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Winter season, frequent hand washing, and irritant patch test reactions to detergents are associated with hand dermatitis in healthcare workers

Adrienne Callahan, BA[1], **Elma Baron, MD**[1], **Desta Fekedulegn, PhD**[2], **Michael Kashon, PhD**[2], **Berran Yucesoy, PhD**[3], **Victor J. Johnson, PhD**[3], **Diana Santo Domingo, MD**[1], **Brent Kirkland, MD**[1], **Michael I. Luster, PhD**[3], and **Susan Nedorost, MD**[1]

[1]Department of Dermatology, University Hospitals, 11100 Euclid Avenue, Lakeside 3500, Cleveland, OH 44106

[2]Department of Biostatistics and Epidemiology, Health Effects Laboratory Division, National Institute for Occupational Safety and Health, Morgantown, WV 26505

[3]Department of Toxicology and Molecular Biology Branches, Health Effects Laboratory Division, National Institute for Occupational Safety and Health, Morgantown, WV 26505

Abstract

Background—Irritant hand dermatitis (IHD) is common in healthcare workers.

Objective—We studied endogenous irritant contact dermatitis threshold by patch testing, and exogenous factors such as season and hand washing for their association with IHD in healthcare workers.

Methods—Irritant patch testing with sodium lauryl sulfate (SLS), sodium hydroxide (NaOH) and benzalkonium chloride (BAK) at varying concentrations was measured in 113 healthcare workers. Examination for hand dermatitis occurred at one month intervals for a period of six months in the Midwestern US.

Results—Positive patch testing to low concentration SLS was associated with IHD (p=0.0310) after adjusting for age, gender, ethnicity, season, history of childhood flexural dermatitis, mean indoor relative humidity, glove and hand sanitizer usage). Subjects with a positive patch test to SLS were 78% more likely to have occurrence of IHD (IRR=1.78, 95% CI: 0.92, 3.45). Hand washing frequency (≥ 10 times a day; IRR=1.55, 95% CI: 1.01, 2.39) and cold season (IRR=2.76, 95% CI: 1.35, 5.65) were associated with IHD. No association was found between history of childhood flexural dermatitis and IHD in this population.

Corresponding Author: Susan Nedorost, Department of Dermatology, University Hospitals, 11100 Euclid Avenue, Lakeside 3500, Cleveland, OH 44106-5028, stn@case.edu, Phone: 216-844-7814, Fax: 216-844-8993.

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Conclusions—Both genetic and environmental factors are important in the etiology of IHD and should be considered in designing strategies to protect, educate and treat susceptible individuals.

Key phrases

irritant contact dermatitis; patch testing; occupational; season; healthcare workers

Introduction

Irritant hand dermatitis (IHD) occurs regularly in occupational populations with an estimated annual incidence of 0.7 workers per 1,000[1]. A high prevalence has been reported in specific occupational groups who do wet work in low humidity conditions, such as healthcare workers[2–4]. A retrospective review of healthcare workers showed that 61% of healthcare workers developed IHD[5]. Another study conducted among nurses showed that hand washing more than 15 times per work shift increased the risk of IHD with an odds ratio (OR) of 2 (95% CI:1.2–3.4)[6].While it is clear that IHD is a problem in the healthcare worker community, the underlying contribution of endogenous (i.e., genetic) and exogenous (i.e., environmental) causes have not been well-separated.

Epidermal barrier function and the innate immune system are endogenous factors that play a strong role in the development of IHD[7]. Disruption of the stratum corneum allows irritants to better traverse the epidermal barrier, where they are sensed by pathogen receptors that trigger components of the innate immune system, including stimulation of phagocytes and release of pro-inflammatory cytokines[8]. The resulting inflammatory response from this activation can lead to the development of IHD. Specific polymorphisms of pro-inflammatory cytokine tumor necrosis factor-alpha were found to be associated with reaction to low concentrations of the irritants SLS and BAK[9] as well as with the development of ICD[10]. Irritant patch testing using both SLS and NaOH has also been noted as a possible identifier for individuals at high risk of dermatitis in different occupational settings[11, 12]. This suggests a possible role for patch testing in elucidating genetic predisposition to IHD. A history of atopic dermatitis (AD), defined in this study as having a history of childhood flexural dermatitis, has been shown to be associated with the development of IHD[13–15]. Barrier dysfunction and innate immune system differences may contribute to an endogenous potential for developing IHD.

