

Occupational Contact Allergens: Are They Also Associated With Occupational Asthma?

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Background Workplace exposures that can potentially cause both allergic occupational contact dermatitis (AOCD) and occupational asthma (OA) are not clearly identified.

Methods Occupational contact allergens (OCAs) were identified using North American Contact Dermatitis Group (NACDG) data. Reference documents and systematic reviews were used to determine whether each OCA had been reported to potentially cause OA. The presence or absence of a sensitizer notation in occupational hygiene reference documents was also examined.

Results The 10 most common OCAs were: epoxy resin*, thiuram, carba mix, nickel sulfate*, cobalt chloride*, potassium dichromate*, glyceryl thioglycolate, p-phenylenediamine*, formaldehyde* and glutaraldehyde*. Seven (indicated by *) were determined to be possible causes of OA. Information on sensitizing potential from OH reference materials contained conflicting information.

Conclusions Several common OCAs can also potentially cause OA. Inhalation and dermal exposures to these agents should be controlled and both OA and AOCD should be considered as possible health outcomes. Increased consistency in sensitizer notations is needed. *Am. J. Ind. Med.* © 2012 Wiley Periodicals, Inc.

KEY WORDS: occupational exposures; allergy; occupational dermatitis; occupational asthma; sensitizer notations

INTRODUCTION

Traditionally, research related to occupational contact dermatitis (OCD) and occupational asthma (OA) has been

done in separate organ system silos, with the work focusing on either lung disease or skin disease, but rarely the two together. In the workplace, workers are exposed to chemicals that may cause both irritant and allergic effects, in the skin and lung, by both dermal and inhalation routes of exposure. Agents causing responses in both systems are not well documented, and are not always recognized in the occupational or clinical settings.

In addition, there is an emerging body of research that examines whether each route (dermal and inhalation) of exposure is capable of inducing sensitization and response in the other system. It has been shown in animal models that dermal exposure can cause sensitization which upon first inhalation exposure (in a naïve animal) results in an asthma-like response [Herrick et al., 2002; Klink and Meade, 2003; Vanoirbeek et al., 2004; Zhang et al., 2004; Lehto et al., 2005]. There are also case reports in the literature of workers having both AOCD and OA in

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Contract grant sponsor: Workplace Safety and Insurance Board; Contract grant number: 06031.

Disclosure Statement: The authors report no conflicts of interests.

Institution: This work was completed at the University of Toronto in Toronto, Canada.

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Accepted 21 December 2011

DOI 10.1002/ajim.22015. Published online in Wiley Online Library (wileyonlinelibrary.com).

response to the same chemical [De Raeve et al., 1998; Guarneri et al., 2008; Moulin et al., 2009].

The evidence from animal models and human case reports shows that there is a need to better understand the relationships between inhalation and dermal routes of exposure, and between respiratory and skin responses, to workplace chemicals in order to develop appropriate prevention strategies.

Patch testing is an important clinical tool in the diagnosis of allergic contact dermatitis (ACD). The North American Contact Dermatitis Group (NACDG) is a group of dermatologists across the United States and Canada who have agreed to patch test patients to standard sets of allergens according to a standardized protocol and pool their data for surveillance and research purposes [Zug et al., 2009]. Members are dermatologists trained in patch testing and experienced in the diagnosis of occupational skin disease; two of the thirteen members of the NACDG are located in Canada. The group uses standardized methods for patch testing and interpretation of results, and also regularly reviews the results of the pooled patch test results from their clinics.

The NACDG database offers an opportunity to examine contact allergens in a large clinical population. There is no equivalent database containing data on airway sensitizers.

The aim of this study was to identify the most common occupational contact allergens (OCAs) in the Canadian portion of the NACDG data, and to determine whether these agents were also airway sensitizers using the peer-reviewed occupational asthma literature. The secondary aim was to identify whether or not the common OCAs were noted as skin or respiratory sensitizers in common occupational hygiene (OH) reference documents.

MATERIALS AND METHODS

De-identified patient data were obtained for the two Canadian NACDG sites for the period January 1, 2001 to December 31, 2006. This data represented three 2-year cycles of NACDG data collection. All patients were patch tested with a standard screening series of 65 allergens (standard tray); a standardized technique was followed in all cases [Pratt et al., 2004]. Informed consent was obtained from all patients as required by each study center's human research committee. This study was approved by the St. Michael's Research Ethics Board.

