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OFFICE ILLNESS

The Worker, the Work and the Workplace

Berndt Stenberg

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ABSTRACT

This thesis addresses health problems related to indoor environmental factors in office workers. The overall aim is to increase knowledge about the relationship between the occurrence of perceived symptoms and potential risk indicators, and about methodological issues of relevance for future research and preventive work.

The work started with the clinical observations in patients working in buildings with indoor air problems. Signs of seborrhoeic dermatitis, erythematous facial skin conditions and itching conditions on the trunk were noted. Another point of departure was the attribution of facial skin symptoms to VDT work by patients. A questionnaire-based prevalence study of symptoms compatible with the Sick Building Syndrome (SBS) and facial skin symptoms in 4,943 office workers formed the basis for two case referent studies, one focusing on SBS, the other on facial skin symptoms in VDT workers.

The prevalence of SBS was three times higher in women than men. The prevalence was higher in young persons and in atopics. Facial skin symptoms showed the same pattern. Psychosocial work load, paper and VDT work were also risk indicators for SBS and for skin symptoms. The symptom excess in women was analyzed with reference to differences in biological or acquired risks and different illness and reporting behaviour. In spite of inequalities in social conditions at home and at work and differences in physical working conditions, these differences could only explain a small part of the gender difference. The odds ratio for SBS in women was lowered from 3.4 in the crude analysis to 3.0 in the multivariate analysis. Effect modification was in most cases stronger in men and the clinical validation of the questionnaire refuted the hypothesis that women over-report symptoms. The results indicate that the gender difference in symptom prevalence is part of a general pattern common to psychosomatic illnesses.

In the case referent study of SBS, atopy, psychosocial work load, buildings built or renovated after 1977, the presence of photocopiers and a low outdoor air flow rate were risk indicators. The association between air quality and the occurrence of SBS symptoms was demonstrated by a flow-response relation between the outdoor air flow rate and SBS symptoms. In the case referent study of skin symptoms in VDT work, psychosocial work load, electric background fields, the presence of fluorescent lights with plastic shields and low cleaning frequency were risk indicators. The clinical findings in the two case groups and their referents supported the applied relevance of the studies. Compared with the referents, the SBS cases had more work-related facial erythema, seborrhoeic dermatitis and general pruritus, while skin symptom cases, had more work-related facial erythema than their referents.

The results show that SBS symptoms and facial skin symptoms have a multifactorial background with constitutional, psychosocial and physical risk indicators. As the indoor air quality is a determinant of SBS symptoms, and the building itself is but one source of indoor air pollution, it is suggested that the name Sick Building Syndrome (SBS) be replaced by Indoor Air Syndrome (IAS).

Key words: Sick Building Syndrome, Indoor Air Syndrome, facial skin symptoms, constitutional factors, psychosocial factors, indoor air quality, outdoor air flow rate, electromagnetic conditions, VDT work

ORIGINAL PAPERS

This thesis is based on the following papers

I Stenberg B. Skin complaints in buildings with indoor climate problems. *Envir Int* 1989; 15: 81–84.

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

III Stenberg B, Wall S. Why do women report sick building symptoms more often than men? *Soc Sci Med*. In press.

IV Stenberg B, Eriksson N, Höög J, Sundell J, Wall S. The sick building syndrome (SBS) in office workers. A case referent study of personal, psychosocial and building–related risk indicators. *Int J Epidemiol*. In press.

V Stenberg B, Eriksson N, Hansson Mild K, Höög J, Sandström M, Sundell J, Wall S. Facial skin symptoms in VDT workers. A case referent study of personal, psychosocial, building– and VDT–related risk indicators. Submitted for publication.

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GLOSSARY & DEFINITIONS

Clinical terms

"Office Illness"
A concept which has been used in Sweden to designate multi-symptomatic complaints perceived by office workers and attributed to such factors as work with carbonless copy paper, indoor air quality factors and work at a Visual Display Terminal (VDT).

Seborrhoeic dermatitis
A scaling dermatitis of the face, the scalp and the upper trunk. Associated with oily skin, seborrhoea, and a history of dandruff and a proneness to facial erythema.

Rosacea
A disease primarily affecting facial skin and characterized by proneness to flushing, facial erythema, oedema, papules, pustules and widened superficial blood vessels (teleangiectasis). Involvement of the eyes is common.

Atopic dermatitis
A chronically relapsing eczema characterized by itching and dry skin and often affecting the skin folds (flexural dermatitis). It is often also localized to the face and the hands in adults. The eczema is associated with allergic rhinitis (hay fever) and allergic asthma.

General symptoms
Includes symptoms such as headache, dizziness, fatigue, and difficulties on concentrating.

Epidemiological terms

Aetiologic cases
With a given outcome, exposure factors and study population, aetiologic cases are those cases among the exposed that would be reduced if the exposure were eliminated. Aetiologic cases can be used to estimate the potential public health impact of a certain exposure.

Case report
The case report is a detailed profile of a single subject documenting unusual or unknown features of a disease or the patient's exposure history. Case reports can lead to the formulation of a new hypothesis. The case report can be expanded to *case series*.

Case referent study
A study that starts with the identification of persons with a certain outcome (cases) and a suitable reference group (referents). The relationship between an attribute (such as an exposure or a personal factor) and the outcome is examined by comparing the cases and the referents with regard to how often the attribute is present in each of the groups.

Clinical study
A term used here to designate a study which is neither a case report/series nor an observational study. The study describes clinical features of a group of patients with common characteristics, such as the reasons for referral to clinical examination.

Cross-sectional study
A study of the relationship between diseases (or other outcomes) and other variables of interest as they exist in a defined population at one particular time or during a specified time span. Synonym: *prevalence study.*

Experimental study
A study in which conditions are under the direct control of the investigator. In epidemiology, a study in which a population is selected for a planned trial of a regimen whose effects are measured by comparing the outcome of the regimen in the experimental group with the outcome of another regimen in a control group. Ideally, the experiment is blinded and the subjects randomly allocated to experimental or control group.

Follow–up study
A study in which individuals or populations, selected on the basis of whether they have been exposed to or possess a certain characteristic, are followed to assess the outcome of the exposure or the effect of the characteristic.

Observational study
A non–experimental study where changes or differences in one characteristic are studied in relation to changes or differences in others, without the intervention of the investigator. Observational studies include cross–sectional, follow–up and case referent studies.

Odds Ratio
The odds is the probability of the occurrence of an event to that of non–occurrence. The odds ratio is the ratio between two such odds. The odds ratio is used to illustrate the strength of the relationship between the occurrence of the outcome and the independent variables (the risk indicators).

Prevalence
The proportion of individuals in a given population with a given disease (or other characteristic) at a designated time.

Survey
A non–experimental population–based study.

Technical terms

Indoor Air Quality
An assessment of how well the air satisfies present standards of thermal conditions (temperature, relative humidity and velocity), concentrations of oxygen and carbon dioxide, and concentrations of gases, vapours, particles and radionuclides that can have deleterious effects or that can be perceived as objectionable by the occupants.[1)] Accordingly, in the Nordic guideline "Indoor Climate – Air Quality" (NKB 1991) is stated: "The quality of air is considered satisfactory if the great majority of visitors, on entry into the room, perceive the air as acceptable, if the air does not cause irritation to skin, mucous membranes or airways, not even in persons who are somewhat more sensitive than normal, if there is no risk of sensitization and if the risk of health effects after long–term exposure is negligible. Nor must the quality of air give rise to disease".

Outdoor air flow rate
Here used as the amount of outdoor air that reaches a room through the ventilation system. Recirculated air is not included. Often expressed as air changes per hour or as litres per second and person (L/s,p).

Notes: Most of the definitions derive from Last JM. A Dictionary of Epidemiology. 2nd Edition. New York: Oxford University Press, 1988.

1) The definition is cited from Woods JE. Air quality control strategies for health, comfort, and energy efficiency. In Berglund B, Lindvall T, Sundell J. (Eds) Indoor Air. Recent Advances In the Health Sciences and Technology. Swedish Council for Building Research, Stockholm, Sweden 1984, 43–50.

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1 INTRODUCTION

Work-related multi-symptomatic illnesses appearing in the office environment have been reported with increasing frequency since the 1970s. Working with carbonless copy paper has been cited as a cause of mucosal, skin, and general symptoms in employees in workplaces where large amounts of paper were handled in small, warm, poorly ventilated rooms.[1] Similar symptoms, supposedly caused by the building itself, have been reported under different names, the "Sick Building Syndrome" (SBS) being the most commonly used. SBS, as described by WHO,[2] is characterized by dryness and irritation of the airways, the eyes, and the skin, and general symptoms such as headache, nausea, and fatigue. Since the 1980s, yet another "office illness" has appeared. Skin symptoms, usually facial skin symptoms and signs, have been reported among Visual Display Terminal (VDT) workers.[3]

During the past twelve years, an increasing number of patients has been referred to the Department of Dermatology in Umeå from different workplaces where indoor air quality (IAQ) problems have been reported by the local medical services. The clinical observations in these patients were one starting point for this thesis (Paper I). Another point of departure was the case report of nine cases with VDT-related facial skin problems presented at the conference on *Work with Display Units (WWDU)* held in Stockholm in 1986.[4] The symptoms and signs had much in common with skin symptoms reported by occupants of buildings with IAQ problems[2] (Paper I) and a connection between VDT work and other indoor environment factors was suggested.[4]

A review of the pertinent literature is presented with a focus on peer-reviewed papers. Exceptions are made for reports often cited in papers in this field. Although the thesis largely addresses multi-symptomatic complaints, the focus is on skin symptoms. My own unpublished experience from clinical work in occupational dermatology at the Department of Dermatology, Umeå, is referred to as *clinical experience*.

1.1 Work with carbonless copy paper (CCP) and other paper brands

Carbonless copy paper (CCP) was introduced in the 1950s by the National Cash Register Company as NCR ("no carbon required") paper. Medical complaints attributed to work with CCP have been reported since the 1970s. There are basically two types of CCP. One type transfers colour from the top sheet, with the undersurface coated with a carbon paper like film, mechanically to the copy sheet. A typical example is an airline ticket. In the other type of CCP the colour forming chemicals are held on the undersurface of the top sheet, most commonly in microscopic capsules made of gelatin, gum arabicum, carboxymethylcellulose or synthetic co-polymers. The colour formers are prepared in a colourless state and dissolved in a solvent. The colour formers are released by pressure breaking the capsules. When absorbed into the top layer of the copy sheet, often coated with alkaline clay, they are converted to coloured products. Most case reports refer to work with the latter type of CCP. These types of CCPs have been shown to emit volatile substances, such as solvents.[5]

1.1.1 Case reports

Case reports from England,[1] Japan,[1] Sweden,[6] Denmark,[7] Belgium[8] and the US,[9,10] have shown a set of symptoms and signs involving the skin, eyes and upper and lower respiratory tract. Systemic symptoms, such as headaches, drowsiness and nausea, have also been reported. In most cases the reactions have been judged to be non-immunological. The skin symptoms

and signs reported are dry skin,[1,6] eczema/rash on hands and face,[1,7,8,10,12-14] burning lips and face,[1,6,7] flushing[9] and urticaria/angioedema.[9-11]

Reports on immunological reactions, such as allergic contact dermatitis from CCP are extremely rare. One positive patch test to *p*-toluene sulfonate of Michler's hydrol (PTSMH)[12] and one to crystal violet[14] have been reported. A case with contact urticaria and airway obstruction with a concomitant increase in prostaglandin F_2 and tromboxane B_2 has also been seen.[11] Whether this reaction was immunological or non-immunological could not be deduced.

Multi-symptomatic complaints, resembling those reported from work with CCP, have only occasionally been reported from other brands of paper or paper associated exposures. Facial erythema, eye irritation, and headaches attributed to vapour from a wet toner used in a photocopier has been described.[15] Similar symptoms have been reported in a repair man working with dry toner machines[16] as well as single cases of papillitis of the tongue from photocopying[17] and rhinitis from laser printer exposure.[18] Most reports on skin symptoms attributed to paper exposure, other than CCP, refer to contact dermatitis without signs of mucosal involvement or systemic symptoms.

1.1.2 Observational studies

There are a few questionnaire-based surveys of health effects of work with CCP from Denmark,[7,19] the US[20] and Sweden.[21] They have reported an exposure-response relation between the amount of paper exposure and the prevalence of skin and mucosal symptoms, as well as to general symptoms such as headache. Another Swedish study found an association between skin symptoms and a certain type of CCPs with desensitizing ink.[22]

1.1.3 Experimental studies/tests

Skin tests and challenge tests have been performed in addition to those mentioned under case reports. Skin patch, scratch or prick tests have shown very few positive reactions and it has been difficult to judge whether these test reactions have explained the clinical symptoms.[23] In a number of challenge tests, reactions in the upper and lower airways have been registered.[9, 11,24]

1.1.4 Clinical experience

Complaints from work with CCP were common in the 1970s, in the 1980s the number of patients referred with such complaints decreased. During the past ten years some patients have attributed their facial skin symptoms to exposure to photocopies or the use of photocopiers. In a number of those patients, placebo controlled blind challenge to vapours from dry toner has evoked a strong facial erythema. Quite commonly patients with multi-symptomatic complaints attributed to IAQ problems report worsening of symptoms from exposure to newly produced photocopies or reading fresh newspapers. Positive patch tests to "office allergens" or test reactions indicating contact allergy to substances in paper products are rarely seen.