However, various environmental factors can also contribute to skin inflammation, including winter season, handwashing, and glove use. Low temperature and low relative and absolute humidity (such as during the winter season) tended to be risk factors for and contributed to the development of IHD[16]. Higher levels of handwashing were also found to be associated with the development of hand dermatitis[17–19]. Overall, it is not evident whether endogenous or exogenous factors make a stronger contribution to the development of IHD, and for that reason, it would be helpful to evaluate all these factors in the same population.

In the present study we investigated potential associations of irritant patch test response, hand washing frequency, personal history of AD and season with development of hand dermatitis in a group of health care workers in order to investigate both potential endogenous (genetic) and exogenous (environmental) factors in the development of IHD.

Materials and Methods

Population and Definitions

This study was approved by the University Hospitals Case Medical Center IRB (08-05-20). Our population consisted of adult health care workers (e.g., nurses, physicians, and

technicians) with no active inflammatory skin disease requiring prescriptive treatment (including atopic dermatitis) who wash their hands at least eight times a day. Subjects who had been on immunomodulatory medications, those who intentionally exposed skin at the patch test sites to more than one-hour of natural sunlight daily, received ultraviolet therapy or used a tanning salon, and those who were pregnant or planned on becoming pregnant were excluded. The volunteers were examined and their medical history was assessed prior to enrollment. Each volunteer underwent informed consent and a questionnaire was given to assess volunteers' health status, medical history, job details and living habits, including any exclusion criteria previously listed.

Subjects (n=113) were recruited from a Midwestern academic health center via word of mouth and IRB-approved flyers. Of the 113 who participated in the study, 10 were screen/enrollment failures with incomplete information and one subject had missing value for IHD at baseline. These 11 participants were excluded prior to statistical analyses leaving a cohort of 102 subjects. Further examination of the remaining participants revealed that 12 were prevalent cases of IHD since they were diagnosed with IHD at the baseline assessment. That is, there was mild hand dermatitis present without history of severe disease requiring medical treatment. History of severe dermatitis was used as proxy to exclude allergic contact dermatitis as we did not patch test our subjects for allergens. Because irritant hand dermatitis is seasonal and we enrolled subjects during both hot and cold months, we included subjects with IHD at baseline to avoid biasing our cold-month recruits by excluding those prone to IHD. Statistical analyses were therefore conducted using two sets of samples; first we examined occurrences of IHD using data that included the 12 prevalent cases (n=102) who could have recurrence, and second we removed the 12 prevalent cases and examined incidence of IHD using n=90 subjects who initially were known to be free of IHD at baseline.

For the purpose of our study, atopic dermatitis and a history of childhood flexural dermatitis are used synonymously. A history of childhood flexural dermatitis (not solely respiratory atopy) was assessed by questionnaire. Subjects were enrolled throughout the entire calendar year (2006) that included both warm and cold weather. Subjects were clinically assessed for the presence or absence of hand dermatitis by a dermatologist or a single trained UHMC Skin Studies Center staff on a monthly basis for six months. Dermatitis classification was based on objective skin symptoms. Active dermatitis was characterized by erythema, papules, vesicles, and/or fissures, exhibiting a clear eczematous picture. Minor dermatitis was exhibited as erythema, slight chapping, and scaling of the skin. Seasonal variation (i.e. resolving dermatitis with warmer weather) within subjects suggested the dermatitis seen was irritant contact dermatitis, not allergic contact dermatitis.

Irritants and patch testing

Sodium lauryl sulfate (SLS), sodium hydroxide (NaOH), and benzalkonium chloride (BAK) were used as irritants. Each irritant has a slightly different mechanism of irritation. As a detergent, SLS emulsifies the fat within the SC to penetrate the skin barrier, while NaOH is a hygroscopic caustic element that penetrates the skin barrier, and BAK is directly cytotoxic[20]. The study had an initial phase where 20 subjects were enrolled and tested with an expanded dose range. Aqueous solutions of SLS (99% pure) were tested at the following concentrations: 0.1%, 0.25%, 0.5%, 1.0%, 2.5%, 5.0%, 10% and 20%. NaOH was tested at ranges of 0.1%, 0.25%, 0.5%, 1.0%, 2.5% and 5.0%. BAK was tested at concentrations of 0.1%, 0.5%, 1.0%. Distilled water served as a negative control. The above 20 subjects were part of the 113 subjects enrolled for the study. Test materials were applied in 0.2 milliliter volumes to 7 mm Finn Chambers (Allerderm, Petaluma, CA) and affixed to the intact, non-inflamed skin of the back.

