Susceptibility to hand eczema in high risk occupations: Contribution of genetic and environmental factors
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WET WORK AND HAND ECZEMA IN APPRENTICE NURSES; PART I OF A PROSPECTIVE COHORT STUDY

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ABSTRACT

Background /Objectives
Environmental exposure and personal susceptibility both contribute to development of hand eczema. Here, we report an investigation on wet work exposure and its influence on the risk of developing hand eczema in apprentice nurses.

Methods
A prospective cohort study was performed among 721 Dutch apprentice nurses. Participants recorded wet work exposure and symptoms of hand eczema using specially designed diary cards.

Results
For 533 apprentice nurses, a follow-up time of 1 – 3 years was completed. Diary cards were supplied by 383 students. The 1-year period prevalence of hand eczema was 23% in the first year, 25% in the second year and 31% in the third year of follow-up. Eighty-one new cases of hand eczema developed, most of which occurred during the first year of follow-up. In approximately one-third of the participants, wet work exposure exceeded the national guidelines. Frequent hand washing during traineeships [odds ratio (OR) 1.5; 90% confidence interval (CI) 1.0 – 2.3], frequent hand washing at home (OR 2.3; 90% CI 1.5 – 3.7) and having a side job involving wet work (OR 1.6; 90% CI 1.0 – 2.4) were independent risk factors for hand eczema.

Conclusion
As a considerable number of apprentice nurses had already developed hand eczema during traineeships, more attention should be paid to skin protection in vocational education.
INTRODUCTION

Occupational hand eczema is one of the most common occupational diseases in industrialized countries; it usually is a manifestation of irritant or allergic contact dermatitis, irritant contact dermatitis being the most common form in the workplace, accounting for 50-80% of the cases. A major cause of irritant contact dermatitis in the workplace is ‘wet work’, that is, frequent or long-lasting contact with water, soaps or detergents (e.g. during hand washing). Contact with disinfectants and prolonged wearing of occlusive gloves are also considered to be wet work. Other well-known occupational exposures able to cause irritant contact dermatitis are oils, lubricants and solvents. In occupations with high exposure to wet work or to other skin threatening agents, for example nursing, hairdressing, the printing industry and the metalworking industry, the 1-year prevalence of hand eczema was reported to be between 20% and 30%. In comparison, the 1-year prevalence found by (mainly Scandinavian) epidemiological studies among the general population between 18 and 69 years of age ranges from 9% to 14%.

Although skin exposure is a prerequisite for developing occupational hand eczema, the risk is influenced by personal susceptibility. A well-known personal risk factor for the development of occupational hand eczema is the presence of atopic dermatitis, a chronic inflammatory skin disease whose main symptoms are dry skin, itching, and erythematous lesions. A history of atopic dermatitis is currently used to identify susceptible individuals in occupational prevention programs in Germany and in the Netherlands. Furthermore, recent findings suggest that loss-of-function mutations in the gene encoding for the epidermal protein filaggrin (FLG) increase the risk of contact dermatitis via impairment of the skin barrier. Also, the effects of polymorphisms in genes encoding for inflammatory cytokines have been shown to be of influence. Incorporation of the examination of these newly discovered polymorphisms into existing susceptibility screening or in health surveillance programs used in high-risk occupations may contribute to a better identification of susceptible individuals and to personalized prevention. However, the effects of susceptibility genes are difficult to assess quantitatively, owing to the complex interplay between genetic polymorphisms, atopic dermatitis, and occupational exposure. We therefore aimed to gain more insight in the relative effects of personal susceptibility factors and exposure by using a prospective cohort study design.

Apprentice nurses were chosen as the study population, for two reasons. First, a population of apprentices is not, or is minimally, affected by a ‘healthy worker effect’ as compared with a population of workers with long-term occupational experience, where some of the susceptible individuals may have left the occupation because of the development of hand eczema. Second, the nursing occupation was chosen because nurses are known to have a relatively high exposure to wet work and an associated increased risk of hand eczema. Owing to hygiene regulations, nurses frequently have to wash and disinfect their hands. Exposure to water, disinfectants, soaps and occlusive gloves is common, as is contact with latex or medication ingredients, which may cause allergic contact dermatitis. The impact of hand eczema may be exceptionally
great in the healthcare sector, because nurses who have developed hand eczema have difficulties in maintaining hygiene standards; the application of disinfectant or soap to damaged skin can be painful, so affected nurses may try to lower the frequency of hand washing and disinfection. In addition, bacterial colonization (e.g. with *Staphylococcus aureus*) has been shown to be more prevalent on damaged skin than on intact skin. Thus, prevention of hand eczema is important not only for the workers, but also for hospital hygiene and infection prevention.

Our goal was to examine the influence of both wet work exposure and personal susceptibility factors on the risk of developing hand eczema in a prospective cohort study among apprentice nurses. Here, we present the baseline characteristics of this cohort, the exposure to wet work during follow-up, and the occurrence of hand eczema in relation to exposure. The influence of personal susceptibility factors is described elsewhere.

