INDIVIDUAL AND ENVIRONMENTAL RISK FACTORS FOR HAND ECZEMA IN HOSPITAL WORKERS

by

Eskil Nilsson

Umeå University 1986
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ABSTRACT

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Eskil Nilsson, Departments of Dermatology, Sundsvall Hospital, S-851 86 Sundsvall and Umeå University, S-901 85 Umeå Sweden.

Individual and environmental risk factors in hand eczema have been investigated in a prospective cohort study of 2452 newly employed hospital workers with a follow-up time of 20 months. Current hand eczema was analyzed in 142 wet hospital workers from this cohort with respect to the etiologic importance of irritants, allergens and contact urticants. The density of the microflora and the effect on the microflora of topical treatment with a potent corticosteroid were studied in 20 patients with hand eczema.

‘Wet’ hospital work was found to increase the odds of developing hand eczema only twice compared to ‘dry’ office work. Nursing children under four years old and the lack of a dish-washing machine significantly increased the risk of contracting hand eczema. Unfavourable combinations of these domestic factors increased the risk as much as wet work. A history of atopic dermatitis approximately tripled the odds both in wet as well as in dry work.

Histories of earlier hand eczema (HHE), metal dermatitis (HMD) and of atopy were analyzed as risk factors for hand eczema in 1857 women in wet work. HHE increased the odds by a factor of 12.9 and created a subdivision of the population into high risk individuals and normal risk individuals. HHE was found in half of the subjects with atopic dermatitis, in one quarter of the subjects with atopic mucosal symptoms and in one fifth of the non-atopics. A HMD increased the odds by a factor of 1.8. This increase was seen as a high risk level in subjects with HHE and as a normal risk level in subjects with no HHE. A history of atopic disease as a complement to information about HHE and HMD increased the odds by another 1.3 times. The predicted probability of developing hand eczema ranged from 91% in subjects with a combination of HHE, HMD and atopy to 24% in subjects with none of these risk factors.

Subjects with AD were found to suffer a more severe form of hand eczema with significantly higher figures for medical consultation, sick-leave, termination due to hand eczema, early debut, permanent symptoms and vesicular lesions.

Amongst the patients investigated for current hand eczema high risk individuals were overrepresented. It was claimed in 92.3% of the cases that trivial irritant factors had elicited the current episodes of hand eczema. In 35% of the cases the exposure to the irritant took place largely at home. Although contact sensitivity and contact urticaria were fairly common, they mostly seemed to be of minor importance in the etiology of the current hand eczema.

Staphylococcus aureus colonized eczematous lesions of the hands in 18/20 patients. The density exceeded 10^5 colony forming units/cm^2 in 15/20 patients. Only three of these patients showed signs of clinical infection. Successful topical treatment with a potent corticosteroid significantly reduced the colonization of S. aureus.

Key words: Hand eczema, prospective study, hospital workers, irritants, contact allergy, contact urticaria, atopy, metal dermatitis, multivariate regression analysis, evaluation of risk factors, microflora, S. aureus in hand eczema.
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A B S T R A C T

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


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ABBREVIATIONS

AD  Atopic dermatitis
AMS Atopic mucosal symptoms
NA  Non-atopics
HMD History of metal dermatitis
HHE History of earlier hand eczema
OR  Odds ratio
PP  Predicted probability
INTRODUCTION

Hand eczema is a disorder of multifactorial etiology. There is general agreement that individual and environmental factors may interact in a complex manner to elicit this common disorder. To date knowledge of the interplay between endogenous and exogenous factors is very limited. Extending this knowledge must be considered a high priority task in the struggle to discover the nature of hand eczema. There are many advantages to be gained from an improved understanding of the relative importance of individual and environmental factors. The accurate classification of hand eczema, occupational counselling, medico-legal considerations, prognostic speculations and the outcome of therapeutic measures are all dependent on the extent to which endogenous and exogenous factors contribute to the etiology of hand eczema. This study has been designed to throw some light on this complex problem.

REVIEW OF THE LITERATURE

HAND ECZEMA

Prevalence. Epidemiological studies of hand eczema in various populations have recorded a rather wide range of prevalence figures. Agrup (1) estimated that the prevalence of hand dermatitis in the general population in southern Sweden was 1.2-3.4%. As a part of a study on nickel allergy Peltonen (2) examined the hands of 980 subjects in Finland and found hand eczema in 4%. In a study in northern Norway (3) 14.667 adult subjects were asked about the occurrence of allergic hand eczema during the preceding twelve months. A positive reply was given by 4.9% of the men and 13.2%
of the women. The age of the women influenced the prevalence. Thus
15% of women between 25-34 years of age reported hand eczema while
for women between 45-49 years the figure was only 9.2%. In a pre-
valence study in the Netherlands an episode of eczema of the hands
and forearms lasting for three weeks and occurring during the past
three years was used as a criterion for a case of hand eczema.
In this study the prevalence figures for 1982 were 4.5% for men
and 10.0% for women (4). A representative sample consisting of
1961 Danish women reported a history of hand eczema in 22% (5). In
a Finnish study of 617 wet hospital workers, predominantly women,
44% had past or present hand eczema (6).

The various results recorded in these investigations reflect some
of the problems innate in prevalence studies of hand eczema. As
hand eczema is a periodic disorder figures based on a single exa-
mination will underrate the prevalence. Prevalence studies cover-
ing periods of time must rely on anamnestic information with its
limitations regarding accuracy of diagnosis. Another aspect of the
problem is how severe a dermatitis of the hands has to be before
it can be diagnosed as eczema. The difference in prevalence be-
tween the two sexes and the importance of wet work is obvious from
the figures.

Classification. Classification of hand eczema may be based on the
morphologic description of the eczema with terms such as vesicu-
lo-squamous, nummular, wedding-ring, fingertip, hyperkeratotic
and pompholyx (7). These names refer to clinical features and say
very little or nothing about the etiology. A common way to classi-
Hand eczema is according to etiologic aspects. Thus the terms irritant or allergic contact dermatitis of the hands are used depending on the cause.

As stated by Epstein hand eczema is almost always multifactorial and therefore simple etiologic classifications are doomed to failure. In order to avoid the frustrating struggle with some of the classifications Epstein proposed that hand eczema should be analyzed for its endogenous and exogenous factors (8).

**ATOPIC DERMATITIS**

**Epidemiology.** The incidence of atopic disease varies widely in the great number of existing investigations. A very complete survey of this topic has been given elsewhere (6). Differences in diagnostic criteria and selection of the population studied regarding age, race and geographic distribution are all probable explanations for the differences found. The cumulative incidence of atopic disease varies from 15-25% in most reports (9). In a study on 7000 adult twin pairs in Sweden 18% had or had had atopic disease (10). In another Swedish study on 1325 unselected 7-year-old school children 15.1% had atopic disease and 8.3% had or had had atopic dermatitis (11).

**Diagnosis.** Attempts to define this dermatological disorder were made as early as in 1892 when Besnier (12) observed a familial disposition and noted that the disorder which he named prurigo diathésique occurred in association with allergic rhinitis, asthma.
and sometimes gastrointestinal symptoms. The term atopy was introduced by Coca & Cooke in 1923 and means a strange disease (13). The word is Greek and can be translated as 'out of place'. In modern terminology the term atopy includes allergic rhinoconjunctivitis, bronchial asthma, atopic dermatitis, and certain forms of gastrointestinal allergy and urticaria.

A transferable factor was found in the serum of allergic persons by Prausnitz & Küstner in 1921 (14). This transferable factor has been identified as immunoglobulin E (IgE) and methods have been developed to measure the total and specific amount of IgE (15-19). Atopic individuals are commonly defined as having an increased liability to form IgE antibodies when exposed to environmental antigens. This commonly used generalization is true for allergic rhinitis and allergic asthma but not for atopic dermatitis. The dermatitis which occurs in atopics is not a typical atopic disease since the importance of allergic factors is uncertain (20-22). Approximately 20% of patients with severe flexural eczema have normal serum IgE levels (22).

No absolute diagnostic criteria exist for atopic dermatitis. Diagnostic guidelines have been proposed by Hanifin & Rajka (23). These guidelines are based on a few basic and many minor criteria. Lammintausta introduced a prognostically useful definition of the skin condition in subjects with atopic mucosal symptoms and non-atopics. This condition was named atopic skin diathesis and was defined as follows:
a) dry skin  
b) a history of a low pruritus threshold for two or three of the following non-specific irritants: sweat, dust, rough material  
c) white dermographism and  
d) facial pallor/infraorbital darkenings

Atopic skin diathesis was found in 35% of the subjects with atopic mucosal symptoms and in 18% of the non-atopics. This diathesis was found to significantly increase the risk of hand eczema among employees engaged in wet work (6).

Hand eczema in atopic dermatitis. Several reports exist in which a correlation has been found between hand eczema and a personal or family history of atopy (1, 24-29). Atopic disease and especially atopic dermatitis in childhood as risk factors for hand eczema in adults have been the subject of two large studies during the last few years. One study has been carried out by Lammintausta on wet hospital workers in Turku, Finland (6) and the other by Rystedt on selected groups of atopics in Stockholm, Sweden (9). In both studies an increased risk of developing hand eczema was found in subjects who had had atopic dermatitis in childhood. Both authors also found that a considerable number of subjects with earlier atopic dermatitis managed to work in high risk occupations without developing hand eczema. Atopic skin diathesis, as defined by Lammintausta, significantly increased the risk of hand eczema in subjects with atopic mucosal symptoms and in non-atopics. In subjects with atopic dermatitis Rystedt identified the following cli-
nical markers as significantly increasing the risk of hand eczema: eczematous involvement of the hands in childhood, widespread dermatitis in childhood, persistent body eczema and dry/itchy skin. In subjects with atopic mucosal symptoms and in non-atopic individuals it was found that dry/itchy skin significantly increased the risk of hand eczema (9). Neither of these two studies was prospective and it was not possible to calculate the relative importance of individual versus environmental risk factors in the development of hand eczema.

