bias due to awareness of exposure may affect symptom reporting, but is unlikely to affect physiological measurements. Moreover, the participation rate was high (100%). We found a selection effect in relation to building dampness, since one of the initial workers developed a severe asthma a few months after the flooding, and could no longer work in the damp building. This case of new onset of dampness-related asthma within a small group of exposed office workers, indicate that selection effects should not be neglected in studies on health effect of building dampness.

Building dampness is associated with an increase of symptoms compatible with the SBS; as well as asthma and asthmatic symptoms (Bornehag *et al*., 2001). These conclusions are mainly based on the large number of cross-sectional questionnaire studies. In our study, with a quasi-experimental design, we found an increase of both symptoms and signs of impaired tear film stability and eosinophilic inflammation in the nasal mucosa. A decrease in tear film stability has previously been observed in a cross-sectional study, comparing hospital workers in two damp buildings, with workers in two buildings without signs of building dampness (Wieslander *et al*., 1999). There are some previous studies supporting the hypothesis that exposures related to building dampness may cause an eosinophilic inflammation in the airway mucosa. An increased concentration of ECP in serum and eosinophilic granulocytes in blood were found in subjects living in damp dwellings, including dwellings with water damage and flooding (Norbäck *et al*., 1999). A significant positive association between serum ECP and the indoor concentration of viable bacteria, and total moulds in the bedroom has also been reported (Björnsson *et al*., 1995). An increase of ECP, lysosyme and albumin in nasal lavage fluid was observed in one school study with water leakage exposure. Finally, an increase of both ECP, MPO and albumin in nasal lavage fluid was observed in an office building with pronounced microbial growth in the construction (Wålinder *et al*., 2001b). The study design did not allow us to draw any definite conclusions about the causative agent in the damp building. One mould species (*Trichoderma sp.)* was present only in the damp building, and there was an increase of many MVOC. Some recent publications indicate that indoor exposure to *Trichoderma sp*. may have a health significance. In one case-control study from Finland, an increased risk of developing asthma in adulthood was related to IgE antibodies to *Trichoderma*, but not to other moulds (Jaakkola *et al*., 2002).

CONCLUSION AND IMPLICATIONS

Subjects previously exposed to a flooded building with growth of *Trichoderma sp*. experienced an increase of ocular, nasal and respiratory symptoms, reduced tear film stability, and signs of eosinophilic inflammation in the nasal mucosa after 2 days of re-exposure. The results imply that intervention studies with physiological measurements can be a useful tool to study the mechanisms behind health impairment in damp buildings. From a preventive point of view, measures should be taken to minimize dampness and microbial growth, and health consequences of water leakage and flooding should not be neglected.

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