

Occupational dermatoses in health care workers evaluated for suspected allergic contact dermatitis

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Background: Occupational skin diseases, including allergic contact dermatitis (ACD), irritant contact dermatitis, and allergic contact urticaria (ACU), occur commonly among health care workers (HCWs).

Purpose: To evaluate the aetiology of the various skin diseases afflicting HCWs evaluated for suspicion of ACD and/or ACU and to identify the most common allergens among HCWs found to have ACD and/or ACU.

Methods: A total of 1434 patients underwent patch testing. The demographic data and most common allergens for HCWs ($n = 100$) and non-HCWS ($n = 1334$) were compared.

Results: HCWs were statistically more likely than non-HCWS to be female, have hand dermatitis, and have a history of atopy. HCWs were also more likely to have work-related ACD especially to quaternium-15, thiuram, carba mix, glutaraldehyde and benzalkonium chloride, and to have ACU to latex.

Limitations: This study was retrospective and is subject to the resultant biases of all such investigations. Only patients suspected of having ACD and who underwent patch testing are included in our database. The prevalence of ACD and ACU is likely to be higher than that seen in the general HCW population.

Conclusions: Our results underscore the importance of thoroughly evaluating HCWs for ACD and ACU with the use of expanded standard allergen series and prick or radioallergosorbent testing to latex.

Key words: allergic contact dermatitis; health care workers; patch test; occupational. © Blackwell Munksgaard, 2008.

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Occupational skin disease occurs commonly among health care workers (HCWs). The disease spectrum includes allergic contact dermatitis (ACD), irritant contact dermatitis (ICD), allergic contact urticaria (ACU), and cutaneous infections as well as work-related exacerbations of endogenous diseases such as atopic dermatitis, dyshidrotic eczema, and psoriasis. Endogenous disease may coexist or be exacerbated by exogenous disease, and it has been well recognized that hand dermatitis in particular is often multifactorial. ACU among HCWs secondary to latex has been extensively studied and may also coexist with other disease states such as ACD and/or atopic disease. The prevalence of latex allergy in this population has been estimated to be 2.8–10.7% (1, 2). The prevalence of positive patch test reactions among

HCWs has been reported to range from 17% to 62.9% (3–5). Despite the high rate of positive patch reactions among HCWs, few published studies are available, none of which is from the USA, in which the patch test response is correlated with the clinical diagnosis of relevant ACD.

In this retrospective study, we report the various skin diseases afflicting HCWs evaluated for suspicion of ACD and/or ACU and the most common allergens among HCWs found to have ACD and/or ACU. In addition, we examine the demographic characteristics particular to this patient population.

Patients and Methods

Between 1 July 1994 and 30 June 2006, a total of 1434 patients with suspected ACD presented to

American Dermatology Associates, (Shawnee, KS, USA) and underwent patch testing. American Dermatology Associates is one of the participants in the North American Contact Dermatitis Group (NACDG). NACDG centres conduct patch testing using a standardized allergen series and standardized screening methods. Prior to testing, patients completed a standardized NACDG questionnaire, which included demographic, medical, and occupational information. Patients were asked to report a history of atopic dermatitis, as defined by the criteria set forth by Hanifin and Rajka (6). As part of the occupational history, occupations were coded using the 1980 Bureau of Census occupation codes (7).

Patients were patch tested in a standardized manner using Finn Chambers (Epitest Ltd Öy, Tuusula, Finland) on Scanpor tape (Norgesplaster Aksjeselskap, Vennesla, Norway). The patches were applied to the patient's back as previously described (8). Test allergens were purchased from Chemotechnique Diagnostics AB, Malmö, Sweden. Allergens were applied on Mondays, and patients were examined at both 2 and 4 days by one of the authors (DVB). Reactions were graded on reaction morphology as previously defined (9). Reactions of +, ++, or +++ were considered allergic, while reactions scored ?+ were doubtful. Dermatitis site, dermatitis type, exposure source, and relevance were also noted. The relevance of a positive patch test to the clinical diagnosis of ACD was defined as follows: 1 = definite (the patient had a positive test reaction to a product to which he or she had been exposed and that contained an allergen to which he or she had reacted in its purified form); 2 = probable (the patient had experienced a known contact with a product known to contain an allergen to which he or she had reacted in its purified form); 3 = possible (the patient probably had contact with a product known, or suggested, to contain an allergen to which he or she had reacted in its purified form); 4 = past (the patient had prior episodes of ACD after being exposed to an allergen to which he or she had reacted in its purified form) (10).

