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Exposure to skin irritants – validation of questions and epidemiological aspects

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ABSTRACT

Hand eczema is common, and is the most frequent occupational skin disease. Exposure to skin irritants contributes to hand eczema. Common skin irritants are water, detergents, chemicals and foodstuffs. The aim of this thesis was to study exposure to skin irritants in the general population in relation to gender, age and occupation, and in individuals with and without hand eczema. A further aim was to validate questions regarding occupational exposure to skin irritants.

In the first study, 182 individuals with hand eczema and 182 without hand eczema, matched for age and sex, participated in telephone interviews regarding exposure to skin irritants at work and during leisure time (Study I). In the second study a validation was performed of self-reported occupational exposure to water, chemicals, foodstuffs, gloves and hand washing, in five different occupations (Study II). Forty participants completed a questionnaire before the start of a working day and observers subsequently registered the exposure during the working day. In another study, a validation was performed as above, in 40 nurses/assistant nurses working in six different geriatric wards (Study III). The participants answered questions regarding exposure to water (frequency and total time of exposure), gloves, hand disinfection and moisturizers. Finally, in an epidemiological study, as part of a public health survey 18,267 gainfully employed individuals aged 18–64 years answered questions regarding occupational water exposure (Study IV).

About 20 % of individuals in the general population reported occupational skin exposure to water (Study IV). Furthermore, 7 % reported exposure of more than 2 hours and 6 % of more than 20 times a day. Women reported more water exposure at work compared with men. The youngest group, aged 18–29 years, reported more water exposure than did the older groups. Eighty per cent of the population reported wet exposure during leisure time, for half an hour or more a day, and women were more exposed than men (Study I). Individuals who reported wet exposure at work also reported more wet exposure in their leisure time. No statistically significant differences were seen regarding exposure to water, hand washing or chemicals in individuals with and without hand eczema. The correlation between self-reports and observations regarding exposure to water, gloves and foodstuffs were strong, while they were moderate regarding hand washing. There was a tendency to overestimate all exposures (Study II). In nursing the correlations between self-reports and observations were strong for hand disinfection and moisturizers. They were moderate for frequency of water exposure and weak for total time of exposure to water (Study III). The nurses/nurse assistant nurses overestimated their exposures, to water in particular.

In conclusion, one-fifth of the general population are occupationally exposed to water and half of the them are highly exposed. Wet exposure during leisure time is common and individuals with high water exposure at work also tend to have high wet exposure in their leisure time. Women have more wet exposure than men both at work and at leisure. Individuals with and without hand eczema seem to have similar exposure to skin irritants. Despite some tendency to overestimate the exposure in the validation studies, the questions are considered useful for surveying exposure to skin irritants.

Key words: correlation, epidemiology, gender, gloves, hand disinfection, high-risk occupation, observation, self-report, skin irritant, survey, validation, water, wet work
LIST OF PUBLICATIONS

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals.


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<tr>
<td>ACD</td>
<td>allergic contact dermatitis</td>
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<tr>
<td>Da</td>
<td>dalton</td>
</tr>
<tr>
<td>ICD</td>
<td>irritant contact dermatitis</td>
</tr>
<tr>
<td>ICU</td>
<td>intensive care unit</td>
</tr>
<tr>
<td>IgE</td>
<td>immunoglobulin E</td>
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<tr>
<td>IOM</td>
<td>Institute of Occupational Medicine</td>
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<tr>
<td>LC</td>
<td>Langerhans cell</td>
</tr>
<tr>
<td>NRL</td>
<td>natural rubber latex</td>
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<tr>
<td>PVC</td>
<td>polymer of vinyl chloride</td>
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<td>UV</td>
<td>ultraviolet</td>
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CONCEPTS AND DEFINITIONS USED

**Atopic dermatitis:** an itchy, more or less chronically relapsing inflammation of the skin. The rash often has flexural distribution in childhood, with papules, excoriations and lichenification.

**Correlation:** a statistical measure used to investigate the degree of association between two variables measured on an ordinal or continuous scale.

**Eczema:** an inflammatory skin reaction histologically characterized by spongiosis, with varying degrees of acanthosis and a superficial perivascular lymphohistiocytic infiltrate.

**Hapten:** compounds of low molecular weight, mostly <400 dalton (Da). Haptens are too small to induce contact allergy by themselves and must therefore bind to macromolecules in the skin in order to form complete antigens.

**High-risk occupations:** occupations in health care, services and manufacturing, with expected high wet exposure, according to a previous classification (Meding and Järvholm, 2002).

**Low-risk occupations:** in this thesis, all occupations not categorized as high-risk occupations were designated low-risk occupations.

**Validity:** a measure used to assess the degree of accordance between a value known to be the “truth” and a value estimated from a study sample.
1 INTRODUCTION

Hand eczema is a common disease in the general population and is the most common occupational skin disease (Diepgen and Coenraads, 1999). Exposure to skin irritants contributes to hand eczema (Dickel et al., 2002a; Diepgen and Coenraads, 1999; Uter et al., 1999a). Common skin irritants are water, detergents, chemicals and foodstuffs. Some occupations are associated with a higher risk of hand eczema, including jobs in health care, the service industries and production (Lind et al., 2007; Funke et al., 2001; Forrester and Roth, 1998; Nielsen, 1996). In most epidemiological studies on the subject, job titles are used as a proxy for exposure to skin irritants, and occupations are classified as high- or low-risk occupations for hand eczema (Meding and Järvolm, 2002; Lerbaek et al., 2007a). Although exposure to skin irritants is essential for development of hand eczema, there are few if any population-based studies on such exposure.

Knowledge about exposure to skin irritants in occupational life and during leisure time is useful in occupational guidance and in preventive measures to reduce hazardous skin exposure. When surveying exposure to skin irritants through questionnaires it is desirable to use validated questions.

This thesis focuses on exposure to the most common skin irritants, water exposure in particular. In an epidemiological study, occupational exposure to water in the general population was studied in relation to gender, age and occupation (Study IV). In another population-based study, exposure to skin irritants, both in occupational life and during leisure time, was studied in individuals with and without hand eczema (Study I). Furthermore, in studies II and III, validation was performed of questions regarding skin exposure, which will hopefully be useful in future epidemiological or interventional studies.
2 BACKGROUND

2.1 HAND ECZEMA

Hand eczema is common in the general population and the 1-year prevalence of hand eczema in individuals of working age in Sweden is about 10% (Meding and Järnholm, 2002). Exposure to skin irritants, in occupational life as well as during domestic work and leisure time, is known to contribute to hand eczema (Dickel et al., 2002a; Diepgen and Coenraads, 1999; Uter et al., 1999a). Contact allergy likewise contributes to and causes hand eczema (Diepgen and Coenraads, 1999). A previous history of atopic dermatitis is a well-known risk factor for hand eczema (Bryld et al., 2003; Lammintausta et al., 1991). The aetiology of hand eczema is often multifactorial and it may therefore be difficult to determine the role of atopic dermatitis, contact allergy, and exposure to skin irritants in an individual with hand eczema. Furthermore, recent studies have indicated that genetic factors other than atopic constitution can contribute to hand eczema (Lerbaek et al., 2007b; Bryld et al., 2003).

2.1.1 Irritant contact dermatitis

Skin disease that is caused by exposure to skin irritants is referred to as “irritant contact dermatitis (ICD)”. Common skin irritants are water, detergents, foodstuffs and chemicals. The clinical picture of ICD can vary a great deal. In its mild form the irritant reaction is characterized by dryness and small fissures. When the eczema is more acute it presents with erythema, vesicles and oedema. Sometimes necrosis can be seen. Invisible symptoms, such as stinging, burning and itching, are common.