1.1.5 Summary

The cited literature as well as the clinical experience indicate that most symptoms attributed to work with CCP are non-immunological reactions. Although most reports on paper-related symptoms refer to work with CCP, similar symptoms reported in association with the handling

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av

Berndt Stenberg

Umeå 1994

ABSTRACT

OFFICE ILLNESS – The Worker, the Work and the Workplace

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This thesis addresses health problems related to indoor environmental factors in office workers. The overall aim is to increase knowledge about the relationship between the occurrence of perceived symptoms and potential risk indicators, and about methodological issues of relevance for future research and preventive work.

The work started with the clinical observations in patients working in buildings with indoor air problems. Signs of seborrhoeic dermatitis, erythematous facial skin conditions and itching conditions on the trunk were noted. Another point of departure was the attribution of facial skin symptoms to VDT work by patients. A questionnaire–based prevalence study of symptoms compatible with the Sick Building Syndrome (SBS) and facial skin symptoms in 4,943 office workers formed the basis for two case referent studies, one focusing on SBS, the other on facial skin symptoms in VDT workers.

The prevalence of SBS was three times higher in women than men. The prevalence was higher in young persons and in atopics. Facial skin symptoms showed the same pattern. Psychosocial work load, paper and VDT work were also risk indicators for SBS and for skin symptoms. The symptom excess in women was analyzed with reference to differences in biological or acquired risks and different illness and reporting behaviour. In spite of inequalities in social conditions at home and at work and differences in physical working conditions, these differences could only explain a small part of the gender difference. The odds ratio for SBS in women was lowered from 3.4 in the crude analysis to 3.0 in the multivariate analysis. Effect modification was in most cases stronger in men and the clinical validation of the questionnaire refuted the hypothesis that women over–report symptoms. The results indicate that the gender difference in symptom prevalence is part of a general pattern common to psychosomatic illnesses.

In the case referent study of SBS, atopy, psychosocial work load, buildings built or renovated after 1977, the presence of photocopiers and a low outdoor air flow rate were risk indicators. The association between air quality and the occurrence of SBS symptoms was demonstrated by a flow–response relation between the outdoor air flow rate and SBS symptoms. In the case referent study of skin symptoms in VDT work, psychosocial work load, electric background fields, the presence of fluorescent lights with plastic shields and low cleaning frequency were risk indicators. The clinical findings in the two case groups and their referents supported the applied relevance of the studies. Compared with the referents, the SBS cases had more work–related facial erythema, seborrhoeic dermatitis and general pruritus, while skin symptom cases, had more work–related facial erythema than their referents.

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Key words: Sick Building Syndrome, Indoor Air Syndrome, facial skin symptoms, constitutional factors, psychosocial factors, indoor air quality, outdoor air flow rate, electromagnetic conditions, VDT work

of other types of paper, suggest that the difference in irritative potential between different brands of paper are quantitative rather than qualitative.

It is difficult to find office workers with exposure to only one type of paper and without exposure to other factors that have been reported to cause similar symptoms as CCPs. With very few exceptions,[19] the cited studies have not controlled for potential confounders. After a comprehensive investigation undertaken at the Swedish National Institute for Occupational Health it was concluded that many other factors influencing the indoor air quality and the indoor environment could explain medical complaints reported from work with CCP.[25] Using the frequency of paper handling as an exposure estimate is a surrogate, as the emissions of volatile and particulate agents may differ from one brand to another and with age of the paper and also from used to unused paper. Emissions from CCPs is one source for indoor air pollution and thus a potential cause for IAQ-related symptoms, but for methodological reasons such an association can be difficult to verify in observational studies.

1.2 Indoor Air Quality (IAQ) problems - the Sick Building Syndrome (SBS)

During the past 25 years health problems related to IAQ factors have received increased attention. "Sick" buildings were reported in the 1950s but have become a major occupational health problem in the last two decades.[2,26] In 1982 a World Health Organization expert group described the Sick Building Syndrome (SBS) as a combination of general, mucosal and skin symptoms, Table 1.[2]

Table 1. Prevalent symptoms reported by occupants of buildings with indoor air quality problems (WHO)[2]

eye, nose, and throat irritation
sensation of dry mucous membranes and skin
erythema
mental fatigue
headache, high frequency of airway infections, and cough
hoarsness, wheezing, itching, and non-specific hypersensitivity
nausea, dizziness

This is merely a list of symptoms reported among inhabitants of buildings with IAQ problems and is not an accepted clinical syndrome. Consequently, the concept of SBS has been given a different meaning by various investigators, skin symptoms are often excluded by Anglo-American investigators.[27] Criteria for the definition of SBS were recently suggested. These include specific symptoms and signs and odour or taste sensations combined with requirements for the prevalence of symptomatic inhabitants within the building. The cause must not be exposure to a single agent.[28]

SBS is commonly separated from "building related illnesses" (BRI) or "building related diseases" comprising established illnesses where the indoor environment factor causing the symptoms is often known, such as hypersensitivity pneumonitis, humidifier fever and Legionnaire's disease.[27] In some reviews, however, BRI includes SBS.[29,30] BRI is said to occur more frequently in buildings where SBS symptoms are prevalent.[31]

1.2.1 Case reports

Case reports describing clinical findings in people supposedly suffering from SBS are very rare. While some reviews have stated that SBS is characterized by the lack of clinical signs and that the perceived symptoms disappear when leaving the building,[32] others have pointed out the gradual onset and long duration of the symptoms.[33]

There are reports from outbreaks of "low humidity occupational dermatoses" in indoor workers. The common exposure factor found was a relative humidity around 35% and the symptoms disappeared when the humidity was raised to 45–50%. The clinical findings were pruritus and urticaria on covered areas of the body and a scaling dermatitis on the face, scalp, and ears.[34,35] These findings are similar to those reported from our department in employees of buildings with IAQ problems (Paper I).

Twenty office employees in the US were examined in connection with an outbreak of multi-symptomatic complaints after their office building underwent major renovation. Eighteen were said to meet the criteria for SBS, three had recent onset of asthma. No visible clinical signs were reported. Three subjects developed chronic symptoms consistent with multiple chemical sensitivity.[36]

1.2.2 Observational studies

Observational studies in SBS are summarized in Table 2. From the US, where IAQ problems are reported to be prevalent,[27] the literature predominantly comprises investigations of "problem buildings".[27,37,38] In a summary of the National Institute for Occupational Safety and Health (NIOSH) experience of approximately 450 field investigations of such buildings,[39] the primary problems found were inadequate ventilation (52%), contamination from inside (17%) or outside the building (11%), from microbiological growth (5%) or building fabric (3%) or were unknown (12%). In studies including "non-problem buildings", some of the risk indicators reported are female gender, low age, photocopying, crowding and volatile organic compounds (VOC).[40–42]

Several European cross-sectional studies of predominantly "non-problem buildings" from the UK,[43,44] Denmark,[19,45] Sweden,[46] Finland[47] and the Netherlands[48] have been published. Some of the major risk indicators reported for SBS symptoms are atopy,[46,47] female gender,[19,44,47,48] low job category,[19,44] unfavourable psychosocial factors,[19,46–48] handling of CCP and photocopying,[19] VDT work[19,46] and mechanical ventilation and/or air-conditioning.[43,44,45,48] Two Swedish studies of "problem" and control buildings[49,50] and one longitudinal study of primary schools[51] identified concentration of total volatile organic compounds (TVOC) and respirable dust, current smoking, wall to wall carpets and unfavourable psychosocial climate as risk indicators.

Office lighting has been suggested as one cause of symptoms, but this was not verified in a study focusing on this issue. There was however an association between the perception of glare and headache.[52] Indoor air humidity has been recorded in several studies, in one Finnish study symptom prevalences were lower in humidified buildings.[53] Several studies have reported an increased prevalence of symptoms in air-conditioned buildings[54] suggesting that microbial

growth in the ventilation system may induce symptoms.[44,54] A relationship between the prevalence of symptoms and airborne viable bacteria and fungi has, however, only rarely been verified.[55] Beta–1,3–glucan, an agent present on the cell wall of fungi and certain bacteria, was found to be associated with cough and skin symptoms in a Swedish study.[56]

There have been few observational studies with clinical findings as the outcome. A Swedish study is of particular interest as it focuses on reactions in children.[57] It is one of the studies on which the WHO list of SBS symptoms[2] is based (Lindvall T, personal communication). Dry and eczematous skin on the face and extremities were more frequently found among children in day care centres with IAQ problems compared with control buildings. The prevalence of foam at the inner eye canthus, which may reflect the condition of the tearfilm, has been found to be lower among office workers compared with a control population.[58]

Table 2. Main features of and results from observational studies on the sick building syndrome

OBSERVATIONAL STUDIES

Author Year of publication Country	Design Method	Return/ participation rate	Control for confounding	Results
Amelius et al 1982 (S) [57]	Selected problem and non-problem buildings, questionnaire, clinical examination	Not stated	No	Dry and erythematous skin in face and on extremities, eye and nose symptoms significantly more prevalent among children in problem day care centres compared with control buildings
Turiel et al 1983 (US) [40]	Problem and control building, questionnaire, measures of chemicals, microorganisms, thermal climate	62–66%	No	Significantly more symptoms in problem building, no measured IAQ factor was judged to be responsible for symptoms
Taylor et al 1984 (US) [41]	Problem and control building, questionnaire, chemical measures	94–85%	Yes	Increased prevalence of symptoms associated with female gender, low age, use of photocopiers, crowded areas, no association with measured agents
Finnegan et al 1984 (UK) [43]	Selected problem and non-problem buildings, doctor administered questionnaire	75–94%	No	Higher symptom prevalence in air-conditioned than in naturally ventilated buildings
Whorton et al 1987 (US) [38]	Problem building, questionnaire, chemical measures	96%	No	No association between measured agents and symptoms
Burge et al 1987 (UK) [44]	Selected problem and non-problem buildings, questionnaire	92%	No	Increased symptom prevalence associated with female gender, low position, mechanical ventilation systems and air-conditioning
Skov et al 1989, 1990 (DK) [19, 45]	Selected non-problem buildings, questionnaire, measures of thermal climate, CO_2, HCHO, VOC, particles, microorganisms	80%	Yes	Increased symptom prevalence associated with female gender, job category, handling of CCP and photocopying, VDT work, psychosocial work strain, organic floor dust, carpets, crowding, supply air systems, open shelves and fleecy material
Robertson et al 1989 (UK) [52]	Selected buildings, questionnaire, lighting measures	97%	No	No significant association between lighting levels and symptom prevalence within each building, higher symptom prevalence in air-conditioned than in naturally ventilated building
Franck et al 1989 (DK) [58]	Selected office employees and controls from general population	76–100%	Yes	The prevalence of foam in the inner canthus was significantly lower in office workers; female gender and use of make-up was associated with low occurrence of foam

Norbäck et al 1989 (S) [49]	Selected workers in presumed "sick" building and reference groups, questionnaire, measures of VOC, CO_2, HCHO and thermal climate	89%	No	CO_2 levels were higher in presumed "sick" buildings and many symptoms were more prevalent among workers in "sick" buildings than among industrial and hospital workers
Norbäck et al 1990 (S) [50]	Selected "sick" buildings, questionnaire, measures of VOC, CO_2, HCHO and thermal climate	95%	Yes	Increased symptom prevalence associated with hyperreactivity, infection proneness, smoking, static electricity, unfavourable psychosocial factors and concentration of TVOC
Norbäck et al 1990 (S) [51]	Selected buildings with wall-to-wall carpets and control buildings, questionnaire, measures of VOC, CO_2, HCHO and thermal climate	91–94%	Yes	Persistent symptoms were associated with concentration of VOC, wall-to-wall carpets, hyperreactivity and unfavourable psychosocial factors; incident symptoms were associated with concentration of respirable dust, smoking and psychosocial factors; removal of carpets were related to a decrease in symptom prevalence
Hodgson et al 1991 (US) [42]	Non-problem buildings, questionnaire, measures of CO, CO_2, VOC, particles and thermal climate	Not stated	Yes	Increased prevalence of mucosal and general symptoms associated with VOC, crowding, layers of clothing and lighting intensity; skin symptoms associated with gender
Jaakkola et al 1991 (SF) [47]	Selected building, questionnaire, measures of air flow rate, thermal climate, CO_2, HCHO and particles	82%	Yes	Increased symptom prevalence associated with female gender, allergy history, ETS, psychosocial factors and high temperature; no association with air flow rate
Norbäck et al 1991 (S) [46]	Random sample, general population, questionnaire, job matrix, limited hygienic information	74%	Yes	Increased symptom prevalence associated with childhood exposure to ETS, urban residency, fresh paint, pre-school children in family, history of atopy and nickel allergy, infection proneness, hyperreactivity, static electricity, VDT work and psychosocial work strain
Reinikainen et al 1991 (SF) [53]	See Jaakkola et al 1991	69–74%	Yes	Air humidification was associated with lower symptom prevalence
Zweers et al 1992 (NL) [48]	Selected problem and non-problem buildings, questionnaire, CO_2, thermal climate, noise, and luminance measures	67%	Yes	Increased symptom prevalence associated with female gender, history of allergy, low work satisfaction, low control over temperature and air-conditioning
Harrison et al 1992 (UK) [55]	Selected problem and non-problem buildings, doctor administered questionnaire, measures of microorganisms, thermal climate	88%	No	Increased symptom prevalence associated with high levels of airborne viable bacteria and fungi
Rylander et al 1992 (S) [56]	Selected problem and non-problem buildings, questionnaire, measures of endotoxins and beta-1,3-glucan	99%	No	Significant association between amount of glucan and dry cough and itching skin, and between endotoxin and skin rash