The use of 20% SLS is the minimum level classified as irritant (R38) by EEC (regulatory guideline of European Union) criteria[21] and served as a positive control. Subjects wore the patch tests for 24 hours and reactions were graded immediately upon removal by visual assessment of the patch sites using a 3-point grading scale of increasing irritation (0: no reaction; +: weakly positive reaction characterized by mild erythema across most of the treatment site; ++: strong positive reaction characterized by spreading erythema with edema). Positive patch tests were assessed for erythema, induration, and crusting. Irritancy, unlike allergy, is appropriately determined at 24 hours after exposure, and is often characterized by crusting at the patch test site.

In the first phase, individual differences in skin response (responders/non-responders) were observed starting at concentrations of 2.5 % SLS, 1 % NaOH and 0.5% BKC. Based on this, the concentration range for the second phase was set as: SLS: 2.5%, 5.0% and 20%; **NaOH:** 1%, 2.5% and 5.0% and **BAK:** 0.5%, 1.0% and 2.5%. In the rest of the study, patients had nine patch tests of three test substances applied to the intact skin of the back.

Statistical Analysis

Descriptive statistics were calculated for the demographic characteristics. Comparison of demographic characteristics (age, gender, and ethnicity) and other factors (history of childhood flexural dermatitis, season, and hand washing frequency) between those with positive vs. negative response to the patch test was conducted using t-test (for continuous variables) and chisquare or fisher's exact test (for categorical variables). Subjects were considered responders to irritant patches if they showed irritancy at concentrations of 2.5% for SLS, 1% for NaOH, and 0.5% for BKC. Ethnicity was reduced to two categories, Caucasian and non-Caucasian. From the self-reported hand washing frequencies, subjects were classified as low frequency or high frequency hand washers using 10 washes per day as the cutoff. Analyses were also performed using hand washing as a continuous variable.

For each participant, we had the date of assessment at baseline and the subsequent 6 visits. For each of these assessments (the baseline and the 6 follow-up visits), a new binary variable (0/1) reflecting a cold or warm season was derived. An assessment period was classified as warm (0) if it fell between April and September and cold (1) if it fell between October and March. Then a cumulative variable that reflects the number of times a participant was seen during a cold season was developed by summing the binary variables from all of the seven assessment periods (the baseline and the 6 subsequent visits). An overall season for a participant was assigned as cold if the participant was assessed on at least 4 cold seasons; warm otherwise. Associations of dermatitis with the irritant patch tests results (responders/non-responders), frequency of hand washing, history of childhood flexural dermatitis and season were analyzed using the Poisson regression where the incidence rate ratios (IRR) was computed as the measure of association when the analyses was based on subjects of free of IHD at baseline (n=90). When the 12 prevalent cases were included the analyses (n=102) the measure of association is referred to as the prevalence ratios (PR). Using data from the follow-up period, the number of positive assessments of IHD was developed for each participant. This discrete count variable that ranges from 0 to 6 was used as the outcome variable of interest in the Poisson regression analyses. The time interval from baseline to end of follow-up was calculated and served as the exposure period (offset) to compute incidence rates of IHD and the corresponding measure of association. The analyses were conducted first using n=102 subjects including the 12 prevalent cases of IHD and then excluding the 12 prevalent cases (n=90). All analyses described in this manuscript were generated using SAS/STAT software, Version 9.2 of the SAS system for Windows (SAS Institute, Cary, NC).

Results

Descriptive characteristics of the study population at baseline are presented by patch test result in Table 1. The study participants had a mean age of 32 years (± 9.6), washed their hands on average 12 times per day (± 5.7) and were composed of 64% females and the majority was Caucasian (76%). 46 of the 90 subjects with no baseline hand dermatitis developed hand dermatitis at least once during the course of the study. The number of times a participant had IHD ranged from zero to five (1.2 ±1.4); 43% had zero count, 28% had one, 18% had two or three, and the remaining 11% had 4 or 5 counts of IHD.