EXOGENOUS FACTORS IN HAND ECZEMA

Irritants. The first line in the capacity of the skin to protect itself against external exposure is the surface film, sometimes called the acid mantle because its pH is on the acid side (30). The buffer capacity of the surface film varies amongst individuals and also from one body region to another (31, 32). The main protective function in the skin rests with the stratum corneum (32-34). The flexibility and cohesion of the horny layer are dependent on the water content (35-36). Reduction of the water-holding substances will decrease the water content of the stratum corneum and cracks and chapping will develop (37-39). Cell-wall lipids protect the water-holding substances (40). Detergents remove lipids and water-holding substances and cause a predisposition to chapping (35, 41). A breakdown of the natural resistance of the skin leads to increased water vapor loss and the integrity of the skin barrier can be measured by transepidermal water loss (42-44).
Acute irritant dermatitis may be caused by strong irritants after a single or a few applications. Hand eczema may also occur after repeated assaults by weak irritants over a long period of time. This dermatitis has been named 'wear and tear' dermatitis and 'traumiterative dermatitis' (45). There is no test which can determine whether an irritant is relevant to a patient's dermatitis. Thus the evaluation of the relative importance of irritants in patients with hand eczema has to be a clinical decision. Discussions of irritants are usually focused on chemicals, solvents, acids, alkali and surfactants. However, dry air, low humidity, cold, wind and friction may be important contributory factors (8). It is very difficult to obtain scientific documentation of the widely-held opinion that contact with irritants is the most common cause of hand eczema. Clinical evidence that surfactants aggravate hand eczema is, however, overwhelming (8). Thus various kinds of wet work involve occupational hazards to the hands (29, 46-50).

Some people seem particularly prone to develop irritant dermatitis (51, 52). Irritable skin seems to depend on constitutional factors but so far it has not been possible to identify individuals who are particularly susceptible to irritants (53). Long clinical experience has shown that atopic skin has a reduced resistance to irritants and consequently has an increased tendency to develop irritant dermatitis especially on the hands. According to the recent findings by Lammintausta and Rystedt this reduced resistance does not seem to occur in all subjects with a history of atopic dermatitis as a considerable number managed to work in risk occupations without developing hand eczema (6, 9). In subjects
with atopic mucosal symptoms and in non-atopics Lammintausta identified atopic skin diathesis which was found to increase the risk of irritant hand eczema (6). These observations indicate that a reduced resistance to irritants does not occur in all subjects with atopic dermatitis and may occur in subjects with atopic mucosal symptoms and in non-atopics.

Allergic contact dermatitis of the hands. A lot of interest has been focused on delayed contact sensitivity in the etiology of hand eczema. Figures for allergic contact dermatitis among hand eczema patients vary considerably (1, 29, 54). The most important reason for this variation is probably the selection of the patient populations tested. A positive patch test in a patient with hand eczema does not mean that a contact allergy is relevant for the current hand dermatitis. Judging the relevance of a positive patch test in hand eczema may be very difficult. An allergen is considered a primary cause of the dermatitis if elimination leads to a complete cure. It is only too common for an allergen to be of doubtful relevance. The proven contact allergy may be only a contributory or aggravating factor or of no significance at all to the dermatitis.

There has been no prospective study on the importance of a delayed contact allergy as a risk factor in hand eczema. A retrospective study on wet hospital workers found that hand eczema was significantly more common amongst subjects with contact allergy. However, a considerable number of workers with contact sensitivity to nickel and fragrance mix had managed to work without deve-
loping hand eczema (6). Amongst hospital workers the following sensitizers are reported to be common: rubber gloves, formaldehyde, chloroxylenol, penicillin, streptomycin, neomycin, piperazine, phenothiazines, hand creams, nickel and glutaraldehyde (55).

Atopy and contact sensitivity. Delayed hypersensitivity to candida, trichophytin, tuberculin and other bacterial and viral antigens is diminished in patients with atopic dermatitis (56-61). Dinitrochlorobenzene (DNCB) which sensitizes over 90% of the normal population has been found to sensitize a lower proportion of atopic patients (56, 62-64). Sensitivity to RHUS-antigen was found in 15% of atopics whereas 61% of non-atopics were sensitized (65).

The occurrence of delayed contact dermatitis and positive patch tests in patients with atopic dermatitis is a subject which produces contradictory findings. One study found a positive patch test reaction in 28% of AD patients as compared to 9% of psoriatics (66). In another study on 4000 patients, of whom 233 had atopic dermatitis, a positive patch test reaction was no more frequent in the atopics (26). Most studies on the prevalence of contact sensitivity in patients with atopic dermatitis have produced figures between 15% and 35% (1, 6, 26, 67, 68). Some investigators have found nickel allergy to be more common in atopic individuals (69-71) whereas other investigators have found no such correlation (72-75). Judging the relevance of a positive patch test in a patient with hand eczema may be even more frustrating in atopics than in non-atopics. In atopics it must be assumed that endogenous factors and an increased sensitivity to
Irritants play an important part in the etiology of the hand eczema. Forsbeck et al. (28) found that contact allergy was as common in AD patients without hand eczema as in patients with hand eczema. This finding highlights the problem of the relevance of contact allergy in subjects with atopic dermatitis and hand eczema.

**Contact urticaria.** Contact urticaria (CU) may be defined as a wheal-and-flare response elicited from within a few minutes up to half an hour after skin exposure to various agents. The term (contact urticaria syndrome) was proposed in 1975 to cover a broad spectrum of clinical manifestations which may be provoked by the causative agent (76). The following staging for this syndrome is proposed by von Krogh & Maibach (77).

Cutaneous reactions only:

- **Stage 1:** localized urticaria dermatitis
  
  non-specific symptoms (itching, tingling, burning etc)

- **Stage 2:** generalized urticaria

Extracutaneous reactions:

- **Stage 3:** bronchial asthma
  
  rhinoconjunctivitis
  
  oro-laryngeal symptoms
  
  gastro-intestinal symptoms

- **Stage 4:** anafylactoid reactions
Non-Immunological Contact Urticaria (NICU). In NICU the reaction is elicited without previous sensitization in most exposed individuals. A release of histamine and other vasoactive substances without involving immunological mechanisms is thought to be the cause (78). This type of contact urticaria is probably very common. Many chemicals in common use have the ability to provoke NICU in a large number of normal individuals (77). Agents such as benzoic acid, sorbic acid, cinnamic acid and cinnamic aldehyde are potent urticariogenic substances. When exposure is optimal a majority of individuals will react with contact urticaria after application of rather high concentrations to intact skin. In lower concentration they may provoke erythema but not a true urticarial reaction. Thus the frequency and strength of NICU are influenced by the concentration of the individual chemicals and even by the chemical composition of the vehicle (79).

Immunological Contact Urticaria (ICU). Evidence of an allergic mechanism in contact urticaria has been rare. Immunological mechanisms may be suspected when there has been a period of sensitization, the reaction is strong, tests on controls are negative and passive transfer test is positive. IgE specific for the antigen has been found in some cases (80-83). Urticaria may also be caused by allergic mechanisms in which specific immunoglobulin G and perhaps immunoglobulin M may activate the complement cascade through the classical pathway (84-86).
While atopics and non-atopics do not differ with respect to NICU (79) it is likely but poorly documented that ICU is more common among atopics.

Uncertain Mechanism Mediated Contact Urticaria (UMCU). This type of contact urticaria refers to reactions for which the mechanisms are unknown (77). Von Krogh & Maibach have updated the contact urticaria syndrome and listed most of the substances known to elicit contact urticaria in the three groups (77, 87).

The diagnosis of contact urticaria had to be based on a careful history of immediate reactions. Diagnostic tests guided by the case history may be performed on intact skin as open, occlusive or intradermal and on slightly affected or previously affected skin as open or occlusive tests. A stepwise test procedure has been recommended by von Krogh & Maibach (77, 87).

Contact urticaria in hand eczema. In a study of 33 food-handlers with recurrent hand eczema it was found that exposure of the hands to various proteins aggravated the hand eczema. Itching, erythema, urticarial swelling and dyshidrotic vesicles were observed within 10-30 minutes after contact between the incriminating protein and the affected skin. Contact urticaria was found in 9 cases of whom 3 reacted only when the suspected food was exposed to eczematous skin. In total 25 showed a positive scratch test with food such as chicken, seafood, vegetables and spices. The term 'protein contact dermatitis' was introduced to describe this phenomenon (88). Immediate reactions which aggravate chronic hand dermatitis
have been reported by other authors. Thus lettuce and endive (89), wheat flour, turkey and lamb (90) and apple and potato (91) have been found to aggravate or elicit hand dermatitis. Some of the patients in these studies reacted with positive tests only on previously dermatitic skin or after intradermal tests.

Although case reports on contact urticaria are numerous the epidemiology in the general population and in populations with hand eczema is unknown except for the study on food-handlers by Hjorth & Roed-Petersen (88).

Colonization of Staphylococcus aureus. The nose, axillae, perineum and toe-webs are the only common resident carrier sites of _S. aureus_ on human skin. Normal skin from other locations yields _S. aureus_ in about 5% of the population (92). Higher carrier rates will be found when individuals are followed up over periods of time (93). The carriage rate of _S. aureus_ on normal hands has been studied in various populations. In 13% of nasal carriers _S. aureus_ was cultured by the 'fingerprint' technique compared to 4% of non-carriers (94). In a study of 361 patients prepared for operation it was found that 24% carried _S. aureus_ on their hands (95). Among hospital staff who had just completed a ward round or treatment 68% carried _S. aureus_ on their hands compared with 25% of those engaged in other duties in the same ward or who had just washed their hands (96). A study on 50 nurses and 50 controls found that 28% of both groups carried _S. aureus_ on their hands. The mean density was however lower among the nurses. A higher percentage of the nurses carried _S. aureus_ on their hands persistently during a three-month period (97).
Various dermatitic conditions carry *S. aureus* more frequently than normal skin. Candidiasis in intertriginous regions carries *S. aureus* in 60% (98), psoriatic plaques are colonized with *S. aureus* in 20-50% (99-102). In a review article by Leyden (103) the following frequency and density of *S. aureus* were reported in various dermatitic conditions: seborrhoic dermatitis 21% with a density of 13 000 cfu/cm², neurodermatitis 90% with 600 000 cfu/cm², exfoliative erythroderma 100% with 2 000 000 cfu/cm², chronic familial benign pemphigus 90% with 4 000 000 cfu/cm² scaling interdigital athlete's foot 6% with 30 000 cfu/cm², macerated interdigital athlete's foot 11% with 500 000 cfu/cm². Dermatitic skin in atopics has shown both a high carriage rate and high counts of *S. aureus* (104, 105). Although it is well-known from clinical experience that *S. aureus* is commonly isolated from eczematous lesions of the hands no systematic quantitative study has been performed on the microflora of hand eczema.
A I M S O F T H E S T U D Y

1. Epidemiological: To investigate the relative importance of some individual and environmental factors in the etiology of hand eczema in newly employed hospital workers.