The potential for irritancy of substances is determined by its chemical and physical properties. Concentration, volume, application time and duration of irritant exposure will determine the outcome. Environmental conditions such as temperature and humidity, and to some extent endogenous characteristics such as body region, age, skin and race influence the risk (Morris-Jones et al., 2002; Foy et al., 2001; Yoshikawa et al., 1994; Cua et al., 1990; Rougier et al., 1986). Atopic dermatitis is a predisposing factor for ICD (Bryld et al., 2003; Lammintausta et al., 1991). Cumulative repeated minor skin exposure to e.g. water and detergents can cause damage to the skin barrier (Bornkessel et al., 2005). Chronic ICD is caused by repetitive exposure to damaging factors. During wet work the clinically normal skin can be damaged at a sub-clinical level by repeated exposure of the skin to water, among other irritants. In a dry climate, the damage to the skin may change from damage at a sub-clinical level in the summertime to visible ICD in wintertime. Nails can also be involved in chronic ICD.

The diagnosis of ICD is based on clinical examination and history of skin exposure at work and during leisure time. Often there is a combination of allergic contact dermatitis (ACD) and ICD. To enable exclusion of ACD, it is necessary to perform patch testing. ICD has an unfavourable prognosis. In a Dutch study, 5 years after initial diagnosis 50 % still had medium and 32 % severe hand dermatitis (Jungbauer et al., 2004a). Because of the vulnerability of the skin in
atopic dermatitis often occur concurrently on the hands.

In ICD, keratinocytes, Langerhans cells (LCs), intercellular lipids and blood vessels are damaged and subsequent release of cytokines creates an inflammation similar to that seen in ACD. The renewal of the stratum corneum is impaired by the ICD. When using gloves, hydration of the skin occurs and may lead to release of cytokine mediators. Histological examination of a skin biopsy does not differ between ACD and ICD. Treatment of ICD should comprise a reduction in exposure to skin irritants.

2.1.2 Allergic contact dermatitis

Allergic contact dermatitis is the clinical manifestation of the exposure to a chemical to which an individual is contact-sensitized. Contact allergy, “type IV allergy” or delayed contact hypersensitivity is common. For instance, in a Danish population-based study 19 % had one or more positive patch tests (Nielsen et al., 2002). In contact allergy a distinction has to be made between the induction phase (sensitization) and the elicitation phase. The induction phase starts with the first contact with the hapten and is completed when an individual is sensitized, that is, when the individual has an immunological memory of a sensitizer and is capable of giving a positive ACD reaction. The overall process takes 3 days to several weeks. The elicitation phase is fully developed within 1–2 days of a subsequent contact with the hapten and results in the clinical manifestation of ACD (Rustemayer et al., 2001).

As the hapten comes in contact with the skin the induction phase starts. The hapten penetrates into the epidermis where it associates with skin macromolecules (proteins) and forms antigens that are taken up by the LCs. The LCs that carry the antigen activate and migrate to the lymph nodes. In the paracortical T-cell area they present the antigen to naïve T-cells that become activated. Activated T-cells release cytokines. These induce proliferation and differentiation of T-cells into specific memory cells that are released into the lymphatics and then enter the bloodstream.

Upon renewed contact with a hapten, the LCs present the antigen to the specific memory T-cells. The T-cells activate, which leads to a local reaction with release of cytokines and chemokines, attracting more T-cells, and an eczematous reaction will develop within 48 hours.

Nickel is the most common contact allergen. Other common contact allergens are perfumes, preservatives and cobalt (Thyssen et al., 2007). To confirm the ACD diagnosis, patch testing needs to be performed. Individuals are tested with a standard patch test series. The relevance of each positive patch test reaction should be considered. ACD, ICD and atopic dermatitis often occur concurrently on the hands and it can be difficult to determine the role of the different causes.
2.1.3 Atopic dermatitis

Atopic dermatitis is an itchy, more or less chronically relapsing inflammation of the skin. The rash often has flexural distribution in childhood, presenting with papules, excoriations and lichenification. Individuals with atopic dermatitis have increased susceptibility to skin irritants, and epidemiological data have shown that ICD is more common among individuals with atopic dermatitis than in individuals without this condition (Bryld et al., 2003; Lammintausta et al., 1991). Atopic dermatitis is frequently associated with other atopic conditions, such as hay fever, conjunctivitis and asthma in the individual or in the family. The respiratory manifestations of atopy seem to be less predictive of skin vulnerability to ICD compared with atopic dermatitis (Meding and Järvholm, 2004; Conti et al., 1996; Lammintausta et al., 1991).

2.2 SKIN EXPOSURE

Exposure to skin irritants occurs daily in occupational life and during leisure time. Common skin irritants are water, detergents, foodstuffs and chemicals. The use of protective gloves can be considered as a dermal exposure as well as prevention of exposure to harmful agents (Wahlberg, 2005; Ramsing and Agner 1996a; 1996b). Water and detergents are the most common skin irritants. All exposures contribute to, or worsen, hand eczema. Low indoor humidity, cold temperatures and mechanical friction may also be considered as dermal exposure (MacMullen and Gawkrodger, 2006; Yoshikawa et al., 1994). Ideally, skin exposure should be measured both quantitatively and qualitatively but unfortunately there are few validated methods for measuring dermal exposure. The existing methods usually measure the amount of the material deposited on skin, and not the length of exposure.

2.2.1 Water

Repeated exposure to water and hand washing is a common cause of ICD. Water alone could act as a mild irritant in repeatedly exposed individuals, and may dissolve a small number of lipids and, besides, influence and reorganize the intracellular lipid structure. In a German study, repeated water exposure caused an increase in blood flow, mild changes in permeability barrier function, stratum corneum hydration, and pH values (Bornkessel et al., 2005). Persistent water contact can produce cytotoxic changes in the epidermal cells and predispose the individual to developing ICD from other irritants such as detergents and hand disinfectants.

2.2.2 Chemicals

Many chemicals are powerful irritants acting by different mechanisms, i.e. organic solvents extract superficial and intercellular lipids and reduce the capacity of the skin barrier to retain water (Boman and Wahlberg, 2006). Chemicals can be toxic as well, and they may cause the whole range of reactions, from mild irritation to chemical burns and necrosis. E.g. in nursing, ethanol and isopropanol, used in alcohol-based hand disinfectants, extract the lipids from the skin.
2.2.3 Foodstuffs
Exposure to almost any foodstuff may cause skin irritation mainly by repeated exposure, which may cause minor trauma to the skin. In certain highly exposed occupations, as in the fishing industry, as many as 80% of workers have been reported to develop ICD on their hands (Halkier-Sørensen and Thestrup-Pedersen, 1988). Exposure to foodstuffs often involves concomitant exposure to water.

2.2.4 Detergents
Detergents are surface-active agents which reduce the surface tension between two non-miscible liquids and impair the skin barrier as a result of removal of intracellular lipids, making it more vulnerable to water and other skin irritants, such as solvents. Detergents are used in soaps, shampoos, shower creams and cleansing agents.

2.2.5 Gloves
In all four studies included in this thesis work, glove use was classified as skin exposure. Glove use can reduce exposure to damaging factors of the skin, but may also be a risk factor for developing or worsening hand eczema, owing to e.g. humidity in the gloves. It can therefore be considered a form of dermal exposure (Wahlberg, 2005). Short-term use probably gives a lower risk, but continuous and protracted use may contribute to hand eczema (Ramsing and Agner, 1996a; 1996b). The use of cotton gloves underneath the occlusive gloves may prevent negative effects on the skin barrier (Ramsing and Agner, 1996b). The gloves used in health care are made of polyvinyl chloride (PVC), natural rubber latex (NRL), synthetic rubber or polyethen. PVC gives good protection against water and detergents, as well as foodstuffs and blood, and is non-allergenic. Gloves made of rubber can cause allergy to rubber chemicals added in the production of the gloves. Gloves made of NRL can cause immunoglobulin E (IgE)-mediated allergy.