During each 2-year study period the standard patch test tray included sixty-five (65) allergens; changes to this standard tray are made between cycles. Generally, the allergens removed have low rates of positive response, and the allergens added are emerging as more common allergens. Fifty-eight (58) allergens were common to all three NACDG cycles included in this analysis. None of the

fourteen allergens excluded were known, common occupational allergens.

For each patient, the physician assigned up to three diagnostic codes which indicate the diagnosis. The work-relatedness of the diagnosis was also recorded by the physician as a separate variable (yes, no, unsure, or not tested). For all patients, their response to each of the individual 58 allergens was recorded as allergic, unknown, negative, or not tested. The work-relatedness for each individual allergen (separate from the diagnosis) was recorded as yes, no, unsure, or not tested. Additional information on the subjects' age, sex, and race was included in the data.

Diagnosis of Occupational Allergic Contact Dermatitis

Subjects were considered to have allergic contact dermatitis (ACD) if any of the three diagnostic codes were "allergic dermatitis." Subjects were considered to have occupational-related ACD (AOCD) if there was a diagnostic code of "allergic dermatitis" and if the overall diagnosis was coded as occupationally-related (yes). Subjects where the overall occupationally-related variable was coded as "unsure" were not included as cases of AOCD for this analysis.

Determination of Occupationally-Relevant Positive Patch Test Responses

Occupational contact allergens (OCAs) were identified using the response code (allergic) and the work-relatedness code (yes) assigned to the individual allergens tested. The number of individual positive patch test (PPT) responses that were coded both as occupational (allergen specific) and allergic (allergen specific) were counted for each allergen. As the OCAs were determined based on individual allergen responses, it was possible for a single subject to contribute multiple times to the OCA frequency table.

Differences between occupational and non-occupational ACD cases were tested using ANOVA (continuous variables) and chi-square (categorical variables) tests. All analyses were conducted using SAS v9.2 [SAS Institute Inc., 2008].

Determination of Whether OCAs May Also Cause OA

Whether each of the ten most common OCAs was also a potential cause of work-related asthma was determined using two reference documents that are considered authoritative sources of information among the

occupational asthma research community. Where no information was available in the reference sources, the peer-reviewed literature was searched systematically.

The first source for determining whether an OCA has been associated with OA was “*Asthma in the Workplace*,” edited by Bernstein et al. [2006]. If the allergen was listed in “Appendix – Agents Causing Occupational Asthma with Key References” (p.825), the allergen was considered to have been associated with OA.

Second, the United Kingdom Health and Safety Executive’s 2001 publication “*Asthmagen?*” was consulted [UK Health and Safety Executive, 2001]. “*Asthmagen?*” reported on all substances which were suspected of being respiratory sensitizers under the European Union’s (EU) 1996 criteria. If the allergen was listed as meeting the criteria it was considered to be associated with OA.

In cases where a search of the peer-reviewed literature was required, a systematic review strategy was followed. All alternate names for the allergen listed in the manufacturer’s documentation (Chemotechnique® Diagnostics, Vellinge, Sweden) as well as alternate names listed in the HazMap on-line database [National Institutes of Health, 2009] were used. Searches were completed for each allergen (all alternate names) combined with occupational asthma. Searches were limited to human studies published on or before December 31, 2010. The systematic search strategy was completed in three separate databases: Ovid MEDLINE, TOXLINE, and EMBASE. Results from the three database searches were combined for each OCA and all articles were reviewed.

Based on data gathered from the two reference materials and the systematic review of the peer-reviewed literature, each of the ten most common OCAs was classified into one of four categories describing the level of evidence linking the agent with OA:

Established, the OCA is listed in either *Asthma in the Workplace* or *Asthmagen* as a potential cause of OA;

Possible, the OCA is not listed in either *Asthma in the Workplace* or *Asthmagen*, but there is some evidence in the peer-reviewed literature (e.g. case reports), OR the evidence in *Asthma in the Workplace* and *Asthmagen* is conflicting;

Negative, studies have investigated the OCA in OA etiology and found negative results;

No evidence located, no evidence of the role of the OCA in the etiology of OA was located.

Determination of Skin Sensitizer Notation Status

Three sources of information available to practicing occupational hygienists were reviewed to assess whether

the 10 most common OCAs identified were listed as possible sensitizers. The sources reviewed were the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) handbook [American Conference of Governmental Industrial Hygienists (ACGIH), 2008], the National Library of Medicine’s HazMap Occupational Exposure to Hazardous Chemical database [National Institutes of Health, 2009] and the NIOSH Pocket Guide to Chemical Hazards [National Institute for Occupational Safety and Health, 2007].

