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Sign of Eye Irritation in Female Hospital Workers and the Indoor Environment

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Abstract The relationships between indoor environment factors and signs of eye irritation were studied in a sample of female personnel with (n=112) and without (n=64) mucous membrane symptoms working in 36 nursing departments at geriatric hospitals in the municipality of Trondheim, Norway. The indoor climate was characterised by high room temperature (interquartile range 23.0–23.7°C), low relative air humidity (interquartile range 17–26%) and high outdoor airflow rate, as indicated by low indoor levels of carbon dioxide (interquartile range 490–650 ppm). An altered microbial flora was observed in nine of the departments, and *Aspergillus fumigatus* was found in three of these. Five of the hospitals were situated in urban parts of the municipality near roads with heavy traffic. In the initial analyses decreased tear-film stability (BUT) was observed in subjects working in departments with increased dust settlement rate (P=0.03), in hospitals situated in urban areas with heavy traffic (P<0.001), and in subjects working in departments with presence of *A. fumigatus* (P=0.04). Increased conjunctival staining (CS) was related to alteration of the microbial flora. In the final multivariate analyses statistically significant relationships were observed between BUT and dust settlement rate and urban vicinity of workplace and between CS and alteration of the microbial flora.

Key words Tear-film break-up time; Vital staining; Microbial flora; Traffic pollution; Dust settlement.

Practical Implications
Clinical tools such as measurements of break-up time and vital staining of the cornea might be useful tools in documenting environmental effects on the eyes, not only in chamber studies but also in the field. The results illustrate the significance of good hygienic standards causing low concentrations of airborne particles, prevention on microbial growth in buildings and ventilation systems, and suggest that improvement of ambient air quality could be positive from a health point of view.

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Introduction

Eye irritation is a common complaint in the general population and particularly in certain indoor climates (Norbäck and Edling, 1991; Wieslander et al., 1999). In indoor climate surveys eye symptoms have often been studied as a part of the so-called sick-building syndrome (SBS), a concept established from observations of increased occurrence of a certain type of symptoms in people occupying some type of buildings (WHO, 1983, 1986; Apter et al., 1994). In a random sample of the general Swedish population, the prevalence of eye symptoms was 16% and of swollen eyelids 6% (Norbäck and Edling, 1991). In the same study the prevalence of eye symptoms among health care and social workers was 20%. Another Swedish study among workers at geriatric hospitals showed a prevalence of eye symptoms of 36% with a great variations between different building ranging from 0–71% (Nordström et al., 1999). In a Norwegian office study the reported prevalences of eye irritation among men and women were 24% and 37%, respectively (Lenvik, 1993).

Objective methods to study the external parts of the eyes have seldom been applied in epidemiological studies of environmental effects. The application of such methods in epidemiological studies may increase the understanding of the aetiology and mechanisms behind indoor environmental symptoms. Measurements of tear film break-up time (BUT), as well as self-reported break-up time, have been performed in studies in offices, hospitals, and experimentally (Norn, 1969; Franck, 1986; Wong et al., 1996). Stability of the tear-film measured by BUT was reduced in personnel working in sick-buildings (Franck, 1986; Muzi et al., 1998) and in buildings with increased concrete hu-

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midity (Wieslander et al., 1999). Staining of the conjunctiva has been used to study epithelial desquamation (v Bijsterveld, 1969; Norn, 1973). Increased conjunctival staining has been related to sick-buildings (Franck, 1986) and to increased dust exposure (Kjærgaard, 1992).

In buildings with mould growth in the ventilation system or on internal surfaces, increased counts of fungi may be observed, with the increase in *Aspergillus spp.* and *Penicillum spp.* being particularly noticable (Flannigan and Miller, 1994). These characteristics have been utilised by consultants in practical investigations, by qualitative and quantitative comparison of the indoor and outdoor microbial flora (Flannigan, 1992). An approach based on viable sampling and cultivation at room temperature and 37°C have been described (Ahlen, 1995). Among the *Aspergillus* species, *A. fumigatus* is reported to be the most important potential pathogen for persons with reduced immunity (Pieckova and Jesenska, 1999).

There is a growing concern about particulate pollution and cleaning in the indoor environment (Raw et al., 1993; Gyntelberg et al., 1994). Methods for assessments of dust settlement rate and cleanliness have been developed based on the collection of dust on foils, where the amount of dust is determined as area covered by dust in percent of total surface area. A guideline for indoor environment quality proposes 1–1.5% as a limit for surfaces close to persons or easily accessible (Schneider et al., 1994).

In this study, we focused on eye irritation as expressed by tear film stability and vital staining of the conjunctiva and indoor temperature, humidity, carbon dioxide, dustiness, micro-organisms, and the influence of urban vicinity of the workplace. The aim of the study was to investigate possible relations between these factors and the physiological measures of eye irritation.