2.2.6 Mechanical and physical forces
Pressure, friction, abrasion, penetration and pounding can cause skin damage (MacMullen and Gawkrodger, 2006). Temperature, radiation, ultraviolet (UV) light, atmospheric humidity and air flow also negatively influence the skin barrier and may contribute to hand eczema.

2.2.7 Moisturizers
Moisturizers are designed to smooth the skin and increase the water content in epidermis, e.g. by creating an occlusive film and because they contain water-binding substances. They can restore, retain or increase moisture in the stratum corneum and enhance the skin barrier. Using moisturizers when suffering from occupational skin exposure has been shown to be beneficial in preventing hand eczema (Halkier-Sørensen and Thestrup-Pedersen, 1993).
2.3 METHODS FOR MEASURING SKIN EXPOSURE

Removal techniques and visualizing techniques have previously been used to investigate contact allergen exposure or exposure to toxic agents.

2.3.1 Removal techniques

These techniques remove chemicals deposited on the skin, followed by analysis of the compounds. For example, tape stripping has been used in assessments of dermal exposure to acrylates (Surakka et al., 1999). Hand wash sampling is another technique where the contaminant is removed from the skin by either hand washing or hand rinsing (Lind et al., 2004). These techniques are useful when assessing exposure to some chemicals but they are not suitable for assessing water exposure. Neither are surrogate skin techniques with patch sampling suitable, or they have limited use in estimating exposure to skin irritants.

2.3.2 Visualizing techniques, and observations

Fluorescent tracers can be used both for qualitative and for quantitative measurements (Cherrie et al., 2000). A suitable tracer is added to the exposure. Ultraviolet light is then used to identify the agents in exposed areas. The technique can be useful for exposure to chemicals but it is not useful for exposure to other skin irritants. Video techniques have been used for measuring dermal exposure to irritants such as cutting fluids (Wassenius et al., 1998). Observations performed by an observer have been used to assess exposure to skin irritants in areas such as nursing (Jungbauer et al., 2004b).

2.3.3 The Institute of Occupational Medicine wet-work sampler

An electronic sensor has been developed, which detects wetness from evaporative cooling and is worn on the finger. Called the “Institute of Occupational Medicine (IOM) wet-work sampler”, it is a practical tool to measure the duration and number of occasions when hands are wet (Cherrie et al., 2007). The output signal is recorded in electronic memory and the frequency and duration of exposure are calculated using a simple data processing algorithm. The device has been tested in a variety of environmental conditions and for a standardized wet-work task. Not yet in clinical use, the IOM wet-work sampler has the potential to provide reliable measurements of wet exposure that may be used to assess the risk of ICD.

2.3.4 Questionnaire

When estimating skin exposure in epidemiological and interventional studies, questionnaires are often used. Some questionnaires comprise questions regarding exposure to skin irritants but in other questionnaires job titles have been used as a proxy for exposure. The questions used regarding skin exposure have not previously been validated.

Validation of questions regarding exposure can be accomplished in different ways. Self-reports in a questionnaire can be compared with blood samples, urinary or saliva metabolites (Post et al., 2005). Self-assessed exposures could be compared with observations, where the observations
constitute the gold standard. In this thesis the self-reported exposures were compared with observations made by observers, and registered on a hand-held computer.
3 AIMS OF THE STUDIES

The overall aim of this thesis was to estimate exposure to skin irritants in the general population, and in individuals with and without hand eczema, in relation to gender, occupation and age. Furthermore, the aim was to validate questions regarding occupational exposure to skin irritants, useful when surveying exposure.

Study I
The aim was to study self-reported skin exposure in individuals with and without hand eczema in the general population.

Studies II and III
The aim was to validate questions regarding exposure to skin irritants, by comparing self-reports and observations.

Study IV
The aim was to study occupational skin exposure to water in the general population.
4 MATERIALS AND METHODS

4.1 STUDY POPULATION

4.1.1 Study I

A random sample of 3,000 individuals aged 20–65 years was drawn from the population register in Göteborg, Sweden. They were asked to answer a postal questionnaire. Answers were obtained from 2,218 individuals. Hand eczema was identified by the question, “Have you during the past 12 months had hand eczema on some occasion?” Of 215 individuals with hand eczema, 63 men and 119 women agreed to participate in a telephone interview. A total of 182 individuals, matched for age and sex, who in the questionnaire denied having, or having had, hand eczema, constituted the controls in the study. Some occupations in health care, services and manufacturing were categorized as high-risk occupations for hand eczema, according to a previous classification (Meding and Järvholm, 2002), and all other occupations were designated as low-risk occupations.

4.1.2 Study II

The study group consisted of 40 volunteers, 13 men and 27 women, who worked in five different occupations. Four were high-risk occupations for hand eczema, where high exposure to skin irritants was expected. The occupations selected were car mechanic, hairdresser, kitchen worker and intensive care unit (ICU) nurse. Office worker was selected as an occupation with expected low exposure to skin irritants. Eight individuals in each occupation were included in the study.

4.1.3 Study III

The study group consisted of 40 individuals, 36 female and four male volunteers, 13 of whom were nurses and 27 assistant nurses. The study was performed in three different geriatric clinics in six different regular wards in Stockholm, Sweden.

4.1.4 Study IV

A total sample of 57,009 individuals aged 18–84 years was drawn from the population register in Stockholm, Sweden, in 2006 (Stockholm County Council Public Health Survey, 2006). A total of 8,000 individuals, sample A, were randomly drawn from the total population in the county, and 49,009 individuals, sample B, were stratified by region. The total sample is regarded as a stratified sample. Altogether 47,931 subjects were of working age, i.e. 18-64 years old. All of these 47,931 individuals were asked to answer a postal questionnaire. Answers were obtained from 27,994 individuals. In total 19,430 individuals were gainfully employed.

Of the gainfully employed individuals, 18,267 (8,669 men and 9,598 women) answered the questions regarding water exposure in the questionnaire. Some occupations in health care, services and manufacturing were categorized as high-risk occupations for hand eczema, according to a previous classification (Meding and Järvholm, 2002). In the present study, all
other occupations were designated as low-risk occupations. In Table 5, regarding the occupations mostly exposed to water, restrictions were made to only include occupations comprising at least 50 individuals in the sample.

4.2 INTERVIEW

4.2.1 Study I

A trained nurse interviewed the 364 subjects by telephone using a standardized questionnaire. The questions concerned skin exposure and use of protective gloves at work and during activities outside work.

4.3 QUESTIONNAIRES

4.3.1 Study I

The main questions used in the interview were –

1. Are your hands, at work, exposed to water and detergents?\textsuperscript{a}
2. Are your hands, at work, exposed to chemicals?\textsuperscript{a}
3. Are your hands, at work, exposed to foodstuffs?\textsuperscript{a}
4. How many hours a day, at work, do you use protective gloves?
5. How many hours a day, in leisure time, do you use protective gloves?
6. How many hours a day, in leisure time, do you have ‘wet hands’?\textsuperscript{a}

* $\square$ < $\frac{1}{2}$ hr $\square$ $\frac{1}{2}$–2 hrs/day $\square$ >2 hrs/day
* Response alternatives questions 1-6

7. How many times, a day, do you wash your hands? ............

\textsuperscript{a}Time without protective gloves.