2. Clinical: To study the importance of irritants, allergens and contact urticants in a selected group of newly employed wet hospital workers with hand eczema.

3. Bacteriological: To study the density of the microbial flora and i.e. *S. aureus* in hand eczema and the effect on the microflora of a potent topical corticosteroid.
Study design and study population (I-II). The study has been performed as a prospective cohort study. The cohort was collected from June 1979 to June 1981 and consisted of 2651 newly employed workers in four hospitals in the county of Västernorrland in northern Sweden. At the preemployment examination, previous skin diseases were recorded but played no part in the selection for employment. A follow-up questionnaire was sent to the employees and answers were received from 2452 subjects (92.5%) after a median observation time of 20 months (range 18.5-24.0). The frequency of atopic disease in the defaulters did not differ from that found in the total cohort. Table I shows the number of employees, percentage of females and median age of the occupational groups. Nursing staff included all kinds of staff working with patients. The following subgroups were included: ward maids 964, nurses/assistants 233, psychiatric nurses 122, nursing assistants 117, physicians 55, children's nurses 36, dental staff 31, occupational therapists 36 and chiropodists 1. Nursing staff and kitchen workers/cleaners performed wet work while office workers and caretakers/craftsmen performed mainly dry work.

<table>
<thead>
<tr>
<th>Occupational Group</th>
<th>Number</th>
<th>Female (%)</th>
<th>Median age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nursing staff</td>
<td>1613</td>
<td>87.7</td>
<td>25</td>
</tr>
<tr>
<td>Kitchen workers/cleaners</td>
<td>457</td>
<td>93.4</td>
<td>23</td>
</tr>
<tr>
<td>Office workers</td>
<td>269</td>
<td>91.8</td>
<td>22.5</td>
</tr>
<tr>
<td>Caretakers/craftsmen</td>
<td>113</td>
<td>16.8</td>
<td>29</td>
</tr>
</tbody>
</table>
Patients (III). The patients in this study consisted of 142 subjects from the total cohort employed in hospital wet work who consulted a dermatologist because of current hand eczema. 91% of them were women and the mean age was 26.2 years. 72% were employed in nursing occupations, 16% were cleaning personnel and 12% were kitchen workers.

Patients (IV). Twenty patients, 16 females and 4 males, with hand eczema were studied. The age of the patients ranged from 13-61 years. Patients who had received local or systemic antibiotics or local corticosteroids within the last two weeks were excluded as were patients with severe suppuration, tenderness, adenopathy and fever.
METHODS

PAPERS I-II

Diagnosis of atopy and metal dermatitis. At the preemployment examination any history of atopic disease was noted by a specially trained occupational nurse in a standardized manner. Atopic dermatitis was accepted as a diagnosis if there was a history of itching, relapsing dermatitis starting in infancy or childhood with a typical distribution. Subjects with past or present atopic dermatitis were recorded together. Atopic mucosal symptoms were accepted as a diagnosis if hayfever or asthma occurred when the subject was exposed to pollen or furred animals. No other diagnostic tests or criteria for atopic disease were used.

A history of metal dermatitis was derived from a questionnaire in which the employees were asked about an itching rash related to exposure to metal buttons, cheap jewelry or wristwatches.

Criteria for hand eczema. At the preemployment examination the employee was informed that the study concerned hand eczema and was given some brief information about the symptomatology of hand dermatitis. The occurrence of hand eczema during the period studied was identified in the follow-up questionnaire. The employee was then asked to characterize his/her eczema using one or more of the following five alternatives:

1. dry and chapped skin with rashes and small cracks
2. itching red macular and papular skin lesion
3. small vesicles
4. ruptured vesicles or excoriated skin
5. rough skin with cracks and scaling

The employee was asked about medical consultation, sick-leave and if he/she had left his/her current work because of hand eczema. The time of onset and the nature, periodic or permanent, of the eczematous symptoms were also recorded. Those who had stated in the questionnaire that they had suffered from hand eczema without seeking medical advice were asked why they had not done so. In a separate question the employee was asked about hand eczema prior to the current work. The reliability of identification of hand eczema by questionnaire has been checked in this study using 146 patients who attended the dermatological clinic with a hand dermatitis which they suspected was eczema. Of these patients, only four had diagnoses other than eczema. One had palmar keratoderma, two had pustular dermatosis of the palms and one had scabies.

Occupational exposure. Approximately 50% of the employees worked part-time and 1/3 had changed their work for other occupations at the follow-up.

Domestic work. Six anamnestic parameters which reflect domestic manual work from different points of view were recorded: the nursing of children younger than four years of age; members of the household; hours of housekeeping per week; hours per week spent working with the hands on a hobby; use of washing machine and dish-washer. The purpose was to investigate the correlation between these parameters and the risk of developing hand eczema.
Statistical methods. The multifactorial problem in this study has been analyzed using a multivariate logistic regression technique (106). The risk of developing hand eczema was calculated as predicted relative odds ratios. The odds ratio (OR) expresses the relationship between the odds (01) of getting hand eczema (E1) in one group (01=E1/(1-E1)) compared to odds (02) of hand eczema (E2) in a second group (02=E2/(1-E2)). E1 and E2 denote the proportion of hand eczema in the two groups. Then the odds ratio (OR) will be

$$OR=\frac{02}{01}=\frac{E2(1-E1)}{E1(1-E2)}$$

The risk in per cent of developing hand eczema has been statistically calculated and is expressed as predicted probability (PP).

The Student's t-test was used to compare relative frequencies.

Three multivariate regression analyses of the interrelationship between individual and environmental factors will be presented. The following factors were used in the three analyses.

The first analysis (A1): AD, AMS, NA and occupation.

The second analysis (A2): AD, AMS, NA, domestic factors and the three occupations dominated by women.

The third analysis (A3): AD, AMS, NA, HMD and HHE in women in wet hospital work.
Characterization of hand eczema. The following factors regarding hand eczema prior to the present work were recorded: time from onset, periodicity and occupation at onset. The patients' opinions about factors which elicited the current hand eczema and contact urticaria were sought. The state of the current hand eczema and diagnosis of ongoing eczema at sites other than the hands, were noted.

Patch tests. Epicutaneous testing was carried out on 120/142 patients using the European standard series except for caine mix and fragrance mix. Benzalconium chloride 0.1% and coal tar 5% were added to the standard series.

An additional series of agents was tested on 55/120 consecutive patients. This series consisted of disinfectants, preservatives, emollients, perfumes and colourings. Most of these were present in products in common use in the hospitals. The following were included: lauromacrogol as it is, macrogol as it is, carbopol 1%, EDTA 1%, propyl gallate 1%, sorbic acid 2.5%, triethanolamine 5%, chlorocresol 2%, merthiolate 0.1%, chloracetamide 0.1%, patent blue V 2%, quinoline yellow 2%, ethanolamine 5%, chlorhexidine gluconate 1%, BHT 2%, bronopol 1%, propylene glycol 20%, isopropyl myristate 20%, cetyl alcohol 5%, cetrimide 0.1% and 0.01%, eucalyptol 2% and hexachlorophene 1%. The European standard test series was supplemented with the addition of caine mix and fragrance mix when testing these 55 consecutive patients.
The Finn Chamber technique was used with exposure to the allergen for 48 hours. The tests were read after 72 hours.

**Prick tests.** For contact urticaria, prick tests were carried out as open tests on the upper back. They were read after 15-30 min. Histamine was included as a positive and saline as a negative control. If the mean diameter of the wheal subtracted from the negative reference was 3 mm or more, the reaction was regarded as positive. Prick tests were performed on 41 out of 49 patients with a positive history. Eight patients declined to have prick tests for various reasons.

A screening series for contact urticaria was conducted as a supplement to substances suspected from case histories. Included in the 'hospital screening series' were three chemically identified substances (formaldehyde 2%, benzalconium chloride 0.1% and isopropyl myristate 20%). The test series included some complex chemicals and agents which were all in common use in the hospitals: i.e. two liquid soaps (Blido, Barnängen); three disinfectants (hand spirit, M-spirit and Hibiscrub); four emollients (Atrix, Sumabless, Helosan and Calmuril), a green rubber glove and a paper towel which was tested wet.

**Statistics.** Student's t-test was used to compare relative frequencies. A significance level of 5% was chosen.
Characterization of hand eczema. The eczema was characterized by:
erythema, papules, infiltration, vesicles, erosions, fissures, crusts and signs of clinical infection with exudation and yellow crusts. The extension of the lesion was estimated and recorded as small (<1/3), medium (1/3-2/3) and large (>2/3) in relation to the total area.

Sampling technique. The sampling technique of Williamson & Kligman (107) was employed with some modification. A sterile silicone rubber cylinder (inner area 5.3 cm²) was placed on the sampling site of the skin and filled with 2 ml 0.1% Triton X-100 in 0.075M phosphate buffered saline pH 7.9. After scrubbing for one minute with a disposable 10 μl inoculating loop (Nunc A/S, Roskilde, Denmark) the liquid was transferred to a locally-produced anaerobic transport device. To facilitate sampling from the fingers a special sampling device was constructed. In a piece of silicone rubber tubing (length 60 mm, inner diameter 20 mm) two holes with a diameter of 14 mm for thick fingers or 11 mm for thin fingers were cut opposite each other. The sampling device was mounted on a finger, and filled with the detergent buffer. The oval enclosed on a finger of 14 mm diameter was 3.89 +/- 0.26 cm² (mean +/- SD of 4 experiments) and that on a finger of 11 mm diameter 3.37 +/- 0.21 cm². In finger samples an estimated area of 3.6 cm² was used in all calculations regardless of finger diameter. Before treatment, samples were taken from three sites; 1) from the most pronounced eczematous lesions; 2) from skin affected only with
erythema and 3) from clinically normal skin of the hands. After treatment the same skin areas were resampled.