**METHODS**

**Subjects**

Subjects were recruited from 15 different Dutch schools that prepare students for a career in nursing or care-giving with intermediate vocational education (six schools) or higher vocational education (nine schools). Students were eligible for participation if they had recently started a traineeship with a duration of at least 10 weeks, or were expecting to do so within the next few weeks. No further inclusion criteria were applied. The only exclusion criterion was the presence of chronic inflammatory disease (e.g. psoriasis and rheumatoid arthritis), because these diseases and their respective treatments may interfere with the inflammatory skin reactions related to hand eczema. After permission had been obtained from the schools’ management boards, a school visit was organized, usually shortly before the start of the traineeships, during which the researchers informed the students about the study by means of a classroom presentation. Students were invited to participate in the study on a voluntary basis. A small gift was given for participation. Ethical approval was obtained from the Medical Ethical Committee of the Academic Medical Center, Amsterdam, The Netherlands.

**Baseline Questionnaire**

Students willing to participate filled in a questionnaire including items on demographic information, personal and family history of eczema, rhinitis, conjunctivitis and asthma, allergies and/or symptoms following exposure to dust, animals, pollen, foods, metals and wool, present or past skin diseases, presence of any chronic disease, medication use, present or past skin complaints regarding the hands or fingers, and exposure to wet work during previous jobs/apprenticeships, secondary jobs, and leisure or household activities. Atopy was defined as having experienced two or more of the following: symptoms following exposure to common allergens (respiratory or skin complaints after contact with animals, plants/pollens, dust, or food), rhinitis, conjunctivitis, or asthma.
Atopic dermatitis was assessed using the UK working party criteria ‘questions only’ definition, in which onset below 2 years of age was replaced by onset below 5 years of age as a proxy of ‘childhood dermatitis’. This modification was made to increase sensitivity according to the rationale of the International Study of Asthma and Allergies in Childhood (ISAAC). To explore the existence of selection bias, during a subset of school visits to six of 15 schools the questionnaire was completed by all apprentices regardless of their participation in the study.

**Wet work exposure during follow-up**

During their traineeships, the apprentices regularly recorded the wet work activities that they performed by using diary cards specifically designed for this purpose. These diary cards were pocket-sized, folding cards of thick paper, with multiple checkboxes on which wet work activities could be ticked off directly during a shift (see Supplementary file and Table 3 for the different wet work activities included on the diary cards). The cards were carefully made and were piloted in a small number of student nurses to make them as user-friendly as possible. One card was used for one shift; either morning, late shift, or night shift. In addition, questions on possible secondary jobs were present on the reverse side of the diary card.

The diary cards were sent to the apprentices periodically by regular mail. A set of two cards at a time plus a return envelope was sent every 2-4 weeks, depending on the length of the traineeship. The apprentices were free to choose the specific day and shift on which they filled in the diary card. If no cards had been returned near the end of the traineeship, participants were contacted by email or telephone to retrieve information about their last traineeship and possible symptoms retrospectively.

**Definition of outcome measures**

Skin symptoms of the hands or fingers were recorded simultaneously with the exposure data on the reverse side of the diary cards. Participants were asked to indicate whether they had experienced any of redness, scaling, itch, fissures, vesicles or papules on the hands or fingers, and whether these symptoms had lasted for > 3 days. Following the classification for screening proposed by Vermeulen et al., ‘hand eczema’ was defined as the presence of one or more of fissures and redness, fissures and itch, fissures and scaling, vesicles, or papules, plus a duration of > 3 days or recurrence (symptoms reported more than once).

As these criteria were developed for identifying cases of hand eczema in a working population, we were concerned that by using this definition, we would miss early-stage symptoms that may progress into hand eczema. Therefore, we used in addition a more lenient definition, ‘mild hand eczema’, defined as the presence of one or more of redness and itch, redness and scaling, itch and scaling, fissures and redness, fissures and itch, fissures and scaling, vesicles, or papules, all irrespective of duration or recurrence.
Without specification, (mild) hand eczema refers to any episode of (mild) hand eczema during follow-up. In some approaches, first episodes and recurrent episodes of hand eczema during traineeships are discerned, irrespective of the participant’s history of hand eczema at inclusion. A first episode of hand eczema in a student without hand eczema history up to inclusion is equivalent to ‘incident hand eczema’. As the exact date of onset of hand eczema was often not known (owing to the fluctuating course of the symptoms and spot-check-like sampling methods of the diary cards), the presence of hand eczema was treated as a binary variable during each traineeship. In the calculation of incidence rates, the length of a participant’s traineeship was used as an equivalent for person-years in the denominator. Participants who had developed hand eczema during their first traineeship were excluded from the calculation of incidence rates during the second traineeship, etc.

**Consultation of occupational physician by students with suspected hand eczema**

Students who reported symptoms of hand eczema at inclusion or during follow-up received an invitation for a free consultation by an occupational physician specializing in dermatology problems. Depending on the student’s preferences, either a visit or a telephone consultation was arranged. If possible, telephone consultations were supported by photographs of the skin symptoms provided by the student. The occupational physician diagnosed the skin condition according to a standardized protocol, taking into account morphology and indications for aetiology (atopic dermatitis, exposure to irritants and allergens). Possible diagnoses were:

- Irritant contact dermatitis, specified according to the presence or absence of concomitant atopic dermatitis,
- Allergic contact dermatitis, specified according to the presence or absence of concomitant atopic dermatitis,
- Atopic dermatitis,
- Combination of irritant-, and allergic contact dermatitis, specified according to the presence or absence of concomitant atopic dermatitis,
- Other.