4.3.2 Studies II and III

Questionnaires were handed to the participants by the observer immediately before the start of a working day. The subjects filled in the questionnaire and handed it back to the observer. Questions regarding gender, occupation, age and work hours per day were also included. The observers gave no further instructions or information.
Questions used in Study II

Questions in the questionnaire regarding skin exposure were –

1. Are your hands, at work, exposed to water?\textsuperscript{a}
2. Are your hands, at work, exposed to chemicals?\textsuperscript{a}
3. Are your hands, at work, exposed to foodstuffs?\textsuperscript{a}
4. How many hours a day, at work, do you use occlusive protective gloves (rubber or plastic)?
   * ☐ Not at all ☐ < \frac{1}{2} \text{ hr/day} ☐ \frac{1}{2}–2 \text{ hrs/day} ☐ 2–5 \text{ hrs/day} ☐ >5\text{hrs/day}
   * Response alternatives questions 1–4

5. How many times a day do you wash your hands at work?
   ☐ 1–10 times ☐ 11–20 times ☐ >20 times

\textsuperscript{a}Time without protective gloves.

Questions used in Study III

Questions on skin exposure asked in the questionnaire were –

1. How many hours a day, at work, do you use occlusive protective gloves (rubber or plastic)?
2. Are your hands, at work, exposed to water?\textsuperscript{a}
   * ☐ Not at all ☐ < \frac{1}{2} \text{ hr/day} ☐ \frac{1}{2}–2 \text{ hrs/day} ☐ 2–5 \text{ hrs/day} ☐ >5\text{hrs/day}
   * Response alternatives questions 1–2

3. How many times a day, at work, are your hands exposed to water?\textsuperscript{a}
4. Are your hands, at work, exposed to hand disinfection?
   † ☐ Not at all ☐ 1–10 times ☐ 11–20 times ☐ >20 times
   †Response alternatives questions 3–4

5. How many times a day, at work, do you use moisturizers?
   ☐ Not at all ☐ 1–2 times ☐ 3–5 times ☐ >5 times

\textsuperscript{a}Time without protective gloves.
4.3.3 Study IV

The questionnaire used in this study comprised 90 questions regarding physical and mental health, social relations, economic status, and work. Questions in the questionnaire asked regarding skin exposure were –

1. Are your hands, at work, exposed to water?\(^a\)
   - □ Not at all
   - □ < ½ hr/day
   - □ ½ hr–2 hrs/day
   - □ > 2–5 hrs/day
   - □ > 5 hrs/day.

2. How many times a day, at work, are your hands exposed to water?\(^a\)
   - □ Not at all
   - □ 1–10 times
   - □ 11–20 times
   - □ 21–30 times
   - □ > 30 times

\(^a\)Time without protective gloves.

4.4 OBSERVATIONS

The observations were performed in Study II and III during one working day or two half days (one morning and one afternoon) for each participant. The duration of each exposure was registered continuously in real time during the whole working day except for lunch breaks, using a hand-held (palmtop) computer. Six circular fields on the computer display corresponded with exposure to water, chemicals, occlusive gloves, foodstuffs, hand washing, and “no exposure”, respectively. Every time a subject was exposed to one of the substances the observer marked the appropriate circle on the display with the pen, and timing was initiated. When the exposure was discontinued for any reason the observer marked “no exposure” or a circle with another exposure. When gloves were used no other exposure was registered.

In Study II, two observers (observers 1 and 2) observed the car mechanics, hairdressers, kitchen workers and ICU nurses. A third observer (I.A.) observed the office workers. To ensure inter-observer reliability, two observers (observers 1 and 2) simultaneously observed the same worker during a working day. One hairdresser and one kitchen worker were chosen for this purpose.

4.5 DATA ANALYSIS AND STATISTICS

4.5.1 Study I

The data were analysed using SAS software, version 8.2 (SAS Institute Inc., Cary, NC, USA). Matched analyses comparing exposure in cases and controls, and changes in exposure over time, were performed using the sign test. For comparison of prevalence in men and women, chi-square statistics or Fisher’s exact test (for fewer than five cases) was used.
4.5.2 Studies II and III

The FIT software system (J. Held, Swiss Federal Institute of Technology, Zurich, Switzerland) was used for data collection (Held and Manser, 2005). The data were then transferred to a personal computer for analysis. The software calculated and saved the start, stop and total time of the observations. Information on the number of times the fields in the circles were activated during a work shift, and the mean duration of each event, was also supplied. The measurements gained through observation were considered as the gold standard. The time was continuously measured in the observations. For statistical analysis, SSPS, version 13.0 (SSPS Inc, Chicago, IL, USA), was used.

In Study II the correlation between recorded data and data from the questionnaire was calculated using Spearman’s rank correlation. To assess concordance among observers an intraclass correlation was calculated (Schrout and Fleiss, 1979).

In Study III the correlation between recorded data and data from the questionnaire was calculated using Pearson’s correlation.

4.5.3 Study IV

In the analysis, data were weighted by region. Thus, the proportion of those reporting occupational skin exposure to water can be regarded as an estimate of the proportion in the whole of the Stockholm County population. The weighting procedure was operationalized by giving the heaviest weight to the proportion linked to the region comprising most inhabitants. The lowest weight was given to the proportion linked to the region comprising the fewest inhabitants. All other proportions were given weights in between these two extremes.

For statistical analysis, SPSS, version 15.0 (SPSS Inc., Chicago, IL, USA), was used. Chi-square tests were performed to test possible differences between men and women regarding exposure time and frequency. Proportion $t$-tests were performed to observe possible differences between men and women in exposure time for half an hour or more and more than 2 hours, respectively, as well as exposure frequency of more than ten times and more than 20 times, in the three different sectors of high-risk occupations. When doing the statistical analyses the weighting variable was not used.
5 RESULTS

5.1 STUDY I

5.1.1 Exposure in relation to hand eczema

Water and detergents, wet hands and hand washings were the most frequent exposures (Table 1). There were statistically significant differences between hand eczema cases and controls regarding occupational exposure to foodstuffs and protective gloves. Similar frequencies of wet hands during domestic/leisure time were reported by cases and controls (Table 1). Very few persons used protective gloves for domestic work for half an hour or more a day.

*Table 1. Self-reported occupational and domestic exposure to skin irritants.*

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Cases (n = 182)</th>
<th>Controls (n = 182)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Occupational</strong>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water and detergents (hr/day) ≥ ½</td>
<td>20</td>
<td>15</td>
<td>0.26</td>
</tr>
<tr>
<td>Chemicals (hr/day) ≥ ½</td>
<td>5</td>
<td>5</td>
<td>1.0</td>
</tr>
<tr>
<td>Foodstuffs (hr/day) ≥ ½</td>
<td>7</td>
<td>1</td>
<td>0.007</td>
</tr>
<tr>
<td>Protective gloves (hr/day) ≥ ½</td>
<td>25</td>
<td>14</td>
<td>0.012</td>
</tr>
<tr>
<td><strong>Domestic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wet hands (hr/day) ≥ ½</td>
<td>80</td>
<td>80</td>
<td>1.0</td>
</tr>
<tr>
<td>Protective gloves (hr/day) ≥ ½</td>
<td>8</td>
<td>1</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Occupational and domestic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand washings (n/day) ≥ 11</td>
<td>36</td>
<td>31</td>
<td>0.35</td>
</tr>
</tbody>
</table>

*Occupationally active cases (n=129) and controls (n=132).