Identification of the microflora. The samples were diluted tenfold ($10^{-1}$, $10^{-2}$, $10^{-3}$) in peptone yeast broth (108) and plated in an anaerobic glove box. Brain Heart Infusion Agar (BHIA), Lab M, London, England; Trypticase Soy Agar (TSA), Difco, Detroit, Michigan, USA; and TSA + 0.5% Tween 80, Kebo Lab, Stockholm, Sweden, were incubated aerobically at $37^\circ$C for two days and BHIA also anaerobically at $37^\circ$C for five days. All bacterial colonies with different morphology were quantified from the appropriate dilution and identified when the number of colony forming units (cfu) reached $10/cm^2$, which was the technical boundary of quantitative estimation. Coagulase-negative staphylococci were identified according to the simplified scheme of Kloos & Schleifer (109). Staphylococci were separated from micrococci by their ability to produce acid aerobically from glucose (110). Corynebacteria were divided into lipophiles and non-lipophiles by the growth of lipophiles on TSA + 0.5% Tween 80 (111). Peptostreptococci, propionibacteria and Sarcina sp. were identified according to the VPI Anaerobe Laboratory Manual (108).

Before quantitative bacteriological analyses different bacterial species were combined into three main groups: (1) S. aureus, (2) other aerobes, and (3) anaerobes.
Treatment. Treatment given was 0.05% clobetasol propionate cream (DermovatR, Glaxo) and an emollient (Essex creamR, Essex) in the following intermittent schedule. Clobetasol propionate cream was applied twice daily on days 1, 2, 3, 4, 8, 9, 12 and 14. The inert cream base was used on days 5, 6, 7, 10, 11 and 13. The patients were seen after fourteen days and new samples were taken from the same sites as before treatment using the same technique.

Antibacterial effect of clobetasol propionate. The in vitro antibacterial effect of clobetasol propionate (2000, 1000, 500, 250, 125, 62, 31 and 16 μg/ml) on S. aureus was investigated using the agar dilution technique in ASM-PDM agar (Biodisc AB, Stockholm, Sweden) using $10^5$ cfu as inoculum.

Statistics. Geometric means of groups of bacteria were compared with paired $t$-tests (112). A significance level of 5% was chosen.
RESULTS

Prevalence of individual risk factors. Of the total cohort studied we considered 22.6% to be atopics. A history of atopic dermatitis was seen in 10.2% including 4.1% with both atopic dermatitis and atopic mucosal symptoms. Pure atopic mucosal symptoms were found in 12.4%. The prevalence figures for atopy were essentially the same in the four occupational groups. A history of metal dermatitis was reported by 26.3% of the women in wet hospital work and was more common in atopics than in non-atopics. The following relative frequency for HMD was found: AD 36.5% (p<0.001), AMS 31.4% (p<0.05) and NA 24.1%. A history of earlier hand eczema was reported by 22.4% of the women in wet hospital work. The following figures for earlier hand eczema were found: AD 48%, AMS 24%, NA 18%, HMD 36% and subjects without HMD 17%. A history of metal dermatitis was more common in atopics (46.9%) and non-atopics (40.0%) subjects with HHE than in atopics (26.7%) and non-atopics (20.5%) without HHE (p<0.001).

Hand eczema in the four occupations. Hand eczema prior to the current work had occurred in 21.7% of the nursing staff, in 20.4% of the kitchen workers/cleaners, in 23.5% of the office workers and in 8.2% of the caretakers/craftsmen.

Table II shows the total occurrence of hand eczema in the four occupations during follow-up. The difference in hand eczema between wet and dry work is small and seems to diminish in the more severe forms of hand eczema. It is open to question whether
Table II  Hand eczema in occupational groups; median observation time: 20 months

<table>
<thead>
<tr>
<th></th>
<th>Nursing staff</th>
<th>Kitchen workers/cleaners</th>
<th>Office workers</th>
<th>Caretakers/craftsmen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number in the group (*)</td>
<td>1599</td>
<td>450</td>
<td>264</td>
<td>110</td>
</tr>
<tr>
<td>Hand eczema (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- by questionnaire</td>
<td>41</td>
<td>37</td>
<td>25</td>
<td>17</td>
</tr>
<tr>
<td>- as cause of medical consultation</td>
<td>9.8</td>
<td>14</td>
<td>7.6</td>
<td>7.3</td>
</tr>
<tr>
<td>- as cause of sick-leave</td>
<td>1.9</td>
<td>3.6</td>
<td>1.5</td>
<td>0</td>
</tr>
<tr>
<td>- as cause of termination of current work</td>
<td>2.0</td>
<td>2.4</td>
<td>0.4</td>
<td>0</td>
</tr>
</tbody>
</table>

(*) A small deficit due to incomplete questionnaires.

the figures really reflect the importance of the current work as a causal factor for hand eczema, as 50% had been working part-time and 1/3 of the workers had left their jobs at the time of the follow-up. However, no significant difference in the occurrence of hand eczema was seen between full-time and part-time workers and only 5.8% of the employees with hand eczema reported that the eczema started after the cessation of work.

Hand eczema in atopics. Hand eczema prior to the current work had occurred in 52.5% of the subjects with atopic dermatitis, in 21.7% of the subjects with atopic mucosal symptoms and in 16.3% of the non-atopics. During the follow-up subjects with atopic dermatitis
Table III. Hand eczema in atopics and non-atopics in hospital work

<table>
<thead>
<tr>
<th></th>
<th>Nursing staff</th>
<th>Wet work</th>
<th>Dry work</th>
<th>Caretakers/craftsmen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AD</td>
<td>AMS</td>
<td>NA</td>
<td>AD</td>
</tr>
<tr>
<td>Total number in the group</td>
<td>164</td>
<td>196</td>
<td>1239</td>
<td>49</td>
</tr>
<tr>
<td>Hand eczema (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- by questionnaire</td>
<td>61</td>
<td>46</td>
<td>37</td>
<td>63</td>
</tr>
<tr>
<td>- as cause of medical consultation</td>
<td>31</td>
<td>14</td>
<td>6.2</td>
<td>35</td>
</tr>
<tr>
<td>- as cause of sick-leave</td>
<td>7.3</td>
<td>1.5</td>
<td>1.3</td>
<td>8.2</td>
</tr>
<tr>
<td>- as cause of termination of current work</td>
<td>5.5</td>
<td>2.0</td>
<td>1.5</td>
<td>11</td>
</tr>
</tbody>
</table>

AD = atopic dermatitis with or without atopic mucosal symptoms
AMS = atopic mucosal symptoms
NA = non-atopics
had higher frequencies of hand eczema than subjects with atopic mucosal symptoms and non-atopics (Table III). The difference between the groups increased in the more severe forms of hand eczema. Sick-leave because of hand eczema was fairly uncommon (0-3.4%) in most occupations but for subjects with atopic dermatitis employed in wet work occupations, the figures were higher (7.3-8.2%). Of the subjects on sick-leave, 75% had been absent from work for less than one month. Most employees with hand eczema do not consult a doctor. The following reasons were given by 677 employees: the hand eczema was mild (69.0%), the employee treated himself with various topical remedies (43.9%), the eczema healed fast spontaneously (36.5%) and other reasons (17.4%).

Hand eczema in women in wet hospital work. Table IV gives the figures for the occurrence of hand eczema in women in wet hospital work. From the total figure it can be seen that hand eczema was reported by 41% and only 2.4% had been on sick-leave. 2.2% had left their current work because of hand eczema. Atopic dermatitis, metal dermatitis and earlier hand eczema increased the occurrence of hand dermatitis. Many subjects with hand eczema had suffered their first bout of eczema prior to the current wet work. The following figures for HHE in subjects with current hand eczema were found: AD 68%, AMS 45%, NA 42%, HMD 55% and without HMD 42%. Thus 46% of all subjects with current eczema had had hand eczema before the observation period.
<table>
<thead>
<tr>
<th>Hand eczema (20 months)</th>
<th>Total</th>
<th>AD</th>
<th>AMS</th>
<th>NA</th>
<th>HMD</th>
<th>No HMD</th>
<th>HHE</th>
<th>No HHE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>1857</td>
<td>194</td>
<td>227</td>
<td>1436</td>
<td>487</td>
<td>1342</td>
<td>410</td>
<td>1423</td>
</tr>
<tr>
<td>Current hand eczema (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>by questionnaire</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- medical consultations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- sick-leave</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- terminations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AD = atopic dermatitis with or without mucosal symptoms
AMS = atopic mucosal symptoms
NA = non-atopics
HMD = history of metal dermatitis
HHE = history of earlier hand eczema

Table IV. Current hand eczema in 1857 women in 'wet' hospital work
Figure 1. Predicted relative odds ratio for hand eczema in atopics and non-atopics in the occupational groups. NA, AMS and AD as defined in Table III.

Multivariate regression analysis of risk factors. In the regression analysis named A1 the following factors were found to significantly influence the occurrence of hand eczema: atopic dermatitis ($F=54$, $p<0.0001$), occupation ($F=14.4$, $p<0.0001$). Figure 1
shows a summarized schematic description of the predicted relative odds ratios of developing hand eczema for atopics and non-atopics in the four occupations. Subjects with atopic dermatitis showed odds approximately three times higher than non-atopics in both wet and dry work. Nursing staff showed odds approximately three times higher than caretakers/craftsmen and twice as high as office workers. The group termed caretakers/craftsmen was small and the prediction is therefore uncertain in this group. The predicted probability of hand eczema for this analysis ranges from 16% in non-atopic caretakers/craftsmen to 62% in nursing staff with atopic dermatitis (Table V).