Among patients with a history of (i) localized and/or generalized cutaneous itching, burning, stinging, or hives following exposure to latex and/or (ii) allergic rhinoconjunctivitis and/or (iii) asthmatic symptoms, and/or (iv) anaphylactic symptoms, the diagnosis of contact urticaria to latex was made by 1 of 3 methods: (i) a positive latex immunoglobulin E or radioallergosorbent (RAST) test (the units for a positive RAST test are determined by the laboratory in which the test is performed; in our study, a positive test was defined as ≥ 5 U/ml), (ii) a positive latex prick test

[defined as a wheal and flare equal to or greater than that elicited by the positive histamine (1 mg/ml) control] to either a latex glove eluate or purified latex resin, and/or (iii) a positive use test.

For this study, HCWs were defined as those expected to have significant contact with patients, gloves, and hand disinfectants. Included among the HCW group were physicians, dentists, podiatrists, registered nurses, physician assistants, dental hygienists (DHs), licensed practical nurses, dental assistants (DAs), health aides, nursing aides/orderlies/attendants, and health-diagnosing practitioners not elsewhere classified. Occupations that were excluded from the study include pharmacists, veterinarians, mental health workers, clinical laboratory technicians, physical/occupational/respiratory therapists, and optometrists.

All data were entered, retrieved, and evaluated using a computer database (Access and Excel; Microsoft, Seattle, WA, USA). A chi-squared test was performed to determine statistical significance of difference between 2 populations. *P*-values less than 0.05 were considered significant. Prevalence ratios were calculated to express the risk of allergen sensitization between HCWs and non-HCWs using OPENEPI[®] software (<http://www.openepi.com>; Open Epi, Atlanta, GA, USA).

Results

Of the 1434 patients who underwent patch testing, 100 patients were classified as HCWs based on their primary occupation. Registered nurses (54%), nursing aides/orderlies/attendants (13%), and physicians (11%) were the most common occupations represented in our HCW sample. A demographic comparison between HCWs and non-HCWs is shown in Table 1.

The most common sites for dermatitis among HCWs were hand (60%), face (13%), and scattered/generalized (10%). The most frequent sites among non-HCWs were hand (28%; *P* < 0.001), face (15%), and scattered/generalized (15%). Of the 60 HCWs with hand dermatitis, 32 (53%) were

Table 1. Demographic comparison of HCWs and non-HCWs

	Female (%)	History of atopic eczema (%)	Average age (years)	Occupationally related allergic contact dermatitis (%)
HCWs	84.0	19.0	41.6	31.0
Non-HCWs	59.1	11.2	47.6	12.6
<i>P</i> -value*	<0.001	<0.025	<0.007	<0.0001

HCWs, health care workers.

**P*-values less than 0.05 are considered significant.

nurses. HCWs were more likely than non-HCWs to have a history of atopic eczema ($P < 0.025$).

53% of HCWs and 51% of non-HCWs had a diagnosis of ACD. The distribution of all relevant positive allergens among HCWs and non-HCWs is given in Table 2. 31% of HCWs had a diagnosis of occupational ACD, while 12.6% of non-HCWs had occupational ACD (Table 1). The distribution of relevant work-related allergens among HCWs and non-HCWs is given in Table 3.

22% of HCWs and 11% of non-HCWs had a diagnosis of ICD ($P < 0.01$). 13% of HCWs and 0.004% of non-HCWs had a diagnosis of contact urticaria ($P < 0.001$). 6% of HCWs and 2% of non-HCWs had a diagnosis of both ACD and ICD. One HCW had a diagnosis of ACD, ICD, and ACU.

The most common relevant allergens among HCWs with ACD are shown in Table 4. For comparison, the prevalence of positive reactions to these allergens among non-HCWs with ACD is also outlined. Statistically significant differences between HCWs and non-HCWs were seen for the incidence of allergic reactions to benzalkonium chloride (BAC) ($P < 0.025$), carba mix ($P < 0.01$), glutaraldehyde ($P < 0.001$), quaternium-15 ($P < 0.001$), and thiuram mix ($P < 0.001$). Table 5 delineates those allergens found occupationally relevant among HCWs.