Table 2 presents results of the association between each irritant patch test and hand dermatitis. The results from the two sets of analyses (n=102 vs. n=90) are in agreement. Significant associations between the responses on the SLS irritant patch tests and dermatitis were observed (Table 2). After adjusting for age, gender, ethnicity, season, history of childhood flexural dermatitis, mean indoor relative humidity, glove and hand sanitizer usage, the occurrence rate of dermatitis is 87% larger for those who were diagnosed with IHD at baseline for SLS patch test compared to those who did not respond to the lowest level SLS patch test (PR=1.87, 95% CI:1.06, 3.31, n=102). Exclusion of the prevalent cases at baseline slightly attenuated the association (IRR=1.78, 95% CI: 0.92, 3.45, n=90).

There was a significant association between the frequency of hand washing and irritant dermatitis (Table 2). After adjusting for covariates, those who wash their hands more than 10 times per day are 55% more likely to have occurrence of IHD compared to those who wash their hands less than 10 times per day (PR=1.55, 95% CI: 1.01, 2.39, n=102). The association between hand washing and occurrence of dermatitis remained significant after exclusion of the prevalent cases (IRR=1.95, 95% CI: 1.16, 3.29). The analysis based on continuous hand washing indicates that for one unit increase in frequency of hand washing per day, the incidence rate of IHD increases by 4% (IRR=1.04, 95% CI: 1.01, 1.07, Table 2).

There was also a significant association between season and dermatitis (IRR=2.76, 95% CI: 1.35, 5.65, n=90, Table 2); the risk of developing IHD during the cold months is nearly three times as much as the risk during the warm months

We examined the association between the SLS patch test and IHD stratified by frequency of hand washing excluding the prevalent cases. The result showed that, among those with low frequency of hand washing (≤10, n=47), the incident rate of developing IHD is 6 times larger for those who were diagnosed with IHD at baseline for SLS patch test compared to those who did not (IRR=6.01, 95% CI: 1.13, 31.9). However, among those who wash their hands more frequently (n=40), there was no significant association between SLS patch test and IHD (IRR=1.09, 95% CI: 0.50, 2.40).

Overall, the association between a history of childhood flexural dermatitis and irritant hand dermatitis was not statistically significant (Table 2).

Discussion

SLS, a detergent, is the most representative of hand cleanser chemicals regularly used by our subjects of the three irritants we studied. In this population of health care workers who used hand washing as the primary method of hand hygiene, a positive patch test to SLS has the potential to be indicative of future occurrence of IHD. SLS is the irritant most often used to demonstrate irritant contact dermatitis in experimental settings, but the concentrations used and populations studied vary widely[22–25]. For example, Smith *et al.* also patch-tested subjects with descending concentrations of SLS from 20 to 0.1% and determined their

irritant threshold to SLS. Similarly, they found an association with a lower irritant threshold and development of hand dermatitis[12].

In workers with exposure to irritants other than SLS, other predictive tests may be more useful. Berndt *et al.* conducted irritation tests with dimethyl sulfoxide (DMSO), NaOH, and SLS and also measured transepidermal water loss in a group of metal workers[11]. Participants were followed up over 2.5 years for the development of IHD. They reported that a combination of short irritation tests with DMSO and NaOH and the measurement of skin moisture identified metal workers at high risk for hand dermatitis.

In contrast to previous reports, we did not find a relationship between history of childhood flexural dermatitis and the development of IHD[14, 15, 26]. Nilsson *et al* worked with newly employed hospital staff including nurses, office workers, kitchen workers, and craftsmen[15]. These subjects were followed-up for 20 months and atopic dermatitis was found to be a risk factor for developing IHD. In addition, subjects with atopic dermatitis developed more severe hand eczema than those without atopic dermatitis. Kaukiainen *et al.* studied hand dermatitis in Finnish construction painters and also reported atopic dermatitis as a risk factor for IHD[14]. However, in these studies, subjects were workers presenting for medical attention for hand dermatitis, whereas our study involved workers with frequent hand hygiene who continued to perform wet tasks in the workplace.

Our results showed that a history of childhood flexural dermatitis is not a determining risk factor for IHD development in a population of health care workers, many with long-term employment requiring frequent hand washing. Workers with severe hand dermatitis often have allergic contact and atopic dermatitis in addition to IHD and subjects with history of severe dermatitis were excluded from our study; none of our workers had severe hand dermatitis after enrollment. By focusing on workers currently employed, the ‘healthy worker’ effect may also have eliminated atopic dermatitis sufferers who left employment due to severe hand dermatitis. Our strict definition of atopic dermatitis as having a history of childhood flexural dermatitis without including respiratory atopy may be another reason we have not demonstrated an association with atopic dermatitis.