Material and Methods

Subjects

This investigation was performed as part of a study of complaints related to the indoor climate in the staff at geriatric hospitals in the municipality of Trondheim (145,000 inhabitants) which is situated in the middle part of Norway (at 63°N). A self-administrated questionnaire, with symptom questions identical to those of the MM-040B Örebro-questionnaire (Andersson and Stridh, 1992; Andersson, 1998), was used to identify subjects with and without mucous membrane symptoms (MMS). The questionnaire was posted to all female employees at the nursing departments (n=1,165) of 14 geriatric hospital units, during the spring of 1995. There were 821 persons (70%) who responded.

The study population consisted of 197 female nursing respondents, who reported at least one mucous membrane symptoms (MMS) of the eyes, nose or upper airways every week during the last three months, and 144 females who reported no such symptoms giving a total of 341 subjects. Of these, 176 responders (52%, 112 with and 64 without MMS) volunteered to participate in clinical examinations. Two subjects were excluded from the study because of fever during the week prior to the examination.

The clinical examinations were performed at the Department of Occupational Medicine at the University Hospital of Trondheim, from November 1995 to March 1996, in a period with cold weather (monthly mean temperature −3.2 to 0.9°C) making artificial heating necessary. The temperature at the Department of Occupational Medicine was constant during the clinical examinations (22.3±0.3 °C), while indoor relative humidity varied (range: 12 to 35%) mainly depending on the outdoor temperature.

Personal characteristics

Among the participants (n=174) the median age was 43 years (range: 22–64 years), 36% of the subjects were current smokers, and there were 13% who in the initial questionnaire stated to have had a history of childhood eczema. Among those who did not participate (n=165) the median age was 42 years (range: 20–67 years), 52% of the subjects were current smokers, and there were 8%, who in the initial questionnaire stated, they had a history of childhood eczema.

Ocular measurements

The two conditions investigated were tear film stability measured by break-up time (BUT) and epithelial desquamation measured by degree of conjunctival staining (CS).

Measurement of BUT, the time period to rupture of the tear film following a complete blink, was performed after transferring 10 µl of sterile 1% Na-flourescein dye to the lower lid using a sterilised glass rod. The subjects were told to blink once and then to keep their eyes open while staring directly into a slit lamp. The time was taken from the first blink until spots or lines indicating break-up of the tear-film were observed on the corneal surface. Three consecutive measurements were recorded (Norn, 1969) in each eye. In the analyses the average of the measurements from both eyes was used. The measurements of BUT took place before the conjunctival staining.

The degree of conjunctival staining (CS) was assessed after installing 10 µl of vital dye (1% Rose-Bengal dye or 1% Lissamine-Green B dye) onto the lower eyelid with a glass rod. After the subjects had blinked normally for 1–2 min in order to distribute the dye, the nasal, temporal, upper and lower parts of the bulbar conjunctiva of both eyes were examined with a slit lamp. Conjunctival scoremarks were categorized into three categories; 0: <10 dots, 1: 10–50 dots and 2: >50 dots (Franck, 1986). A total CS score (sum of all scores in both eyes) was calculated. The Rose-Bengal dye was used in the first 2 months of the study due to problems with the manufacturing of the Lissamine-Green B dye at the local pharmacy.

Environmental factors

The indoor environmental factors considered in the study were room temperature, relative humidity, indoor carbon dioxide, dust settlement rate, and microbial flora. The measurements were performed during daytime, after breakfast over a single period of 4–6 h. In addition, hospital vicinity to heavy trafficked roads was included as a proxy variable for indoor traffic pollution. The measurements were performed from December 1995 to February 1996.

The 14 geriatric hospitals entailed 18 buildings, with 36 nursing departments. The ages of the buildings ranged from 3 to 75 years. There were no humidification or air-cooling devices in any of the buildings. Indoor smoking was partly restricted. In some departments smoking was restricted to certain areas, in others the residents were allowed to smoke in the main living areas and/or in their rooms. In general the staff were not allowed to smoke indoors. Some visible sign of dampness or microbial growth were observed in two of the buildings.

Outside the hospitals outdoor temperature and relative humidity (Vaisala Humidity & Temperature indicator HMI 31; Vaisala OY, Helsinki, Finland) were measured. Inside in the main living area temperature, relative humidity and carbon dioxide (Telaire koldioxidmätare; Telaire Europe AB, Delsbo, Sweden) were measured. The measurements were made at three different locations (1.1 m above the floor) in each department. For each location the mean value were recorded. In the analyses the average of the three locations were used.

Dust settlement rate was measured during 1 week with a dust detector (BM-Dustdetector, N. P. Klock, Nivå, Denmark) by a laser extinction meter expressed as area covered by dust in percent of total surface areas. The measurements were performed on standardised steel plates, which were placed horizontally 1–1.5 m above the floor, and were collected dust for one week. The surfaces were protected with three barrels and the personnel were instructed not to touch the surface. The average of three samples from each steel plate was recorded. The dust settlement rate was measured at two locations in each department. Prior to use the steel plates were cleaned with ethanol.