CCP = Carbonless Copy Paper
ETS = Environmental Tobacco Smoke
VDT = Visual Display Terminal
CO = Carbon monoxide
HCHO = Formaldehyde
CO_2 = Carbon dioxide
IAQ = Indoor Air Quality
VOC = Volatile Organic Compounds

1.2.3 Clinical studies

Eye symptoms have been studied in the population of the Danish Town Hall Study.[19, 45] In people suffering from work-related eye symptoms, signs of dryness, such as low Break Up Time (BUT) and corneal erosions, were noted.[59] Nasal symptoms, reported by inhabitants in dwellings with IAQ problems have been investigated by a Swedish group, using stereometric measurements of the nasal mucosa after histamine provocation. These individuals had obvious signs of nasal hyperreactivity.[60]

The immunological response was studied in a work force because of symptoms appearing soon after the renovation of their office. Antibodies to albumin conjugates of formaldehyde, toluene diisocyanate, and trimellitic anhydride were found in 12 of 14 full-time employees. There was no reference group but such findings were not seen in 100 asymptomatic healthy city dwellers investigated in a prior study.[61] A medical evaluation of two office work forces, allegedly suffering from SBS, found few, generally minor abnormalities at general medical examination. Neurological and neuropsychological examinations documented mental status, cerebellar and neuro-behavioural deficits.[62]

1.2.4 Experimental studies

Experimental studies are summarized in Table 3. Symptoms from the lower airways are considered to be more infrequent than those from upper airways.[2,28] Building-related asthma has been reported separately from SBS, but the prevalence of both phenomena appear related and cases of either condition are sometimes reported within the same building.[31] In a Swedish experimental study a decrease in forced vital capacity (FVC) during work was demonstrated in teachers working in a school where there were problems with damp/mould.[63]

Results from the humidification of office environments associated with a decrease in the prevalence of symptom,[64] failed to confirm results from some observational studies indicating that humidification is a risk factor.[43,44] Chamber tests with the humidification of clean air have shown that dry air is not perceived differently from humidified air.[65,66] Experiments with air ionization have also produced conflicting results.[67-70]

Most experiments performed on IAQ-related health problems have either used challenge tests with volatile organic compounds (VOC) or registered changes in symptom-reporting following changes in ventilation rates. A standardized mixture of VOCs, stated to be representative of the indoor air in offices,[71] has been used for challenge tests both in symptomatic individuals[71] and in healthy control subjects.[72-74] The observed effects are mucosal irritation and general symptoms. Conjunctival exposure to CO_2 has induced eye symptoms, a reaction that was predicted by skin irritancy tests.[75] In two of the VOC experiments, inflammatory reactions were verified by an increase in white blood cell counts in tear and nasal fluid.[72,74]

As the ventilation rate is the single most important determinant of indoor air quality, results from experimental studies of the effect of different outdoor air flow rates on perceived symptoms have attracted special attention. Results, however, have been conflicting.[40,47,76,78] For outdoor air flow rates at or below 10 litres/second and person (L/s,p), however, the results, with few exceptions, show an association between low flow rates and a high prevalence of symptoms.[79] In one of the ventilation experiments, the type of fluorescent lighting was also changed. As lighting changes were associated with changes in symptom reports it was suggested that photochemical smog, produced indoors by fluorescent light, could be one source of indoor air pollution.[78]

Table 3. Main features of and results from experimental studies on the sick building syndrome

EXPERIMENTAL STUDIES

Author Year of publication Country	Design	Exposure	Outcome	Results
Andersen et al 1973 (DK)[65]	Randomized, blinded, healthy subjects	Four levels of relative humidity	Perceived humidity and temperature	No difference in perceived humidity
Andersen et al 1974 (DK)[66]	Single blind, healthy subjects	Two levels of relative humidity	Perceived humidity, nasal mucus flow, nasal and bronchial flow resistance, skin resistance	No differences noted
Hawkins 1981 (UK)[67]	Double blind, selected problem building	Air ionization and sham exposure	Perceived IAQ and symptom reports	Increased rating of alertness, air freshness and reduced symptom reports during ionization
Turiel et al 1983 (US)[40]	Open	All outside air vs recirculation	Concentration of indoor pollutants, perceived IAQ	The concentration of pollutants and perceived odour increased at low outdoor air flow rates
Sterling et al 1983 (US) [78]	Selected problem building	Varying air flow rates and type of lighting	Perceived IAQ and lighting condition and symptom reports	Complaints and symptom reports decreased when outdoor air flow rate increased and when fluorescent lamps with less UVA light were used
Hawkins et al 1984 (UK)[68]	Blinded, employees of problem building	Air ionization and sham exposure	Symptom reports	Reduction only in lethargy during ionization
Mølhave et al 1986 (DK)[71]	Double blind, selected subjects with history of symptoms of dryness	Two levels of VOC mixture and sham exposure	Perceived IAQ and mucosal irritation, performance tests	IAQ was perceived as worse and odour and mucosal irritation increased during VOC exposure; memory test performance decreased
Finnegan et al 1987 (UK) [69]	Blinded, occupants of a "sick" building	Air ionization and sham exposure	Symptom reports and perceived IAQ	No differences noted except for a decrease in upper respiratory tract infections and nausea in the high negative ion period
Kjaergaard et al 1989 (DK)[72]	Double blind, randomly selected healthy subjects	Three levels of n-decane and sham exposure	Perceived odour, symptoms, BUT and cytology	Mucosal irritation, odour intensity, and conjunctival PMNs increased at exposure, BUT decreased; skin and mucosal irritancy tests predicted mucosal symptoms
Jaakkola et al 1991 (SF)[47]	Blinded, selected building	Different ventilation rates	Symptom reports	Reduced ventilation caused significant increase in symptoms

Table 3. Continued

Kjaergaard et al 1992 (DK)[75]	Blinded, randomly selected subjects	Conjunctival exposure to CO_2 at varying concentrations	Eye symptoms	Subjects with SBS symptoms had lower threshold; skin irritancy test predicted reactivity
Wyon 1992 (S)[70]	Single blind, selected building with test, reference and placebo area	Varying air flow rates, cleaning routines, temperature and lighting, aircleaning, air ionisation, humidification and antistatic measures	Symptom reports, blink rate, skin signs, nasal congestion, BUT	Both symptoms and signs were reduced by lower temperature and lighting glare and by humidification and air ionization
Reinikainen et al 1992 (SF)[64]	Blinded, cross-over, selected work sites	Air humidification vs natural conditions	Perceived IAQ and symptom reports	Significantly less dryness and allergic symptoms and increased perception of stuffiness during humidification
Hudnell et al 1992 (US)[73]	Blinded, selected healthy subjects	VOC mixture and sham exposure	Perceived IAQ and symptoms	Eye and throat irritation, headache and drowsiness increased during VOC exposure
Koren et al 1992 (US)[74]	Selected healthy subjects	VOC mixture and sham exposure	Nasal lavage, PMN counting	Significant increase in PMNs after VOC exposure
Menzies et al 1993(US)[76]	Double blind, randomized, crossover, selected bildings	Different outdoor air flow rates	Symptom reports	No significant effect
Dahlqvist et al 1993 (S)[63]	Open, selected problem building	Working week and leisure time	Symptom reports and measured pulmonary function	Thirteen out of 15 subjects had a fall in FVC during a working week in wintertime
Jaakkola et al 1994 (SF)[77]	Blinded, crossover, selected buildings	No vs 70% recirculation of air	Symptom reports	No differences in symptom reports noted

BUT = Break Up Time
IAQ = Indoor Air Quality
UVA = Ultraviolet light 320–400 nm
CO_2 = Carbon dioxide
PMN = Polymorphnuclear Leucocytes
VOC = Volatile Organic Compounds
FVC = Forced Vital Capacity
SBS = Sick building syndrome

1.2.5 Clinical experience

Patients referred to us for IAQ-related complaints have been examined and in many cases followed for a number of years. Some of these patients are described in Paper I. It is our impression that a number of patients with symptoms that initially were related to the workplace and that diminished when being away from the building for some time, develop chronic symptoms and signs. A number of our patients with IAQ-related symptoms have also been examined by oto-laryngologists. The most commonly reported signs in the upper airways are dryness and redness of the mucosa. A low baseline saliva production is often found in these patients (Östberg Y., personal communication). In one patient with alleged IAQ-related eye and skin symptoms, we have registered a gradually shortening of BUT which was normalized after one month's sick-leave.

Challange tests in patients with IAQ-related symptoms have shown that the probable source for offending pollutants can be building-related (wall paint and plastic flooring) and work-related but not building-related (toner from photocopiers and photochemicals). Polluted supply air has also evoked symptoms in challenge test.

Quotation from patient's file: The symptoms started with the perception of dry eyes and dry facial skin. Some months thereafter the facial skin started to feel hot and swollen and an erythema developed on the cheeks. Then the throat became dry and the nose crusty. At the beginning, the symptoms disappeared over the week-end, now it takes weeks away from work until the symptoms diminish. What annoys the patient most is the fatigue that forces her to rest for some time after work before she can start her house work. After some time she noticed that the symptoms are worsened in crowded areas, such as in buses and in supermarkets, and from diesel car exhausts, perfumes and fresh newspapers.

1.2.6 Summary

The clinical characteristics of IAQ-related symptoms are still very sparsely investigated. Studies using objective methods, however, indicate that SBS symptoms in the mucosa and the skin can be verified by an examiner, but probably require the development of suitable methods. The long-term clinical course has not been studied.

Because of methodological shortcomings the validity of many cited results from observational studies can be questioned. Central problems are the operationalization of the outcome and the exposure assessments. As there is no agreed definition for SBS, the defined outcome varies from one study to another. In many cases this problem is not even considered. Some studies include symptoms, such as hand eczema, that have never been on the list of IAQ-related symptoms. In some instances, symptoms included in the WHO definition of SBS, such as hyperreactivity and infection proneness, are used as risk indicators. Low response rates in questionnaire studies are rarely accompanied by an analysis of drop-outs, and until recently there was little attempt at controlling for potential confounders.

In exposure assessments, surrogates for actual measurements are often used without any discussion of the possible relevance of the surrogate and the duration and intensity dimensions of the exposure are seldom considered. Methodological problems make studies of measured VOCs as risk indicators difficult to interpret both with regard to the definition of VOC, to the different methods used and to the representativeness of spot measurements for exposure over a period.[80]

Few double blind and randomized experimental studies have been performed. Conflicting results from experiments and observational studies may to some extent be due to the lack of knowledge about causative factors and lack of relevant monitoring of exposure.

Humidification can, in one situation, be curative for dry skin and mucous membranes, while in other situations it may enhance indoor air pollution. Similarily, the effect of ionization is dependent on the situation. A positive effect of air ions should only be expected when particulate pollutants cause the symptoms. Experiments with standardized VOC mixtures may not reflect the working situation because of variations in the concentration of single agents from one place to the other.