Our study also showed that certain exogenous factors such as winter season and handwashing frequency contribute to the development of IHD. This confirms what has been previously reported in the literature[16] [17] [18] [19], as well as showing both results for the first time in a single population of healthcare workers. In Cleveland, Ohio, where our study took place, the year is typically divided into 6 months of cold and 6 months of warm weather. Winter seasonality highlights the contribution of low indoor humidity conditions in the development of IHD, as well as the importance of educating workers susceptible to these environments.

The significant association of hand dermatitis in our study with winter season also confirms that the majority, if not all, of our subjects suffered from IHD without secondary allergic contact dermatitis. As we did not patch test for allergic contact dermatitis, we may have missed any cases of allergic contact dermatitis due to winter gloves or hand emollient used in winter. However, irritant contact dermatitis is more common than allergic contact dermatitis, so we assumed most to all of our cases were that of irritant hand dermatitis. Also, irritant contact dermatitis tends to be milder than its allergic counterpart; most of our subjects’ dermatitis was mild and we had no subjects graded as having “severe” dermatitis, supporting a diagnosis of irritant contact dermatitis.

Although our evidence showed that hand washing frequency is associated with the development of IHD, we cannot make quantitative conclusions about the association between hand hygiene and dermatitis because we selected subjects who were frequent hand

washers. In addition, we used the 24-hour closed patch test method, which does not mimic real-life chronic irritant exposure. A repeat open patch testing method would be a better model, but such a method was not feasible within the limits of the study. In addition, our population may have been subjected the 'healthy worker effect', unwittingly excluding any workers that may have left their occupation due to disabling hand dermatitis. Finally, our results may not be translatable to a population using hand hygiene products that differ from SLS.

In summary, our findings showed that a positive patch test reaction to low concentration of SLS is associated with the development of hand dermatitis in this population. Hand washing frequency and cold season were also associated with IHD development. We plan to conduct genetic analysis from blood samples already obtained from this cohort to characterize genetic risk factors for the development of IHD. Both genetic and environmental factors are important in the etiology of hand dermatitis and should be considered in designing strategies to protect, educate and treat susceptible individuals in occupational and non-occupational settings.

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Table 1

Baseline characteristics of study participants according to patch test response (Yes/No) to the irritants (prevalent cases excluded)

Variable	All subjects	SLS, 2.5%			BKC, 0.5%			NaOH, 1%		
	N=90	Yes N=63	NO N=26	p-value	Yes N=59	NO N=31	p-value	Yes N=62	NO N=15	p-value
Age (%)										
20–30	55.4	49.1	68.0	0.4294	63.3	50.9	0.4436	69.2	50.0	0.3866
30–40	26.5	31.6	16.0		23.3	28.3		15.4	32.8	
40–50	8.4	8.8	8.0		10.0	7.6		15.4	8.6	
≥50	9.6	10.5	8.0		3.3	13.2		0.00	8.6	
Gender (%)										
Male	35.6	38.3	26.9	0.3079	32.3	37.5	0.6249	35.7	34.4	1.0000
Female	64.4	61.7	73.1		67.7	62.5		64.3	65.6	
Ethnicity (%)										
Caucasian	76.1	78.7	69.2	0.3453	80.7	73.7	0.4643	78.6	75.8	1.0000
Other	23.9	21.3	30.8		19.4	26.3		21.4	24.2	
Atopy (%)										
Positive	19.3	22.9	11.5	0.2191	32.3	12.3	**0.0234**	14.3	22.6	0.7208
Negative	80.7	77.1	88.5		67.7	87.7		85.7	77.4	
Season (%)										
Warm	55.6	52.4	65.4	0.2609	67.7	49.2	0.0917	73.3	53.2	0.1579
Cold	44.4	47.6	34.6		32.3	50.8		26.7	46.8	
Hand washing freq. (%)										
<10/day	55.8	57.6	50.0	0.5146	53.3	57.1	0.7346	42.9	55.9	0.3779
≥10/day	44.2	42.4	50.0		46.7	42.9		57.1	44.1	
Age	31.8 ± 9.6	32.8 ± 9.2	30.0 ± 10.4	0.2277	29.8 ± 8.4	32.9 ± 10.1	0.1567	29.5 ± 9.1	31.9 ± 8.7	0.3761
Hand washing freq.	11.9 ± 5.7	12.0 ± 6.2	11.8 ± 4.6	0.8766	12.3 ± 5.7	11.7 ± 5.8	0.6619=	11.4 ± 3.8	12.4 ± 6.4	0.5892
Sanitizer use (%)										
Yes	65.0	68.3	60.0	0.4603	60.0	67.9	0.4857	42.9	68.3	0.1211