The prevalence of thiuram mix and formaldehyde allergy was $3.6\times$ (CI 15–38%) and $1.75\times$ greater (CI 10–32%), respectively, in HCWs than in non-HCWs. The prevalence of glutaraldehyde allergy was $15\times$ greater in HCWs than in non-HCWs (CI 6–25%). Among HCWs, 9 were employed within the dental profession (dentist, DA, or DH). The prevalence of glutaraldehyde allergy among these patients was 56% (CI 21–86%); among HCWs employed outside of the dental profession, the prevalence of glutaraldehyde allergy was 5% ($P < 0.01$).

There were a total of 19 patients in our database with a diagnosis of ACU to latex. 13 (68%) had a concomitant diagnosis of ACD, and 3 patients

Table 2. Distribution of relevant patch test reactions among HCWs and non-HCWs with a diagnosis of allergic contact dermatitis

	HCWs ($n = 53$) ^a	Non-HCWs ($n = 680$) ^a
Definite relevance	20 (37.7%)	159 (23.4%)
Probable relevance	30 (56.6%)	278 (40.9%)
Possible relevance	32 (60.4%)	381 (56.0%)
Past relevance	12 (22.6%)	158 (23.2%)

HCWs, health care workers; n, number of unique patients.

^aPer cent of relevant reactions $>100\%$ because of a given patient having more than 1 relevant positive reaction.

Table 3. Distribution of relevant reactions among HCWs and non-HCWs with occupationally related allergic contact dermatitis

	HCWs ($n = 31$) ^a	Non-HCWs ($n = 168$) ^a
Definite relevance	12 (38.7%)	74 (44.0%)
Probable relevance	19 (61.3%)	95 (56.5%)
Possible relevance	18 (58.0%)	101 (60.1%)
Past relevance	6 (19.4%)	34 (20.2%)

HCWs, health care workers; n, number of unique patients.

^aPer cent of relevant reactions $>100\%$ because of a given patient having more than 1 relevant positive reaction.

(16%) were also diagnosed with ICD. 68% of patients in our database with latex ACU were HCWs, 79% were female, and 21% of patients had a history of atopic eczema. The hand (74%) was the most common site for dermatitis among patients with ACU. The average age for this subset of patients was 41.9 years.

The most common concomitant delayed-type allergens among patients with both ACU and ACD were quaternium-15 (26%), formaldehyde (21%), and cocamide diethanolamine (DEA) (16%). 11% of patients were also positive to each of the following allergens: thiuram mix, carba mix, fragrance mix, myroxylon pereirae, and DMDM hydantoin.

Discussion

We found that HCWs referred for patch testing are statistically more likely to be women. This phenomenon has been seen in other investigations

Table 4. The most common relevant occupational and non-occupational allergens among HCWs with allergic contact dermatitis (prevalence given as percentage) in comparison with non-HCWs

	HCWs ($n = 53$) (%) ^a	Non-HCWs ($n = 685$) (%) ^a	P-value*
Quaternium-15, 2% pet.	34.0	13.7	<0.001
Thiuram mix, 1% pet.	24.5	6.9	<0.001
Formaldehyde, 1% aq.	18.9	10.8	<0.1
Carba mix, 3% pet.	15.1	5.4	<0.01
Fragrance mix, 8% pet.	13.2	12.7	<1
Glutaraldehyde, 1%, pet.	13.2	0.88	<0.001
Nickel sulfate, 2.5% pet.	11.3	17.1	<1
Myroxylon pereirae, 25% pet.	9.4	11.7	<1
Cobalt chloride, 1% pet.	9.4	8.6	<1
Benzalkonium chloride, 0.1% aq.	7.5	2.3	<0.025
Methylchloroisothiazolinone/ methylisothiazolinone, 100 ppm aq.	7.5	5.7	<1

aq., aqueous; HCWs, health care workers; pet., petrolatum.

*P-values less than 0.05 are considered significant.

^aPer cent of relevant reactions $>100\%$ because of a given patient having more than 1 relevant positive reaction.