If allergic contact dermatitis was suspected, the apprentice nurse was referred to a hospital dermatology department specializing in occupational dermatology and allergy (Department of Dermatology, VU University Medical Centre, Amsterdam, The Netherlands). In addition, the apprentices received advice on preventive measures and skin care.

**Final questionnaire**

At the end of the study period of 3 years, an email questionnaire was sent to all apprentices who were still participating in the study. This final questionnaire included
items on symptoms experienced during follow-up, localization, duration, recurrence and date of first occurrence of the symptoms, consultation of general practitioners or dermatologists, changes in hand hygiene behaviour as a result of symptoms, changes in hand hygiene behaviour as a result of participation in the study, use of protective hand cream, information on traineeships and side jobs, and smoking. Participants who did not respond to the email questionnaire after up to three reminders received a paper version.

**Statistical analysis**
Demographic characteristics, prevalence of atopic dermatitis, rhinitis or asthma and prevalence of hand eczema symptoms at baseline were compared between participants and non-participating classmates by calculating the percentage differences and 95% confidence intervals (CIs) based on a binomial distribution.

For the analysis of associations between exposure factors and the presence of (mild) hand eczema during follow-up, data from the exposure cards were used. For each apprentice, the data of each wet work activity from all cards of one traineeship were averaged, and the mean values per person were subsequently used in a mixed models design. Hand eczema is a disease with a fluctuating course, and the recovery time may be as short as a few days. Thus, the apprentice nurses would have time to recover from hand eczema in between traineeship periods. We therefore assumed that the probability of hand eczema developing in one traineeship does not depend on the exposure in previous traineeships. Each traineeship of one participant was therefore counted as a separate entity, and data from participants who entered a second or a third traineeship were entered as multiple records in the database. This, however, results in the problem that, regardless of susceptibility, participants who contributed data for multiple traineeships would have had more opportunities to develop hand eczema than those who had been followed for only one traineeship. Therefore, a mixed models design was used in the analyses, with participant identification number included as random effect (procedure GENLINMIXED in SPSS™). In such a mixed model, the within-subject correlation is taken into account. First, univariate mixed models were performed with each exposure factor separately as independent variable. Exposure factors showing a $p$-value of $< 0.20$ were included in a multivariate mixed model. In the univariate and multivariate mixed models, 90% CIs were used as these correspond to one-sided testing with $p < 0.05$.

**RESULTS**

**Subject characteristics and follow-up**
Between September 2008 and February 2011, a total of 728 apprentices signed up to participate in the study. Seven were excluded because of chronic inflammatory disease, leaving a cohort size of 721. The characteristics of the study population at
baseline are shown in Table 1. In addition, Table 1 includes a comparison of participants and non-participants in a subset of six schools. A history of atopic dermatitis, rhinitis, and asthma and lifetime prevalence of hand eczema were significantly more prevalent in participants. Reporting of hand eczema symptoms at baseline was significantly associated with a history of atopic dermatitis, rhinitis and asthma (data not shown). Associations between hand eczema and personal susceptibility factors are presented in Part II of this cohort study.25.

Fig. 1 presents a flow scheme of the study population in time. One hundred and eighty-eight participants (26%) were lost to follow-up shortly after they had completed the inclusion questionnaire, or were excluded from the analysis for another reason, for example because they had not performed any traineeship or had missing information about exposure or hand eczema symptoms during follow-up. Thus, 533 of the 721 included participants (74%) were followed for 1, 2 or 3 years. One hundred and fifty-nine apprentices quit their participation before the end of the study period: 62 for practical reasons (e.g. quit apprenticeship or changed career, went abroad, or entered a long period of only theoretical classes), 48 for motivational reasons (e.g. being too busy or not motivated to keep on filling in the diary cards).

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td># students signed up:</td>
<td>190</td>
<td>361</td>
<td>177</td>
</tr>
<tr>
<td>Excluded because of chronic inflammatory disease:</td>
<td>0</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Completed inclusion questionnaire:</td>
<td>190 + 355 + 176 = 721</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excluded from analysis (no follow-up data):</td>
<td>146</td>
<td>281</td>
<td>106</td>
</tr>
<tr>
<td>Year 1: N=146</td>
<td>10</td>
<td>136</td>
<td>149</td>
</tr>
<tr>
<td>Year 2: N=417</td>
<td></td>
<td>268</td>
<td></td>
</tr>
<tr>
<td>Year 3: N=374</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quit participation during follow-up:</td>
<td>10 + 149 = 159</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1. Flow scheme of study population.
Table 1. Characteristics of the study population and comparison of participants with non-participants