Table V. Predicted relative odds ratios (OR) and predicted probability (PP) for hand eczema in the occupational groups

<table>
<thead>
<tr>
<th></th>
<th>NA</th>
<th>AMS</th>
<th>AD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>PP %</td>
<td>OR</td>
</tr>
<tr>
<td>Nursing staff</td>
<td>3.2</td>
<td>37</td>
<td>4.1</td>
</tr>
<tr>
<td>Kitchen workers/ cleaners</td>
<td>2.7</td>
<td>33</td>
<td>3.5</td>
</tr>
<tr>
<td>Office workers</td>
<td>1.5</td>
<td>22</td>
<td>2.0</td>
</tr>
<tr>
<td>Caretakers/ craftsmen</td>
<td>1.0</td>
<td>16</td>
<td>1.3</td>
</tr>
</tbody>
</table>

AD, AMS, NA as defined in Table III.
In the regression analysis named A2 the following factors significantly increased the occurrence of hand eczema: atopic dermatitis (F=54, p<0.001), occupation (F=14.4, p<0.0001), children younger than four years old (F=13.9, p<0.001) and lack of dish-washing machine (F=8.6, p<0.05). From the population in this analysis 16.4% had children younger than 4 years old and 70.4% had no dish-washing machine. Figure 2 shows the odds ratios for hand eczema in atopics and non-atopics in the different occupations when consideration was taken of the importance of the significant domestic parameters. The predicted odds for the most favourable and the most unfavourable combinations of the two significant domestic parameters in the occupations have been outlined. The odds for hand eczema in an occupation is twice as high for subjects with the most unfavourable combination of domestic factors as for subjects with the most favourable combination. Office workers with an unfavourable combination of domestic parameters show as great a risk of developing hand eczema as wet workers with a favourable combination of home factors. Wet work in combination with unfavourable domestic factors increased the odds by four times compared to dry work and a favourable combination of domestic factors. The predicted probability of hand eczema for this analysis ranges from 18% in non-atopic office workers with the most favourable combination of domestic factors to 72% in nursing staff with atopic dermatitis and the most unfavourable combination of domestic factors (Table VI).
Figure 2. Predicted relative odds ratios for hand eczema in atopics with the most favourable and unfavourable combinations of domestic work. NA, AMS and AD as defined in Table III.
Table VI. Predicted odds ratios (OR) and predicted probability (PP) for hand eczema in atopics and non-atopics with the most favourable and unfavourable combinations of significant domestic factors.

<table>
<thead>
<tr>
<th></th>
<th>NA OR</th>
<th></th>
<th>AMS OR</th>
<th></th>
<th>AD OR</th>
<th></th>
<th>OR PP %</th>
<th></th>
<th>OR PP %</th>
<th></th>
<th>OR PP %</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Nursing staff +C -D</td>
<td>4.1</td>
<td>48</td>
<td>5.5</td>
<td>55</td>
<td>11.4</td>
<td>72</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kitchen/cleaning +C -D</td>
<td>3.5</td>
<td>44</td>
<td>4.6</td>
<td>50</td>
<td>9.5</td>
<td>68</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nursing staff -C +D</td>
<td>2.1</td>
<td>32</td>
<td>2.7</td>
<td>38</td>
<td>5.6</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Office workers +C -D</td>
<td>2.0</td>
<td>31</td>
<td>2.6</td>
<td>37</td>
<td>5.5</td>
<td>55</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kitchen/cleaning -C +D</td>
<td>1.7</td>
<td>28</td>
<td>2.3</td>
<td>34</td>
<td>4.7</td>
<td>51</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Office workers -C +D</td>
<td>1.0</td>
<td>18</td>
<td>1.3</td>
<td>23</td>
<td>2.7</td>
<td>38</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

+C = children < 4 years old  
-C = no children < 4 years old  
+D = dish-washing machine  
-D = no dish-washing machine

In the regression analysis called A3 the following factors were found to influence the occurrence of hand eczema: history of earlier hand eczema (F=540, p<0.0001), history of metal dermatitis (F=68, p<0.001) and atopic dermatitis (F=38, p<0.001). Figure 3 shows the interrelation of HHE, HMD and atopy in a summarized schematic description of the predicted relative odds ratios of hand eczema. HHE increased the odds by 12.9 times and created a subdivision of the population into two groups which differ considerably as regards risk of developing hand dermatitis. HMD further increased the odds by 1.8 times and AD and AMS by another 1.3 times. The predicted probability of hand eczema in this analy-
sis ranges from 24% in non-atopic subjects without HMD and without HHE to 91% in subjects with AD, HMD and HHE (Table VII).

Figure 3. Relative odds ratios for hand eczema in the various groups during 20 months of 'wet' hospital work. HHE = history of hand dermatitis; AD, AMS, NA as in Table III; HHE, HMD as in Table IV.
Table VII. Predicted relative odds ratios (OR) and predicted probability (PP) for hand eczema and its consequences in women in wet work.

<table>
<thead>
<tr>
<th></th>
<th>Hand eczema</th>
<th>Medical consultation</th>
<th>Sick-leave</th>
<th>Changed work</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>PP%</td>
<td>PP%</td>
<td>PP%</td>
</tr>
<tr>
<td>AD</td>
<td>31</td>
<td>91</td>
<td>57</td>
<td>14</td>
</tr>
<tr>
<td>AMS</td>
<td>31</td>
<td>91</td>
<td>42</td>
<td>5.6</td>
</tr>
<tr>
<td>HMD-NA</td>
<td>23.1</td>
<td>88</td>
<td>28</td>
<td>5.6</td>
</tr>
<tr>
<td>AD</td>
<td>17.3</td>
<td>84</td>
<td>53</td>
<td>6.6</td>
</tr>
<tr>
<td>AMS</td>
<td>17.3</td>
<td>84</td>
<td>37</td>
<td>2.6</td>
</tr>
<tr>
<td>HHE-No HMD-NA</td>
<td>12.9</td>
<td>80</td>
<td>25</td>
<td>2.6</td>
</tr>
<tr>
<td>AD</td>
<td>2.4</td>
<td>43</td>
<td>48</td>
<td>22</td>
</tr>
<tr>
<td>AMS</td>
<td>2.4</td>
<td>43</td>
<td>34</td>
<td>9.5</td>
</tr>
<tr>
<td>HMD-NA</td>
<td>1.8</td>
<td>36</td>
<td>22</td>
<td>9.5</td>
</tr>
<tr>
<td>AD</td>
<td>1.3</td>
<td>30</td>
<td>44</td>
<td>11</td>
</tr>
<tr>
<td>AMS</td>
<td>1.3</td>
<td>30</td>
<td>30</td>
<td>4.3</td>
</tr>
<tr>
<td>No HHE-No HMD-NA</td>
<td>1.0</td>
<td>24</td>
<td>19</td>
<td>4.3</td>
</tr>
</tbody>
</table>

Medical consultation: AD p<0.001, HHE p<0.01
Sick-leave: AD p<0.01, HMD p<0.05
Changed work: AD p<0.01

Severity of hand eczema. The consequences of the current hand eczema in women in wet work as regards medical consultation, sick-leave and termination of work due to hand eczema were analyzed statistically. It was found that AD (F=35.4, p<0.001) and HHE (F=9.4, p<0.01) increased the need for medical consultation. Atopic dermatitis (F=6.7, p<0.01) and HMD (F=6.1, p<0.05) in-
creased sick-leave and AD (F=7.3, p<0.01) increased the terminations due to hand eczema. The predicted probability of medical consultation, sick-leave and termination were found within the following ranges: medical consultation 19-57%, sick-leave 2.6-22%, termination 3.9-14% (figures as a percentage of the total number for current hand eczema). Figures for medical consultation, sick-leave and termination in the various groups are given in Table VII. Table VIII shows that vesicular lesions, permanent symptoms and onset within four months were significantly more common in subjects with atopic dermatitis. 'Dry and chapped skin with rashes and small cracks' was recorded as the only symptom of the current hand eczema in 24% of subjects with atopic dermatitis, in 43% of subjects with atopic mucosal symptoms (p<0.01 vs AD) and in 46% of the non-atopics (p<0.01 vs AD).

Table VIII. Severity of hand eczema

<table>
<thead>
<tr>
<th></th>
<th>AD</th>
<th>AMS</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of employees with</td>
<td>145</td>
<td>119</td>
<td>634</td>
</tr>
<tr>
<td>hand eczema</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Vesicular lesions</td>
<td>44</td>
<td>22**</td>
<td>22***</td>
</tr>
<tr>
<td>Permanent symptoms</td>
<td>20</td>
<td>10*</td>
<td>6.1***</td>
</tr>
<tr>
<td>Onset of hand eczema with</td>
<td>76</td>
<td>59**</td>
<td>54***</td>
</tr>
<tr>
<td>the first 4 months of occupation</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*) p<0.05, versus AD; **) p<0.01, versus AD; ***) p<0.001, versus AD
Investigated patients (III). Past or present atopic dermatitis with or without mucosal symptoms was found in 46% of the subjects. Atopic mucosal symptoms without a history of atopic dermatitis were seen in 12% and 42% were considered non-atopics. A history of metal dermatitis appeared in 41%.

Earlier hand eczema in investigated patients. Hand eczema prior to current employment occurred in 66.7% of the subjects. No difference was found between atopics and non-atopics in the occurrence of previous hand eczema. The time lapse since the onset of earlier hand eczema ranged from 4 months to 30 years (mean 5 years). The periodicity of earlier hand eczema was characterized as once or twice in 7.5%, sometimes in 52.5%, often in 39.8% and permanently in none. Occupation at the time of onset of the earlier eczema was given as wet work by 40.1%, industrial work by 4.2% and dry work by 16.2%, while 39.4% did not connect the onset of hand eczema with any occupation.

Current hand eczema in investigated patients. The current hand eczema was considered by 92.3% of the employees to be elicited by external contacts. Water, cleaning agents, physical factors, disinfectants, food stuffs and the wearing of gloves were the most commonly reported causes. Contact with eliciting factors was considered to take place mostly at work by 57.2%, equally at work and at home by 21% and mostly at home or in leisure time by 13.8% of the patients. A history of contact urticaria was reported by 49/142 (34.5%) and was more common after exposure to substances in the home. Various kinds of food, cleaning agents and animals were
most commonly considered to provoke contact urticaria at home and in leisure time. The agents most commonly reported at work were cleaning agents, vegetables and rubber gloves.

State of current hand eczema. At the time of the investigation, 100/142 patients had eczema of the hands. Recent hand dermatitis, without clinical signs of ongoing eczema except for minor erythema and dry or chapped skin, was seen in 42/142 patients. The following sites of the current hand eczema were noted: interdigital and dorsal aspects of the fingers 82%, palms of fingers 32%, dorsa of hands 41%, palms of hands 28% and finger-tips 15%. Vesicles were present in 43%, erosions and/or crusts in 33% and lichenifications in 11%. The lesions itched in 61% of the patients with ongoing hand eczema.