Table 5. The most common relevant occupational allergens among HCWs with occupationally related allergic contact dermatitis (prevalence given as percentage)

	HCWs (<i>n</i> = 31) (%) ^a
Thiuram mix, 1% pet.	35.5
Quaternium-15, 2% pet.	29.0
Formaldehyde, 1% aq.	22.6
Glutaraldehyde, 1% pet.	22.6
1,3-Diphenylguanidine, 1% pet.	12.9
Myroxylon pereirae, 25% pet.	9.7
Benzalkonium chloride, 0.1% aq.	9.7
Cocamide DEA, 0.5% pet.	9.7
Fragrance mix, 8% pet.	9.7
Nickel sulfate, 2.5% pet.	9.7

aq., aqueous; HCWs, health care workers; pet., petrolatum.

^aPer cent of relevant reactions >100% because of a given patient having more than 1 relevant positive reaction.

(5, 9, 11). In our study population, the hand was the most common site for dermatitis for both HCWs and non-HCWs; however, HCWs were statistically more likely than non-HCWs to have hand dermatitis. Similar findings have been noted by others (3, 12–16).

Nettis et al. (4) reported a history of atopic eczema among 6.9% of HCWs, while Holness and Mace (11) found 18% of HCWs had a history of atopic eczema. The prevalence of atopic eczema in our population of HCWs was 19%, which was statistically higher than that among non-HCWs. We suspect that this results not from an overrepresentation of atopics among HCWs but rather that HCWs with an atopic background are more likely than their non-HCW counterparts to develop problems with ICD and/or ACD of the hands because of their enhanced exposure to wet-work and allergens in the work place, respectively (17–20).

In our study, HCWs were no more likely to have ACD than their non-HCW counterparts. This finding is to be expected given the inherent bias of this study; for example, only patients suspected of having ACD were included. Nonetheless, the allergens to which HCWs reacted differed somewhat. The most common relevant allergens among HCWs with ACD were quaternium-15, thiuram mix, formaldehyde, carba mix, and fragrance mix. HCWs were significantly more likely than non-HCWs to be allergic to quaternium-15, thiuram mix, and carba mix. Formaldehyde allergy was higher in HCWs than non-HCWs; however, this difference did not reach statistical significance in our population, probably because of the ubiquity of formaldehyde in the general, not only medical, environment. The same is likely true for fragrance mix where the rate of positive reactions between HCWs and non-HCWs did not differ.

In our study, 40% of HCWs with ACD had positive reactions to thiuram mix or carba mix. The higher rates of reactivity to thiurams and carbamates are most likely because of the use of gloves among HCWs. This has been noted in studies from Germany and other European countries (4, 5, 16).

The enhanced rate of allergy to quaternium-15, a widely used formaldehyde-releasing preservative in personal care products such as liquid soaps and moisturizers, among HCWs may be because of washing and moisturizing the hands with increased frequency relative to non-HCWs. In addition, some HCWs may come into contact with quaternium-15 in products used primarily for patient care, such as the nurse who bathes patients. The higher, although not statistically significant, rate of formaldehyde allergy among HCWs (19%) in our study may be because of low levels of exposure to formaldehyde released from quaternium-15 and other formaldehyde-releasing preservatives. In addition, sources of direct formaldehyde exposure (e.g. that among pathologists) may be operative, but not sufficiently so to achieve statistical significance.

HCWs were also statistically more likely than non-HCWs to be allergic to glutaraldehyde ($P < 0.001$). Dental personnel are especially likely to have reactions to glutaraldehyde (9). In an age and sex-controlled study conducted by patch testing a voluntary cohort of randomly recruited, healthy DHs and DAs versus non-dental professionals, Ravis et al. (21) found a statistically significant disparity in the rates of glutaraldehyde sensitivity among healthy dental personnel versus healthy control subjects (10.9% versus 0.2%; $P = 0.02$). The preponderance of reactions among DHs and DAs suggested to these authors that the present safety practices among DHs and DAs were largely ineffective in protecting against sensitization to glutaraldehyde in sterilizing solutions (21). Thus, it is not surprising that among the 9 HCWs whom we evaluated and who were employed within the dental profession (dentist, DA, or DH), the prevalence of glutaraldehyde allergy was 56%; while among HCWs employed outside the dental profession, the prevalence of glutaraldehyde allergy was only 5% ($P < 0.01$). HCWs exposed to glutaraldehyde should familiarize themselves with the current Occupational Safety and Health Administration (OSHA) guidelines for its safe use (22).