Conflicting results from ventilation studies may result from differences in emissions leading to different indoor air quality despite similar outdoor air flow rates. Design features, such as very short experimental study periods, may also explain why some studies have failed to demonstrate an effect on symptom reports from low ventilation rates.[76, 77]

When observational studies with strong design features, such as defined and motivated outcome and exposure variables, high response rate and control for confounding are taken into account, female gender, atopy, unfavourable psychosocial conditions, photocopying and work in crowded areas are consistent risk indicators.[19,41,42,45,47,48]

Compilations of observational and experimental studies also strongly indicate that air-conditioning and outdoor air flow rates below 10 L/s,p are associated with an elevated occurrence of SBS symptoms.[54,79]

1.3 Work at Visual Display Terminals (VDTs)

Facial skin symptoms related to VDT work appeared in Great Britain and Norway in the late 1970s.[81–85] Since 1985 this issue has become of major concern to local company health services and a topic of considerable controversy in Sweden. There are also cases reported from the US[86,87] and Japan.[88]

1.3.1 Case reports

In the case series facial skin complaints are commonest, with sensory symptoms, erythema and signs of rosacea.[4,83,85,87,88] In one case dryness and erythema of the hands and forearms was seen.[86]

1.3.2 Observational studies

The observational studies are summarized in Table 4. Three surveys of VDT-related skin complaints have been reported from the US and the UK. One showed an association between VDT use and the prevalence of skin symptom at one work site[89], two failed to show any such relation.[90,91] Two Swedish studies have been published and both reported an exposure-response relationship between the amount of VDT work and the occurrence of skin complaints.[92,93] In one survey,[92] people who complained of skin symptoms were examined by occupational dermatologists.[94] Subjects with seborrhoeic eczema, acne and rosacea were over-represented in the exposed group. However, in the other study objective skin signs did not show this pattern.[93]

A longitudinal study, emanating from a prior cross-sectional study[92], showed an increased incidence of skin symptoms in VDT workers with intensive VDT work.[95] The effect was modified by company type, suggesting an impact from locale-specific factors such as indoor climate factors or job-specific factors such as stress. A recent Swedish cross-sectional study reported a tendency for increased occurrence of seborrhoeic eczema, nonspecific erythema and skin symptoms among VDT users compared with non-users. Psychosocial and organizational

conditions were associated with skin symptoms and facial erythema while photosensitive skin type and low relative humidity were related to an increased prevalence of seborrhoeic eczema. No association was found between measured VDT-related electromagnetic fields and skin symptoms or signs.[96] The prevalence of skin complaints among plasma display users in Singapore was found to be similar to that found among those using cathode ray tubes.[97]

1.3.3 Clinical studies

Clinical studies of referred patients have not shown any specific VDT-related skin disease.[3] Seborrhoeic dermatitis, acne and rosacea have been the most prevalent diagnoses observed[3,98] and routine histopathological examination of VDT exposed subjects have shown similar findings to those in a control group.[99]

1.3.4 Experimental studies

Experimental studies are shown in Table 5. An experiment has demonstrated that the deposition of particles onto the cheek of an operator increases with the intensity of the electrostatic field.[100] The investigator suggested that irritant aerosols cause the observed rashes. This hypothesis was not supported by an experiment performed on patients with VDT-related skin symptoms. The effect of exposure to VDTs with powerful or no electrostatic fields did not differ in a double blind provocation study. High relative humidity, which reduces the electrostatic charge, did not prevent reactions.[101]

Preliminary reports from double blind provocation tests with electromagnetic fields on VDT workers have so far not presented evidence for alternating fields as a cause of symptoms.[102-104] Stress has been studied as a cause for the skin reactions.[105] VDT users with skin symptoms had higher levels of stress-sensitive hormones during work and reported more occupational work strain compared with employees without symptoms. From these findings the investigators proposed a model, techno-stress, in which the working conditions rather than the VDT itself cause the symptoms.

Table 4. Main features of and findings from observational studies on skin symptoms in visual display terminal users

OBSERVATIONAL STUDIES

Author Year of publication Country	Design Method	Return/ Participation rate	Control for confounding	Results
Murray et al 1981 (US)[89]	Selected work sites, questionnaire	37-51%	No	Skin symptoms were more prevalent among VDT users at one work site
Frank 1983 (US)[90]	Selected work sites, questionnaire	40%	No	No significant difference between VDT users and non-users
Knave et al 1985 (S)[92]	Selected work sites, questionnaire	91%	Yes	Skin symptoms were more prevalent among female VDT users
Lidén et al 1985 (S)[94]	Employees with symptoms invited, clinical examination	77%	No	Seborrhoeic eczema, acne, rosacea and perioral dermatitis as a group were more prevalent among VDT users
Berg et al 1990 (S)[93]	Random sample of employees in selected work sites		Yes	Facial skin complaints were more prevalent among VDT users, no difference in skin signs
	questionnaire, clinical examination	97% 92%		
Koh et al 1990 (SG)[97]	Selected work sites, questionnaire	97%	No	No significant difference between CRT and PD operators
Carmichael et al 1992 (UK)[91]	Selected work sites	41%	No	No significant difference between VDT users and non-users
Bergqvist et al 1992 (S)[95]	Selected work sites, follow up, questionnaire	82-97%	Yes	An increased incidence of skin problems was associated with extensive VDT work; the effect was modified by company type
Bergqvist et al 1994 (S)[96]	Selected work sites,		Yes	Seborrhoeic eczema, erythema and skin symptoms tended to be more prevalent among VDT users; psychosocial and organizational factors were associated with symptom occurrence; photosensitive skin was associated with seborrhoeic eczema; no association between measured fields and symptoms
	questionnaire, clinical examination, measures of electro-magnetic fields	92% 85% 83%		

CRT = Cathode Ray Tube PD = Plasma Display VDT = Visual Display Terminal

Table 5. Main features of and findings from experimental studies on skin problems in visual display terminal users

EXPERIMENTAL STUDIES

Author Year of publication Country	Design	Exposure	Outcome	Results
Cato Olsen 1981 (N) [100]	Open	ES fields	Deposition of particles onto face-mounted subtrates	Elevated ES potentials increased the deposition
Swanbeck et al 1989 (S) [101]	Randomized, double blind, referred VDT users	ES, B-VLF fields from VDTs, different levels of RH	Skin symptoms and signs	No significant difference between exposures
Sandström et al 1989 (S) [102]	Blinded, referred VDT users	E and B fields of VDT type, 50 Hz	Skin symptom reports	B-ELF and E-VLF increased symptom intensity in some patients
Hamnerius et al 1992 (S) [103]	Double blind, referred patients, with "hypersensitivity" to electrical equipment	E and B fields of VDT type	Skin symptoms, temperature, conductance, peripheral blood flow, pulse rate	No significant difference between exposures
Franzén et al 1992 (S) [104]	Double blind, selected subjects with "hypersensitivity" to electricial equipment	E and B fields	Detection of exposure	Two subjects detected exposure significantly more often than expected by chance
Berg et al 1992 (S) [105]	Open, invited VDT users with or without symptoms	VDT work , leisure	Itching behaviour, perceived mental strain, stress hormones	Symptomatic persons had higher itching frequency, perceived higher mental strain and had elevated stress hormones during work

B = Magnetic field E = Electric field ELF = Extremely Low Frequency (picture refreshment frequency) ES = Electrostatic
RH = Relative Humidity VDT = Visual Display Terminal VLF = Very Low Frequency (line frequency)

1.3.5 Clinical experience

Since 1985 over 200 patients have been referred to our department for alleged VDT-related skin conditions. Nine out of ten patients are women and the symptoms have often started in relation to changes in working conditions. Sensory symptoms mimicking a sunburn with facial erythema are common, sometimes accompanied by eye irritation, periorbital swelling and facial eczema. One out of ten patients also report irritation on the back of the hands. The symptoms are aggravated during winter-time and 10–20% of the patients report worsening of the symptoms when being close to TV-sets, fluorescent tubes and other electric devices. Sun light is often reported to worsen the symptoms until a protective suntan is developed.

The most common conditions are rosacea, facial erythema and telangiectasia, seborrhoeic and atopic eczema and acne. Routine blood tests are normal as are photo tests on facial skin. Routine histopathology does not differ from that normally found in patients with similar, but non-VDT-related, conditions. Patients with isolated skin symptoms seem to have a good prognosis for work in the office environment. Most patients can continue with, or return to VDT work after some measures have been taken. In many cases shortening VDT work is enough. Many patients report that the application of filters reducing the alternating electric fields or the change to liquid crystal display (LCD) screens permits them to extend their VDT work before symptoms develop. Those reporting multiple systemic symptoms from electric devices are worse off and have difficulties in adapting to office work, even after measures have been taken. It is our impression that these two groups of patients generally represent different types of personality and that psychological factors of possible importance for the symptoms are more often found in the latter group.

Quotation from patient's file: The patient has been working with different VDTs for some years without any problems. The symptoms started when her old VDT was replaced by a new "low radiation" colour screen. The work situation was not changed in any other aspect. The symptoms started with the sensation of a strong sunburn but from the beginning there was nothing to see on the skin. Gradually the facial skin became swollen and red over the cheeks, forehead and chin. Skin symptoms developed after a few hours of daily VDT work. When she tried to use her old VDT she could work double the time at this screen before symptoms were perceived. After some months symptoms were worsened by watching television, being close to flourescent lights and by sunlight.

1.3.6 Summary

With the exception of the Swedish studies, the cited surveys have had low response rates or no control for confounders. In studies with a strong design in these respects, there is a consistent pattern showing an exposure-response relation between the amount of VDT work and the prevalence of self-reported skin symptoms. Whether VDT work induces or aggravates skin diseases has not definitely been resolved. Reported skin symptoms and signs are predominantly localized to facial skin.

The cause of the symptoms is still obscure. Experiments with static electric fields have given inconsistent results. However, if skin symptoms are evoked by irritants in the ambient air of the workplace, and whose deposition onto the skin is influenced by the static electric field, experiments in clean air would not be expected to confirm this mechanism. Consequently such experiments should be conducted at the workplace where the symptoms started or in similar IAQ conditions. Until now there is no observational study showing an association between measurement of electromagnetic fields and skin problems and experiments contradict such an association. Stress as a risk factor is not refuted by any study. Skin symptoms in VDT users,

although reported from three continents, are most commonly reported from Sweden. No single factor serves as a good explanation for the geographic distribution of complaints and reports.

2 AIMS

2.1 Overall aims

This thesis focuses on health problems attributed to indoor air quality and other indoor environmental factors, such as work at video display terminals (VDTs), with special emphasis on facial skin problems. As these types of health problems have only to a limited extent been subject to research there is still a considerable lack of basic knowledge about both their nature and prognosis as well as risk factors for these ailments.

The clinical observations in patients referred to the Department of Dermatology at Umeå University Hospital became one point of departure for an interdisciplinary project, the Office Illness Project in Northern Sweden, where medical staff have cooperated with engineers and experts in medical physics and indoor environment as well as with sociologists.

The overall aim is to increase knowledge both about the occurrence of perceived symptoms and potential risk indicators, and about methodological issues. The intention is to lay the ground for future research, for the prevention of illnesses caused by indoor environment factors and to better care for the patients by taking personal, psychosocial as well as physical factors into account.

2.2 Specific aims

The specific aims are

- to document clinical observations from patients with IAQ-related skin complaints (Paper I)
- to estimate the prevalence of symptoms compatible with SBS in office workers and facial skin symptoms in VDT users (Papers II, III)
- to assess the relationship between the occurrence of symptoms and personal, psychosocial and physical factors of relevance for the indoor environment at home and at work (Papers II, III, IV, V)
- to explore the clinical relevance of a study model based on questionnaire-reported symptoms in the light of previous clinical observations (Papers IV, V) and
- to discuss the concepts of "sick" buildings and the "Sick Building Syndrome" in the light of the results (Paper III, this thesis)

3 MATERIAL AND METHODS

Figure 1 shows the design of the investigations that supplied the data for this thesis.

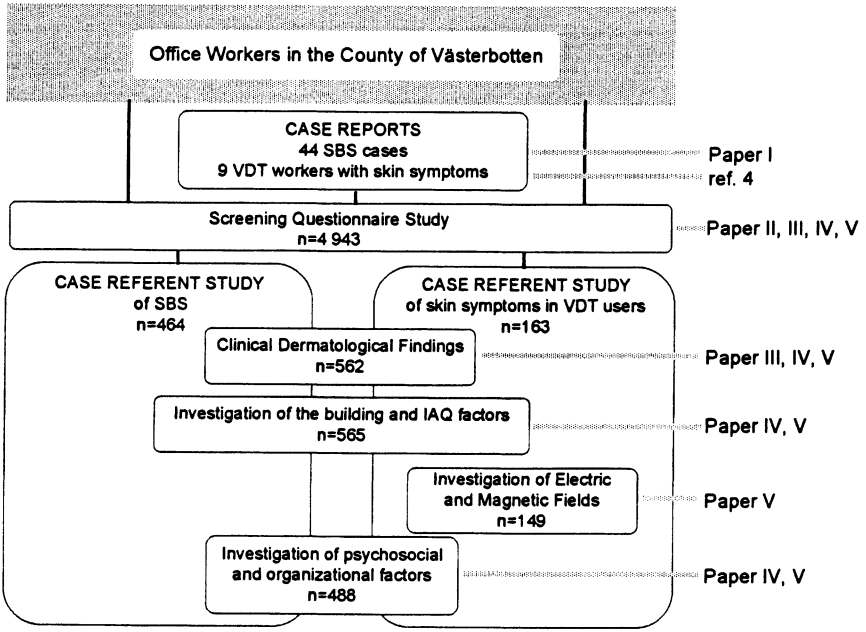

Figure 1. The investigations supplying data for paper I-V. The screening study and the case referent studies are parts of the Office Illness Project in Northern Sweden.

3.1 The patients and the buildings of the case report on SBS

Clinical investigations were performed on 77 outpatients from seven workplaces during 1982 to 1986. Patients were referred because of symptoms related to work within a particular building or part of a building. Patients with eczema were tested for standard and office allergens. Standard allergens include about 20 substances that are known to be common causes of contact allergy, such as rubber chemicals, metals, such as nickel and cobalt, and preservatives, such as formaldehyde. Office allergens include substances in paper, photocopying processes, and printing inks. The workplaces were four office buildings, one museum, one newspaper office (composing room), and one hospital. The buildings were identified as "sick" buildings by the local health services. The rationale for this standpoint was an "unexpectedly" high prevalence of symptoms compatible with SBS among the employees. As there were no reference figures known for this region this judgement was highly subjective. Findings from technical investigations of relevance for the indoor air quality were inadequate ventilation performance (all buildings), damage due to damp (three buildings), abnormal emissions from surface materials (one building), microbiological growth (one building) and emissions from work activities (one building). Four buildings, from which 44 patients were referred, were office buildings located in the County of Västerbotten.