5.1.2 Exposure in relation to gender and age

Occupational exposure to water and detergents, and hand washings were more frequent among women than men (Table 2). Men more often reported exposure to chemicals than women did. In domestic work and during leisure time, women reported wet hands for longer time periods compared with men. Gainfully employed women below 30 years of age reported more frequent occupational exposure to water and detergents compared with older women.
Table 2. Self-reported occupational and domestic exposure in relation to gender.

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Women (n = 238) (%)</th>
<th>Men (n = 126) (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Occupational</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water and detergents (hr/day) ≥ ½</td>
<td>21</td>
<td>10</td>
<td>0.010 a</td>
</tr>
<tr>
<td>Chemicals (hr/day) ≥ ½</td>
<td>3</td>
<td>10</td>
<td>0.003 a</td>
</tr>
<tr>
<td>Foodstuffs (hr/day) ≥ ½</td>
<td>5</td>
<td>2</td>
<td>0.28 b</td>
</tr>
<tr>
<td>Protective gloves (hr/day) ≥ ½</td>
<td>18</td>
<td>22</td>
<td>0.40 a</td>
</tr>
<tr>
<td><strong>Domestic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wet hands (hr/day) ≥ ½</td>
<td>89</td>
<td>63</td>
<td>0.001 a</td>
</tr>
<tr>
<td>Protective gloves (hr/day) ≥ ½</td>
<td>6</td>
<td>2</td>
<td>0.19 b</td>
</tr>
<tr>
<td><strong>Occupational and domestic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand washings (n/day) ≥ 11</td>
<td>42</td>
<td>17</td>
<td>0.001 a</td>
</tr>
</tbody>
</table>

*aOccupationally active women (n=164) and men (n=97)

*a chi-square test.

*b Fisher’s exact test.

5.1.3 Exposure and occupation

People in jobs classified as high-risk occupations reported more frequent exposure to water, chemicals, foodstuffs and gloves and more frequent hand washings compared with those in low-risk occupations. Of 15 individuals with exposure to foodstuffs 14 also reported exposure to water and detergents for half an hour or more a day.

However, about half of those in high-risk occupations reported exposure to water and detergents for less than half an hour a day and ten or fewer hand washings a day. Furthermore, 11% of those in jobs classified as low-risk occupations reported exposure to water and detergents for half an hour or more a day and 25% of these reported more than ten hand washings a day.

There was a correlation between occupational exposure to water and detergents and wet work at home. Forty-nine per cent of those with occupational exposure to water for half an hour or more a day, compared with 25% of those with such occupational exposure for less than half an hour a day (p<0.001), also reported wet hands during domestic work for more than one hour a day.
5.2 STUDY II

Self-reported skin exposure in relation to observed exposure is presented in Table 3. There was a strong correlation between self-reports and observations regarding total skin exposure to water, gloves and foodstuffs, and a moderate correlation regarding frequency of hand washing (Table 3). A tendency to overestimate was found for all the exposures. For water, 21/40 overestimated the exposure.

Table 3. Self-reported skin exposure in relation to observed skin exposure during a working day in 40 volunteers, expressed as underestimation, correct estimation or overestimation. The correlations between self-reports and observations are presented.

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Underestimation</th>
<th>Correct</th>
<th>Overestimation</th>
<th>Correlation*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>5</td>
<td>14</td>
<td>21</td>
<td>0.68</td>
</tr>
<tr>
<td>Chemicals</td>
<td>3</td>
<td>24</td>
<td>13</td>
<td>0.73</td>
</tr>
<tr>
<td>Foodstuffs</td>
<td>1</td>
<td>28</td>
<td>11</td>
<td>0.67</td>
</tr>
<tr>
<td>Occlusive gloves</td>
<td>8</td>
<td>21</td>
<td>11</td>
<td>0.72</td>
</tr>
<tr>
<td>Hand washing</td>
<td>1</td>
<td>30</td>
<td>9</td>
<td>0.37</td>
</tr>
</tbody>
</table>

* Spearman’s rank correlation coefficient.

The total mean observation time per individual was 494 minutes (i.e. 8.23 hours). The longest total exposure times for water were observed in hairdressers, and for occlusive gloves in ICU nurses. Hairdressers were exposed to skin irritants for a mean of 62% of the working day. The corresponding percentage for ICU nurses, kitchen workers and car mechanics was 24%, 27% and 3%, respectively. The mean exposure time to water for ICU nurses was 1 minute per working day (hand washing excluded).

Results from observations performed simultaneously by two observers are presented in Figure 1. The observations by the two observers showed good concordance, with an intraclass correlation coefficient of 0.897–0.999.
Hand-washing
Chemicals
Foodstuffs
Occlusive gloves
Water
"No exposure"

Observer 1 Observer 1
Observer 2 Observer 2
Kitchen worker Hairdresser

Figure 1. Results regarding skin exposure from observation of one kitchen worker and one hairdresser by two observers simultaneously. The proportions of different exposures during the working day are shown.

5.3 STUDY III

Self-reported skin exposure in relation to observed exposure is presented in Table 4. The Pearson correlation varied between 0.25 and 0.68. A tendency to overestimate was found for all exposures. Thirty-three out of 40 individuals overestimated the total time of water exposure compared with 15/40 regarding the number of exposure periods.

Table 4. Self-reported skin exposure in relation to observed exposure during a working day in 40 volunteers, expressed as underestimation, correct estimation or overestimation. The correlations between self-reports and observations are presented.

<table>
<thead>
<tr>
<th></th>
<th>Underestimation</th>
<th>Correct</th>
<th>Overestimation</th>
<th>Correlation*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protective gloves</td>
<td>3</td>
<td>13</td>
<td>24</td>
<td>0.40</td>
</tr>
<tr>
<td>Water (exposed time)</td>
<td>0</td>
<td>7</td>
<td>33</td>
<td>0.25</td>
</tr>
<tr>
<td>Water (no. of exposures)</td>
<td>4</td>
<td>21</td>
<td>15</td>
<td>0.52</td>
</tr>
<tr>
<td>Hand disinfection</td>
<td>7</td>
<td>23</td>
<td>10</td>
<td>0.68</td>
</tr>
<tr>
<td>Moisturizers</td>
<td>2</td>
<td>22</td>
<td>16</td>
<td>0.62</td>
</tr>
</tbody>
</table>

*Pearson’s rank correlation.
The total mean skin exposure time in nurses and assistant nurses was 96 minutes per working day, including glove use. The mean exposure time to water was 9 minutes per working day and the majority of the water exposure periods observed were due to hand washing. The longest mean total exposure times during a working day were observed for protective gloves, being 83 minutes in assistant nurses and 27 minutes in nurses. For nurses as well as for assistant nurses, the mean duration of each exposure to gloves was 6 minutes.

5.4 STUDY IV

Self-reported occupational skin exposure to water is presented in Table 5. Altogether 16.2 % of individuals reported total exposure time for half an hour or more a day and 12.9 % reported exposure of more than ten times a day. Furthermore, 6.9 % reported exposure of more than 2 hours and 6.0 % of more than 20 times a day. Considering the answers to both the questions, 19.2 % of the population reported exposure for half an hour or more and/or more than ten times a day. The percentage reporting exposure of more than 2 hours and/or of more than 20 times was 9.2 %.

When using the two different questions about water exposure (for half an hour or more and more than ten times a day) to identify water-exposed individuals, there was overlap between the two questions. The majority of exposed individuals were identified by the question on length of water exposure, but 15 % were exclusively identified by the question on frequency. When a higher limit (more than 2 hours and/or more than 20 times) was used, 25 % of exposed individuals were exclusively identified by the question regarding frequency.
Table 5. Reported occupational skin exposure to water in the gainfully employed population aged 18–64 years.