Finally, HCWs were also statistically more likely than non-HCWs to be allergic to BAC; however, the prevalence of allergy among HCWs was only 8%. BAC is widely used in alcohol-based, waterless hand disinfectants and as a

preoperative skin antiseptic, a disinfectant for surgical instruments, and treatment of burns, ulcers, and infected wounds. BAC is also found in cosmetics, deodorants, mouthwashes, dentifrices, lozenges, and ophthalmic preparations (23). HCWs may be more likely than non-HCWs to be exposed to BAC as an occupational contactant. Nettis et al. reported a positive reaction to BAC among 9.7% of HCWs with occupational ACD (4). The low rate of BAC allergy among both HCWs and non-HCWs may reflect its potential as a strong cutaneous irritant, rather than a sensitizer (24). Given its irritant properties, the final concentration of BAC is typically sufficiently below that which would induce sensitization in most of the exposed population.

Given the bias of this study, the overall incidence of ACD did not differ between HCWs and non-HCWs. Nonetheless, the occupationally relatedness of the ACD did. 58.5% of cases of ACD among HCWs were occupationally related versus 24.5% of cases among non-HCWs. The 5 most common allergens were thiuram mix, quaternium-15, formaldehyde, glutaraldehyde, and 1,3-diphenylguanidine. Interestingly, 1,3-diphenylguanidine, a component of carba mix, was identified more frequently than carba mix itself is a relevant allergen in occupational ACD. 1,3-diphenylguanidine is used as an accelerator in the rubber vulcanization process; the likely exposure source for HCWs with occupational ACD is gloves. Of note, as manufacturers seek to reduce sensitizing thiurams from gloves, we and others have noted a rising incidence of carba mix, including 1,3-diphenylguanidine, allergic patch test reactions (25).

HCWs were statistically more likely than non-HCWs to suffer from ICD (22% of HCWs versus 11% of non-HCWs; $P < 0.01$), the majority of them (86%) were occupationally related. Our finding of an enhanced rate of ICD among HCWs is not novel (3, 26). Jungbauer et al. evaluated the role of soap and water, hand alcohol, and gloves in programs to prevent ICD in nursing personnel (27). The results of this study justify the conclusion that, when the hands were not visibly soiled, hand alcohol was the preferred disinfectant over soap and water. In contrast, the efficacy of gloves in reducing ICD was variable. This is not surprising given the findings by Burke et al. (27) of a strong association between glove wearing and the incidence of skin irritation among general dental practitioners, especially the female respondents.

Among our patients, HCWs were significantly more likely than non-HCWs to have ACU to latex (13% of HCWs versus 0.004% of non-HCWs; $P < 0.001$). There are few good studies designed

to look at the incidence of immediate hypersensitivity to latex in the USA. Among hospital workers most likely to be exposed to latex gloves, the rate of latex ACU has been reported to range from a low of 5.5% to as high as 17% (28, 29). Thus, our findings are consistent with what has been reported. Of concern is the fact that the number of HCWs presenting with ACU to latex has not declined over time (22% of HCWs prior to 2000; 16% of HCWs after 2000.) This is in contrast to reports from other countries where regulations banning powdered latex gloves have resulted in a significant decrease in the incidence of latex ACU (30, 31).

68% of patients with latex ACU were HCWs, 79% were female, and 21% of patients had a history of atopic eczema. The hand (74%) was the most common site for dermatitis among patients with ACU. Similar data have been reported by many others, particularly the association between atopic dermatitis and ACU (32–39).

Among the 19 patients in our database with a diagnosis of ACU to latex, 3 patients (16%) were also diagnosed with ICD and 13 (68%) with ACD, a percentage much higher than reported by either Holness and Mace (11) or Nettis et al. (32). The reason for this difference is unknown but may in part be because of our use of an expanded HCW's series, in addition to the already expanded NACDG standard series. Thus, some of the contact allergens that we identified as causative for ACD, such as cocamide DEA, DMDM hydantoin, cocamidopropyl betaine, and propylene glycol, may have been missed by other investigators using only a more limited standard screening series.

HCWs with unexplained eczematous dermatitis and/or urticaria should be evaluated by patch testing and/or RAST/prick testing. A patch test series for HCWs should include those allergens listed in Tables 4 and 5. Additionally, any chemical to which the patient is exposed must be explored as a potential allergen, and the patient should be tested accordingly. As noted above, we found such non-standard allergens as cocamide DEA, DMDM hydantoin, cocamidopropyl betaine, and propylene glycol to be responsible for ACD in our HCWs.

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