Viable microbiological samples were collected with a centrifugal air sampler (Biotest RCS sampler; Biotest, Solihull, UK) and agar strips (Hycon Agar Stripes; Biotest, Solihull, UK). The substrates used for sampling were Tryptic Soy Agar (total counts) and Rose-Bengal-agar for moulds. The sampling volume was 40 l/min and the sampling time was 8 minutes pr agar. At least two sampling locations in each department were chosen: one in the middle of the living room and one close to the exhaust air duct. If a mechanical air supply existed, a third sample was taken near the air supply duct. Outdoor samplings were used as reference. The samples were incubated at room temperature (22°C) and at 37°C for 1–2 weeks. Major alterations of the composition of the indoor microbial flora as compared to the outdoor sample taken at the same time were identified by visual inspection of the stored media. An altered microbial flora in one or more of the samples was considered as an indication of microbial amplification in the building or ventilation system. In addition presence of *A. fumigatus* in any of the indoor samples was noticed.

All the measurements and classifications of the microbial flora were done without knowledge of the results from the initial questionnaire survey or the clinical examination.

Urban vicinity was considered as a proxy of traffic pollutants in the indoor environment. Four of the hospitals were situated in the inner city of the municipal and one fifth were situated near a main road outside the city hub, where traffic was the main source of outdoor air pollution, especially during the wintertime, when studded tyres are in use by most of the vehicles. The hospitals were situated near roads with an approximate traffic density at 20–25,000 vehicles per 24 h. In the inner city, during the actual period, the maximum outdoor levels of CO were 14 μg/m^3 (on an 8-h average) and the maximum levels of total dust were 250 μg/m^3 (on an 24-h average). No measurements of indoor traffic pollution were performed at the geriatric hospitals.

No information about the results of the measurements was relayed to the hospital units before the clinical examinations were completed.

Statistical analysis

Due to a non-normal distribution of the physiological parameters, non-parametric tests (Kendall's rank correlation test or, when appropriate, the Mann-Whitney U-test) were used in the initial bivariate analyses, to address possible relationships between physiological findings, personal characteristics and environmental factors. The analyses were done in two steps. First, possible correlations between continuous variables were addressed, and second, possible relationships between physiological findings and dichotomised environmental factors were addressed. These analyses were performed on non-transformed data. In the text the correlation coefficient "Kendall's tau-b", and the P-values for the correlation test and the Mann-Whitney U-test are given.

After log-transformation of the BUT and the total CS score, the residuals approximate a normal distribution. Therefore multiple linear regression analyses were applied to address possible relationships between the environmental factors and the biological measures, with adjustment for possible confounding factors (age, childhood eczema, and current smoking status). The regression analyses were done in three steps. First, all relevant environmental factors were entered into the model one by one (model A), and then together (model B and C). Adjustments for three possible confounding factors (age, current smoking and childhood atopy) were made in all models. In model C, additional adjustment for persistent mucous membrane symptoms was performed.

In the text the regression coefficient (b) and the 95% confidence interval (95% CI) are given on a logarithmically scale. Upper and lower confidence limits with the same sign (+/−), indicate a level of significance of more than 0.05 (e.g. P-values <0.05).

Collinearity diagnostics were applied for the multiple regression models (Hamilton,1992). A high correlation between coefficients in the models and a tolerance below 0.2 were used as indicators of collinearity problems. All the data were analysed by the SPSS for Windows version 9.0 (Statistical Product and Service Solutions (SPSS), Chicago, IL, USA).

The protocol of the study was approved by the Ethical Committee for Medical Research in Mid-Norway and the Norwegian Data Inspectorate Board.

Results

Environmental factors

The climatic conditions at the nursing departments at the time of the clinical examinations were characterised by low outdoor temperatures ranging from −12–+5 °C (median 0.3 °C) and by indoor temperatures ranging from 21.7–25.1 °C. Median values for temperature, relative humidity, carbon dioxide and dust settlement rate are given in Table 1. The average differences between measured temperature, relative humidity, carbon dioxide and dust settlement within the same departments were 0.2 °C, 1%, 50 ppm and 0.1%, respectively. An altered microbial air flora was detected in nine of the nursing departments. In three of these departments growth of *A. fumigatus* was identified and only in samples from the air supply duct. The microbial air flora in the two buildings with visible indications of dampness or microbial growth in the building construction was characterised as normal. A positive association between temperature and growth of *A. fumigatus* was observed (Mann-Whitney U-test, $P<0.001$).

Ocular measurements and personal factors

The median value of BUT was 8.0 s. with a range from 1.3–85 s (n=174). The total conjunctival staining (CS) score ranged from 0–8 with a median value of 2 (n=132). Decrease in BUT was observed with increasing age (Kendall's tau-b=−0.17, P=0.001). The influence of age was most pronounced in subjects older than 40 years. Decreased BUT was also observed in subjects with mucous membrane symptoms compared with subjects without such symptoms (Mann-Whitney U-test, P=0.04). There were no significant relationship between BUT and a history of childhood eczema. Regarding the total CS score, the amount of stains was observed to be higher in current smokers compared to non-smokers (Mann-Whitney U-test, P=0.04). No significant relationships were observed between total CS score and age and childhood eczema.