<table>
<thead>
<tr>
<th>Exposure time</th>
<th>Total (%)</th>
<th>Women (%)</th>
<th>Men (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all</td>
<td>66.6</td>
<td>62.0</td>
<td>71.6</td>
</tr>
<tr>
<td>&lt;½ hr per day</td>
<td>17.2</td>
<td>17.4</td>
<td>16.9</td>
</tr>
<tr>
<td>½ hr–2 hrs per day</td>
<td>9.3</td>
<td>11.5</td>
<td>6.8</td>
</tr>
<tr>
<td>&gt;2 hrs–5 hrs per day</td>
<td>4.3</td>
<td>5.7</td>
<td>2.8</td>
</tr>
<tr>
<td>&gt;5 hrs per day</td>
<td>2.6</td>
<td>3.4</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Women v. men $p<0.001$.

<table>
<thead>
<tr>
<th>Exposure frequency</th>
<th>Total (%)</th>
<th>Women (%)</th>
<th>Men (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all</td>
<td>42.2</td>
<td>38.2</td>
<td>46.7</td>
</tr>
<tr>
<td>1–10 times/day</td>
<td>44.9</td>
<td>44.2</td>
<td>45.5</td>
</tr>
<tr>
<td>11–20 times/day</td>
<td>6.9</td>
<td>9.7</td>
<td>3.9</td>
</tr>
<tr>
<td>21–30 times/day</td>
<td>3.2</td>
<td>4.5</td>
<td>1.8</td>
</tr>
<tr>
<td>&gt;30 times/day</td>
<td>2.8</td>
<td>3.4</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Women v. men $p<0.001$.

Women reported more occupational water exposure than did men, and the youngest subjects, aged 18–29, reported the highest exposure. A total of 17.7 % of individuals had occupations classified as high-risk occupations for hand eczema. Of these, 59.0 % reported water exposure for half an hour or more and/or more than ten times a day, and 32.1 % reported daily exposure of more than 2 hours and/or of more than 20 times. The corresponding figures in low-risk occupations were 10.9 % and 4.3 %. The occupations with the most extensive exposure to water are presented in Table 6. The individuals in high-risk occupations reported a wide range of exposure, from none (“not at all”) to more than 5 hours or more than 30 times a day. Women in health care as well as in the service industries reported more occupational water exposure than did men in these occupations (data not shown). In manufacturing the differences found between men and women were not statistically significant. Women were significantly more exposed than men in the same occupations. For example, in nursing 34.5 % of the women reported exposure to water for more than 2 hours a day compared with 16 % of the men.
Table 6. The range of answers from individuals in the ten occupations most highly exposed to water (more than 2 hrs and/or more than 20 times per day). The classification of the occupations was based on the international standard, ISCO 88, 3 digit level.

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>&lt;½ hr</th>
<th>≥ ½-2 hrs</th>
<th>&gt;2-5 hrs</th>
<th>&gt;5 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cook</td>
<td>3.0</td>
<td>12.3</td>
<td>32.5</td>
<td>31.1</td>
<td>21.3</td>
</tr>
<tr>
<td>Kitchen worker</td>
<td>3.9</td>
<td>16.3</td>
<td>25.0</td>
<td>31.1</td>
<td>23.6</td>
</tr>
<tr>
<td>Hairdresser</td>
<td>5.0</td>
<td>18.7</td>
<td>23.3</td>
<td>31.0</td>
<td>22.0</td>
</tr>
<tr>
<td>Cleaner</td>
<td>7.6</td>
<td>14.2</td>
<td>24.0</td>
<td>21.6</td>
<td>32.6</td>
</tr>
<tr>
<td>Dental assistant, child minder</td>
<td>6.6</td>
<td>31.5</td>
<td>34.3</td>
<td>17.6</td>
<td>9.9</td>
</tr>
<tr>
<td>Assistant nurse</td>
<td>14.2</td>
<td>39.7</td>
<td>30.9</td>
<td>10.4</td>
<td>4.9</td>
</tr>
<tr>
<td>Painter</td>
<td>4.3</td>
<td>30.8</td>
<td>37.6</td>
<td>11.9</td>
<td>15.4</td>
</tr>
<tr>
<td>Nurse</td>
<td>12.0</td>
<td>43.4</td>
<td>33.4</td>
<td>8.6</td>
<td>2.6</td>
</tr>
<tr>
<td>Machine tool setter and operator</td>
<td>36.8</td>
<td>22.8</td>
<td>29.7</td>
<td>8.0</td>
<td>2.6</td>
</tr>
<tr>
<td>Biomedical analyst</td>
<td>10.2</td>
<td>58.7</td>
<td>15.5</td>
<td>11.5</td>
<td>4.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>1-10 times</th>
<th>11-20 times</th>
<th>21-30 times</th>
<th>&gt;30 times</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cook</td>
<td>0.2</td>
<td>17.6</td>
<td>18.3</td>
<td>27.0</td>
<td>37.0</td>
</tr>
<tr>
<td>Kitchen worker</td>
<td>6.1</td>
<td>26.1</td>
<td>18.0</td>
<td>22.7</td>
<td>27.2</td>
</tr>
<tr>
<td>Hairdresser</td>
<td>2.6</td>
<td>39.8</td>
<td>29.5</td>
<td>16.5</td>
<td>11.6</td>
</tr>
<tr>
<td>Cleaner</td>
<td>7.4</td>
<td>40.6</td>
<td>16.2</td>
<td>9.9</td>
<td>25.8</td>
</tr>
<tr>
<td>Dental assistant, child minder</td>
<td>3.2</td>
<td>45.8</td>
<td>28.4</td>
<td>13.6</td>
<td>8.9</td>
</tr>
<tr>
<td>Assistant nurse</td>
<td>4.6</td>
<td>38.5</td>
<td>32.5</td>
<td>16.9</td>
<td>7.5</td>
</tr>
<tr>
<td>Painter</td>
<td>1.8</td>
<td>64.0</td>
<td>18.6</td>
<td>9.9</td>
<td>5.7</td>
</tr>
<tr>
<td>Nurse</td>
<td>5.7</td>
<td>46.2</td>
<td>29.7</td>
<td>12.1</td>
<td>6.3</td>
</tr>
<tr>
<td>Machine tool setter and operator</td>
<td>13.2</td>
<td>63.2</td>
<td>11.8</td>
<td>3.5</td>
<td>8.2</td>
</tr>
<tr>
<td>Biomedical analyst</td>
<td>6.0</td>
<td>52.2</td>
<td>29.8</td>
<td>7.9</td>
<td>4.1</td>
</tr>
</tbody>
</table>
6 DISCUSSION

As exposure to skin irritants is considered to be essential for development of hand eczema it is of interest to survey exposure to skin irritants (Lerbaek et al., 2007a; Dickel et al., 2002a; Diepgen and Coenraads, 1999). There are few population-based studies which focus on exposure to skin irritants, though there are studies regarding wet exposure in relation to hand eczema and some well-known risk occupations (Jungbauer et al., 2004b; Dickel et al., 2002a; Funke et al., 2001; Uter et al., 1999a). Further knowledge regarding skin exposure in relation to gender, age, hand eczema and occupations is desirable and could be useful in prevention measures to reduce skin exposure, and in occupational guidance. In this thesis the focus has been on both epidemiological aspects of skin exposure and validation of questions regarding skin exposure. In a population-based study (Study I) the exposure to skin irritants was investigated in individuals with and without hand eczema at work and during leisure time. To form an opinion about the extent to which the self-estimates regarding exposure to skin irritants reflect true exposure a validation study was performed (Study II). The aim was to validate questions for use in future epidemiological and interventional studies. The questions had to be simple and comparable to be useful in such studies.