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All participants included in cohort n = 721</th>
<th>Subset of six school visits where the questionnaire was filled in by all apprentices regardless of participation</th>
<th>Willing to participate n = 106</th>
<th>Not willing to participate n = 99</th>
<th>Difference (± 95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex (%)</td>
<td>90</td>
<td>91</td>
<td>91</td>
<td>-1%</td>
<td>(-9% – 7%)</td>
</tr>
<tr>
<td>Age at inclusion (years)*</td>
<td>19.5 (18.3 – 20.9)</td>
<td>25</td>
<td>13</td>
<td>11%</td>
<td>(0.6% – 22%) *</td>
</tr>
<tr>
<td>Lifetime prevalence of atopic dermatitis (%)</td>
<td>24.3</td>
<td>25</td>
<td>13</td>
<td>11%</td>
<td>(0.6% – 22%) *</td>
</tr>
<tr>
<td>Persistent atopic dermatitis (started in childhood and still present at time of inclusion) (%)</td>
<td>6</td>
<td>7</td>
<td>3</td>
<td>4%</td>
<td>(-3% – 10%)</td>
</tr>
<tr>
<td>Eczema with onset at &lt; 5 years of age (%)</td>
<td>13</td>
<td>11</td>
<td>4</td>
<td>7%</td>
<td>(-0.3% – 15%)</td>
</tr>
<tr>
<td>Eczema with onset at &gt; 18 years of age (%)</td>
<td>21</td>
<td>21</td>
<td>17</td>
<td>4%</td>
<td>(-7% – 14%)</td>
</tr>
<tr>
<td>History of rhinitis (%)</td>
<td>46</td>
<td>55</td>
<td>34</td>
<td>20%</td>
<td>(7% – 33%) *</td>
</tr>
<tr>
<td>History of asthma (%)</td>
<td>17</td>
<td>24</td>
<td>10</td>
<td>14%</td>
<td>(3% – 24%) *</td>
</tr>
<tr>
<td>Symptoms caused by common allergens (dust, pollen, animals, food) (%)</td>
<td>44</td>
<td>44</td>
<td>33</td>
<td>11%</td>
<td>(-2% – 24%)</td>
</tr>
<tr>
<td>Any symptoms on hands/fingers currently present (at the time of completing the questionnaire) (%)</td>
<td>24</td>
<td>20</td>
<td>18</td>
<td>2%</td>
<td>(-9% – 12%)</td>
</tr>
<tr>
<td>Any symptoms on hands/fingers ever (currently present or in the past) (%)</td>
<td>54</td>
<td>49</td>
<td>37</td>
<td>12%</td>
<td>(-2% – 25%)</td>
</tr>
<tr>
<td>Hand eczema currently present (at the time of completing the questionnaire) (%)</td>
<td>7</td>
<td>4</td>
<td>1</td>
<td>3%</td>
<td>(-3% – 8%)</td>
</tr>
<tr>
<td>Hand eczema ever (currently present or in the past) (%)</td>
<td>16</td>
<td>15</td>
<td>6</td>
<td>9%</td>
<td>(0.4% – 18%) *</td>
</tr>
<tr>
<td>General dry skin (%)</td>
<td>17</td>
<td>18</td>
<td>12</td>
<td>6%</td>
<td>(-4% – 16%)</td>
</tr>
</tbody>
</table>

* Age at inclusion could not be calculated in the subset, because birth date was not known for non-participants.

b Eczema was defined as an itchy rash on the face, flexures, wrists/ankles, hands, or other locations.

* p-value of difference < 0.05.
and 49 for other (unspecified) reasons (Fig 1). There were no substantial differences in baseline characteristics between participants who completed one or more study years and those who were excluded from the analysis. However, of the participants with hand eczema during follow-up, 80% completed their participation until the end of the study period, as compared with 56% of those without hand eczema (chi-square, $p < 0.0001$).

**Hand eczema during follow-up**

Of those participants with sufficient follow-up information ($n = 533$), 285 (53%) reported any symptoms on their hands or fingers at any time during follow-up. The most commonly reported symptom was redness (reported by 38%), followed by itching (31%), scaling (25%), fissures (18%), papules (12%) and vesicles (7%). Of the 445 participants who had no history of hand eczema up to the time of inclusion, 81 (18%) developed hand eczema during the study. Most of these new cases occurred during the first traineeship, with an incidence rate of 36.7/100 person-years in traineeship. The incidence for the second and third year was combined because of the small number of participants in the third year; the incidence rate appeared to be 13.7/100 person-years in traineeship. The median duration of practical training was 20 weeks/year, with interquartile limits from 10 to 20 weeks. Calculation of incidence rates with the total period of follow-up per person instead of only the time in practical training resulted in incidence rates of 20.0/100 person-years and 8.5/100 person-years in the first year and second plus third year, respectively. Of the 88 participants with a history of hand eczema reported at inclusion, 47 (53%) reported hand eczema during their traineeship(s). Thirty-five of these 88 participants had hand eczema at the time of inclusion; 20 of them also reported hand eczema during their first traineeship. The period prevalence rates of mild hand eczema were 33% in the first year, 29% in the second year and 31% in the third year. The period prevalence rates of hand eczema were 21%, 25%, and 31%, respectively.

Figure 2 shows the period prevalence of hand eczema during the subsequent traineeships, differentiated by first and recurrent episodes of hand eczema. Approximately 15% of the participants who were followed during two subsequent traineeships ($n=261$) had hand eczema during both traineeships. In the subset of participants who were followed during three traineeships ($n=68$), a similar percentage had hand eczema during all three traineeships.