Table 1 Median values and interquartile range of temperature, relative humidity, carbon dioxide and dust settlement rate in the 36 nursing departments of geriatric hospitals in the municipality of Trondheim

Environmental factors	Median	Interquartile range
Temperature (°C)	23.2	23.0–23.7
Relative humidity (%)	24	17–26
Carbon dioxide (ppm)	570	490–650
Dust settlement (% surface pr week)	1.6	1.3–2.2

Table 2 Relationships between tear-film break-up time (BUT) and conjunctival staining (total CS score) and environmental factors in geriatric hospitals in the municipality of Trondheim

Environmental factors	BUT (n=174)		Total CS score (n=132)	
	tau-b[1]	P-value[2]	tau-b[1]	P-value[2]
Temperature (°C)	−0.13	0.02	0.02	0.80
Relative humidity (%)	−0.07	0.21	−0.11	0.09
Carbon dioxide (ppm)	0.01	0.82	−0.10	0.12
Dust settlement (% of surface pr week)	−0.17	0.001	−0.05	0.49

[1] Coefficient of correlation (Kendall's tau-b), [2] Two-tailed test for significance

Relationships between environmental and ocular measurements

Possible relationships between environmental measurements and ocular signs were initially addressed by bivariate correlation analyses. As shown in Table 2, relationships were indicated between BUT and temperature and dust settlement rate. In Table 3, the median values and the interquartile range recorded for BUT across two categories of temperature, relative humidity, carbon dioxide, dust settlement rate, and microbial flora are given, together with values obtained in subjects working in departments with identified growth of *A. fumigatus* and situated in the urban areas of the municipality with heavy traffic. A reduced BUT was related to increased temperature, dust settlement rate, altered microbial flora, growth of *A. fumigatus* and vicinity of the hospital. In the bivariate analyses, significant statistical differences were observed for dust settlement, growth of *A. fumigatus*, and urban vicinity of the hospital. When comparing the tear-film stability in personnel working at the six departments with an altered microbial flora without growth of *A. fumigatus* with those in departments with normal microbial flora no differences were observed.

In Table 4, the possible relationships between BUT and four of the environmental factors: temperature, dust settlement rate, growth of *A. fumigatus*, and urban vicinity were addressed by means of multiple linear regression. As indicated by negative regression coefficients, increasing temperature and concentration of airborne particles were associated with BUT, as well as the growth of *A. fumigatus* and urban vicinity of the hospital. When corrections for other environmental factors were done, statistically significant differences in BUT could be demonstrated related to dust settlement and the urban vicinity of the hospital. The differences were statistical, significant even after the adjustment of mucous membrane symptoms. No other relationships were observed between BUT and building or environmental factors.

With respect to conjunctival staining an increased staining of the conjunctiva was observed in depart-

Table 3 Median values and interquartile range (IQR) recorded for tear-film break-up time across two categories of temperature, relative humidity, carbon dioxide, dust settlement rate, microbial flora, growth of *A. fumigatus*, and vicinity of the hospital in the study population of female nursing personnel at geriatric hospitals in the municipality of Trondheim (n=174)

Environmental factors	Cut off points	Tear-film break-up time (BUT)			
		n	Median	IQR	P-value[1]
Temperature (°C)	<23	54	10.0	4.4–16.3	
	>23	120	7.8	4.3–12.8	0.24
Relative humidity (%)	<24	86	8.1	4.2–14.7	
	>24	88	7.9	4.7–13.0	1.00
Carbon dioxide (ppm)	<570	118	7.9	4.2–14.8	
	>570	56	8.0	5.0–14.3	0.48
Dust settlement rate (% of surface pr week)	<1.6	77	9.5	5.1–18.1	
	>1.6	97	7.2	4.2–11.9	0.03
Microbial flora	Normal	113	9.0	4.6–14.7	
	Altered	61	7.2	4.2–13.6	0.32
A. fumigatus	No	139	8.8	4.7–15.3	
	Yes	35	5.4	3.5–12.1	0.04
Urban vicinity of the hospital (heavy traffic)	No	102	10.4	5.6–16.2	
	Yes	72	5.7	3.5–9.6	<0.001

[1] Mann-Whitney U-test (two-tailed)

Table 4 Tree multiple linear regression models with partial regression coefficients (b) with 95% confidence intervals (95% CI) showing occurrence relations between four determinants; temperature (°C), dust settlement (% pr week), growth of *A. fumigatus* (no/yes) and urban vicinity of the hospital (no/yes), on the one hand, and BUT (s), on the other. The environmental factors were first entered one by one (model A), and then together (model B and C). Adjustments for three possible confounding factors (age, current smoking and childhood atopy) were made in all models. In model C, additional adjustment for persistent mucous membrane symptoms was performed. The unit of the regression coefficient (b) is that of the outcome variable per unit change in the independent variable on a log-normal scale (n=174)