The clinical picture was described as a red vesicular scaly eczema in 93%, finger-tip eczema in 6% and neurodermitis in 1%. Ongoing eczema at sites other than the hands was seen in 35/142 (24.6%). Atopic eczema was present in 23, metal dermatitis in 4, seborrhoic eczema in 3, neurodermitis in 2, ichthyosis with eczema in 1, external otitis in 1 and nummular eczema in 1 patient. From these figures, it is obvious that approximately 1/3 of the patients with atopic dermatitis and hand eczema had manifestations at other sites.

The exogenous causes of current hand eczema were judged to be mostly (>50%) of occupational origin in 72%. Of the subjects investigated, 14.8% were on sick-leave for some period because of current hand eczema.
Contact allergy. Delayed contact sensitivity was found in 45 of the 120 patients tested. There were 71 positive tests, of which 54 were relevant. The allergens are listed in order of decreasing frequency in Table IX. Of the patients tested, 68 were atopics and 52 non-atopics. No significant difference between them was seen in the total number of positive tests or in reactions to nickel. Nickel and/or cobalt allergy was found in 25 of the 45 patients with contact allergy. Of all the women tested 83% had had their ears pierced. Contact allergy to nickel was found in 18/88 (20.5%) of those with pierced ears and in 1/18 (5.6%) of those without pierced ears. The difference is significant (p<0.05).

Table IX. Positive patch test reactions in 120 patients

<table>
<thead>
<tr>
<th></th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>nickel</td>
<td>18.2</td>
</tr>
<tr>
<td>cobalt</td>
<td>7.4</td>
</tr>
<tr>
<td>balsam of Peru</td>
<td>5.8</td>
</tr>
<tr>
<td>carba mix</td>
<td>4.1</td>
</tr>
<tr>
<td>formaldehyde</td>
<td>4.1</td>
</tr>
<tr>
<td>benzalkonium chloride</td>
<td>4.1</td>
</tr>
<tr>
<td>PPD mix</td>
<td>3.3</td>
</tr>
<tr>
<td>wood tars</td>
<td>3.3</td>
</tr>
<tr>
<td>thiuram mix</td>
<td>2.5*</td>
</tr>
<tr>
<td>caine mix</td>
<td>1.8*</td>
</tr>
<tr>
<td>fragrance mix</td>
<td>1.8</td>
</tr>
<tr>
<td>colophony</td>
<td>1.7</td>
</tr>
<tr>
<td>chromium</td>
<td>1.7</td>
</tr>
<tr>
<td>P-phenylenediamine</td>
<td>0.8</td>
</tr>
</tbody>
</table>

*) As a % of 55 patients tested.

A history of metal dermatitis was found in 33/68 (48.5%) of the atopics and 18/52 (34.6%) of non-atopics, the difference not being significant. Of 51 patients with a history of metal dermatitis, a
positive patch test to nickel and/or cobalt was obtained in only 19/51 (37.3%). The corresponding figure for atopics was 12/33 (36.4%) and for non-atopics 7/18 (38.9%). Among subjects with no history of metal dermatitis, a positive test to nickel and/or cobalt was found in 4/35 (11.4%) of the atopics and 2/34 (5.9%) of the non-atopics.

In only 2 out of 10 patients allergic to rubber chemicals was there a clear correlation between occupational exposure to rubber gloves and the current hand eczema.

Many patients suspected that they had contact allergy prior to patch testing and had tried to avoid the allergens. Although minor exposure of the hands to the different allergens was common, few patients thought that contact allergy played any significant role as a cause of the current episode of hand eczema.

Contact urticaria. Tables X and XI (113-135) show the figures and relevance for positive prick tests. Substances which occur in the agents tested and known from the literature to elicit contact urticaria have been listed in the tables. One or more positive prick test reactions were seen in 32 out of 41 patients tested. In 22, the positive test(s) was relevant. The total number of positives was 68 and the relevance to contact urticaria on normal or dermatitic skin was 32/68.
Table X Positive prick test reactions in 41 patients tested with the hospital series

<table>
<thead>
<tr>
<th></th>
<th>No.pos</th>
<th>Relevance</th>
<th>Urticariogenic substances (references in brackets)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>(A) Simple chemicals</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>formaldehyde 2%</td>
<td>11</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>benzalkonium chloride 0.1%</td>
<td>5</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>isopropyl myristate 20%</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>(B) Complex chemicals</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>green rubber glove</td>
<td>8</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>paper towel</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>liquid soap (Blido)</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Emollients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calmuril</td>
<td>4</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Atrix</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Helosan</td>
<td>2</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Sumabless</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Disinfectants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hibiscrub</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>hand spirit</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>M spirit</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(*) A complete declaration has not been received from the manufacturer.
Relevance: 1=positive, 2=probable, 3=doubtful
Table XI. Positive prick test reactions in 41 patients tested with substances reported by history as eliciting contact urticaria

<table>
<thead>
<tr>
<th>Substances</th>
<th>No.pos</th>
<th>Relevance</th>
<th>Urticariogenic substances (references in brackets)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>potato</td>
<td>4</td>
<td>4</td>
<td>(125-129)</td>
</tr>
<tr>
<td>tomato</td>
<td>3</td>
<td>3</td>
<td>(88, 129)</td>
</tr>
<tr>
<td>carrot</td>
<td>1</td>
<td>1</td>
<td>(123, 129)</td>
</tr>
<tr>
<td>pear</td>
<td>1</td>
<td>1</td>
<td>(130)</td>
</tr>
<tr>
<td>orange</td>
<td>1</td>
<td>1</td>
<td>(131)</td>
</tr>
<tr>
<td>Proteins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>milk</td>
<td>2</td>
<td>2</td>
<td>(132)</td>
</tr>
<tr>
<td>meat</td>
<td>1</td>
<td>1</td>
<td>(88, 90, 133)</td>
</tr>
<tr>
<td>fish</td>
<td>1</td>
<td>1</td>
<td>(88, 134, 135)</td>
</tr>
<tr>
<td>Animals</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cat hair</td>
<td>1</td>
<td>1</td>
<td>(136)</td>
</tr>
<tr>
<td>dog hair</td>
<td>1</td>
<td>1</td>
<td>(136)</td>
</tr>
<tr>
<td>Chemicals</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cleaning agents (Rent Extra)</td>
<td>2</td>
<td>2</td>
<td>perfumes (121-123)</td>
</tr>
<tr>
<td>emollient (HTH)</td>
<td>1</td>
<td>1</td>
<td>perfumes (121-123), cetyl alcohol (124)</td>
</tr>
</tbody>
</table>

Relevance: as in Table X.
In 24 atopics a total of 46 positive prick tests was seen, and in 17 non-atopics 22. Although the figure in the atopics was higher, the difference is not significant.

Most patients with relevant contact urticaria were aware of it prior to testing, and if possible they avoided the substances responsible. Some with a positive test for the complex chemicals in the hospital screening series remembered a history of immediate reaction on the hands especially on dermatitic skin. In a small number of patients, predominantly those who reacted to rubber and disinfectants, immediate urticarial reaction caused real problems because of the difficulty of avoidance. In two patients, prick tests were positive to both benzalconium chloride and the emollient Helosan which contains it.

**Morphology of hand eczema in the bacteriological study (IV).** The eczematous lesions sampled showed the following morphology before treatment: erythema with papules and/or infiltration was noted in 20/20, vesicles in 16/20, erosions, fissures and crusts were seen alone or in combination in 14/20, signs of clinical infections with exudation and yellow crusts were seen in 3/20. Because of the localization of the eczematous lesions a majority (43/56) of all samples taken at the first visit were from fingers and only 13/56 from other parts of the hands. The extent of the eczematous lesions was estimated as small in 4/20, medium in 14/20 and large in 2/20 patients. Nine of the patients were on sick-leave during treatment. At follow-up the eczematous lesions were suppressed and the skin was essentially normal-looking in 18/20 patients and in the other 2/20 patients the eczema was much improved.
Table XII. Frequency of isolated bacteria before and after topical treatment with clobetasol propionate

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Eczema n = 20</th>
<th>Erythema n = 16</th>
<th>Normal skin n = 20</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>Before</td>
</tr>
<tr>
<td><strong>Aerobes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>18</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>S. epidermidis</td>
<td>6</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>S. warneri</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>S. cohnii</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>S. capitis</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>S. hominis</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>S. hemolyticus</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>S. saprophyticus</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Micrococcus species</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Corynebacteria</td>
<td>0</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Coliform bacteria</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Peptostreptococci</td>
<td>8</td>
<td>11</td>
<td>10</td>
</tr>
</tbody>
</table>

1) lipophilic
2) non-lipophilic
3) all isolates from the non-atopic group of patients
4) after treatment skin was normal-looking in 18/20 patients
Microbial flora and effect of treatment. The incidence of the isolated organisms is shown in Table XII. Before treatment the incidence of \textit{S. aureus} in eczema was 18/20, in erythema 13/16 and in normal skin 8/20. Treatment with clobetasol propionate reduced the incidence of \textit{S. aureus} in the three sampling sites to 6/20, 4/16 and 2/20 respectively.