3.2 The hypothesis for the epidemiological studies

In our hypothesis, constitutional factors are fundamental for SBS symptoms and for skin symptoms in VDT workers. Psychosocial stress, mediated by stress-related hormones, is supposed to either cause symptoms or make the individual more susceptible to other risk factors, or both. The indoor air quality is supposed to be the major physical determinant of SBS symptoms. The indoor air quality is a function of particulate and volatile emissions and elimination (ventilation). As the ventilation has to balance all pollution sources it is considered to be a more fundamental determinant than single emission sources.

In VDT workers with skin symptoms, electromagnetic conditions are added as hypothetical physical determinant of symptoms. Thus, besides constitutional factors, the epidemiological studies assess the relative importance of stress states, indoor air pollution and electromagnetic conditions as determinants of symptoms.

3.3 The source population

The source population for the epidemiological studies was office workers in the County of Västerbotten, the primary catchment area for the University Hospital of Umeå. The County of Västerbotten is situated in the northern part of Sweden, latitude 63–65° north and longitude 15–21° east, Figure 2.

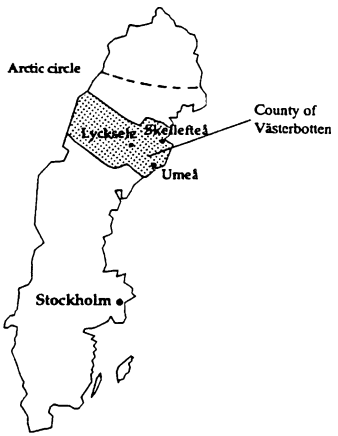

Figure 2. Map of Sweden indicating the location of Lycksele, Skellefteå and Umeå in the County of Västerbotten.

3.4 The study population

All workplaces with office workers were classified and listed by staff at the county Labour Inspectorate. From this list, a proportional stratified sample was drawn so as to be representative of the number of office workers in three cities, one with an inland climate and few industries (Lycksele) and two coastal cities, one industrialized (Skellefteå) and the other the administrative centre of the county (Umeå). The minimum number of employees was set to ten per office and the chances of an office being included were proportional to the number of

employees there. All workers spending more than half their working hours in the office building during the three preceding months were included in the study population. A questionnaire was mailed to 5,986 office workers, making up approximately one third of all office employees in the county. The study was designed to yield a sufficient number of cases for the subsequent case referent studies.

3.5 The prevalence study

The questionnaire has been used in Swedish surveys and most of the questions have been validated previously. In preliminary data from the supplier of the questionnaire the sensitivity of questions on general and mucosal symptoms was 70–100% (unpublished data). In a pilot study we found the sensitivity of dermatological questions to be 60–70%. The specificity for all questions was high, 90–100%. The validation of all symptom questions, based on patients' symptom history and signs at clinical investigation, applies to the period prevalence of symptoms. The questionnaire included questions about demographic and personal factors, work characteristics and conditions, building characteristics and other factors of relevance for the indoor air quality at work and at home, perception of psychosocial conditions and physical climate and perceived symptoms. Symptoms were registered regardless of perceived work-relation. There was one question asking whether the respondents attributed perceived symptoms to indoor environment factors. Data acquisition lasted from late October until December 1988. A recall period of three months was used for symptoms.

The return rate was 95.7%, but 13% of the respondents had to be excluded. The main reasons were absence from work during the period under study or not fulfilling the criterion of spending at least half their working hours in the office. Due to the low drop-out rate the analysis of non-response was limited to telephone interviews with forty people. The most frequent reasons for not responding were "forgetfulness", "haven't got time","quit work" and "tired of questionnaires". Nothing indicated that perceived symptoms had influenced the willingness to respond. The proportion of missing values was low, for symptom questions 1–1.5%. A total of 4,943 questionnaire forms have been processed. "SBS cases" was used as one outcome in the prevalence study (Papers II, III). An "SBS case" was here defined as an employee reporting weekly occurrance of at least one general, one mucosal and one skin symptom included in the WHO descripton of SBS.[2] This is incongruent with the definition given in Paper II where a monthly occurrence of general symptoms is stated.

3.6 Common features of the case referent studies

The measurements at the work sites and the clinical examination were performed from January until April 1989 during which period the temperature in the region is normally low enough to induce the use of recirculation of air. Neither cases and referents nor examiners and investigators knew whether an employee was classified as a case or as a referent.

3.6.1 Clinical dermatological examination

All cases and referents were invited to a clinical dermatological examination including a history of previous health problems, current symptoms during the recall period and the use of cosmetics, soaps and creams. Skin signs in the face, scalp and on upper trunk were noted and a dermatological diagnosis was made based on the history and the signs. Workplace relation was

estimated from information on diminishing symptoms when not at the work site. The examination was completed with a "stinger test" of facial skin, a method used for estimating skin sensitivity to cosmetics.[106] An aqueous solution of 10% lactic acid, applied with a cotton swab in the naso–labial fold, was used to induce a stinging reaction on the cheek.

3.6.2 Investigation of psychosocial and organizational factors

The screening questionnaire included questions about perceived psychosocial work factors. At the time of the clinical examination, an extensive questionnaire addressing psychosocial and organizational factors was distributed.[107]

3.6.3 Investigation of indoor environment factors

Some data of relevance for the indoor environment of the workplace were collected through the questionnaire, such as signs of damage to the building, VDT work and handling of paper. So were, for the dwelling, data on the heating and ventilation system, carpeting, pets, environmental tobacco smoke (ETS), signs of damage and condensation on windows (Paper II).

For each case and referent, data were collected at the work site regarding the office building in general and the work room in particular. Some individuals were excluded since their workplace had undergone important physical changes since the time of the questionnaire, one to five months prior to the plant visit. The outdoor air flow rate, temperature and humidity were measured on one occasion. In parallel, the room size, surface materials, age of furniture, smoking habits, cleaning routines, occurrence of humidifiers, photocopying machines and laser printers were recorded. Basic facts about the building were gathered from the occupational health engineer.[108]

3.6.4 Definitions of independent variables

The presumed determinants were operationalized in a large number of variables. From previous analyses of data from the Office Illness Project in Northern Sweden (Papers II, III)[107–111] a limited number of statistically or theoretically important risk indicators were entered into the analyses described in this thesis. Table 6 presents the type of variables, source of the data and specifies the theoretical effects. Many of the variables are surrogates for measurements of the postulated risk factors. In the following, variables that have been defined are listed with reference to the Paper in which the definition occurs.

Personal factors

Asthma/rhinitis (II–V), *atopic dermatitis* and *atopy* (IV, V).

Seborrhoeic dermatitis, rosacea, migraine and *photosensitive skin* (IV, V).

Smoking habits (II, III) and *marital status* (III).

Exposure factors at home

Condensation (II–V), *ventilation system, damage indices* and *environmental tobacco smoke* (III).

Working conditions and exposure factors at work

Position (II–V), *public/private employment* (II, III) and *psychosocial indices* (II–V).

Virtual age of the building, *type of work room*, and type of *flooring* (IV, V).

Amount of *VDT work* (II, III and V) and *paper index* (II–V).

The presence of *photocopiers* (IV, V), *room and building damage index* (III), signs of *problems of damp/mould* (IV) and *outdoor air flow rate* (IV, V).

3.7 The case referent study of SBS

3.7.1 Outcome

An "SBS case" was defined as an employee reporting at least one general symptom every month and at least one mucosal and one skin symptom every week. The symptoms used for the definition (Paper II) are compatible with the WHO description of SBS.[2] The criterion for general symptoms had to be broadened from weekly to monthly occurrence in order to generate a sufficient number of cases.

Referents, not fulfilling all the symptom criteria, were pair–matched for three potential confounders, age (±5 yrs), gender and geographical area. All cases and referents had less than one hour of daily VDT work. The rationale for this restriction was that we intended to compare clinical findings among these "non VDT workers" with findings among VDT workers reporting skin symptoms. VDT work as a risk indicator was mainly assessed in the prevalence study.

3.7.2 Dimensioning and power

From all subjects that fulfilled the case criteria 225 were randomly drawn. With an equal number of matched referents, an estimated power of 0.9, a level of significance of 0.05, the lowest detectable relative risk was 1.9 for a determinant with a prevalence of 0.5 in the study population. A small number of surplus cases and referents were added to compensate for possible drop–outs. There were 232 matched pairs.

3.8 The case referent study of facial skin symptoms in VDT workers

3.8.1 Outcome

A "case" was defined as an employee reporting itching, stinging, tight or burning sensations in facial skin and facial erythema or dry skin every week during the recall period. Referents were pair–matched in the same manner as in the case referent study of SBS. All cases and referents had at least one hour of VDT work every day.

3.8.2 Dimensioning and power

From a total of 133 cases, 75 were randomly drawn. With an equal number of matched referents, an estimated power of 0.9, a level of significance of 0.05, the lowest detectable relative risk was 3.3 for a determinant with a prevalence of 0.5 in the study population. With the addition of surplus cases there were 85 matched pairs.

3.8.3 Investigation of electromagnetic conditions

In addition to the above described measurements, investigations of electric and magnetic factors were performed in this study. These measurements included temperature, relative humidity, body potential, background and VDT related electric and magnetic fields and other VDT characteristics.[112]

3.8.4 Definitions of independent variables

In the analyses in this thesis only a small number of variables were included by the same criteria as for the variables described above.

Exposure factors at work

Electric background field and *VDT-related magnetic field (ELF)* are defined in Paper V.

Table 6. Variables under study, source of the data and hypothetical effects

Variables	Source of data	Hypothetical effects
Emission sources		
At home		
Building characteristics	screening questionnaire	new buildings and buildings with signs of water damage emit pollutants
Surface materials	screening questionnaire	wall-to-wall carpets store pollutants
At work		
Building characteristics	screening questionnaire workplace investigation	new buildings and buildings with signs of water damage emit pollutants
Room characteristics	screening questionnaire workplace investigation	open plan offices are more crowded and more often polluted by emissions from office machines; fluorescent tubes and heating system influences electromagnetic, light and IAQ conditions
Surface materials	workplace investigation	wall-to-wall carpets store pollutants, plastic flooring emits pollutants
Working conditions	screening questionnaire	paper emits particles and volatile pollutants, VDT work entails exposure to physical and psychosocial factors that induces symptoms or enhances the inclination to react to other factors
Elimination		
Type and performance of ventilation at home	screening questionnaire	naturally ventilated dwellings and buildings with signs of condensation on windows may have insufficient elimination of pollutants
Ventilation performance at work	workplace investigation	office buildings with low outdoor air flow rates accumulate pollutants
Electromagnetic conditions		
Background and VDT-related fields	workplace investigation	induce symptoms or influences inclination to react to other factors
Psychosocial factors at work		
Perceptions	screening questionnaire psychosocial questionnaire	influence inclination to react to other factors or induce symptoms from stress hormones
Personal factors		
Age	screening questionnaire	older employees have dry mucous membranes and skin and are more sensitive to stress and are thus more liable to react
Gender	screening questionnaire	women are more prone to react because of unfavourable physical and psychosocial conditions
Marital status	screening questionnaire	single persons with children living at home have higher stress load and are more liable to react
Smoking habits	screening questionnaire	increases inclination to react/emits pollutants
Constitutional traits	screening questionnaire clinical examination	previous conditions increases likelihood of reacting

IAQ = Indoor Air Quality VDT = Visual Display Terminal

4 RESULTS

The results from the different studies form a complex but comprehensive pattern. The number of clinical conditions observed in the case reports, with relation to IAQ problems and VDT work, are limited and are consistent with characteristics that have been observed in previous case reports. There was also a considerable number of consistent risk indicators comprising personal, psychosocial as well as physical exposure factors.

4.1 The clinical impression (Paper I)

The most prevalent conditions found among individuals working in buildings with stated IAQ problems fall into three main groups: signs of seborrhoeic dermatitis; erythematous facial skin conditions and itching conditions on the trunk (Table 1, Paper I). The groups are not absolutely separated as seborrhoeic dermatitis is associated with facial erythema and with follicular lesions on the trunk.

In all buildings but one, the association between the clinical conditions and IAQ factors was circumstantial. In employees of the newspaper office (building No. 6), a restrainer used in a photocopying process was shown to elicit visible skin signs in double blind placebo controlled challenge tests.

4.2 Symptoms by age and gender (Papers II, III)

All the studied symptoms were significantly more prevalent in women, with the exception of difficulties in concentration and scaling/itching the scalp or ears, (Table 5, Paper II). The prevalence of SBS cases defined as weekly occurrence of at least one general, one mucosal and one skin symptom, was 11.9% in women and 3.9% in men, and the prevalence was higher in young persons (Figure 4, Paper III). The corresponding figures for skin symptoms cases were 6.8% and 2.5%, and skin symptoms had the same age distribution as SBS.

The symptom excess in women was analyzed with questionnaire data as gender was matched for in the case referent studies. The analysis was made with reference to common hypotheses for the symptom excess found in women in studies of non-lethal illnesses, namely *differences in biological or acquired risks and different illness and reporting behaviour.* The prevalence of atopy, which is a constitutional trait often cited as a risk indicator for SBS, did not differ in women and men. With respect to acquired risks, women were, compared with men, more often smokers, had a lower position at work and were more often publicly employed, handled larger amounts of paper and perceived higher psychosocial work strain. These conditions were identified as risk indicators for SBS symptoms in a crude analysis. Adjustment for the gender distribution however, showed that most risk figures were confounded by gender. Even though the pattern remained, smoking, low position and public employment were no longer statistically significant risk indicators. Part-time work, which was more common in women, reverted from increased to decreased risk figures after adjustment for gender (Figure 3, Paper III). Part-time work is the only important gender difference found, acting in favour of women with respect to potentially adverse effects from IAQ factors at work. An analysis of skin symptom cases showed similar results with respect to confounding.