Less than one-third of the apprentices invited by the occupational physician accepted the invitation. The main reasons for declining were that the symptoms had resolved spontaneously, that symptoms could be controlled easily by using skin care products on their own initiative, that treatment had already been started by the subject’s own general practitioner or dermatologist, or that the subjects just considered it to be ‘not necessary’. A consultation was successfully arranged in 52 cases. Table 2 shows that 90% of the cases seen by the occupational physician were diagnosed with contact dermatitis.
Fig. 2. Reported hand eczema (HE) during traineeships (period prevalence) in the first, second and third year of follow-up in a prospective cohort of apprentice nurses.

Table 2. Diagnoses of suspected skin symptoms in 52 apprentice nurses who were examined by a specialized occupational physician

<table>
<thead>
<tr>
<th>Diagnose</th>
<th>n (%)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irritant contact dermatitis without atopy</td>
<td>21 (40)</td>
<td>-</td>
</tr>
<tr>
<td>Irritant and/or allergic contact dermatitis without atopy</td>
<td>5 (10)</td>
<td>Including 2 cases of protein contact dermatitis</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>2 (4)</td>
<td>-</td>
</tr>
<tr>
<td>Irritant contact dermatitis in combination with atopic dermatitis</td>
<td>14 (27)</td>
<td>Including 3 cases of irritant-provoked AD</td>
</tr>
<tr>
<td>Irritant and/or allergic contact dermatitis in combination with atopic dermatitis</td>
<td>7 (13)</td>
<td>Including 2 cases where atopic constitution was unclear</td>
</tr>
<tr>
<td>Other / unclear</td>
<td>3 (6)</td>
<td>-</td>
</tr>
</tbody>
</table>

Exposure to wet work in subjects with completed diary cards

A total of 2291 diary cards were returned, representing exposure data of 383 apprentices. Exposure-reponse relationships were studied in this subset of participants. Different types of wet work reported on the diary cards are shown in Table 3 and Fig. 3. The most reported type of wet work was hand washing, followed by the use of hand alcohol gel rubs, wearing of gloves, and other types of wet work such as contact with water and soap (e.g. when washing a patient) or disinfectants (e.g. when cleaning
medical equipment). The type of wet work exposure differed between healthcare sectors; for example, hand disinfection with alcohol gel rubs constituted a great deal of the exposure in hospitals, whereas in other sectors, hand washing was the most frequent wet work activity (Fig. 3).

**Table 3. Exposure to wet work during one work shift as reported by 383 apprentice nurses**

<table>
<thead>
<tr>
<th>Wet work activity</th>
<th>% of apprentices reporting this activity minimally once a shift</th>
<th>Frequency per shift, median (25% - 75%)</th>
<th>Maximum frequency per shift</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hand washing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>water only</td>
<td>86</td>
<td>3 (1 – 5)</td>
<td>19</td>
</tr>
<tr>
<td>water and soap</td>
<td>99</td>
<td>6 (4 – 9)</td>
<td>21</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>8 (6 – 12)</td>
<td>31</td>
</tr>
<tr>
<td><strong>Hand disinfection (alcohol gel rub)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>87</td>
<td>5 (2 – 11)</td>
<td>30</td>
</tr>
<tr>
<td><strong>Wearing occlusive gloves</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With a duration of &lt; 5 min per occasion</td>
<td>85</td>
<td>3 (1 – 4)</td>
<td>13</td>
</tr>
<tr>
<td>With a duration of 5-14 min per occasion</td>
<td>74</td>
<td>2 (1 – 3)</td>
<td>12</td>
</tr>
<tr>
<td>With a duration of 15-29 min per occasion</td>
<td>34</td>
<td>1 (1 – 2)</td>
<td>7</td>
</tr>
<tr>
<td>With a duration of &gt; 30 min per occasion</td>
<td>11</td>
<td>1 (1 – 2)</td>
<td>4</td>
</tr>
<tr>
<td>Total (all occasions)</td>
<td>93</td>
<td>4 (2 – 6)</td>
<td>24</td>
</tr>
<tr>
<td><strong>Contact with water (other than hand washing)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With a duration of &lt; 1 min per occasion</td>
<td>75</td>
<td>2 (1 – 3)</td>
<td>13</td>
</tr>
<tr>
<td>With a duration of 1-14 min per occasion</td>
<td>64</td>
<td>2 (1 – 2)</td>
<td>10</td>
</tr>
<tr>
<td>With a duration of &gt; 15 min per occasion</td>
<td>12</td>
<td>1 (1 – 2)</td>
<td>6</td>
</tr>
<tr>
<td>Total (all occasions)</td>
<td>89</td>
<td>3 (1 – 4)</td>
<td>24</td>
</tr>
<tr>
<td><strong>Contact with soap or detergents</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(other than hand washing)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With a duration of &lt; 1 min per occasion</td>
<td>59</td>
<td>2 (1 – 3)</td>
<td>16</td>
</tr>
<tr>
<td>With a duration of 1-14 min per occasion</td>
<td>78</td>
<td>2 (1 – 3)</td>
<td>16</td>
</tr>
<tr>
<td>With a duration of &gt; 15 min per occasion</td>
<td>23</td>
<td>1 (1 – 2)</td>
<td>8</td>
</tr>
<tr>
<td>Total (all occasions)</td>
<td>88</td>
<td>4 (1 – 5)</td>
<td>23</td>
</tr>
<tr>
<td><strong>Contact with disinfectants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(other than alcohol gel rubs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With a duration of &lt; 1 min per occasion</td>
<td>44</td>
<td>2 (1 – 3)</td>
<td>16</td>
</tr>
<tr>
<td>With a duration of 1-14 min per occasion</td>
<td>21</td>
<td>2 (1 – 2)</td>
<td>16</td>
</tr>
<tr>
<td>With a duration of &gt; 15 min per occasion</td>
<td>2</td>
<td>2 (1 – 2)</td>
<td>9</td>
</tr>
<tr>
<td>Total (all occasions)</td>
<td>52</td>
<td>2 (1 – 3)</td>
<td>27</td>
</tr>
</tbody>
</table>
The German TRGS 401, the only existing guideline addressing wet work exposure that we know of, recommends that, if the total duration of wet work exposure exceeds 2 hr/day, protective measures should be taken. A Dutch expert group involved in the definition of guidelines for occupational contact dermatitis stated that a frequency of wet work exposure of > 20 times/day is a risk factor for developing occupational contact dermatitis. For 111 of the 383 participants (29%), the mean wet work exposure exceeded 2 hr/day, or the maximum frequency of hand washing or disinfection exceeded 20 times/day. The frequency of exceeding 2 hr/day of wet work and/or frequent hand washing or disinfection differed between healthcare sectors; 43% of the participants in hospital traineeships reported exposure exceeding these cut-offs, as compared with 17% of participants working in nursing homes, 12% of participants working in disabled care, 11% of participants working in homecare, and 6% of participants working in psychiatry. The difference between hospitals and each of the other sectors was statistically significant (all chi-square, \( p < 0.0001 \)).

