Journal of Occupational and Environmental Hygiene, 10: 597–608
ISSN: 1545-9624 print / 1545-9632 online
Published with license by JOEH, LLC
DOI: 10.1080/15459624.2013.818236

Prevention Guidance for Isocyanate-Induced Asthma Using Occupational Surveillance Data

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Data from Washington State's work-related asthma surveillance system were used to characterize isocyanate-induced asthma cases occurring from 1999 through 2010. Injured worker interviews and medical records were used to describe the industry, job title, work process, workers' compensation cost, and exposure trends associated with 27 cases of isocyanate-induced asthma. The majority (81%) of cases were classified within the surveillance system as new-onset asthma while 19% were classified as work-aggravated asthma. The workers' compensation cost for isocyanate-induced asthma cases was $1.7 million; this was 14% of the total claims cost for all claims in the asthma surveillance system. The majority of cases (48%) occurred from paint processes, followed by foam application or foam manufacturing (22%). Nine of the asthma cases associated with spray application occurred during application to large or awkward-shaped objects. Six workers who did not directly handle isocyanates (indirect exposure) developed new-onset asthma. Two cases suggest that skin contact and processes secondary to the isocyanate spray application, such as cleanup, contributed to immune sensitization. Surveillance data provide insight for the prevention of isocyanate-induced respiratory disease. Key observations are made regarding the development of work-related asthma in association with a) paint application on large objects difficult to ventilate, b) indirect exposure to isocyanates, c) exposure during secondary or cleanup processes, and d) reports of dermal exposure.

Keywords work-related asthma, occupational asthma, workers compensation, cost, indirect exposure, dermal

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INTRODUCTION

Isocyanates are widely recognized as a common cause for occupational asthma.[1–3] The goal of occupational health surveillance is to inform prevention activities aimed at improving worker health. Many countries administer surveillance programs for occupational respiratory disease. Surveillance systems in both the United Kingdom's West Midlands and in Great Britain name isocyanates as the leading cause of occupational asthma.[4,5] Additionally, Great Britain's surveillance system reports "vehicle paint sprayers" as one of two occupations having the highest rates of new asthma cases per year.[5] The national asthma surveillance system in the United States ranks isocyanates among the top 10 causes for occupational asthma.[6] Washington State conducts work-related asthma surveillance and identifies isocyanates as the 11th most common cause for occupational asthma in Washington State[7]

In addition to asthma, isocyanates are associated in several countries with hypersensitivity pneumonitis.[8–15] Dermal exposure to isocyanates is known to cause irritation and contact dermatitis.[16–18] More significant is the role that dermal exposure may play in the development of isocyanate-induced asthma.[19,20] Animal toxicity studies suggest that skin contact with isocyanates can lead to systemic respiratory sensitization.[21–25] Human epidemiological studies are limited, but do show an association between dermal exposure and respiratory disease.[26–28]

Beyond respiratory disease, there are at least six cases of fatal exposure to isocyanates reported in the literature. A total of three fatal asthma cases are reported for MDI exposure in three different processes: truck bed liner application, foundry work, and foam operation.[29–32] Two fatal cases were identified for exposure in auto painting in the 1980s, one specified toluene diisocyanate, and the other case was caused by an unspecified isocyanate in automotive paint.[31,33,34] Finally, there is one fatal case associated with exposure to an unidentified isocyanate while spray painting in furniture manufacturing.[35]

Occupational health surveillance has the potential to characterize isocyanate-induced asthma so that research, policy, and educational outreach can be strategically directed to specific industries or applications for disease prevention. Isocyanate-induced asthma cases identified in the surveillance system described here occurred during the period 1999–2010. Cases were reviewed in-depth to characterize the job title, process description, isocyanate species, and workers' compensation costs associated with the asthma case. The purpose of this review was to identify isocyanate-based processes

associated with asthma, and to characterize exposure to help inform prevention activities.