Nursing is by tradition regarded as wet work and as a high-risk occupation for developing hand eczema (Jungbauer et al., 2004b; Forrester and Roth, 1998; Smit and Coenraads, 1993) though work-related skin exposure in nursing has probably changed over time. In Study II the nurses/assistant nurses showed a tendency to overestimate their exposure to skin irritants, why it was found to be of interest to perform further studies on exposure in nursing (study III). Finally, the two questions regarding exposure to water in Study III were used in a public health survey (Stockholm County Council Public Health Survey, 2006) in which data were collected regarding physical and mental health, social relations, economic status and work. In Sweden the social security number gives the unique possibility to perform population-based studies, and similar surveys have regularly been done since the 1970s. This makes it possible to follow developments in work-related diseases over decades. In 2006, more than 18,000 individuals of working age answered the questions in the survey. Skin exposure to water was then studied in relation to gender, age and occupation (Study IV).

6.1 SKIN IRRITANTS

6.1.1 Wet exposure

Occupational water exposure often correlates to concurrent exposure to foodstuffs, detergents and other chemicals, and can be looked upon as a proxy for wet exposure. About one-fifth of the general population in Stockholm reported occupational exposure to water, and half of these acknowledged water exposure of more than 2 hours and/or more than 20 times a day, which exposure most likely has a damaging effect on the skin barrier (Lerbaek et al., 2007a; Uter et al., 30
1999a; 1999b; Nielsen, 1996). What was noticeable was that 25% of the individuals exposed to water for more than 2 hours and/or more than 20 times per day at work were exclusively identified by the question regarding frequency of exposure. Although the relationship between frequency of water exposure and skin damage is not fully established, it seems reasonable that exposure of more than 20 times a day impairs the skin barrier. Frequency of exposure should therefore be taken into consideration and be further investigated in future studies.

Wet exposure during domestic/leisure time was frequent and it is noteworthy that few studies investigate exposure during leisure time (Bauer et al., 2001). Eighty per cent of all individuals reported wet exposure during leisure time, which stresses the importance of enquiring about and reducing the non-occupational exposure as well as the occupational exposure (Study I).

Hand washing is an important part of wet exposure and women reported more hand washings compared with men through the day (Study I). Half of the individuals in high-risk occupations reported more than ten hand washings per day, compared with one-fourth of the individuals in low-risk occupations (Study I). When observed, only a few individuals washed their hands more than 20 times during the working day in studies II and III. In nurses and assistant nurses, a large part of water exposure during the working day was linked to hand washing (Study III).

Exposure to chemicals often entails wet exposure, e.g. when exposed to hand disinfection, cutting fluids and detergents. Only 5% of the individuals reported occupational exposure to chemicals other than detergents, and men reported more exposure to chemicals at work than did women (Study I). In Study III, nurses/assistant nurses were exposed to hand disinfection in mean 22 times per day at work. Studies indicate that hand disinfection may be less damaging to skin compared with hand washing and may therefore reduce the risk of hand eczema (Kynemund-Pedersen et al., 2005; Jungbauer et al., 2004c; Winnefeld et al., 2000).

6.1.2 Gloves

In this thesis work, glove use was considered a skin irritant, mainly because of humidity collected in the gloves, although short exposure time to occlusive gloves probably lowers the risk of hand eczema (Wahlberg, 2005; Ramsing and Agner, 1996a; 1996b). The mean exposure time for gloves was 65 minutes/day in nurses and assistant nurses, but the duration of each glove exposure period was short (Study III). Despite the short exposure periods of glove use in nursing, the skin barrier may be impaired following exposure to water, detergents, and hand disinfection or presence of other chemicals underneath the gloves.

6.2 HIGH-RISK OCCUPATIONS

As expected, individuals in high-risk occupations reported more exposure than did individuals in low-risk occupations. The most highly exposed individuals were cooks, kitchen workers, hairdressers and cleaners. There was a wide range of answers regarding water exposure from those in risk occupations and 41% of those in high-risk occupations reported occupational
exposure to water of less than half an hour and/or ten times a day (Study IV). This stresses the difficulties when using job titles as a proxy for exposure as it gives an underestimation of the hand eczema risk. Due to misclassification risky environments may even be missed. Individuals with high exposure, at work, to water and detergents also more often had wet exposure in their leisure time. This relationship stresses the importance of eliciting total exposure to skin irritants during the day.

In Study IV, 17.7% of the general population in Stockholm were employed in risk occupations for hand eczema. The most extensive water exposure was reported by individuals working in health care and in the service sector. Preschool teachers, who were not categorized as a high-risk occupation in the thesis, also reported extensive water exposure. In manufacturing, wet exposure has probably decreased over the years, because of changes in work procedures, although many jobs may still be considered high-risk occupations for hand eczema because of friction and glove use.

Nursing is traditionally regarded as wet work and a risk occupation for hand eczema (Jungbauer et al., 2004b; Forrester and Roth, 1998; Smit and Coenraads, 1993). As the nurses and assistant nurses in Study III were not randomly chosen, the data obtained by observation regarding their exposure to skin irritants should be interpreted with caution. In studies II and III, nurses/assistant nurses had very limited exposure to water when observed, less than 10 minutes during a working day. Nursing is probably a risk occupation because of extensive use of gloves and hand disinfection, not because of water exposure. National registers regarding occupational skin disease give the incidence of hand eczema as being 0.2–1.5/1,000 in nurses, compared with an average of 0.8/1,000 in the total work force, which indicates an only slightly increased risk of developing hand eczema in nursing (Skoet et al., 2004; Diepgen, 2003; Dickel et al., 2002b; Cherry et al., 2000).

In this thesis work, 27 occupations in health care, services and manufacturing were categorized as high-risk occupations, according to a previous classification (Meding and Järvholm, 2002). All other occupations were designated as low-risk occupations. In a Danish study, “high-risk work for hand eczema” has been defined as employment in nine occupations previously shown to have a high risk for hand eczema (Lerbaek et al., 2007a). When using the definition from the Danish study 10% of the population in Study IV can be said to have been employed in high-risk occupations. Furthermore, about 7% of that population were employed in high-risk occupations as well as being exposed to water for half an hour or more and/or more than ten times at work per day. The corresponding figures when using the classification as in this thesis were 18% and 10%. Consequently, a proportion of water-exposed individuals will not be identified using the Danish definition.
6.3 GENDER AND AGE
Women were more exposed to water at work than men (Studies I and IV), and many female-dominated occupations comprise wet work, e.g. hairdressing, kitchen work and nursing. Furthermore, women were more exposed than men within the same jobs, which could be interpreted as men having more administrative work tasks than women. Women had more wet exposure than men during leisure time as well, probably owing to more domestic tasks. The youngest individuals, aged 18–29, reported the most extensive water exposure at work, probably owing to more low-qualified work at the beginning of their working life (Study IV). In the other age groups no apparent differences in exposure to water were seen.

6.4 HAND ECZEMA
The individuals with and without hand eczema reported similar exposure to skin irritants at work and in their leisure time, although glove use was more common in individuals with hand eczema (Study I). The reasons why individuals with hand eczema do not reduce their wet exposure are unknown, but may include ignorance about the adverse effects that skin irritants have on their hand eczema and/or lack of motivation to reduce exposure in occupational life and during leisure time. The causality between exposure to skin irritants and hand eczema has not been studied in this thesis.