Variable	All subjects	SLS, 2.5%			BKC, 0.5%			NaOH, 1%		
	N=90	Yes N=63	NO N=26	p-value	Yes N=59	NO N=31	p-value	Yes N=62	NO N=15	p-value
No	35.0	31.7	40.0		40.0	32.1		57.1	31.7	
Glove use (%)										
Yes	82.0	82.3	80.8	0.8688	86.7	79.7	0.4159	80.0	81.9	0.8602
No	18.0	17.7	19.2		13.3	20.3		20.0	18.1	
Mean humidity *	32.1 ±	30.1 ±	37.6 ±	0.0154	35.1 ±	30.5 ±	0.1248	38.6 ±	30.7 ±	0.0397
	13.5	12.2	15.3		14.0	13.1		16.3	12.6	
Mean temperature *	48.9 ±	47.6 ±	52.4 ±	0.0091	50.3 ±	48.2 ±	0.2222	52.8 ±	47.9 ±	0.0268
	7.9	7.1	8.9		7.9	7.9		8.4	7.4	

P-values compare the distribution of categorical covariates or mean values of continuous covariates by categories of the patch test result for each irritant; p-values are from chi-square test of independence or Fisher's exact test for categorical covariates, and from t-test for continuous covariates.

* Mean humidity and temperature data were obtained from the National Climatic Data Center and were not collected as part of the study protocol

Table 2

The association between the exposure variables and development of IHD

	Including the 12 prevalent cases (n=102)						Excluding the 12 prevalent cases (n=90)					
	Unadjusted			Multivariate adjusted			Unadjusted			Multivariate adjusted		
Exposure[+]	**PR**	**95% CI**	**P-value**	**PR**	**95% CI**	**P-value**	**IRR**	**95% CI**	**P-value**	**IRR**	**95% CI**	**P-value**
SLS, 2.5% (yes vs. no)[1]	2.67	1.55, 4.58	0.0004	1.87	1.06, 3.31	0.0310	2.86	1.52, 5.36	0.0011	1.78	0.92, 3.45	0.0887
BKC, 0.5% (yes vs. no)[1]	1.23	0.86, 1.76	0.2631	1.32	0.86, 2.03	0.2077	1.17	0.77, 1.78	0.4492	1.55	0.93, 2.59	0.0941
NaOH, 1% (yes vs. no)[1]	0.78	0.49, 1.25	0.3035	1.30	0.76, 2.21	0.3410	0.83	0.48, 1.45	0.5171	1.60	0.84, 3.04	0.1517
hand washing (>=10 vs. <10)[1]	1.84	1.27, 2.66	0.0011	1.55	1.01, 2.39	0.0481	2.11	1.38, 3.25	0.0006	1.95	1.16, 3.29	0.0123
Frequency of hand washing[1,2]	1.01	0.99, 1.03	0.0593	1.03	1.00, 1.05	0.0236	1.02	0.99, 1.03	0.0562	1.04	1.01, 1.07	0.0086
Season (Cold vs. warm)[3]	1.77	1.11, 2.84	0.0166	1.88	1.12, 3.14	0.0165	2.49	1.29, 4.79	0.0065	2.76	1.35, 5.65	0.0055
Atopy (yes vs. no)[4]	1.19	0.75, 1.87	0.4626	0.86	0.49, 1.49	0.5812	1.41	0.72, 2.26	0.1564	1.08	0.61, 1.93	0.7830

[1] The multivariate model adjusted for age, gender, ethnicity, season, atopy, mean indoor relative humidity, glove and hand sanitizer usage.

[2] Frequency of hand washing was treated as continuous predictor and hence the IRR's represent a multiplicative increase in rate of developing IHD for a unit increase in frequency of hand washing.

[3] The multivariate model adjusted for age, gender, ethnicity, atopy, glove and hand sanitizer usage.

[4] The multivariate model adjusted for age, gender, ethnicity, season, mean indoor relative humidity, glove and hand sanitizer usage;

[+] A separate model was fit for each exposure