Model	Temperature (°C)				Dust settlement (% per week)				Growth of *A. fumigatus* (no/yes)				Urban vicinity of the hospital			
	b	95% CI			b	95% CI			b	95% CI			b	95% CI		
A	−0.20	−0.34	−0.06	**	−0.30	−0.48	−0.12	**	−0.35	−0.64	−0.06	*	−0.50	−0.72	−0.27	***
B	−0.02	−0.24	0.21		−0.30	−0.46	−0.11	**	−0.16	−0.62	0.29		−0.48	−0.71	−0.25	***
C	−0.03	−0.25	0.20		−0.30	−0.47	−0.13	**	−0.09	−0.55	0.36		−0.44	−0.67	−0.22	***

* p<0.05; ** p<0.01; *** p<0.001

ments with an altered microbial flora (median=3) compared to those with normal microbial flora (median=2, Mann-Whitney U-test, P=0.01). The relationship remained statistically significant after adjustment for personal (age, childhood eczema, and current smoking habit) and other environmental factors, such as temperature, dust settlement rate and vicinity of the hospital, by means of multiple linear regression (b=0.17, 95% CI 0.07–0.28). Additional adjustment for mucous membrane symptoms did not change the coefficient significant. A similar result was observed when growth of *A. fumigatus* was considered (b=0.23, 95% CI 0.01–0.44); however, after additional adjustment for mucous membrane symptoms, the relationships were no longer statistically significant. No other relationships were observed between conjunctival staining and building or environmental factors.

Discussion

Our results indicate that environmental factors in hospitals might result in ocular effects, and that these effects persist enough time to be detected at a standardised investigation in another building, at constant room temperature. The most consistent finding was related to dust settlement and urban vicinity of the hospital and reduced tear-film stability. Reduced tear-film stability was also observed in relation to growth of *A. fumigatus* and increased temperature, but only in the initial analyses. Instabilities of the tear-films were also observed to be augmented in departments with elevated temperatures. Increased conjunctival staining was related to altered microbial flora.

The study was performed in a sample of subjects with and without persistent mucous membrane symptoms in their eyes, nose and upper airways (MMS) (from the MM-040 questionnaire). Selection bias due to this two-step selection procedure and the low participation rate (52%) might have occurred. Data from the initial questionnaire survey indicated numerical differences between participants and non-participants. Participants could be somewhat more focused on having a good indoor climate, and more prone to react with immediate type allergy (a history of childhood eczema). However, since we are not studying symptoms, but clinical signs, we do not think that these differences have seriously hampered the conclusions of the study. The low participation rate might partly be explained by the change in the workforce between the initial questionnaire survey (April–May) and the subsequent clinical examination (November–March). Change of job or long-term leave owing to sickness, pregnancy or other reasons were verified in 38 subjects. In addition, some of the head-nurses were not willing to let personnel participate in the clinical examinations in their work-time (verified in 15 subjects).

After two months, with some episodes of serve eye stinging after the use of Rose-Bengal dye, we decided to end the use of this dye, resulting in loss of some CS measurements until the Lissamine-Green B dye was available. This explains the differences in the numbers of females in the study of BUT and CS. The shift of dye might have introduced some bias in the study, however, since Rose Bengal dye and Lissamine-Green B dye are reported to stain mucous protein and areas of devitalised epithelium of the ocular surface in a similar fashion (Manning et al., 1995), we do not think that this shift has introduced any serious bias into the study. Another source of error might be related to the time variability in environmental factors and biological outcomes. In maximum the environmental and clinical examination took place 1 month apart. This time difference might have influenced the results. However, in our experience, factors such as indoor temperature, carbon dioxide, and dust settlement rate are stable over such time periods in large institutions like geriatric hospitals. However, possible misclassification due to variability in time and space is most likely non-differential, resulting in a dilution of the studied effects, and not likely to cause a differential misclassification causing in false-positive results. Therefore, we do not believe that our conclusions are seriously biased by these errors.

The BUT values obtained in this study (median 8.0 s) were comparable with previously reported values from healthy unexposed subjects in Danish chamber studies, applying the same technique. The lowest values from these studies (mean 5.3 s) (Pan et al., 2000) were obtained at 21°C and 24% relative humidity, values characteristically for the indoor climate during the winter season in large parts of Scandinavia, whereas the other studies (mean range 20–38 s) (Kjærgaard et al., 1989) were conducted under conditions typical for the summer season (23°C and 45% RH). However, higher normal values have been reported (Norn, 1969; Lemp and Hamill, 1973; Menger et al., 1985; Wyon and Wyon, 1987). The large range in reported normal values is most likely due to differences in the applied techniques. However, climatic conditions might also play a role as indicated. With respect to conjunctival staining (total CS score), to our knowledge, no other studies have reported results using sum of vital staining scores in the field of indoor climate research.