METHODS

Washington's Workers' Compensation System

Workers' compensation insurance is mandated for all nonfederal employers in Washington State unless they are covered by an alternative workers' compensation program (e.g., Federal Employees' Compensation Act, Longshoremen's and Harbor Workers' Compensation Act). Workers' compensation insurance can be obtained through either (a) the state's industrial State Fund (SF) insurance program administered by the Department of Labor & Industries (L&I) or (b) through self-insurance. The State Fund provides coverage for approximately 1.9 million (about two-thirds) of the workers in the state and 99.7% of all employers. The remaining 450 employers self-insure for workers' compensation. To self-insure, employers must have at least $25 million in assets, an effective accident-prevention program, a minimum of 3 years of business operations, and specific liquidity requirements.[36] Specific occupations and employers that are exempted from mandatory workers' compensation include domestic workers and sole proprietors such as specialty trade contractors. [36]

Distinction between State Fund and self-insured workers is made because while data from both programs are collected into L&I's Workers' Compensation database, less information about self-insurance claims (medical records and claim costs) is typically reported to the state. Because of this, the surveillance system described here reflects primarily State Fund-insured workers. Occupational asthma is a reportable condition in Washington State for health care providers and health care facilities.[37] Cases are to be reported directly to the Safety and Health Assessment and Research for Prevention (SHARP) program, regardless of the insurance source, through confidential case reporting.

Work-Related Asthma Surveillance Program

Washington State's asthma surveillance system has been described in detail.[7] In brief, the surveillance system extracts monthly those workers' compensation claims from the Workers' Compensation database with the word "asthma" (or its misspelling) on the Report of Industrial Injury or Occupational Disease (RIIOD) claim form. Claims are reviewed and educational materials are sent to each claimant. Cases are interviewed by telephone to obtain additional data on workplace exposures and medical history. The surveillance protocols, phone interview, and educational materials were approved by the Washington State Institutional Review Board.

Two primary goals of the surveillance system are to classify the type of asthma and to document the agent causing the asthma. This information is obtained through a questionnaire administered over the telephone with the injured worker. The questionnaire incorporates the Sentinel Event Notification System for Occupational Risks (SENSOR) case classification scheme for occupational asthma adopted by the National Institute for Occupational Safety and Health (NIOSH).[38] There are three SENSOR asthma classifications including: Work-Aggravated Asthma (WAA), New-Onset Asthma with latency (NOA), and new-onset asthma without latency known as Reactive Airways Dysfunction Syndrome (RADS).[38,39]

Within the SENSOR case classification scheme, WAA is defined as work-related exacerbations of a preexisting asthma condition. Workers with a history of symptomatic or treated asthma within the past 2 years and who have an increase in symptoms or use of asthma medications are classified as having work-aggravated asthma.[38,39] Workers with no history of asthma or with preexisting asthma who have been asymptomatic for the past 2 years (e.g., childhood asthma) are considered to have new-onset asthma. NOA refers to sensitizer- or irritant-induced asthma caused by agents that may or may not be previously documented (known) in the medical literature as causes of occupational asthma.

RADS refers to new-onset persistent asthma resulting from a one-time high-dose irritant exposure.[39] The agent(s) that caused the asthma is (are) described by the injured worker during the surveillance interview, and is (are) coded using the Association of Occupational and Environmental Clinics (AOEC) exposure code list.[40] Isocyanates, as an agent, can result in either airway sensitization or act as a respiratory irritant. For cases in which an interview cannot be obtained, medical records that sometimes include Material Safety Data Sheets (MSDS) may be used to code the agent(s) involved in the exposure.

To gain further insight into the isocyanate-induced asthma cases, surveillance interviews and medical records were reviewed by one of the authors and also by a research analyst. Additionally, information to answer the following yes/no questions was sought: 1) if a spray application, was the item large, awkwardly shaped, or a fixed outdoor structure?, and 2) did the injured worker directly handle isocyanates? When an injured worker reported during the surveillance interview or in the medical records that dermal exposure to isocyanates was a factor contributing to his or her asthma, this was noted. These questions were answered in relation to the predominant task performed, or if emergency care was sought, to the task being performed at the time of respiratory distress.

Workers' Compensation Claim Costs

Claim costs for self-insured workers were excluded from the cost summary because these claims have incomplete cost records in the L&I's Workers' Compensation database and cannot be accurately estimated. For State Fund workers' compensation claims the costs presented are based on all costs paid to date for closed claims. For claims that were still active and open ($n = 3$) on the date of extraction (Dec. 15, 2011), the claim costs represent those costs paid to date as well as an estimate of future expected claim costs. Future expected claim costs are estimated by the workers' compensation case reserve unit. Reserves are based on an experienced claim adjudicator's best estimations of claim costs for the life of the claim. If appropriate, reserves are estimated for medical care by injury

type, wage costs, vocational rehabilitation costs, permanent partial disability, pension, and other claim costs. Costs are not adjusted for inflation.