6.5 METHODOLOGICAL ISSUES

6.5.1 Validation
Validated questions are useful for comparing skin exposure in different epidemiological and interventional studies. Although self-reports and observations to estimate skin exposure in nurses have been performed previously, no validation of questions has previously been presented (Jungbauer et al., 2004b). The study group in Study II consisted of 40 volunteers working in four occupations well known to be risk occupations, with frequent exposure to skin irritants, and in office workers with expected low exposure. The number of individuals included in the study, 40, seemed to be a reasonable number for assessing correlations between self-reports and observations, when considering the costs and time needed to perform the observations.

The tendency to overestimate all exposures to skin irritants among individuals in Study II may be an important consideration when evaluating results in future epidemiological studies. However, there was a strong correlation between observations and self-reports of exposure to water, foodstuffs and gloves in Study II. The correlation for hand washing was moderate, although 30/40 individuals estimated their exposure correctly. Using more response alternatives and more time boxes would probably have strengthened the correlations. The risk when using time boxes is that individuals choose a response alternative close to the real exposure time, but it ends up in an adjacent time box, which could weaken the correlations. In Study III, the nurses/assistant nurses
had a tendency to overestimate all their exposures, to water in particular. The correlations between self-reports and observation were strong for hand disinfections and moisturizers, and moderate for gloves. Furthermore, the correlations were moderate for frequency of water exposure and weak for exposure time to water. Therefore, the nurses/assistant nurses estimated frequency more correctly than they estimated total time of water exposure. A possible explanation for the overestimation is that nurses/assistant nurses by tradition experience their work as comprising a large amount of water exposure.

To be useful in further studies and to be generally applicable, the questions should reflect skin exposure during an average working day. For this reason, the participants completed the questionnaire before the start of the working day. There is a small risk that the individuals adjusted their exposure during the working day according to how they had estimated their exposure in their questionnaire. On the other hand, handing in the questionnaire after the working day may not only have strengthened the correlations between self-reports and observation but would also reflect the ability of the individuals to recall their exposure during that specific day. To what extent the observed working day reflected an average working day is uncertain, and for this reason, it would have been desirable to observe the same individuals over several days.

The observation method was easy to learn and the acceptance by participants to be observed was good. To use a hand-held computer to record skin exposure, which has not been done before, simplifies reporting in observational studies. The concordance between the two observers in Study II was very high and the method seems to be reliable and useful for application in further validation and observational studies. The observation method was found not to be suitable in estimating exposure to chemicals although the correlation was strong between self-reports and observations (Study II). The characteristics of the chemical, including volatility, stickiness and viscosity, and the use of contaminated gloves influence the true exposure time.

6.5.2 Questionnaire

In all four studies questionnaires were used. The questions used seem easy to understand and to reflect true skin exposure. The limits for exposure used in the response alternatives of the questions were arbitrary, although exposure of more than 2 hours and for more than 20 times/day is often considered a risk exposure for hand eczema (Lerbaek et al., 2007a; Uter et al., 1999a; Nielsen, 1996). The time was continuously measured in the observation, but in the questionnaire an ordinal response scale was used. The ordinal scale is probably more suitable for subjects, especially when estimating long exposure times. If the questionnaire was designed to give a continuum of answers it would be fair to assume that the participants would report their exposure rounded to the nearest half hour or whole hour. The question regarding hand eczema used in studies I and III has been previously validated and it was found that the question gives some underestimation of the prevalence of hand eczema (Meding and Barregård, 2001).

To be able to assess the total exposure to skin irritants throughout the day it is important to ask about both occupational exposure and exposure during leisure time. The same nomenclature and
wording should be used in the questions regarding exposure in occupational life and during leisure time. The most important skin irritant to assess, both in occupational life and during leisure time, is water. It may be confusing to ask about hand washing and about “water and detergents”. To avoid misinterpretations, detergents should be asked about separately. Almost all the individuals exposed to foodstuffs also reported exposure to water to a large extent, which implies that they will be identified as having a high risk of hand eczema as their water exposure is elicited. When assessing water exposure both time and frequency of exposure should be asked for although the relation between frequency of water exposure and skin damage is not yet fully established.

### 6.6 PREVENTION, AND FUTURE PERSPECTIVES

The knowledge regarding exposure to skin irritants generated from this thesis work can be useful in developing prevention measures and reducing unfavourable exposure in occupational life and at leisure. Some of the occupations regarded as risk occupations for hand eczema were heavily exposed to water but others did not comprise water exposure of considerable proportions. Vocational guidance with regard to advising individuals in career transition with a previous history of atopic dermatitis could be improved.

Exposure to skin irritants during leisure time is an important area to elucidate. Eighty per cent of individuals acknowledged wet exposure during leisure time and individuals who acknowledged wet exposure at work also more often had wet exposure during leisure time (Study I). These data stress the importance of reducing wet exposure during leisure time as well as in occupational life.

Skin protection programmes have been developed in some countries including Denmark (Agner and Held, 2002) and comprise practical instructions relating to skin care, which are aimed to reduce hazardous skin exposure in a risk occupation or at certain workplaces. These programmes are meant to be offered as part of training and educational programmes, and the objective is to improve knowledge about skin care. In Germany occupational exposure to skin irritants has been subject to regulation since 1996, and according to the regulations, wet work is described as wet hands at work for more than 2 hours a day, or hand washing exceeding 20 times a day, or glove use for more than 2 hours a day (Gefährdung durch Hautkontakt – Ermittlung, Beurteilung, Maßnahmen, 2006). The regulations state that for occupations which comprise wet work, a specific prevention programme should be provided. In Sweden, occupational exposure to skin irritants has not been subject to regulation thus far. Introducing regulation in Sweden would be a possible way to prevent hazardous occupational skin exposure and should be further discussed.

Using textile gloves underneath the occlusive gloves may prevent harmful effects of humidity associated with wearing occlusive gloves (Ramsing and Agner, 1996b). Even short exposure periods of glove use can impair the skin barrier because of water, detergents, hand disinfection or other chemicals in the gloves. The adverse effects on the skin barrier when using gloves could be further reduced if the hands are rinsed and dried thoroughly after hand washing and if contaminated gloves are avoided.
Using moisturizers is not considered to constitute skin exposure; on the contrary, moisturizers have been shown to be beneficial in preventing hand eczema in hazardously exposed individuals (Halkier-Sørensen and Thstrup-Pedersen, 1993). In Study III, the nurses/assistant nurses used moisturizers only once a day. Advice on additional use of moisturizers in individuals employed in risk occupations may be valuable in preventing hand eczema.
7 CONCLUSIONS

The most common occupational skin irritant is water and almost 20% of the general population reported occupational water exposure. Furthermore, about 7% reported exposure of more than 2 hours and 6% reported exposure frequency of more than 20 times a day. Exposure during leisure time is common and 80% of the population reported wet exposure at leisure. Furthermore, women and men with high wet exposure at work also tend to have high wet exposure in their leisure time. These findings stress the importance of investigating total exposure to skin irritants during the day. Women have more wet exposure than men, both at work and during leisure time. The youngest individuals, aged 18–29 years (Study IV), were more exposed to water at work than older age groups were. Individuals with and without hand eczema seem to have similar exposure to skin irritants.

When validating questions regarding skin exposure by observation there was a strong correlation between self-reports by questionnaire and observations regarding exposure to water, occlusive gloves and foodstuffs, and a moderate correlation regarding hand washing (Study II). In nursing, the correlations between self-reports and observations were strong for hand disinfections and moisturizers, moderate for gloves and frequency of water exposure, and weak for total time of water exposure (Study III). Despite some tendency to overestimate the exposures in the validation studies, the questions are considered to be useful for surveying exposure to skin irritants.
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9 REFERENCES


MacMullen E, Gawkrodger DJ. Physical friction is under-recognized as an irritant that can cause or contribute to contact dermatitis. Br J Dermatol 2006:154:154-156.