Table XIII. Bacterial counts expressed as colony forming units (CFU) before and after topical treatment with clobetasol propionate

<table>
<thead>
<tr>
<th></th>
<th>Staphylococcus aureus</th>
<th>Other aerobes</th>
<th>Anaerobes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CFU/cm²</td>
<td>CFU/cm²</td>
<td>CFU/cm²</td>
</tr>
<tr>
<td>Normal skin</td>
<td>Before</td>
<td>1.7 ± 0.9</td>
<td>2.1 ± 0.9</td>
</tr>
<tr>
<td>n = 20</td>
<td>After</td>
<td>1.1 ± 0.3</td>
<td>1.9 ± 0.7</td>
</tr>
<tr>
<td>Erythema</td>
<td>Before</td>
<td>3.4 ± 1.4</td>
<td>2.5 ± 0.9</td>
</tr>
<tr>
<td>n = 16</td>
<td>After</td>
<td>1.3 ± 0.6</td>
<td>2.1 ± 0.7</td>
</tr>
<tr>
<td>Eczema</td>
<td>Before</td>
<td>4.8 ± 1.5</td>
<td>2.4 ± 1.2</td>
</tr>
<tr>
<td>n = 20</td>
<td>After**</td>
<td>1.3 ± 0.6</td>
<td>2.4 ± 0.8</td>
</tr>
</tbody>
</table>

* 10. log, geometric mean ± SD
** after treatment skin was normal-looking in 18/20 patient
The bacterial geometric mean counts/cm² before and after treatment are shown in Table XIII. The mean density before treatment of *S. aureus* in eczema was 56 000 cfu/cm², in erythema 2 600 cfu/cm² and in normal skin 45 cfu/cm². The mean count of *S. aureus* in the three sites differs significantly (p<0.01). Treatment reduced the counts of *S. aureus* in the three sampling sites significantly: in earlier eczema to 22 cfu/cm² (p<0.001), in previous erythema to 21 cfu/cm² (p<0.001) and in normal skin to 13 cfu/cm² (p<0.05). The occurrence of other aerobes or anaerobes did not differ significantly in the three sampling sites before treatment. Nor was there a significant reduction in the geometric mean count of these bacterial groups in the three sites after treatment.

Before treatment *S. aureus* constituted 89% of the total aerobic flora in eczema, 73% in erythema and 41% in normal skin. After treatment *S. aureus* constituted 21% of the total aerobic flora in eczema, 22% in erythema and 24% in normal skin. Before treatment *S. aureus* was found in densities exceeding $10^5$ cfu/cm² in the eczematous lesions of 15 patients. Only 1 patient had more than $10^6$ cfu/cm². The three patients with clinical signs of infection had the following counts for *S. aureus*: $3.0 \times 10^5$, $3.2 \times 10^5$ and $2.3 \times 10^6$ cfu/cm². The two patients who did not carry *S. aureus* in their eczematous lesions were non-atopics. The mean count for *S. aureus* in the atopics did not differ significantly from the counts that were found in the non-atopics.
Fifty freshly isolated clinical strains of *S. aureus* were tested for the antibacterial effect of clobetasol propionate *in vitro*. No inhibitory effect of the substance was demonstrated in the dose range tested.
DISCUSSION

The cohort and patients studied. The cohort in this study was dominated by young women newly employed in four Swedish hospitals. Therefore the conclusions may be considered relevant only for similar individuals in similar working conditions. However, as the individual factors were found to be most important in the etiology of hand eczema, the main findings are probably significant for young women in the general population.

The patients with hand eczema who were clinically investigated are not representative of the general population. These patients represent the top of the epidemiologic iceberg of hand eczema and risk individuals are overrepresented. This indicates that it is not possible to draw uncritical conclusions of the nature of hand eczema in the population from a selected group of patients.

This study shows that most eczemas are mild, periodic, often self-limiting and in many cases they can be dealt with by self-treatment measures.

The patients with hand eczema in the bacteriological study were consecutive out-patients in a dermatologic department and were not selected except according to the exclusion criteria and the acceptance requirements for participation in this particular study.

Methodological aspects. The prospective cohort study design used in this investigation has many advantages over retrospective
epidemiologic studies. The design makes it possible to quantitate and compare the relative importance of individual and environmental factors. Furthermore it is possible to follow the first period of employment in a risk occupation. It must be assumed that this period provides the most suitable opportunity for revealing individual differences as regards the risk of developing hand eczema. Various measures with the passage of time will probably equalize the differences between the groups. Thus patients with hand eczema will reduce irritant exposure, use emollients or topical cortico-steroids and high risk individuals especially will change their work and get lost in retrospective studies.

Follow-up in the cohort study was done by questionnaire. The final questionnaire was designed after a pilot-study on 400 employees using a test questionnaire. The total response rate to the follow-up questionnaire was acceptable and the partial drop-out rate for the various questions was limited to a few percent.

It was not possible to study the prevalence of hand eczema by means of clinical examination of each episode of eczema for the whole cohort over a period of 20 months. Therefore, we had to rely on anamnestic information about hand eczema given in the follow-up questionnaire. The combination of information about the symptomatology of hand eczema given before employment followed by a questionnaire was found to be a reliable way of diagnosing hand eczema.
Atopy has been diagnosed exclusively by case history. This imposes limitations, but it is simple and practically useful in a large epidemiological study. As no absolute diagnostic criteria for atopic disease exist we have accepted this compromise.

Prevalence of hand eczema. The prevalence of hand eczema in women prior to their current employment in wet work was 22.4% which corresponds to the figure found in a study of a randomized sample of Danish women (5). Thus any selection of the studied cohort regarding previous hand eczema is unlikely.

The prevalence of hand eczema amongst those engaged in wet hospital work in this study is similar to the one found by Lammintausta (6). Lower prevalence figures have been found in other studies (47, 137, 138). The possible reasons for these discrepancies have been given earlier. The low figure for the occurrence of hand eczema in occupations dominated by men verifies previous findings of the sex difference (1-4).

Prevalence of atopy and metal dermatitis. The prevalence figures for atopy obtained in our study are somewhat higher than the 15.1% found by Kjellman (11) in a study where he questioned 7-year-old children in Sweden. Several investigations exist and varying figures for atopy have been found (6).

The high figure for metal dermatitis may be explained by the fact that the cohort consists predominantly of young women with common exposure to metals.
Individual risk factors for hand eczema. When atopic dermatitis was used as a risk factor for developing hand eczema without considering either previous hand eczema or metal dermatitis it was found to increase the odds approximately three times. This increase was seen in wet as well as in dry work. The figures for hand eczema among wet work employees with atopic dermatitis are similar to those found in a previous study (6).

The regression analysis on women in wet work clearly demonstrated the great importance of information about earlier hand eczema and metal dermatitis. It is obvious that many individuals with earlier hand eczema will suffer from recurrence if they are engaged in wet work. These high risk individuals constitute approximately half of the subjects with AD, one quarter of the subjects with AMS and one fifth of the non-atopics.

One possible explanation for the great importance of earlier hand eczema is that there is an endogenous characteristic of the skin, a skin vulnerability factor, which predisposes the person to develop irritant hand dermatitis. As the population consists of women, it may be assumed that they have been exposed to some degree of irritant occupational and domestic work in the past which sometimes, but not always, may have caused hand eczema. Thus earlier hand eczema may be considered a major indicator of this endogenous factor, which may correspond to the 'atopic skin diathesis' as defined by Lammintausta. This assumption is supported by Lammintausta who identified 'atopic skin diathesis' in 1/3 of the subjects with AMS and in 19% of the non-atopics. Atopic skin
diathesis involved a significantly increased risk of developing hand eczema. No identification of this atopic skin diathesis was made in subjects with atopic dermatitis. It was, however, found in both Lammintausta's and Rystedt's studies that a considerable number of employees with atopic dermatitis had managed to work in wet occupations without developing hand eczema. In the present study 39% of the subjects with AD reported no occurrence of hand eczema and these were predominantly subjects without earlier hand dermatitis.

The importance of endogenous factors in the etiology of hand eczema in subjects with atopic dermatitis is underlined in a study by Rystedt (9). In a report by Forsbeck et al. (28) it was found that 50% of the subjects with AD and current eczema had their first bout of eczema prior to their first employment. In another retrospective study on occupational dermatosis it was found that the relative odds of developing occupational skin diseases were calculated to be 13.5 times higher in atopics than in non-atopics (139).

There are other possible explanations for the great importance of a history of hand eczema. For example hand eczema in the past may leave a non-restored skin barrier for a long time and thus increase the risk of recurrence (140, 141).

A correlation between hand eczema and a history of metal dermatitis could be found on two levels in this study. At both levels
HMD increased the odds by 1.8 times. According to the hypothesis presented, high-risk subjects are those with HMD and an inherited disposition to irritant hand eczema occurring predominantly in atopics. This hypothesis is supported by a finding by Peltonen (142) that almost all nickel sensitive females afflicted with hand eczema were atopics. Further support is provided by the finding that hand dermatitis in nickel sensitive females seems to follow one of two causes: mild and transient or chronic and disabling (143). In addition, it was reported that atopy made the prognosis for hand eczema worse in nickel sensitive women.

Severity of hand eczema. Most hand eczemas were mild with periodic symptoms and the employee could handle the disorder using self-treatment methods. Most subjects with hand eczema also managed to work during the observation period and the figures for sick-leave were very low in most groups thus confirming previous findings that most hand eczemas are mild (6).

Subjects with atopic dermatitis developed a more severe hand eczema than subjects with atopic mucosal symptoms and non-atopics. This difference in severity was not observed by Lammintausta (6) perhaps because her study was retrospective and subjects with atopic dermatitis who get severe hand eczema early on in their careers might have left their jobs and thus have been lost to the study.

Occupational and domestic factors in hand eczema. Wet work only doubled the odds of developing hand eczema over dry office work.
This difference between a high risk and a low risk occupation is unexpectedly small. One explanation may be that the population consists of women and it must be assumed that they are exposed to a considerable amount of irritant domestic work. Two anamnestically available parameters of domestic work namely 'nursing of children younger than 4 years old' and 'no dish-washing machine' were found to correlate significantly with the occurrence of hand eczema, probably because they increased the irritant load to above the average level. These findings verified the clinical experience that the nursing of small children often gives rise to hand eczema amongst women. Furthermore it seems justified to recommend the use of dish-washing machines to people suffering from hand eczema.

The relative importance of wet work may be greater in patients with a vulnerable skin factor. This assumption could not be documented in the present study as no comparison was possible between wet and dry work regarding previous hand eczema and metal dermatitis. However, the clinical investigation of the women in wet work with hand eczema supports this assumption as most of these high risk individuals claimed that their hand eczema had been elicited by trivial irritants.