Decreasing BUT was observed with increasing age and in subjects with reported mucous membrane symptoms. This is in agreements with studies of dry eye conditions, which are reported to increase by age, especially in post-menopausal women (Holly and Lemp, 1977). The increased occurrence in women of dry eye conditions with increasing age might be a result of oestrogen deficiency (De Roetth, 1952), reduced tear quality and production and reduced corneal sensitivity (Mishima et al., 1966). The conjunctival staining was increased in current smokers, compared to non-smokers. This might be due to increased eye exposure to irritants in the cigarette smoke. In accordance with this view, increased conjunctival staining has been demonstrated with increased dust exposure (Kjærgaard, 1992).

Our study was performed during wintertime, in northern Scandinavia, with an indoor climate characterised by high room temperature, and low relative humidity. The low indoor relative humidity was a consequence of high room temperature, low outdoor temperature and high outdoor airflow rate, as indicated by low indoor levels of carbon dioxide. In subjects suffering from dry eyes, tear evaporation is increased (Mathers and Daley, 1996), making these subjects more vulnerable for conditions facilitating increased evaporation (e.g. low relative humidity and high temperatures). This might be one explanation of the observed decrease in tear-film stability observed in persons working in departments with high room temperature. Previous studies have shown increased levels of volatile organic compounds (VOC) related to increased temperature (Norbäck et al., 1990) as well as an interactive effect between VOC and temperature on BUT (Mølhave et al., 1993).

Presence of *A. fumigatus* was identified in samples from the air supply ducts and in buildings without visible sign of building dampness or microbial growth, indicating the ventilation unit as site of the microbial amplification. We consider the observed decrease in tear-film stability among personnel working in departments with presence of *A. fumigatus* to be in agreement with previous studies reporting mucosal effects related to mould exposure (Wålinder et al., 1997; Norbäck et al., 1999, 2000). The weak associations between microbial findings and ocular outcomes observed in this study might be related to the sampling strategy (e.g. few samples, and short sampling time) and the analytical method used in this study (e.g. visual inspection of outdoor and indoor samples). With this tool positive findings might be of significance, while negative findings might be more difficult to interpret, due to the low sensitivity of the method.

The BUT was decreased in subjects working at hospitals situated in the urban region of the municipality. Due to local traffic and geographic conditions in the municipality, the inner city and areas close to the main roads are exposed to higher levels of traffic pollution than other parts of the municipality. During the wintertime the levels of traffic pollutants in these areas periodically exceeds the national air quality guidelines (The Norwegian Board of Health, 1999). In agreement with this view, progressive increases in degree of eye inflammation have been observed following the living zone of patients from suburban areas with low to inner city areas with high air pollution levels (Versura et al., 1999). This study was performed in Bologna, Italy, where the levels of NO_2, dust (PM_{10}), and CO are reported periodically during the wintertime to exceed 90 $\mu g/m^3$, 100 $\mu g/m^3$, and 4.0 mg/m^3, respectively (Ferrecchi et al., 1999). An effect of indoor traffic pollution have also been seen amongst Swedish school employees, where increased sign of nasal inflammation was observed among personnel at schools situated near roads with heavy traffic compared to schools situated in areas without heavy traffic (Norbäck et al., 2000). However, lacking measurements of traffic pollutants in the indoor environments, we could only hypothesize a relationship between increased instability of the tear-film and increased levels of traffic pollutants.

More than half of the employees (56%) worked at hospitals with a dust settlement rate higher than 1.6 % per week. Among employees at these hospitals lower tear-film stabilities were observed. The dust settlement rate might reflect the dustiness or airborne particle concentration at the department, influenced by cleaning procedures, quality of air filtration, hygienic standards of the ventilation unit and sources at the department. Dust concentrations on easily accessible surfaces in offices and kindergartens have shown higher mean values of 2.6% and 4.2%, respectively (Kildesø et al., 1998). These differences probably represent differences in methodology. Our measurements were performed on clean steel plates, which had collected dust for 1 week, reflecting the weekly dust settlement rate, while the other measurements were performed directly on the furniture surfaces reflecting the cleaning practise. In chamber studies, after exposure to house dust, decreased tear-film stabilities have been reported (Mølhave et al., 1985; Pan et al., 2000). Decrease in tear-film stability has also been observed 1 day after exposure (Mølhave et al., 1985), indicative of a subclinical eye inflammation causing a persistent change in tear-film stability. The existence of such persistent change in the tear-film stability due to dust exposure is supported by our findings. This, however, contradicts the common view that BUT only reflects more temporary effects.

Weighted by statistical techniques, dust settlement rate and the vicinity of the hospital seems to be the two most potent environmental factors causing tear-film instability, while an altered microbial flora seems to be the most prominent external factor causing increased staining of the conjunctiva. However, any conjuncture of the relative importance of possible environmental factors might be unsure. We therefore conclude that winter conditions in northern Scandinavia, with low indoor air humidity and high room temperature, increased dust settlement rate and alternation of the indoor microbial flora, particularly with growth of *Aspergillus fumigatus*, were associated with decreased tear-film stability and indications of conjunctival damage. We also hypothesize that increased tear-film stability was associated with traffic pollution. The results illustrate the significance of good hygienic standards causing low concentrations of airborne particles, prevention on microbial growth in buildings and ventilation systems, and suggest that improvement of ambient air quality and lower room temperatures could be positive from a health point of view.