Claims are defined as compensable if they meet a 3-day waiting period for time loss compensation and are further classified as "compensable," "kept-on-salary," "total permanent disability," "fatal," or "loss of earning power." Time loss payments occur over time and in some cases may extend over several years. Both compensable and medical-only (non-compensable) claims from the State Fund are included in this analysis. The indirect cost to employers (e.g., employee turnover, productivity loss, and poor employee morale), the indirect costs to workers, and the administrative costs of managing the claims are not included in the claim costs. The Kruskal-Wallis non-parametric rank test was used to compare the median costs of isocyanate-induced asthma cases with all other asthma cases.

RESULTS

Among the 1,469 cases brought into the asthma surveillance system, there were 27 cases from exposure to isocyanates. Many of the cases are from Washington's manufacturing sector (North American Industry Classification System (NAICS) codes 31–33, Table I) which specializes predominantly in industrial goods (vs. retail goods) and makes up approximately 23% of the state's economy. Washington's leading manufacturing industries include aerospace, secondary forest products, industrial machinery, high-tech assembly, electronics manufacturing, food processing, and medical device manufacturing.

The Standard Occupational Classification (SOC) codes for the 27 isocyanate-induced asthma cases are given in Table II. Table III summarizes the asthma cases by the process causing the asthma, while Table IV provides a high level of detail describing each case. The isocyanates associated with asthma include toluene diisocyanate (TDI), methylene diphenyl diisocyanate (MDI), hexamethylene diisocyanate (HDI), naphthalene diisocyanate (NDI), and isophorone diisocyanate (IPDI). The majority (89%) of isocyanate-induced asthma cases occurred in males, and this is in contrast to "all other" asthma cases which predominantly (59%) occurred in females (Table V). The majority (81%) of isocyanate-induced asthma cases were classified as NOA, including two cases of RADS, which is a type of NOA. In comparison, only 52% of "all other" asthma cases were classified as NOA (Table V). No asthma fatalities occurred from any exposure.

One question answered through the review of surveillance interview data and medical records was the number of spray operation cases (n = 20) which involved large objects difficult to ventilate. Eighteen of the 20 asthma cases involving a spray application had a sufficient description of the object being painted to determine this, and 9 of these 18 cases were found to involve large, awkward, or outdoor (fixed) objects (Table III). These objects are inherently difficult to ventilate effectively because they require laminar airflow over long distances and even with good laminar flow, an awkward shape can result in air turbulence or dead-air spaces. Outdoor objects are typically sprayed without the advantages of mechanical ventilation to help reduce worker exposure. The remaining 9 spray applications involved objects such as automobiles and windows, items that can be and often are painted inside automotive or other spray booths.

A second question answered through data review was whether workers handled isocyanates directly (e.g., operated the spray gun or applicator) or indirectly (e.g., assisted spray

TABLE I. Distribution of Isocyanate-Induced Asthma Cases Across NAICS Code Sector (2-digit) and National Industry (6-digit)

NAICS Code	# Isocyanate-induced asthma cases
23 Construction	
238320 Painting and wall covering contractors	2
238310 Drywall and insulation contractors	1
31–33 Manufacturing	
325510 Paint and coating manufacturing	2
336411 Aircraft manufacturing	2
313230 Nonwoven fabric mills	1
326199 All other plastic product manufacturing	1
327991 Cut stone and stone product manufacturing	1
332321 Metal window and door manufacturing	1
332999 All other misc. fabricated metal product mfg.	1
336214 Travel trailer and camper manufacturing	1
336612 Boat building	1
339950 Sign manufacturing	1
42 Wholesale Trade	
423990 Other misc. durable goods merchant wholesalers	1
54 Professional, scientific, and technical services	
541330 Engineering services	1
81 Other services	
811121 Automotive body, paint, and interior repair and maintenance	8
92 Public administration	
922160 Fire protection	1
924110 Admin. of air and water resources and solid waste mgmt.	1
Total # cases	27

Note: NAICS, North American Industry Classification System, 2007.