Fig. 3. Frequency of wet work (median and interquartile limits) reported by 383 apprentice nurses during 470 traineeships, stratified by healthcare sector. ‘n’ refers to the number of participants who worked in the healthcare sector concerned; the sum of n exceeds 383 because a number of apprentices participated in more than one traineeship.
To study associations between different types of exposure and prevalence of hand eczema reported on the diary cards, generalized mixed models were used. There was some correlation between the different types of wet work, but not to a sufficient extent to disturb the regression approach (highest Spearman $r = 0.56$). In univariate analyses, the frequency of application of hand alcohol gel rubs, the frequency or duration of glove wearing and the frequency or total duration (all episodes summated) of contact with water only did not have a significant effect ($p > 0.20$), and only the frequency of hand washing, the frequency of contact with soap or detergents (other than hand washing) and the frequency of contact with disinfectants (other than hand alcohol gel rubs) were introduced in the multivariate analysis. In the multivariate analysis, only frequent hand washing (more than eight times per shift) was associated with hand eczema during traineeships [odds ratio (OR) 1.5; 90% CI 1.02 – 2.25], and there was a tendency for there to be an effect of contact with soap or detergents (more than four times per shift) (OR 1.5; 90% CI 0.97 – 2.30; Table 4). The effect of hand washing on mild hand eczema was similar to that on hand eczema (OR 1.6; 90% CI 1.16 – 2.32).

**Table 4. Association of different types of wet work with prevalence of hand eczema during traineeships in 383 apprentice nurses (multivariate mixed model)**

<table>
<thead>
<tr>
<th></th>
<th>Mild hand eczema during traineeships (207 episodes)</th>
<th>Hand eczema during traineeships (128 episodes)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio (exp $\beta$)</td>
<td>90% confidence interval</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand washing &gt; 8 times per shift versus &lt; 8 times per shift $^a$</td>
<td>1.6 (1.16 – 2.32)*</td>
<td>1.5 (1.02 – 2.25)*</td>
</tr>
<tr>
<td>Contact with soap or detergents, other than hand washing &gt; 4 times per shift versus &lt; 4 times per shift $^a$</td>
<td>1.3 (0.86 – 1.87)</td>
<td>1.5 (0.97 – 2.30)</td>
</tr>
<tr>
<td>Contact with disinfectants, other than alcohol hand rubs &gt; 2 times per shift versus &lt; 2 times per shift $^a$</td>
<td>1.1 (0.73 – 1.71)</td>
<td>1.1 (0.69 – 1.79)</td>
</tr>
</tbody>
</table>

$^a$ Cut-off points for hand washing, contact with soap or detergents and contact with disinfectants were based on the median reported frequencies (see Table 3).

* $p < 0.10$.

**Exposure outside of traineeships**

Almost half of the participants (46%) reported having a job on the side, of whom 72% were working in healthcare, 15% were working in other sectors involving wet work (e.g. bars and restaurants) and 13% had side jobs not involving wet work. In univariate
analysis, work in healthcare, catering or other side jobs that involved wet work for > 8 hr/week was associated with prevalence of hand eczema during follow-up (OR 1.6; 90% CI 1.04 – 2.37) in comparison to absence or shorter duration of similar work. Hand washing at home > 10 times/day according to the inclusion questionnaire, which was reported by 17% of participants, was associated with hand eczema during follow-up (OR 2.3; 90% CI 1.42 – 3.64) in comparison to < 10 times/day. There was no substantial correlation between the frequency of hand washing at home and that in traineeships (Spearman $r = 0.14$).