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References

Ahlen, C. (1995) Determination of viable microbes in indoor air – what do we gain? In: Flatheim, G., Berg, K.R. and Edvardsen, K.I. (eds). *Proceedings from Indoor air quality in practice. Moisture and cold climate solutions*, Oslo, Moberg & Helli AS, pp. 255–259.

Andersson, K. (1998) Epidemiological approach to indoor air problems, *Indoor Air*, **8 (Suppl. 4)**: 32–39.

Andersson, K. and Stridh, G. (1992) The use of standardized questionnaires in building-related illness (BRI) and sick building syndrome (SBS) surveys. In: Levy, F. and Maroni, M. (eds). *NATO/CCMS Pilot study on indoor air quality. 4th plenary meeting. Epidemiology and medical management of building-related complaints and illnesses. Report on a meeting held in Oslo, Norway 19–21 August, 1991*, Oslo, National Institute of Occupational Health, pp. 47–64.

Apter, A., Bracker, A., Hodgson, M., Sidman, J. and Leung, W.Y. (1994) Epidemiology of the sick building syndrome, *Journal of Allergy and Clinical Immunology*, **2**, 277–288.

von Bijsterveld, O.P. (1969) Diagnostic Tests in the Sicca Syndrome, *Archives of Ophtalmology*, **82**, 10–14.

De Roetth, A.F.M. (1952) Low flow of tears – The dry eye, *American Journal of Ophthalmology*, **35**, 782–787.

Ferrecchi, P., Mazzetti, R., Milia, E., Zanarini, M., Pipitone, E., Morselli, M., Poluzzi, V., Faggioli, A.F., Po, C., Zanini, G. and Rondini, C. (1999) *Relazione annuale sulla qualita' dell'aria 1999 della Città di Bologna*, Bologna, Comune di Bologna, Unita ambiente.

Flannigan, B. (1992) Indoor microbiological pollutants – sources, species, characterisation and evaluation. In: Knöppel, H., Wolkoff, P. (ed). *Chemical, microbiological, health and comfort aspects of indoor air quality–State of the art in SBS. EUR 14289*, Dordrecht, Kluwer Academic Publishers, pp. 73–98.

Flannigan, B. and Miller, D. (1994) Health implications of fungi in indoor environments – an overview. In: Samson, R.A., Flannigan, B., Flannigan, M.E., Verhoeff, A.P., Adan, O.C.G. and Hoekstra, E.S. (eds) *Health implications of fungi in indoor environments*, Air quality monographs, Vol 2. Amsterdam, Elsevier, pp 3–28.

Franck, C. (1986) Eye symptomes and signs in buildings with indoor climate problems ('office eye syndrome'), *Acta Ophtalmologica*, **64**, 306–311.

Gyntelberg, F., Suadicani, P., Nielsen, J.W., Skov, P., Valbjörn, O., Nielsen, P.A., Schneider, T., Jorgensen, O., Wolkoff, P., Wilkins, C.K., Gravesen, S. and Norn, S. (1994) Dust and the sick building syndrome, *Indoor Air*, **4**, 223–238.

Hamilton, L.C. (1992) *Regression with graphics. A second course in applied statistics*, Belmont, Duxbury Press.

Holly, F.J. and Lemp, M.A. (1977) Tear physiology and dry eyes, *Survey of Ophthalmology*, **22**, 69–87.

Kildesø, J., Tornvig, L., Skov, P. and Schneider, T. (1998) An intervention study of the effect of improved cleaning methods on the concentration and composition of dust, *Indoor Air*, **8**, 12–22.

Kjærgaard, S. (1992) *Objective eye changes in the indoor climate – a prospective study* [in Danish with an English summary], Copenhagen, The Danish Building Agency, Ministry of Housing.

Kjærgaard, S.K., Mølhave, L. and Pedersen, O.F. (1989) Human reactions to indoor air pollutants: n-decane, *Environment International*, **15**, 473–482.

Lemp, M.A. and Hamill, J.R. (1973) Factors affecting tear film breakup in normal eyes, *Archives of Ophthalmology*, **89**, 103–105.

Lenvik, K. (1993) Smoking habits, atopy, and prevalence of sick-building syndrome symptoms among office workers in Norway, *Environment International*, **19**, 333–340.

Manning, F.J., Wehrly, S.R. and Foulks, G.N. (1995) Patient tolerance and ocular surface staining characteristics of lissamine green versus rose bengal, *Ophthalmology*, **102**, 1953–1957.

Mathers, W.D. and Daley, T.E. (1996) Tear flow and evaporation in patients with and without dry eye, *Ophthalmology*, **103**, 664–669.