The notations indicating sensitizing potential differed between the OH reference documents. In some cases sensitizing potential was not explicitly noted. The notations that were accepted to indicate the possibility of sensitization resulting from exposure were as follows:

NLM Haz-Map Database: adverse effects ‘Skin’ and ‘Asthma’ as well as potential disease outcomes of ‘Asthma’ and ‘Contact Dermatitis’.

ACGIH TLV Handbook: specific sensitizer notation, ‘SEN’, though this does not differentiate between the systems in which sensitization may occur.

NIOSH Pocket Guide: possible symptoms as ‘Respiratory sensitizer’, ‘Asthma’ or ‘Skin Sensitizer’.

RESULTS

Data received from the NACDG contained 3676 patch test records for the period January 1, 2001–December 31, 2006. In total 1808 (49%) subjects had a diagnosis of allergic contact dermatitis and 619 (17%) subjects had a diagnosis of work-related dermatitis. Overall, 397 subjects (11% of all subjects) met the definition of A OCD.

The ACD and overall population were not observed to have any striking differences in the demographic variables (Table I). There were 354 (10%) subjects who had both an irritant and an allergic diagnosis (data not shown). Among the occupational cases, 20% had both an allergic and an irritant diagnosis ($n = 120$) (data not shown). Among the ACD cases, occupational cases were more likely to be male ($P < 0.0001$) and to be younger ($P < 0.0001$) than the non-occupational cases (Table I).

Common Occupational Contact Allergens

The ten most frequent OCAs (PPT reactions coded as occupational and allergic) were: epoxy resin, thiuram, carba mix, nickel sulfate, cobalt chloride, potassium dichromate, glyceryl thioglycolate, p-phenylenediamine (PPD), glutaraldehyde, and formaldehyde (Table II). In total forty-one allergens were coded as both work-related and allergic in at least one subject.

TABLE I. Basic Descriptive Statistics for the Entire Study Population, Subjects With an Allergic Contact Dermatitis (ACD) Diagnoses and ACD Cases Stratified by Occupational Relatedness

	All patients n (%)	ACD n (%)	AOCD n (%)	Non-Occupational ACD n (%)	P-value
Overall	3676 (100)	1808 (49)	397 (11)	1411 (38)	—
Physician					
A	2167 (59)	1286 (59)	244 (19)	1042 (81)	<0.0001
B	1509 (41)	522 (35)	153 (29)	369 (71)	
Work-related					
Yes	619 (17)	397 (64)	—	—	—
No	2854 (78)	1321 (46)	—	—	
Unsure	203 (5.5)	90 (44)	—	—	
Sex					
Male	1155 (31)	554 (48)	200 (36)	354 (64)	<0.0001
Female	2521 (69)	1254 (50)	197 (16)	1057 (84)	
Race					
White	3265 (89)	1601 (49)	339 (21)	1262 (79)	0.1570
Black	88 (2.4)	45 (51)	15 (33)	30 (67)	
Asiatic	205 (5.6)	105 (51)	27 (26)	78 (74)	
Hispanic	35 (1.0)	11 (31)	4 (36)	7 (64)	
Other	83 (2.3)	46 (55)	12 (26)	34 (74)	
Age (mean, sd)	45.5 (15.9)	45.4 (15.9)	39.3 (11.2)	47.1 (16.6)	<0.0001

Occupational Contact Allergens as Potential Causes of Occupational Asthma

Of the ten most frequent OCAs in our patient population, seven were listed in *Asthma in the Workplace* (all except thiuram, carba mix, and glyceryl thioglycolate) and five were listed in the HSE *Asthmagen* document (some components of epoxy resin systems, nickel sulphite, cobalt chloride, potassium dichromate, and glutaraldehyde) as exposures capable of causing OA (Table III).