TABLE II. Distribution of Isocyanate-Induced Asthma Cases Across Occupations

Standard Occupational Classification (SOC) code	# Isocyanate-induced asthma cases
11 Management Occupations	
119199 Managers, All Other	1
33 Protective Service Occupations	
332011 Firefighters	1
43 Office and Administrative Support Occupations	1
439061 Office Clerks, General	
47 Construction and Extraction Operations	
472061 Construction Craft Laborer	1
472141 Painters, Construction, and Maintenance	3
49 Installation, Maintenance, and Repair Occupations	
491011 First-Line Supervisors of Mechanics, Installers, and Repairers	1
493021 Automotive Body and Related Repairers	1
51 Production Occupations	
512099 Assemblers and Fabricators, All Other	5
514000 Metal Workers and Plastic Workers	2
519112 Painters, Transportation Equipment	1
519121 Coating, Paint, and Spraying Machine Setters, Operators, and Tenders	1
519122 Painters, Transportation Equipment	5
519199 Production Workers, All Other	
53 Transportation and Material Moving Occupations	3
537051 Industrial Truck and Tractor Operators	1
Total # cases	27

Note: SOC, Standard Occupational Classification System, 2010

operations or performed associated tasks nearby). Twenty-four of the 27 asthma cases had enough information for this to be assessed. Six of these 24 workers (25%) developed new-onset asthma from indirect exposure to isocyanates (see Table III and Table IV). These cases include a forklift operator in foam manufacturing (case 8), an equipment technician in foam manufacturing (case 9), an assistant to an attic insulator (case 12), a tire press operator (case 18), a "line tender" supporting a lead sprayer while coating the inside of a sewer pipe (case 3), and one office worker in a collision repair shop (case 22).

A third observation from the surveillance data was two cases in which notable exposure occurred outside of the main spray task with reports of dermal exposure. Case 15 was a truck bed liner applicator, and he indicated that while he always wore a respirator (various types) when spraying the truck liner inside a ventilated booth, he did not wear personal protective equipment (PPE) while trimming masking tape off the vehicles outside the booth (Table IV). The worker indicated that unmasking the vehicle contributed to his symptoms, and this is possible if the isocyanate is not fully cured at the time of vehicle unmasking. Case 4 was an industrial painter who applied coatings in various construction settings. The medical records indicated that while "full PPE" ("full PPE" not defined) was required when spraying the product, the injured worker indicated that the exposure from handling spent containers and from being inside the container storage area contributed to his symptoms (Table IV).

Overall, some type of paint process was responsible for more than half (n = 15, 56%) of the 27 asthma cases from isocyanate exposure (Table III). The majority (8 cases) of painting cases were for exposure to automotive paints (Table IV, cases 20–27). Industrial paint processes were involved in 4 cases including coatings applied to a missile (case 1), industrial equipment (case 2), city sewer pipe (case 3), and in a construction setting (case 4, Table IV). Two painting cases were for coating signs (cases 5 and 6) and one case resulted from painting unspecified materials inside a spray booth (case 7). Five (19%) cases involved foam (Table III): two cases in foam manufacturing (cases 8 and 9, Table IV), two cases in foam packing (cases 10 and 11), and one case in residential foam insulation (case 12). There were two cases for exposure to adhesives in aircraft manufacturing (cases 13 and 14) and two cases in truck bed lining application (cases 15 and 16). Two cases involved the use of molds, one in synthetic rock manufacturing (case 17) and one in plastic tire assembly (case 18). Finally, there was one case for exposure to sealants during insulated glass manufacturing (case 19).

Information on respiratory protection was obtained through data review for 18 (67%) of the 27 cases. Three cases stated clearly that no respiratory protection was worn (2 of these were indirect exposure). Three injured workers referenced using a dust mask. Four injured workers clearly sought improved respiratory protection after symptom onset or asthma diagnosis: one case adopted progressively greater protection through initially using an air-purifying respirator (APR), then a powered-air-purifying respirator (PAPR), and finally a supplied-air respirator (SAR). Seven cases reported using more than one type of respirator. One case reported that while an APR was used, it was often removed so that the worker could breathe. Detailed information as to the effectiveness of respiratory protection programs, fit tests, or training was typically not available in the interview and medical record information.