Contact allergy and hand eczema. The patients with hand eczema who were patch tested had been exposed to the current wet work for 20 months at the most. Thus it must be assumed that sensitization in most patients with contact allergy must have occurred prior to the current work. This assumption is supported by the finding that
no sensitization occurred in connection with the specially designed hospital patch test series. Although sensitization has occurred earlier, hand eczema may recur after occupational or domestic exposure to relevant allergens. Nevertheless, most employees with contact allergy could not correlate the current episode of hand eczema to any obvious exposure to the allergen. It must however be emphasized that allergens such as nickel and balsam of Peru are very common in the environment and some exposure of the hands is inevitable. Delayed contact sensitivity was seen in 38% of the patients tested. In another study of hospital workers, a positive patch test was found in 38% of the patients who had consulted an occupational doctor, and in 26% of all patients tested who had earlier or current hand dermatitis (6). The frequency of contact allergy to individual allergens was essentially similar to that of a previous study of hospital wet workers with hand dermatitis (6). One probable reason for the high figure for nickel allergy is that the patients were predominantly young women, a large number of whom had pierced their ears, which greatly increases the risk of nickel allergy (144, 145). These findings were verified in the present study.

Contact allergy to metals in subjects with metal dermatitis

Contact allergy to nickel and/or cobalt was found in only 37.3% of the subjects with a history of metal dermatitis. In two previous studies, contact allergy to metals was found in 58% and 70% respectively, of women with a history of metal dermatitis (4, 5). A study by Boss & Menné (144) indicates that a history of metal dermatitis is relevant in most cases. They found that although
only 5/13 women with a history of metal dermatitis were allergic
to nickel, 12/13 developed dermatitis when exposed to the sus­
pected ear ring for 48 hours. The irritant effect of nickel is
one possible explanation for the non-allergic cause of metal
dermatitis (146). Patients in the present study were mainly women
with optimal exposure to metals through pierced ears. Furthermore,
atopics were overrepresented. In two recent studies it has been
shown that a positive history of metal dermatitis with negative
test is common in atopics (147, 148). These facts may explain the
high figure for non-allergic metal dermatitis.

Contact urticaria and hand eczema. Contact urticaria with a wheal-
and-flare reaction on normal skin is easily recognized by an
exposed individual and if possible he/she should avoid eliciting
agents. However, contact urticaria does not always appear in the
form of a distinct whealing reaction. In non-immunological contact
urticaria, the concentration and nature of the urticariogenic
substances particularly influence the strength of the reaction. A
low, suboptimal concentration may provoke erythema, while a high
concentration may provoke urticaria (79). Sometimes repeated
exposure may be necessary (113). Exposure of dermatitic skin may
elicit contact urticaria and thus the urticariogenic substances
may be of clinical relevance for dermatitic but not for normal
skin (88-90). The case histories of some patients indicated that
contact urticaria was relevant only for dermatitic skin on the
hands.
Prick tests have been performed to trace urticariogenic substances in the present study. A prick test should be interpreted as positive only with caution. However, substances which produce a positive prick test do have urticariogenic properties which may be of clinical relevance, especially in dermatitic skin if exposure is optimal.

In patients with a history of contact urticaria, prick testing was carried out for two different reasons. Firstly, anamnestically suspected agents were tested, and secondly a screening series was carried out with substances in common use at the hospital. The relevance of the positive reactions varies according to the two reasons for testing. When the test was motivated by the history, a positive result was relevant for contact urticaria. Judging the relevance of a positive prick test in the series is difficult. Some patients with a positive test did have a positive history, and for them the relevance seems obvious. In subjects with a negative history, a positive test is probably of less clinical significance. Some patients may, however, have had signs of weak immediate reactions on eczematous skin which have not been recognized as contact urticaria.

Most reports of contact urticaria are limited to one or a few cases. Little is known about the prevalence and the relevance in different populations with hand eczema (8). Figures in the present study indicate that contact urticaria may be common. Most of the different kinds of food which produced positive prick tests in this study are known from the literature to provoke contact urticaria.
Formaldehyde has been reported as a cause (113-115). A prick test with formaldehyde 0.1-0.6% produced a weak reaction in the study by Anderson & Maibach (113). The high concentration used in this study may explain the high frequency of positive tests. A laboratory assistant with occupational exposure to formaldehyde was the only patient with a relevant prick test.

Rubber is another well-known urticariogenic substance (116-119). Apart from natural latex, the glove tested contained zinc-diethyl-dithiocarbamate (ZDC) which may induce contact urticaria (120). The high frequency of positive prick tests may indicate a non-immunological urticariogenic effect of the glove. This is based on the fact that substances with non-immunological urticariogenic properties give rise to contact urticaria in a large number of exposed individuals (79). This view is supported by the common occurrence of skin complaints in connection with this particular glove. Apart from the rubber glove, few positive prick tests to the complex chemicals were found. Most of them contained one or more substances known to elicit contact urticaria. Further investigations are needed to identify the substance responsible and to clarify the nature and clinical significance of the positive tests found.

**Staphylococcus aureus in hand eczema.** This study shows that hand eczema in atotics as well as in non-atotics is regularly colonized by *S. aureus* in quantities similar to those found in atopic dermatitis (105). Severe atopic dermatitis has shown higher densities of *S. aureus* in some investigations (104, 149). Colonization by *S.
_Staphylococcus aureus_ seems to parallel the severity of the eczema and clinical signs of pyoderma are lacking in most cases in spite of _S. aureus_ counts >10⁵ cfu/cm². Absence of clinical pyoderma in spite of high counts of _S. aureus_ has also been found in studies on atopic dermatitis (104, 105).

The densities of _S. aureus_ after topical treatment with a potent corticosteroid were equal in normal skin and healing eczematous lesions and were similar to those found by McBride et al. (97) on the skin of normal hands. The density of other aerobes and anaerobes did not differ between eczematous lesion and normal skin before treatment and no significant changes were caused by the topical corticosteroid. These findings are in agreement with a study by Chan et al. (150) in which no significant difference in the microflora of normal skin was caused by the application of triamcinolone acetonide compared to white petrolatum base. The density of aerobes other than _S. aureus_ found in this study are similar to previous findings on the palms of healthy individuals (151).

All isolations of a lipophilic corynebacteria in our study were obtained from non-atopics. This is in accordance with a study by Aly et al. (105) on atopic dermatitis where no lipophilic corynebacteria were found in the lesions and very few on normal skin. From these observations it seems possible that atopic skin might differ from non-atopic skin in its colonization by lipophilic corynebacteria.
Intermittent treatment with clobetasol propionate during 14 days produced a highly significant reduction and sometimes elimination of *S. aureus*. A study by Leyden & Kligman (149) on atopic dermatitis showed a slight but non-significant reduction of *S. aureus* after one week's treatment with 0.25% fluocinolone acetonide. The higher mean count of *S. aureus*, the less potent steroid and the shorter treatment period in their study are all possible explanations for the difference found. Our findings also contrast with those of Marples, Rebora & Kligman (152) who studied the effect of triamcinolone acetonide 0.1% on the growth of a single *S. aureus* strain which had been inoculated in experimental skin lesions. This study found that the steroid suppressed the experimental lesions but did not influence the multiplication of the bacteria.

Normal skin has an efficient defence against foreign microorganisms. Many different mechanisms are of importance in this defence. In the eczematous lesion one or more of the defense mechanisms may be disturbed and favour the colonization of bacteria (153). The reason for the selective, heavy colonization of *S. aureus* in hand eczema is unknown. It is well-known, however, that protein A in the cell wall of *S. aureus* has a high affinity to IgG (154) and to fibronectin (155). Both IgG and fibronectin might be present in eczematous lesions, which in turn could favour staphylococcal colonization and multiplication. Therefore a suppression of the eczematous inflammation by the potent topical corticosteroid may eliminate the prerequisites for the colonization of *S. aureus* and offer a possible interpretation of our results.
Corticosteroids in therapeutic concentrations have been reported to inhibit the metabolism of certain microorganisms including *S. aureus* (156). However, this explanation is less likely since we were unable to demonstrate an inhibition of the growth *in vitro* of 50 different strains of *S. aureus* by clobetasol propionate in the dose range 16-2000 mg/ml.
SUMMARY AND CONCLUSIONS

1. The odds for developing hand eczema in wet occupations dominated by women (nursing/kitchen/cleaning work) was only approximately twice that of dry office work. Most eczemas even in wet work were mild and periodic and only a few gave rise to sick-leave. Many sufferers could handle the disorder using self-treatment measures.

2. An increase in the irritant domestic load on women's hands through nursing babies and the simultaneous lack of a dish-washing machine will increase the risk of hand eczema as much as a wet work.

3. A history of atopic dermatitis increased the odds of developing hand eczema approximately three times both in wet and in dry work. As a single factor information about previous atopic dermatitis was of limited value as a predictor of the risk of developing hand eczema.

4. For women with a previously manifested disposition towards hand eczema, the odds of developing hand eczema was 12.9 times higher than for those with no previous hand eczema if they go into wet hospital work. This increase in the risk of hand eczema was great and created a subdivision of atopics and non-atopics in a high risk group and a normal-risk group. Half the subjects with atopic dermatitis, one quarter of the subjects with atopic mucosal symptoms and one fifth of the non-atopics belonged to this high
risk group. This finding indicated that among atopics as well as non-atopics there are two subgroups which differ considerably regarding the risk of developing hand eczema.

5. A history of metal dermatitis increased the odds of developing hand eczema by a factor of 1.8. This increase was seen in individuals in one high risk and one normal risk level. Metal dermatitis may develop as a cause of contact allergy and probably through the irritant or other effects of metals. Metal dermatitis was more common in subjects with vulnerable skin.

6. Information about atopic disease as a supplement to information about previous hand eczema and metal dermatitis was of very limited value when predicting the risk of developing hand eczema in women who start wet work. One important observation was however that subjects with previous atopic dermatitis will suffer from a more severe hand eczema.

7. By means of simple anamnestic information about earlier hand eczema, metal dermatitis and atopic disease it was possible to obtain a very differentiated prognostic information about hand eczema and its consequences in women in wet hospital work.

8. In wet work employees with a disposition to hand eczema who seek medical advice for current hand eczema, trivial irritants in wet and domestic work played an important part in the etiology of the current hand dermatitis. Contact allergy and contact urticaria were fairly common. However, in most patients contact allergy and contact urticaria seemed to be of minor importance in the etiology of the hand eczema.
9. Hand eczema was commonly colonized by *S. aureus* in high counts in atopics as well as in non-atopics. The density of *S. aureus* was high even if the eczema showed no signs of clinical infection. Successful topical treatment of the eczema with a potent cortico-steroid significantly reduced or eliminated the colonization of *S. aureus*.
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