Use of hand cream and changed behaviour regarding wet work exposure

Hand cream was used significantly more often by those who reported symptoms (e.g. itch and fissures) on the diary cards; 66% of participants without symptoms used hand cream, as compared with 84% of those with symptoms (chi-square, $p < 0.0001$). The mean frequencies of hand cream use per day were 1-10 times/day in the group without symptoms and 1-14 times/day in the group with symptoms. In the final email questionnaire, which was returned by 323 participants (response rate of 57%), the participants were asked whether they had changed their behaviour with respect to hand hygiene as a result of having symptoms. Of the 169 participants who reported any symptoms during follow-up in the final questionnaire (52%), 78 (46%) indicated that they had taken measures to reduce their symptoms. The most often reported measure was ‘using more hand cream’ ($n=51$), followed by attempts to reduce the frequency of hand hygiene activities or changing the type of hand hygiene products used ($n=24$), and wearing gloves more often ($n=9$). Eight participants had increased their use of hand alcohol gel rubs as alternative to washing with water and soap. In contrast, 11 participants had decreased their use of alcohol gel rubs, and instead used water and soap more often, because of the stinging sensation that they felt when using alcohol gels.

DISCUSSION

In this prospective cohort of Dutch apprentice nurses, we found that wet work exposure during traineeships varied between different healthcare sectors, and exceeded 2 hr/day and/or included hand washing or disinfection exceeding 20 times/day in 29% of participants. The 1-year period prevalence rates of hand eczema were 23% in the first year of follow-up, 25% in the second year, and 31% in the third year. Eighty-one new cases of hand eczema developed, most of which occurred during the first year of follow-up. In addition, ~15% of participants had recurrence of hand eczema during subsequent traineeships 1 or 2 years later. Frequent hand washing during traineeships (OR 1.5), frequent hand washing at home (OR 2.3) and having a side job involving wet work (OR 1.6) were risk factors for hand eczema during follow-up.
Other studies among nursing apprentices have reported 1-year prevalence rates ranging from 10% to 27% \(^7,^{30,31}\), which is in the range of our results. In a smaller prospective cohort study among Dutch apprentice nurses, a higher incidence rate was also found in the first year of follow-up (19.8/100 person-years) than in the second year (5.2/100 person-years) \(^8\). The same research group found 34 new cases of hand eczema over a follow-up period of (maximal) 33 months in a retrospective cohort of 371 newly employed nurses in a university hospital. The majority had developed the disease within the first 3 months of employment \(^32\). Several prospective cohort studies among apprentice hairdressers \(^5,^8,^9\) and a survey among vocational trainees in a variety of high-risk occupations \(^33\) have also indicated that the incidence of new hand eczema cases is highest shortly after the start of exposure to skin irritants.

To our knowledge, this is the first prospective study on hand eczema in which detailed information on exposure was collected at the individual level for a relatively large cohort. In our study, information on wet work exposure and skin symptoms was collected by means of diary cards, which were regularly sent to the participants. The advantage of the diary card method is that the information obtained supposedly reflects the daily exposure more accurately than retrospective questionnaires. Retrospective self-reporting tends to be influenced by recall bias, as shown by validation studies of questionnaires for self-reporting of wet work exposure among nurses \(^34,^35\). The reported frequency of wet work activities on the cards in our study agreed with recent observational studies of wet work in hospital and geriatric nursing wards, in which the reported frequencies of hand washing, hand alcohol use and glove use were similar to our data \(^34-36\).

The only wet work characteristic associated with (mild) hand eczema during the traineeships was the daily frequency of hand washing, with ORs of 1.6 and 1.5 for mild hand eczema and hand eczema, respectively. Furthermore, there was a tendency for other contact with soap or detergents to also increase the risk of hand eczema. The reported ORs are a fairly good approximation of the corresponding relative risks (hand eczema was reported for 24% of all traineeships observed, and the numbers of traineeships with high and low exposure were approximately equal). As 20 participants had hand eczema both at inclusion and during their first traineeships, it was unknown whether these cases of hand eczema had been caused by exposure during traineeship or were a continuation of pre-existing hand eczema. Repeated analysis excluding these 20 participants showed similar results, namely an increased risk of hand eczema conferred by hand washing and other contact with soap or detergents, but not by contact with disinfectants. These findings are in agreement with earlier epidemiological studies among hospital populations \(^4,^{37,38}\) and with experimental studies showing that soap and detergents are more damaging to the skin than, for example, alcohol-based hand disinfectants \(^39-41\).