TABLE II. Ten Most Common OCAs, Based on the Frequency that Individual PPT Responses to the Allergen Were Coded Both as Work-Related and Allergic

No.	Allergen	n
1	Epoxy resin	49
2	Thiuram	39
3	Carba mix	36
4	Nickel sulfate	22
5	Cobalt chloride	21
6	Potassium dichromate	20
6	Glyceryl thioglycolate	20
8	P-phenylenediamine (PPD)	19
8	Formaldehyde	19
10	Glutaraldehyde	16

Three of the ten most common OCAs in our patient population were not listed in either document: thiuram, carba mix, and glyceryl thioglycolate; the systematic review strategy was completed for each of these agents. The systematic search strategy retrieved the following number

TABLE III. Summary of the Ten Most Frequent OCAs and the Evidence Linking Each to OA in Asthma in the Workplace, UK HSE Asthmagen and PubMed

		Asthma in the Workplace	HSE Asthmagen
1	Components of epoxy resin systems	Yes ^a	Yes ^a
2	Thiuram	Not listed	Not listed
3	Carbamix	Not listed	Not listed
4	Nickel sulfate	Yes	Yes
5	Cobalt chloride	Yes	Yes
6	Potassium dichromate	Yes	Yes
7	Glyceryl thioglycolate	Not listed	Not listed
8	P-phenylenediamine (PPD)	Yes	Watch list
9	Formaldehyde	Yes	No
10	Glutaraldehyde	Yes	Yes

^aEpoxy resins systems contain epoxy monomers and polymers (e.g., bisphenol A, bisphenol F) as well as hardeners (e.g., acid anhydrides and amines). The hardeners are confirmed causes of OA, some epoxy monomers, such as bisphenol A have been associated with OA in a few cases [Kanerva et al., 2000; Hannu et al., 2009; Moulin et al., 2009].

of citations: carba mix—9 articles; thiuram mix—19 articles; and glyceryl thioglycolate—1 article. After review (VA, ST, GL, LH), none of the retrieved articles contained objective diagnostic test results that supported an association between exposure to the OCA and occupational asthma.

Epoxy resin, nickel sulfate, cobalt chloride, potassium dichromate, and glutaraldehyde were classified as having established associations with OA. P-phenylenediamine (PPD) and formaldehyde were classified as possibly associated with OA due to discrepancies between the two reference documents. Thiuram, carba mix, and glyceryl thioglycolate were classified as having no current evidence of causing OA. These categorizations are summarized in Table III.

Sensitizer Notations

Lastly, the presence or absence of a sensitizer notation, or a reasonable equivalent as described in the Methods, was determined for each of the ten most common OCAs in the three OH reference documents (Table IV). The NLM Haz-Map data base was the only source to assign all of the OCAs a skin or contact dermatitis notation (indicating sensitizing or irritant effects); seven were assigned an asthma notation (Table V). All three sources agreed that epoxy resin (or components of epoxy resin systems) and glutaraldehyde were potential sensitizers (either skin or respiratory) but for all other OCAs there was disagreement between the sources.

DISCUSSION

This study generated a list of the ten most common OCAs in the Canadian portion of the 2001–2006 NACDG

population. In 2002 Rietschel et al. published an analysis of the complete NACDG data from 1998 to 2000 and reported that the most common occupational contact allergens in this period were, in descending frequency: thiuram, epoxy resin, carba mix, nickel sulfate, formaldehyde, potassium dichromate, quaternium 15, cobalt chloride, glutaraldehyde, glyceryl thioglycolate, and mercaptobenzothiazole [Rietschel et al., 2002]. With the exception of quaternium 15 and mercaptobenzothiazole, the results presented here are strikingly similar to those of Rietschel et al. This suggests that the results from the 2001–06 Canadian data are at least somewhat representative of the NACDG data as a whole.

A second comparison can be made with the UK's surveillance system data: EPIDERM and the Occupational Physicians Reporting Activity (OPRA). These surveillance schemes group allergens into more holistic groups but results from both indicate that the most common OCAs in the Canadian NACDG population map well to the published EPIDERM and OPRA data [McDonald et al., 2006]. For example, “rubber chemicals and materials”, which would include thiuram and carba mix, were the materials most frequently reported as causing cases of contact dermatitis in both OPRA and EPIDERM from 1996 to 2001 [McDonald et al., 2006]. “Resins and acrylics”, “nickel” and “preservatives” were also in the ten most common agents reported as causes of contact dermatitis during this period. OPRA and EPIDERM do not differentiate between irritant and allergic contact dermatitis; this both explains why “wet work” appears as the second leading cause of dermatitis, and suggests why more of the agents identified in the current study were not more highly ranked in the OPRA/EPIDERM results.