In spite of inequalities in social conditions at home and at work and differences in physical working conditions, these differences could only explain a small part of the gender difference

in symptom reporting (Table 4, Paper III). The odds ratio for female gender as risk indicator for SBS was only lowered from 3.4 in the crude analysis to 3.0 in the multivariate analysis. Effect modification was in most cases stronger in men, indicating that the effect of an exposure in the office may be easier to detect in men. The clinical validation of the skin symptom questions in the questionnaire refuted the hypothesis that women over-report symptoms. On the contrary, the results indicated that the gender difference in symptom prevalence might be even greater than estimated.

4.3 Risk indicators for the sick building syndrome (SBS) (Papers II–IV)

In the analysis of questionnaire data, asthma/rhinitis, condensation in the dwelling, psychosocial work load, paper and VDT work were statistically significant risk indicators in addition to female gender. The case referent study included data from 464 individuals as compared to 4,943 in the questionnaire study. Some changes in the risk pattern were seen. Some of the risk indicators from the questionnaire did not reach statistical significance when added to the strongest risk indicators from the measurements and the clinical examination in the case referent study. Photosensitive skin type was as strong a risk indicator as atopy. The psychosocial work index derived from a questionnaire, specialized on psychosocial and organizational issues, had a stronger association with symptom prevalence than the screening questions in the base questionnaire.

Besides atopy and psychosocial work load, the age of the building, a surrogate variable for emissions from new surfaces, was a risk indicator in the multivariate analysis. So was the presence of photocopiers and a low outdoor air flow rate. The association between air quality and the occurrence of SBS symptoms was shown by analyzing the odds ratio for symptoms with respect to the outdoor air flow rate at different cut-off points (Figure 1, Paper IV). The odds ratio was adjusted for atopy, psychosocial work load index, virtual age of the building and the presence of photocopiers. An apparent flow-response relationship was seen, indicating an association between IAQ factors and SBS symptoms.

4.4 Risk indicators for facial skin symptoms (Papers II, III, V)

The gender and age distribution and the risk indicators for facial skin symptoms in VDT workers were much the same as for SBS symptoms in the questionnaire study. Female gender, asthma/rhinitis, psychosocial work load, VDT and paper work were statistically significant risk indicators in the multivariate analysis. Paper work was a stronger risk indicator for SBS symptoms than for skin symptoms in isolation, while the reverse was noted for VDT work (Tables 7 and 8, Paper II). Similar to the analysis of the gender difference in SBS symptoms, the variables under study could not explain the excess prevalence of skin symptoms in women.

The case referent study of skin symptoms in VDT users was less powerful than the study of SBS cases because only 163 subjects were studied. Atopic illnesses and paper work were close to statistical significance both in bivariate and multivariate analysis. Besides unfavourable psychosocial working conditions and the amount of VDT work, background electric fields, the presence of fluorescent lights with plastic shields and low cleaning frequency were associated in the multivariate analysis with a higher prevalence of symptoms.

4.5 The results vs the hypothesis

At the start of the Office Illness Project a great number of potential risk factors for the symptoms studied were listed. The screening study and the case referent studies have assessed many more variables than those included in this thesis. Many potential risk factors have been refuted in our prior analyses. Table 6 displays the central risk indicators assessed in this thesis and their hypothetical effect.

Indoor air quality factors as determinants of SBS symptoms were supported by the identification of potential emission sources such as newly raised buildings, paper exposure and photocopiers as risk indicators. The association between paper work and low cleaning frequency and skin symptoms support the hypothetical importance of IAQ factors also for skin symptoms in VDT users. Wall-to-wall carpets in the dwellings were not identified as significant pollutants. The importance of eliminating pollutants was supported by the identification of low outdoor air flow rate and condensation on windows as risk indicators.

The role of stress hormones, as inducers of symptoms or as modifiers of the effects from other exposure factors, was emphasized by the results, both with respect to SBS symptoms and skin symptoms in isolation.

With regard to personal factors, the age distribution of SBS and skin symptoms was in conflict with the hypothesis. Contrary to what was expected from biological reasons, young people reported symptoms most prevalently. The analysis of the symptom excess among women also refuted the hypothesis that the difference was mostly due to the studied physical and psychosocial conditions at work and at home.

In VDT work, the mechanism of electrostatic fields enhancing particle deposition on the skin was not supported. On the whole, VDT-related electromagnetic fields as inducers or effect modifiers gained weak support, with the exception of the magnetic field in the ELF range. Unspecified VDT-related conditions as inducers of symptoms however, were supported by the exposure-response relation obtained between time at the VDT and symptom occurrence.

4.6 A public health perspective (Paper III)

From the prevalence of the risk indicators and the associated relative risks (here OR) obtained from the multivariate analysis of the questionnaire data in Paper III, and thereby taking both frequency and the magnitude of the occurrence relation into account, "aetiologic" cases were calculated. As the causal relationships between the outcome and the determinants are unknown, aetiologic cases are here used only to illustrate the potential public health interest of the risk indicators. Figure 3 shows the results expressed as a percentage of all SBS cases. The sum of aetiologic cases exceeds the total number of cases because many cases have, or are exposed to, several risk indicators. The results underline the importance of factors associated with female gender. In addition, two common exposure factors in offices, paper and VDT work, together with psychosocial work conditions seem to be important to further investigate. The fact that one to four hours of daily VDT work supplies more aetiologic cases than extensive VDT work is explained by the fact that more people had only moderate amounts of VDT work. The proportion of aetiologic cases were calculated according to the formula

$$\frac{p(RR-1)}{1+p(RR-1)}$$

where p is the prevalence of the characteristic or exposure and RR is estimated by the odds ratio obtained from logistic regression analysis.

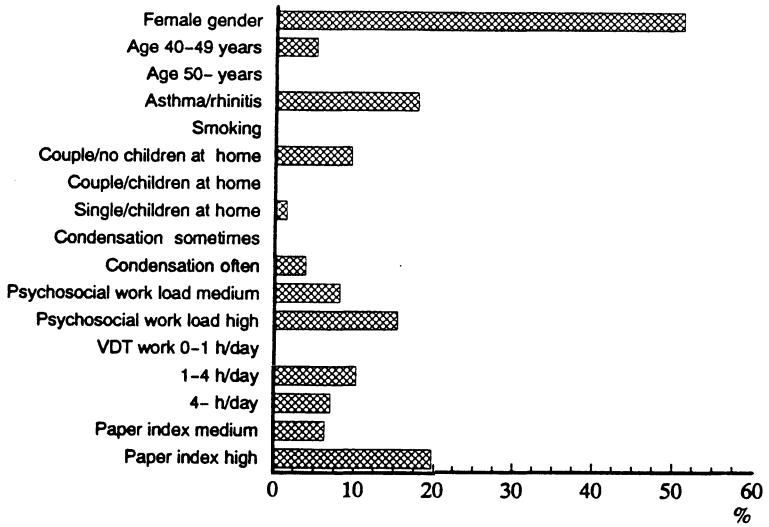

Figure 3. The proportion (in percent) of SBS cases attributed to certain personal characteristics and exposure factors.

4.7 A clinical comparison between SBS cases and skin symptom cases (Papers IV, V)

The clinical findings in the two case groups and their referents are summarized in Tables 7 and 8. The comparisons are based on standard chi-square test. Both case groups reported more sensory symptoms than their referents. SBS cases had more visible eczema and erythema than the referents, among skin symptom cases erythema was more prevalent than among referents. Moreover, compared with the referents, the SBS cases had more work-related facial erythema, seborrhoeic dermatitis and general pruritus, conditions involving the face as well as the trunk. Skin symptom cases, on the other hand, had more work-related facial erythema than their referents.

The results from the "stinger test" were not identical in the case groups. Even if there also was a tendency to stronger reactions in skin symptom cases it was not as obvious in SBS cases.

Table 7. Comparisons of prevalence (in percent) of some previous characteristics of SBS cases and referents and skin symptom cases and referents.

	Acne	Atopic dermatitis	Seborrhoeic dermatitis	Photosensi-tive skin	Migraine
SBS cases	42.2	13.5	22.8	26.0	19.9
Referents	56.7	10.0	16.4	19.4	19.4
p-value	<.01	n.s.	n.s.	n.s.	n.s.
Skin symptom cases	58.8	15.0	20.3	32.9	21.8
Referents	60.8	7.6	14.1	22.8	15.4
p-value	n.s.	n.s.	n.s.	n.s.	n.s.

Table 8. Comparisons of current facial skin symptoms and signs and "stinger test" results (in percent) at clinical examination of SBS cases and referents and skin symptom cases and referents.

	Sensory facial skin symptoms	Dry skin	Eczema	Erythema	"Stinger test" reaction		
					weak	medium	strong
SBS cases	80.8	14.9	16.5	51.0	20.9	38.5	40.6
Referents	43.8	16.9	9.5	40.3	35.5	39.9	24.6
p-value	<.001	n.s.	<.05	<.05		.001	
Skin symptom cases	96.3	12.5	21.3	67.5	25.0	48.8	26.3
Referents	60.8	6.3	15.2	40.5	27.8	40.5	31.6
p-value	<.001	n.s.	n.s.	<.01		n.s.	

5 GENERAL DISCUSSION

5.1 The model/study design

The epidemiological part of this work is based on a model of a clinical problem. We recognize both SBS and skin symptoms in VDT workers as problems of clinical significance. These conditions are seen in patients by clinicians in primary health care as well as in occupational medicine, occupational dermatology, oto-laryngology and lung medicine.

5.1.1 The outcome

SBS cases

The case definition used in Paper IV was based on clinical experience. We were aware of the fact that many patients with IAQ-related symptoms lack skin symptoms and signs. In our hypothesis however, skin symptoms are judged to be signs of significant exposure as patients often report general and eye symptoms early and skin symptoms later in the history. To create a good contrast between cases and referents we chose a "strong" case definition with at least one general, mucosal and skin symptom. One drawback of this definition may be that individuals with constitutional risk factors are favoured by the case selection and that the importance of such factors is overestimated.

The non-specific nature of the symptoms may also create a problem in the assessment of atopy as a risk factor. Atopics may perceive general, mucosal and skin symptoms due to their atopic illness and thus erroneously be identified as risk persons for reporting SBS as defined in a questionnaire. The use of work-relatedness as a criterion for SBS does not help much as other work factors than indoor air quality, such as psychosocial conditions, may cause worsening of atopic symptoms. This problem underlines the need to find better and, if possible objective, criteria for case definitions.

The validation of the questionnaire showed a low sensitivity of the skin symptom questions. The other symptom questions have been validated by other investigators (unpublished data) who found a better sensitivity. Skin symptom questions, comparable to those we have used, have been shown to provide a reasonable estimate of the period prevalence estimated at an interview but they poorly predict the clinical findings at a particular point in time.[113] The gender difference found in our validation motivates stratification for gender in future validations of questionnaires for self-reported health.

The questionnaire used in the Office Illness Project was designed for surveying IAQ-related problems. The sensitivity and specificity of each symptom for predicting SBS cases was estimated. Table 9 shows the results. For screening purposes, high sensitivity is more important than high specificity, and this was guiding when one screening symptom was chosen from each group of symptoms (general, mucosal and skin symptoms). Note that scaling/itching scalp or ears and skin symptoms on hands were not used in the definition of SBS cases.

Table 9. Sensitivity and specificity of different symptoms for diagnosing sick building syndrome in individuals with and without atopy.

Symptom	Sensitivity			Specificity		
	Total	No "atopy"	"Atopy"	Total	No "atopy"	"Atopy"
fatigue	97.5	97.8	97.4	22.3	23.1	18.3
heavy-headedness	87.2	87.9	87.2	52.0	43.4	35.8
headache	80.9			42.6		
nausea	45.2			84.0		
difficulties concentrating	64.8			59.5		
eye symptoms	91.7	91.2	90.6	58.9	60.8	50.5
nose symptoms	78.9			60.6		
hoarse throat	77.6			65.2		
cough	56.3			71.8		
dry facial skin	97.5	97.8	96.6	60.2	61.5	55.3
flushed facial skin	71.6			82.2		
sensory facial skin symptoms	74.9			79.0		
scaling scalp/ears	53.7			75.9		
skin symptoms on hands	57.3			79.2		

SBS = Sick Building Syndrome IAQ = Indoor Air Quality

Among general symptoms fatigue and heavy-headedness both had high sensitivity but fatigue had a very low specificity. Eye symptoms and dry skin were the best screening symptoms from the mucous membranes and the skin. For these four symptoms, figures for individuals with and without asthma/rhinitis, here used as a sign of atopy, are also given in Table 9. As a rule, the symptoms were less specific among atopics. Heavy-headedness, eye symptoms and dry skin seem to be acceptable screening symptoms for SBS. When investigating specific buildings with a potential IAQ problem, the causal emissions may differ from one building to another with respect to characteristics entailing differences in effects. Therefore results from interviews with the occupants should suggest how a questionnaire is worded.