Diagnostic criteria constitute an important issue in epidemiological studies. In this study, we used a symptom-based definition of hand eczema. Previous validation studies have shown that symptom-based classifications tend to overestimate the prevalence of hand eczema, whereas self-reported hand eczema (‘Do you have hand
eczema? underestimates the prevalence. Because we wanted to assess new cases of hand eczema, including mild cases of beginning hand eczema, we deliberately chose to use a symptom-based definition. As a result, the prevalence and incidence of hand eczema may have been slightly overestimated. It is reassuring to some extent that 90% of the 52 apprentices examined by a specialized occupational physician (a subset of approximately one-third of the apprentices classified as having hand eczema) were diagnosed as having irritant or allergic contact dermatitis. However, more than two-thirds of the apprentices invited for a consultation did not contact the physician. The most frequently mentioned reasons for declining the invitation (for example, symptoms had diminished with the use of hand cream on the subject’s own initiative, or the subject did not consider it necessary to consult a physician) indicate that many apprentices considered their symptoms to be mild and not severe enough for them to consult a physician. A similarly low attendance rate was found by Jungbauer et al., who invited 160 healthcare employees reporting symptoms of hand eczema in a questionnaire to consult a specialized occupational dermatology nurse. Less than half (46%) of the invited employees attended the consultation; the reasons for declining the invitation were not known, but it was suspected that individuals with milder complaints were less likely to attend the consultation.

One limitation of our study is that, as indicated in Table 1, subjects with atopic dermatitis, rhinitis and asthma were overrepresented in this cohort, as these atopic features were more common in participants than in non-participants (selection bias). Because atopic dermatitis is a known risk factor for hand eczema, this probably resulted in a higher proportion of participants with increased susceptibility to hand eczema, presumably leading to a slight overestimation of prevalence and incidence rates in apprentice nurses. Although the effects of exposure may be different in participants with atopic dermatitis and in participants without atopic dermatitis, the overrepresentation of atopic dermatitis in the group involved in exposure analysis (n=383) was so small (a frequency of 26% in the 383 participants, as compared with 19% in the unselected subsample of 205 apprentices in Table 1) that its influence on the effect size of the specific wet work activities can be regarded as negligible.

Apparently, having a history of atopic dermatitis does not seem to prevent youngsters from choosing occupations with high skin exposure. The impact of personal susceptibility factors on the risk of hand eczema in this cohort is described in more detail in Part II of this study.

Two recommendations for practice can be made on the basis of the results of this study. First, our results support the advice in the recent guideline on hand hygiene to replace hand washing with hand disinfection using alcohol gel rubs where possible (i.e. if the hands are not visibly dirty) and promote the use of protective gloves. However, some apprentices with hand eczema appeared to prefer the use of water and soap over hand alcohol gel rubs, because of the stinging sensation that they experienced when applying the latter on their damaged skin. This indicates a need for education of vocational students on the effects of different hand hygiene procedures on the skin. Furthermore,
the guideline requires that alcohol gel rubs and suitable protective gloves be available at the workplace. Work sites in nursing homes, and especially in homecare, however, are not always equipped with proper hand disinfection products and the correct type of protective gloves, which hampers nurses’ control over their own exposure.

Second, good access to and a positive attitude of vocational students towards consultation of an occupational physician should be promoted. Also individuals with mild hand eczema may benefit from a consultation with their occupational physician, because, apart from skin care advice, advice on working practices and exposure reduction is important in the case of occupational hand eczema, and this kind of counselling usually goes beyond what occurs in the consultation of general practitioners. Furthermore, timely measures for skin protection at the workplace may prevent mild symptoms from progressing into manifest hand eczema. Education of vocational students on this topic may help to increase attendance of consultations in the future.

In conclusion, this prospective cohort of Dutch student nurses has confirmed that, during vocational training, many apprentice nurses already have too much exposure to wet work and that they are at substantially increased risk of developing hand eczema. More attention should be paid in vocational education to the effects of wet work and to skin protection.

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REFERENCES


SUPPLEMENTARY FILE: FOLDING-CARD FOR RECORDING WET WORK EXPOSURE AND SKIN SYMPTOMS

A. Hand washing
- Water only
- Water + Soap / Shampoo / Showergel
- Water + Other, namely:

B. Hand disinfection (alcohol gel rubs)
- Hand alcohol gel rub

C. Use of gloves
- < 5 min
- 5 – 15 min
- 15 – 30 min
- > 30 min

D. Use of hand cream / moisturizer
- Hand cream

E. Other work tasks where your hands get wet
- Contact with water only
- Contact with water + soap / shampoo
- Contact with disinfectants

F. Use of pre-heated wash towels
- Pre-heated wash towels

Don’t forget to fill in the inside of the card!!

G. To be filled in at the end of your shift:
Did today’s shift deviate from normal shifts regarding wet work?
- No
- Yes, I did more wet work than usual
- Yes, I used gloves more often / longer than usual
- Yes, I did less wet work than usual
- Yes, I used gloves less often / shorter than usual

During the past 2 weeks, has your skin been exposed to water or irritants outside your traineeship? (e.g. working in a bar, doing extra household chores, swimming)
- No
- Yes:
  If yes, what did you do?

On how many days did you do it?

On average, how long did you perform ‘wet work’ per day?

Did you, since the last time you filled in a diary card, experience one or more of the following symptoms on your hands and/or fingers?
- No
- Yes, my hands or fingers clearly showed:
  - Redness
  - Scaling
  - Itching
  - Fissures
  - Vesicles
  - Bumps

Did the symptoms last for more than 3 days?
- No
- Yes

Attention please:
- Did any unusual events occur today, which led to skin exposure to substances that are not mentioned on this diary card?
- Do you have skin complaints on your hands that are not mentioned in the above list?
- Or do you have other comments / remarks?

Then please note your remarks on the backside of this diary card!