TABLE IV. Categorization of Whether Each Common OCA has the Potential to Cause OA Based on Reference Sources and Systematic Literature Review, Where Necessary

		Established	Asthma Causing Agent?		No Current Evidence
			Possible	Negative	
1	Components of epoxy resin systems	X ^a			
2	Thiuram				X
3	Carba mix				X
4	Nickel sulfate	X			
5	Cobalt chloride	X			
6	Potassium dichromate	X			
7	Glyceryl thioglycolate				X
8	P-phenylenediamine (PPD)		X		
9	Formaldehyde		X		
10	Glutaraldehyde	X			

^aEpoxy resin contains epoxy monomers and polymers (e.g., bisphenol A, bisphenol F) as well as hardeners (e.g., acid anhydrides and amines). The hardeners are confirmed causes of OA, some epoxy monomers, such as bisphenol A have been associated with OA in a few cases [Hannu et al., 2009; Kanerva et al., 2000; Moulin et al., 2009].

TABLE V. Summary of Sensitizer Notations for the Ten Most Common OCAs in Common Occupational Hygiene Reference Documents

	ACGIH TLVs	NLM Haz-map health effects		NIOSH Pocket Guide	
	Sensitizer notation	Asthma	Skin OR contact dermatitis	Resp sensitizer OR asthma	Skin sensitizer
Epoxy resin					
Hardener	Yes	Yes	Yes	Yes	No
Monomer	No	Yes	Yes	No	No
Thiuram	Not listed	No	Yes	No	No
Carba mix	Not listed	No	Yes		Not listed
Nickel sulfate	No	Yes	Yes	Yes	Yes
Cobalt chloride	No	Yes	Yes		Not listed
Potassium dichromate	No	Yes	Yes	No	Yes
Glyceryl thioglycolate	Not listed	No	Yes		Not listed
P-phenylenediamine (PPD)	No	Yes	Yes		Not listed
Formaldehyde	Yes	Yes	Yes	No	No
Glutaraldehyde	Yes	Yes	Yes	Yes	Yes

Not listed = agent not listed in the reference material.

These comparisons suggest that, although the small sample size may have caused the results to be influenced by local industry and case clusters, the most common agents observed in the Canadian NACDG data are common occupational contact allergens in other parts of the world.

Determining whether an OCA is related to occupational asthma presented a few challenges, specifically in the case of epoxy resin. The epoxy resin on the NACDG standard tray contains epichlorhydrin and bisphenol A which react to form the epoxy resin monomer diglycidyl ether of bisphenol A (DGEBA or BADGE). However, a worker using epoxy resin systems in the workplace will likely have exposure to both the epoxy resin (DGEBA or BADGE) as well as at least one hardener to ‘cure’ the epoxy. Several common hardeners, including amine and acid anhydride formulas are known to cause occupational asthma; these agents were listed in both reference texts [UK Health and Safety Executive, 2001; Bernstein et al., 2006] as known causes of OA. Epoxy resin monomer, specifically DGEBA, has also been associated with asthma in the peer-review literature [Kanerva et al., 2000; Hannu et al., 2009; Moulin et al., 2009] but was not listed as a cause of OA in either text. It is clear that components of epoxy resin systems are capable of causing AOCD and OA, and that a worker using epoxy resins systems may be at risk for both OCD and OA from separate chemical exposures during the use of epoxy resin systems. For this reason we included both the epoxy resin monomer and the hardeners in our review of the reference documents and literature.

When the common OCAs were cross-referenced with the OA literature, seven of the ten OCAs were determined

to be established or possible causes of OA (epoxy resin, nickel sulfate, cobalt chloride, potassium dichromate, PPD, formaldehyde and glutaraldehyde). A wide variety of workers may be exposed to these common OCAs in various occupational settings [National Institutes of Health, 2009]. Epoxy resins are commonly used in coatings for metal, wood, concrete, or plastic, but are also found in adhesives, castings and electrical components. Nickel sulfate is used as a dye and in the process of electroplating; it can also be found in both coatings and ceramics and is commonly used in the production of other nickel compounds. Cobalt chloride is found in a wide variety of applications including as a laboratory reagent, in the process of electroplating, and as a glass or porcelain pigment. Potassium dichromate can be used in the processes of dyeing, bleaching and leather tanning and can also be found in some types of cement. It can also be present in the health care setting as an antiseptic or astringent, as well as in painting, printing, coating or staining. P-phenylenediamine (PPD) is present in dark hair dyes used by hairdressers, but can also be used in photographic development. Formaldehyde is used in the production of formaldehyde resins, plywood, particle board and urea-formaldehyde foam. Glutaraldehyde is used for sterilization purposes in health care settings. Embalmers and laboratory workers may have exposure to both formaldehyde and glutaraldehyde.