Skin symptom cases

The definition of cases for the study of skin symptoms in VDT users was based on the experience that such patients almost always report marked sensory symptoms from the face and that the clinical signs can be very sparse. Thus sensory symptoms were mandatory for the case definition.

The slight difference between the definitions , with respect to skin symptoms, in the two case groups may affect the outcome in such a way that the comparison of clinical signs between the case groups is biased. Therefore we cannot state that the differences we noted at the clinical

examination are representative of the difference between the two groups in clinical practice. Still the clinical findings in the two case groups agree well with previous case reports. From this we conclude that the findings in the case referent studies have *applied relevance.*

5.1.2 The independent variables

Some problems concerning atopy as a risk indicator have been discussed above. Furthermore, the questionnaire did not entirely cover the concept of atopy, which was defined as a previous or present history of atopic asthma, atopic rhino-conjunctivitis or atopic eczema. The questionnaire was not specific enough to entirely fit this definition.

The assessment of psychosocial and organizational factors was based on questions in the screening questionnaire and on an extensive questionnaire addressing such questions. They have been previousely validated and their importance as determinants of health has been documented.[115] Three main areas of the psychosocial work environment have been assessed in this thesis; work content, work control and social support. The health effects of these factors are supposed to be mediated by stress-related hormones.

Knowledge about the nature of the pollutants causing SBS symptoms is lacking. Chemical analyses of the indoor air are not meaningful at the moment unless in certain situations with specific questions, such as assessments of emissions from plastic flooring or pollution from outdoor car exhausts or in research situations. TVOC is often used as a measure of indoor air pollution. There is experimental support for an association between VOC exposure and SBS symptoms. As already discussed in the literature review, there are, however, methodological problems regarding both the definition of VOC and the measurement methods.[80] In the Office Illness Project analyses of VOC were performed in buildings with high and low prevalence of SBS symptoms. A decrease in TVOC concentration from supply to room air was associated with an increased prevalence of symptoms.[114] "Lost" TVOCs may have been changed to potent matter that was not trapped or analyzed by the method used.

Traditionally, most exposure variables studied in IAQ surveys are surrogates for actual measurements of hypothetical risk factors. The association between the surrogate variable and IAQ factors may be complex, as for the age of a building, or more intelligible, as for condensation on windows. This means that important associations between symptom occurrence and exposure can be obscured by the non-specific nature of the exposure variables. In other cases false associations may be seen due to undetected confounding. Even if we have tried to specify the theoretical effect of the exposure variables future research in this field should be based on a limited number of better defined exposure measurements.

The precision of measurements of ventilation rates and electromagnetic conditions is known. They were measured using well-established methods and calibrated instruments.[112,116,117] There are still problems concerning the comparability of results from different studies of electromagnetic fields. The measurement of electric fields always perturb when measuring magnetic fields and the variation with time can sometimes be substantial (Hansson Mild K., Sandström M., personal communication). The existing standardized methods for VDT measurements are adapted for laboratory conditions. We had to modify some of the measurements for the conditions in the working place. Even if the validity and precision of spot measures are good, the main problem concerns their validity as estimates of exposure over time. When performing the workplace investigations we have aimed at measuring conditions that were, at the least, representative of the recall period of the questionnaire. From measuring the air exchange efficiency we have assumed that the ventilation rates are representative for the whole work room.[110] To provide a representative value for the electromagnetic background

fields we used the mean value of five different measurement points in the room.[112] The exposure situation in other rooms in the workplace is unknown. So is the route of administration to the reaction organ and the dose in most instances.

5.1.3 Sources of potential bias

The odds ratio as a measure of the relationship between independent variables and the occurrence of the outcome was used as it expresses the results in an intelligible way. In the multivariate analyses using logistic regression, the calculations were guided by the hypotheses rather than using a stepwise analysis based solely on significance levels.

The temporal relationship between the exposure and the first appearance of symptoms is unknown as the study was cross-sectional. True causal relations may be obscured if in some individuals, the exposure duration is too short or if there is a biological induction time needed and such conditions are not fulfilled. Actions taken at the workplace because of symptoms may also hinder the identification of important associations. In our study a large proportion of the VDT users had protective devices mounted on their VDT screens lowering the electric fields. Some of these may have been mounted because of skin symptoms. False associations may also be found if the studied symptoms have induced changes in exposure. One such example is probably the association found between the presence of humidifiers and SBS symptoms.[110]

With the exception of the definition of SBS cases which may have favoured atopy as a risk indicator, (see above), we have not found any signs of significant *selection bias* in the prevalence and case referent studies. The prevalence study involved a random sample of employees stratified for geographic area so as to be representative of the geographical distribution of office workers in the county. The drop-out rate was under five percent, and interviews with a sample of non-responders did not indicate any selection bias. A number of referents may have been very similar to cases from a symptomatic point of view. They just did not fulfil all symptom criteria. From the time of the questionnaire until the measurements were taken, a number of cases and referents changed position[114] which can be due to fluctuations in symptom intensity. The misclassification caused by this phenomenon is probably non-differential, resulting in underestimated risk figures. The exclusion of individuals in the prevalence study due to absenteeism poses another problem. They may have been absent because of the symptoms under study causing an underestimation of their prevalence in the study population. If absenteeism due to such symptoms was unequally distributed with respect to some independent variable a selection bias may have occurred, which was beyond our control. A high psychosocial work load affecting the inclination to take sick leave because of the symptoms under study could be one example of this. This would result in an underestimation of psychosocial conditions as risk indicators. The drop-outs in the case referent studies were almost exclusively due to exclusions caused by changes in working conditions between the time of the questionnaire and the examination of the workplace. Even if these cases and referents were replaced the procedure might have weakened the strength of some risk indicators if the changes that caused the exclusions were made because of the symptoms under study.

To minimize the risk of *information bias* we performed the clinical examination and the technical measurements blindly with respect to whether the employees were cases or referents. Consequently the potential misclassification of exposure intensity is probably non-differential, influencing the odds ratios towards 1.

Variables potentially subject to *recall bias* were sparsely used in the analyses. This applies especially to signs of damage to the building construction at work and at home. Even if recall bias may affect the analyses of factors such as paper and VDT work, the exposure–response relationships that were established support an association between the exposure and the symptom occurrence.

Potential *confounding* was controlled by matching and stratification and multivariate analyses. For convenience, the case referent studies were matched for age, gender and geographical area. These risk indicators were assessed in the prevalence study. Stratification was used primarily for gender and atopy. In spite of a matched design both unmatched and matched analyses were used in the multivariate calculations. In the light of the problems associated with loosing observations in the matched analysis, we would probably today prefer an unmatched design.

To conclude, the well–established operationalization of work stress and the measured and observed physical risk indicators, and the relative lack of bias in the epidemiological studies gives the results *theoretical relevance*. The use of surrogate variables is a limiting factor both for the validity and the *efficiency* of the study.

5.2 Agreement with previously published work

Sick Building Syndrome

Some of the major risk indicators found in the Office Illness Project, such as female gender, atopy, and psychosocial work load confirm the results of other reports.[19,41,44,46-48] A thorough analysis of the gender difference has however not been published before and skin symptoms, included in the descriptions of SBS, have not been broadly assessed before. Higher prevalences among young people have been reported by others.[41] Photosensitive skin has not previously been identified as a risk indicator for SBS while the "stinger test" reactivity found in SBS cases, is in line with experimental data showing that this skin "hyperreactivity" predicts conjunctival reactions to n-decane.[72]

Paper and VDT work and the presence of photocopiers are not consistent, although earlier reported risk indicators.[19] Higher symptom prevalences in buildings raised or renovated after 1977 were expected, as buildings raised after the energy crisis in the 1970s have often been cited as problem buildings.[2] This statement has however seldomly been subject to research. The rate-response relationship found between the outdoor air flow rate and symptom occurrence corresponds with prior reports of elevated complaints when the outdoor air flow rate is below 10 L/s,p.[79] Some previously identified risk indicators could not be assessed in our study. Air-conditioning is very rarely used in Sweden, not at all in Västerbotten, and wall-to-wall carpets are also rarely used in offices where many people pass. The indication that plastic flooring may be associated with increased SBS symptom occurrence has not been reported before. A number of reported risk indicators, such as the area of textiles and the amount of open book shelves in the room[45] were not verified. This thesis does not cover the Office Illness Project in total. Other potential risk factors, such as VOCs, were measured in a sample of the buildings, the results have been discussed elsewhere.[114]

Facial skin symptoms in VDT users

The exposure-response relationship found between VDT work and skin symptoms has been reported in previous Swedish studies.[92,93] An assessment of a wide spectrum of personal, psychosocial and physical risk indicators has however not been performed earlier. The importance of psychosocial work conditions verifies other results.[96,105] The association

between electromagnetic fields and skin symptom occurrence has only been studied in one more observational study[96] and their results are in conflict with our findings. Electric heating and fluorescent lights with different types of shielding have not been assessed by other investigators.

The Office Illness Project comprises interdisciplinary studies founded on clinical experience and it is based on measurements of important exposure factors. Furthermore, the results were established using multivariate analysis. These facts render our results a good theoretical relevance compared with many previous studies of the office environment.

5.3 Theoretical considerations on pathogenesis

Constitutional factors

Female gender represents a risk indicator associated with constitutional as well as psychosocial and physical exposures. An analysis of the symptom excess in women indicated that the gender differences in symptom prevalence is part of a general pattern for psychosomatic illnesses. Even if women work under poorer psychosocial and physical conditions than men these inequalities do not explain their symptom excess. We need more knowledge of the differences in life circumstances in a broad sense to better analyze what is inherited and what is acquired. Proneness to dry mucous membranes[118–121] and a more active immune system in women[122] have been noted as constitutional gender differences, but the importance of these and other genetically determined differences must be explored.

Atopy has already been discussed. Photosensitive skin as a risk indicator for SBS symptoms cannot be understood today. A constitutional link between such a skin type and proneness to mucosal and general symptoms should be looked for. A strong "stinger test" reaction was a risk indicator for SBS. This is an interesting finding as it has been shown to be a predictor of mucosal reactions to VOC exposure.[72] The test was originally designed for predicting skin irritancy proneness[106] but these findings indicate a link between skin and mucosal hyperreactivity.

Psychosocial factors

Many of the symptoms studied are psychosomatic in the sense that they may be provoked by the action of stress-related hormones. As the pathogenic mechanisms for IAQ- and VDT-related symptoms are unknown the role of stress-related hormones in these conditions is obscure. There is scientific support for a link between psychological functions and the immune system, "psychoneuroimmunology",[123] but up to now SBS symptoms and skin symptoms in VDT users have not been shown to be mediated by any identified immunological mechanism. A reaction pattern called "techno-stress" has been proposed in which the occupational strain in computer work induces stress reactions which may act as an unconditioned stimulus. The conditioned stimulus would be the VDT environment. Once learned, the response can be elicited by the VDU environment even without stress.[105] The hypothesis was supported by findings of higher levels of stress-related hormones in VDT users with skin symptoms than among controls. The mechanism of conditioning would also be possible with a physical factor as the unconditioned stimulus.

Chemical factors

The nature of the chemical agents and the route of administration to the reaction organ is practically unknown. The skin and the mucous membranes may react to a direct action of chemical substances. Substances can also be absorbed and spread to the reaction organs via the circulation or secreted by glands such as the salivary and lacrimal glands. The mechanism for chemical agents inducing SBS symptoms is not known. Neurogenic inflammation is a pathway distinct from antigen-driven, immune-mediated inflammation and is triggered by the nervous system. Immunological and neurological inflammation may co-exist. In the skin, immunological reactions often induce a powerful itch. The burning sensation and erythema in facial skin reported by patients with IAQ-related symptoms, and especially by VDT users, may be evoked by substance P, which has strong vasodilatory properties. Neutral endopeptidase, a cell-surface enzyme, downregulates neurogenic inflammation by degrading substance P. SBS and multiple chemical sensitivity (MCS), see below, have been proposed to be disorders of this regulation entailing a hypersensitivity to chemical agents.[124] According to this hypothesis, the general symptoms perceived in SBS may be the effect of mediators and regulators produced in the central nervous system by resident cells or by activated cells penetrating the blood-brain barrier.[124] Whether or not psychological stress enhances neurogenic inflammation is unclear.

Electromagnetic factors

The association between the occurrence of skin symptoms and VDT work, background electric fields, VDT-related magnetic (B) fields, certain types of fluorescent light shielding and electric heating suggest a biological response to electromagnetic conditions. These associations however may be confounded by undetected factors and there is little support for the induction of skin symptoms by electromagnetic fields. Challenge tests with VDT-related fields have with few exceptions been negative.[102-104] Besides these challenge tests there is one previous observational[96] and one experimental[101] study addressing the association between skin symptoms and alternating VDT-related electromagnetic fields. Their results also refuted an association between VDT-related electromagnetic fields and skin symptoms. There are, however, findings that show or indicate a biological effect of alternating electromagnetic fields.