Menger, L.S., Bron, A.J., Tonge, S.R. and Gilbert, D.J. (1985) A non-invasive instrument for clinical assessment of the pre-corneal tear film stability, *Current Eye Research*, **4**, 1–7.

Mishima, S., Gasset, A. and Klyce, S.D.J. (1966) Determination of tear volume and tear flow, *Investigative Ophthalmology and Visual Science*, **5**, 264–276.

Muzi, G., dell'Omo, M., Abbretti, G., Accattoli, P., Fiore, M.C. and Gabrielli, R.A. (1998) Objective assessment of ocular and repiratory alternations in emplyees in a sick building, *American Journal of Industrial Medicine*, **34**, 79–88.

Mølhave, L., Kjærgaard, S.K., Attermann, J. and Pedersen, O.F. (1985) *House dust and indoor climate [in Danish with English summary]. Report to Arbejdsmiljøfondet*, Aarhus, Institute of Environmental and Occupational Medicine, University of Aarhus, pp. 1–283.

Mølhave, L., Liu, Z., Jørgensen, A.H., Pedersen, O.F. and Kjærgaard, S.K. (1993) Sensory and physiological health effects on humans of combined exposure to air temperatures and volatile organic compounds, *Indoor Air*, **3**, 155–169.

Norbäck, D., Björnsson, E., Janson, C., Palmgren, U. and Boman, G. (1999) Current asthma and biochemical signs of inflammation in relation to building dampness in dwellings, *International Journal of Tuberculosis and Lung Disease*, **3**, 368–376.

Norbäck, D. and Edling, C. (1991) Environmental, occupational, and personal factors related to the prevalence of sick building syndrome in the general population, *British Journal of Industrial Medicine*, **48**, 451–462.

Norbäck, D., Torgen, M. and Edling, C. (1990) Volatile organic compounds, respirable dust, and personal factors related to prevalence and incidence of sick building syndrome in primary schools, *British Journal of Industrial Medicine*, **47**, 733–741.

Norbäck, D., Wålinder, R., Wieslander, G., Smedje, G., Erwall, C. and Venge, P. (2000) Indoor air pollutants in schools: nasal patency and biomarkers in nasal lavage, *Allergy*, **55**, 163–170.

Nordström, K., Norbäck, D., Wieslander, G. and Wålinder, R. (1999) The effect of building dampness and type of building on eye, nose and throat symptoms in Swedish hospitals, *Journal of Environmental Medicine*, **1**, 127–135.

Norn, M.S. (1969) Desiccation of the precorneal film. I. Corneal Wetting-Time, *Acta Ophthalmologica*, **47**, 865–880.

Norn, M.S. (1973) Lissamine green. Vitale Staining of Cornea and Conjunctiva, *Acta Ophtalmologica*, **51**, 483–490.

The Norwegian Board of Health. (1999) *Bedre byluft. Rapport fra arbeidsgruppe som har vurdert strakstiltaksnivåer, varslingsgrenser og terminologi. IK-2674* [Translated book title: Better urban air quality. Report from a working group, considering alert thresholds, information thresholds and terminology], Oslo, The Norwegian Board of Health.

Pan, Z.W., Mølhave, L. and Kjærgaard, S.K. (2000) Effects on eyes and nose in humans after experimental exposure to airborne office dust, *Indoor Air*, **10**, 237–245.

Pieckova, E. and Jesenska, E. (1999) Microsopic fungi in dwellings and their health implications in human, *Annals of Agricultural and Environmental Medicine*, **6**, 1–11.

Raw, G.J., Roys, M.S. and Whitehead, C. (1993) Sick building syndrome: Cleanliness is next to healthiness, *Indoor Air*, **3**, 237–245.

Schneider, T., Løbner, T., Nilsen, S.K. and Petersen, O.H. (1994) Quality of cleaning quantified, *Building and Environment*, **29**, 363–367.

Versura, P., Profazio, V., Cellini, M., Torreggiani, A. and Caramazza, R. (1999) Eye discomfort and air pollution, *Ophthalmologica*, **213**, 103–109.

WHO. (1983) *Indoor air pollutants exposure and health effects report on a WHO meeting, Nördlingen, 8–11 June 1982*, Copenhagen, WHO Regional Office for Europe (EURO reports and studies 78).

WHO. (1986) *Indoor air quality research report on a WHO meeting, Stockholm*, Copenhagen, WHO Regional Office for Europe (EURO reports and studies 103).

Wieslander, G., Norbäck, D., Nordström, K., Wålinder, R. and Venge, P. (1999) Nasal and ocular symptoms, tear film stability and biomarkers in nasal lavage, in relation to building-dampness and building design in hospitals, *International Archives of Occupational and Environmental Health*, **72**, 451–461.

Wong, H., Fatt, I. and Radke, C.J. (1996) Deposition and thinning of the human tear film, *Journal of Colloid and Interface Science*, **184**, 44–51.

Wyon, N.M. and Wyon, D.P. (1987) Measurement of acute response to draught in the eye, *Acta Ophthalmologica*, **65**, 385–392.

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