Three OCAs were found to have no evidence of an association with OA: thiuram, carba mix, and glyceryl thioglycolate. Glyceryl thioglycolate is found in permanent wave solution used by hairdressers. Thiuram and carba mix are accelerants used in rubber manufacturing, and can be present in the final manufactured rubber product (i.e.

rubber elastic components, rubber gloves, rubber tool hand grips). Components of the carba mix allergen can also be found in carbamate pesticides.

The results suggesting an association between epoxy resin and OA are largely based on the link between amine and anhydride hardeners (used to cure the epoxy resin) with OA rather than from the epoxy monomers themselves, though BADGE (or DEGBA) have been shown rarely in three case studies to be related to OA [Kanerva et al., 2000; Hannu et al., 2009; Moulin et al., 2009].

When the ten most common OCAs identified in the Canadian NACDG data were cross-referenced in the occupational hygiene resources only the NLM NIH Haz-Map database identified all ten as causing skin effects. The ACGIH TLV Hand Book reported only epoxy resin hardeners, formaldehyde and glutaraldehyde as potential sensitizing agents, but does not specify the system of effect. The NIOSH Pocket Book identified epoxy resin hardeners, nickel sulfate and glutaraldehyde as potential respiratory sensitizers as well as nickel sulfate, potassium dichromate and glutaraldehyde as possible dermal sensitizers.

In the ACGIH TLV Hand Book the sensitizer (SEN) notation does not distinguish between the respiratory, dermal or conjunctival organ systems. In both the NLM NIH Haz-Map database and the NIOSH Pocket Book respiratory and dermal effects are separate notations. However, the Haz-Map database does not differentiate between sensitizing and irritant, thus a limitation is that the notations could refer to either allergic or irritants exposure effects.

Though each OH reference document has a slightly different purpose and scope, the contradictory information provided by these sources is problematic. Neither a practicing occupational hygienist nor occupational physician should be required to reference multiple sources for comprehensive information on an occupational exposure. More work is needed to ensure consistency in the application of sensitizer notations if workers are to be sufficiently protected; this process has been proposed in other jurisdictions [Schnuch et al., 2002].

This study analyzed six years of patient data from the two Canadian contributors to the NACDG. The results could reflect local clusters of exposure as one of the centers has a large telecommunications industry with known epoxy exposure. Due to the small number of AOCD cases, the data is perhaps more sensitive to these regional clusters. However, the common OCAs that were identified in this study have previously been reported as some of the most frequent OCAs [Rietschel et al., 2002].

Limitations

There are some limitations with our study to be noted. It must be emphasized that the basis for the list of

common OCAs was a database of patch test data focused exclusively on contact sensitizers. The OCAs identified as possible causes of OA should not be interpreted as common causes of OA, but rather as common contact sensitizers (or common causes of ACD) that are also capable of causing OA. No inference on each OCA's likelihood of causing OA, or frequency of cases, can be made from this study.

There is no source of information on occupational respiratory sensitizers that is comparable to the North American Contact Dermatitis Group database, making it challenging to identify the most common asthmagens at the population level. Although the agents discussed in this study are common contact sensitizers they are not necessarily the most common respiratory sensitizers, they are simply capable of causing OA in some workers.

The practical importance of the current findings are 2-fold: first, there are many OCAs that can also cause OA. Awareness of this by occupational hygienists and clinicians alike needs to be improved. Second, the designation of workplace chemicals as potential skin and/or lung sensitizers is lacking in consistency across databases and agencies.

Results from this study highlight the importance of considering both dermal and inhalation routes of exposure. Analysis of the 2001–2006 data from the NACDG Canadian data showed that of the ten most common OCAs, seven have been associated with OA in the literature. Unrecognized or uncontrolled exposure to these agents through either dermal or inhalation routes of exposure can potentially lead to work-related allergic disease in both the skin and the respiratory system.

ACKNOWLEDGMENTS

The authors would like to thank both the North American Contact Dermatitis Group (NACDG) for providing data access for this study and the Research Advisory Council of the Ontario Workplace Safety and Insurance Board for research funding (grant #06031).

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