Pulsed magnetic fields have been used to promote bone fracture healing.[125] Experiments have shown that these fields have regulatory effects on the function of endothelial cells and fibroblasts.[126-128] There is also epidemiologic data suggesting a carcinogenic effect of exposure to magnetic fields from high voltage transmission lines[129]and occupational exposure to magnetic fields.[130] Results from different studies, however, are not consistent[131] and results from such exposures may not be applicable to the electromagnetic situation in an office in front of a VDT. The shape of the wave, the frequency and the field strength and the mixed exposure to a number of fields hinders comparisons from one set of conditions to another. There is one study, based on measurements of VDT-related fields, showing an increased occurrence of adverse pregnancy outcome in VDT users working with VDTs with high B fields in the ELF range[132] but these results also disagree with other findings.[133]

Other VDT-related factors

There are other physical factors than electric and magnetic fields in the ELF and VLF range associated with VDT work. Chemical emissions , such as flame retardants, from different parts of the VDT device have been suggested as possible causes for skin and mucosal symptoms.[134] No study has so far supported this hypothesis. Another hypothesis suggests that electromagnetic fields or exposure to light emitted by cathode ray tubes and flourescent tubes

causes a reaction mediated by the photosensitive central nervous hormone melatonine.[134] Experiments exploring this hypothesis are going on in Sweden.

5.4 The concepts "sick" buildings and "Sick Building Syndrome"

The concept of "sick" buildings has been used to designate buildings in which the inhabitants perceive irritative symptoms from the eyes, airways and skin together with general symptoms.[2] Some investigators define a "sick" building as a building where an unexpectedly high proportion of the inhabitants report symptoms.[43] Temporarily "sick" buildings and permanently "sick" buildings have been distinguished. The former are newly constructed or remodelled buildings, where the symptoms generally disappear within six months. The second category comprises buildings with common constructional features in which symptoms persist for years. Typical features of the latter category are mechanical ventilation systems, light construction, large indoor textile surfaces, energy-efficiency and airtight building envelopes.[2]

Observational studies published from various continents have clearly shown that the occurrence of "sick" building symptoms, SBS symptoms, is associated with a number of non-building-related factors, such as age, gender, previous hypersensitivity, psychosocial and organizational factors and working conditions such as paper and VDT work. These risk indicators need to be controlled for in prevalence studies. Studies of specific problem buildings also require local control buildings as "normal" prevalences may vary from one region to another because of differences in climate and working conditions. Thus the use of the term "sick" building, where the "sickness" is estimated from symptom occurrence, is not well founded. The concept of "sick" buildings should be abandoned as a high prevalence of SBS symptoms as such does not give any information about the status of the building and as the assessment can be confounded by a number of non-building-related factors. The term might be applicable in those cases where it can be shown that damage to the construction causes symptoms in the inhabitants. As a rule, however, people are sick while buildings may be subject to chemical/physical problems. Buildings judged to have emissions evoking symptoms in its inhabitants are IAQ problem buildings.

Similarly the concept of the Sick Building Syndrome (SBS), attached to "sick" buildings, should also be abandoned. SBS can be replaced by Indoor Air Syndrome (IAS), as it focuses on the indoor air quality as the necessary cause. There is now sufficient data linking the occurrence of SBS symptoms to IAQ factors to justify this terminology. The Swedish term is suggested to be "Inneluft-sjuka". As a syndrome is a set of associated symptoms, Indoor Air Syndrome should not be used for single symptoms such as fatigue, rhinitis or erythema. In these cases terms such as "indoor air-related rhinitis" or "IAQ-related rhinitis" are more proper to use if the association between the exposure and the symptom is plausible.

There is a need for consensus regarding which symptoms and signs should be included in the syndrome. With current knowledge it should be possible to set a number of major and minor clinical criteria for the diagnosis. These criteria must be supplemented by information about exposures recognized as risk factors or other conditions supporting the diagnosis. A high proportion of the occupants of a building reporting symptoms and odour complaints are the kind of condition indicating an IAQ problem. The normal perception of odour is, however, not a symptom and should not be included in the syndrome.

A recent suggestion for criteria for the definition of SBS[28] includes absenteeism and contact with primary health care, but such reactions and actions will be modified by cultural, economical and psychosocial conditions and will be more likely to obscure rather than clarify

the definition of a syndrome. The suggested criteria also state that some symptoms must be more prevalent than others. Such restrictions may hinder the development of knowledge as different exposures may lead to different symptoms. Moreover, the same exposure may induce different symptoms in individuals with different constitutions or reaction patterns. This fact motivates further studies of single symptoms and different syndrome constituents. A similar problem is the use of "work-related" symptoms in surveys. As some symptoms may be more chronic than others, and because "work-relatedness" is a subjective assessment that must be validated, both "work-related" and total symptom occurrence should be analyzed.

Multiple chemical sensitivities (MCS) is a concept with many similarities to IAS. It is commonly used in the US to designate a chronic, multi-symptomatic state, supposedly induced by short-term exposures to certain chemical agents.[135] People suffering from MCS react continuously to chemical exposures in concentrations that do not affect others. MCS is a highly controversal concept, but may represent a type of hyperreactivity, sometimes reported by IAS patients. As both IAS and MCS are poorly understood conditions they may represent over-lapping phenomena.

SBS has also been said to be a form of mass psychogenic illness (MPI) and the diagnosis of MPI or "mass hysteria" can sometimes be an excuse for inadequate investigations of environmental problems.[136] MPI however has characteristics that quite clearly separate such reactions from SBS. MPI affects a population and is often triggered by an event starting a rumour about toxic exposures. Even if the symptoms in many cases are similar, episodes of MPI often disappear as abruptly as they start.[137-138] This contrasts to the insidious start and protracted course commonly seen in outbreaks of SBS.[33] MPI must be separated from psychosomatic illnesses. SBS and VDT-related skin symptoms are psychosomatic in the sense that they are influenced by psychological stress factors.

Skin symptoms in VDT workers have been alleged to be an example of "20th Century disease",[139] sometimes used as a synonym for MCS. VDT workers with facial skin complaints however, do not have a multi-symptomatic condition typical of descriptions of MCS and MPI, and the clinical course does not have the abrupt appearance and clearing characteristic of MPI. This is not contradictory to the view that the mass media may have a role in focusing on VDT work as a threat to health, thus influencing how individuals assess the relationship between symptoms and exposure factors. Another phenomenon, not addressed in this thesis, the perception of "electric hypersensitivity" with multi-symptomatic complaints, bears many similarities with descriptions of MCS.[140]

5.5 Back to the patient

Even if this study does not necessarily permit causal interpretations, the results, in the light of previous studies and clinical experience, provide a basis for tackling the clinical problems. The following check-lists are presently used at the Department of Dermatology and are recommended for use at local health services involved in health problems related to the indoor environment. They illustrate how the present knowledge is applied in the clinical situation. Because of the lack of knowledge about the nature of offending chemicals and the role of electromagnetic factors, the check-lists are in some respects non-specific.

Alleged IAQ-related symptoms

1. Take a thorough medical, hygiene, and social history. When indicated, perform a psychological examination.
2. Try to document the relation between a certain indoor environment and symptoms and observable signs, such as erythema (photo), BUT, peak expiratory flow (PEF), rhinometry etc.
3. If possible, delay treatment until relationships have been documented.
4. Investigate and reduce emissions from damage to the building construction or surface materials.
5. Investigate and reduce unnecessary emissions from apparatus and activities. These include photocopiers in the vicinity of the workplace, handling and storage of large amounts of paper, smoking indoors, inadequate or poorly performed cleaning.[1)]
6. Investigate and, if needed, improve ventilation, including outdoor air flow rate, recirculation rate, efficiency, polluted duct works and supply air quality.
7. When indicated, investigate and reduce emissions from undamaged but strongly emitting surface materials.[2)]
8. Investigate and treat signs of unnecessary psychosocial strain.

[1)] As laser printers can emit similar substances as photocopiers[141] such machines, if frequently used, should preferrably be located in separately ventilated areas. Incorrect cleaning and surface polishing of the flooring can enhance emissions of volatile and particulate agents.

[2)] In situations where the emission source is unknown chemical analyses of the indoor air can give information about strong emission sources, such as polyvinyl chloride (PVC) flooring which has typical emissions.

Because of similarities between risk indicators for IAS and for skin symptoms in isolation, and similarities in clinical signs, attention should also be paid to IAQ factors when complaints are attributed to VDT work.

Alleged VDT-related skin symptoms

1. Take a thorough medical, hygiene, and social history. When indicated, perform a psychological examination.
2. Try to document the relation between VDT work and symptoms and observable signs, such as erythema (photo).
3. If possible, delay treatment until relationships have been documented.
4. Investigate and deal with obvious sources for an IAQ problem, including emission sources and inadequate ventilation, see points 4–7 above.
5. Investigate and treat signs of unnecessary psychosocial strain.
6. Shorten VDT time or try to spread VDT work evenly over time to avoid intense and stressful work situations.
7. Reduce electric fields by protective shields or try alternative VDT technique.[3)]

8. Avoid fluorescent light if it evokes symptoms.[3)]

9. Reduce the exposure to ambient electromagnetic fields by earthing and moving electric devices and cables.[3)]

[3)] These recommendations are widely used in Sweden but the scientific basis for these actions is weak. There are no published experimental studies of the effects of single regimens. They have been reported as beneficial[142] but often a number of actions are taken, why it is difficult to evaluate them separately. Our results provide some support for these recommendations.

The main objective of a thorough medical, hygiene, social and, when indicated, psychological, examination is to find alternative explanations for the alleged cause of the symptoms. Contact allergy must be ruled out as an explanation for skin symptoms. Colophony is one substance, recently reported to be an important paper allergen.[143] When such alternative explanations seem unlikely one proceeds down the list. It should not be used as a recipe but as a check-list and should be used with a generous portion of common sense. In clinical practice we often have to handle problems even when deep knowledge is lacking about the nature of and the cause of the complaints. If, however, hypothetical causes for symptoms are brought forward as true and paid too much attention, we may contribute to an iatrogenic phobia towards such factors. This applies especially to electromagnetic conditions where the scientific support for action is weak. It is not unlikely that insufficiently understood phenomena such as MCS, IAS, VDT-related symptoms and perceived "electric hypersensitivity" to a varying extent contain elements of unjustified avoidance of alleged risk situations.

6 CONCLUSIONS

The occurrence of non-specific general, mucosal and skin symptoms, here used to operationalize the Sick Building Syndrome (Indoor Air Syndrome), is associated with constitutional factors, psychosocial stress factors and IAQ factors. Women report symptoms more often than men and even though there are marked gender differences in working conditions, such factors cannot explain the female symptom excess. Gender is the most important risk indicator to control for in the study of health problems related to the indoor environment.

As the occurrence of SBS symptoms is related to a number of non-building-related factors, and as chemical emissions inducing symptoms can have non-building-related sources, "sick" buildings and the Sick Building Syndrome are inappropriate terms. As IAQ factors are necessary causes of SBS symptoms, demonstrated by a rate-response relationship between the outdoor air flow and the symptom occurrence, Indoor Air Syndrome (IAS) is a more appropriate term.

The occurrence of facial skin symptoms in isolation is, with some exceptions, determined by similar factors to the Indoor Air Syndrome. These exceptions motivate separate analyses of single symptoms and symptom groups. In VDT users, the occurrence of facial skin symptoms is associated with the intensity of VDT work and with electromagnetic conditions or undetected factors related to such exposure.

7 SUGGESTIONS FOR FUTURE RESEARCH

7.1 Symptoms and signs related to IAQ problems and VDT work

More knowledge and better descriptions of the nature of IAQ–and VDT–related symptoms and signs are needed. Systemic studies of outbreaks, case reports, and objective monitoring of symptoms and signs are suitable tools for this. Immunological and psychoneuroimmunological studies may provide greater insight into the pathogenesis of the complex symptom patterns. The association between general, mucosal and skin symptoms observed in the indoor air syndrome (IAS) suggests systematic mechanisms. Whether or not there exist relevant constitutional links between skin and mucosal reactivity, other than atopy and autoimmunity needs to be clarified. Our clinical experience also indicates that studies of both psychosocial and personality factors will increase our understanding of this kind of environment–related health problem.

7.2 IAQ/VDT–related inducers for symptoms and signs

Further observational and experimental studies aimed at identifying agents capable of inducing the symptoms of the indoor air syndrome are also needed. Bacteria and fungi (microorganisms) are among the important potential sources of emissions that produce volatile organic compounds (MVOC). Others include plastic surface materials, such as PVC floorings, and laser printers. The findings that photocopiers are significant risk indicators, suggest that printers using similar technology should also be assessed. In the light of present knowledge of potential confounders, chemical studies may produce valuable data provided that the symptom provoking agents can be analysed using currently available methods.

Further studies of psychological stress factors and electromagnetic conditions are needed to confirm or refute results of previous studies of the skin symptoms in people working at VDTs. Possible interactions between psychological, neurological ad immunological mechanisms should be studies. The crucial issues in future observational studies include the operationalization of the outcome and exposure assessments. The present use of surrogate variables and spot measurements should be replaced by more specific and relevant measures of the long–term exposure.

7.3 Long–term effects of exposure to adverse IAQ factors and work at VDTs

Longitudinal studies with valid exposure measures are needed to answer such questions as whether adverse IAQ factors can induce asthma and whether such factors or conditions related to working at VDTs can induce or provoke chronic skin conditions such as rosacea. As indoor work in office–like environments becomes more common, these studies are important public health issues.

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