Limited information on employment length before diagnosis was available for 24 cases (data not shown). Work history was of somewhat limited value because the length of employment does not necessarily indicate when isocyanate

TABLE III. Summary of the Processes and Trends Associated with Isocyanate-Induced Asthma

Process	# Isocyanate-induced asthma cases	# Cases involving large objects	# Cases indirect exposure
Painting (total cases)	*15*	*7*	*2*
Automotive	8	2	1
Industrial coating	4	4	1
Signs	2	1	–
Unknown	1	–	–
Foam (total cases)	*5*	–	*3*
Manufacturing	2	–	2
Packaging (shipment of goods)	2	–	–
Building insulation	1	–	1
Adhesives in aircraft mfg.	2	2	–
Truck bed liner application	2	–	–
Resin and molds in production mfg.	2	–	1
Sealant	1	–	–
Total	27	9	6

Note: All cases of indirect exposure to isocyanates were classified as New Onset Asthma (NOA).

exposure may have started. For example, the introduction of a new process, product, or job reassignment could create a new exposure after many years of employment. Nonetheless, four (17%) cases were with their employer for 12 months or less before being diagnosed with isocyanate-induced asthma. At the opposite end of employment length, an equal proportion (4 cases, 17%) worked for 20 years or more with their employer before diagnosis. Six (25%) cases worked for 1 to 5 years, 5 (21%) worked 6 to 15 years, and 5 (21%) had worked 16 to 20 years for their employer before developing isocyanate-induced asthma.

The injured worker's employment and health outcome after diagnosis was determined for 16 cases (data not shown). A total of 11 workers left work permanently, while 5 workers returned to the workplace under modifications. At the time records were reviewed, 3 of the 5 returning workers reported a successful return with symptom resolution, 1 worker returned but was looking for a new career, and the final worker returned to work but the medical record did not indicate whether his or her return was successful or not.

The total compensable and medical-only cost for isocyanate-induced asthma was approximately $1.7 million; this was 14% of the total claims cost for asthma claims from all other agents, which totaled $12.5 million (see Table VI). Nearly 78% of the compensable claim cost for isocyanate-induced asthma claims was from 3 claims having at least 1200 time loss days each. In addition to these 3 large time loss claims, there were 5 compensable claims in which a permanent partial disability was awarded for respiratory impairment from exposure to isocyanates. Overall, the median number of lost work days (time loss) for injured workers with isocyanate-induced asthma was 367 days, and this was nine-fold higher than time loss experienced by workers with asthma from all other agents ($p < 0.0005$, Table VI). Similarly, the median cost of compensable claims for workers with isocyanate-induced asthma was approximately $48,000, fourteen-fold greater than the compensable costs for workers with asthma from other agents ($p < 0.0006$). Medical-only costs were not significantly different between the two groups ($p < 0.08$).

DISCUSSION

Review of the 27 isocyanate-induced asthma claims has identified three important observations concerning exposure to isocyanates in the workplace. First, isocyanate-induced asthma is associated with spray application on large, awkward-shaped, or fixed outdoor objects. Second, workers who do not directly handle isocyanates (indirect exposure) can experience an isocyanate dose substantial enough to cause asthma. Third, exposure from secondary tasks such as cleanup and self-reports of dermal exposure contributed to symptoms in two cases. While the majority of cases stemmed from automotive spray applications and processes involving isocyanate-based foam (manufacture, shipment packaging, and insulation) two unusual work processes were identified and are discussed in further detail below. One final observation discussed below regards respiratory protection, and its role in preventing isocyanate-induced asthma.

Three Observations for Exposure Control and Disease Prevention

First, the observation of respiratory disease associated with large-object spraying is supported by exposure assessment conducted by Janko et al. [41] Janko et al. evaluated isocyanate exposures in three categories of spray finishing: continuous spray finishing, auto body repair, and large object spray operations in which the capacity of the spray facility was frequently exceeded by the size and unusual shape of the object being

TABLE IV. Characterization of Isocyanate-Induced Asthma Cases Identified Through a Surveillance System

ID	Job Title	NAICS	Process (Isocyanate)	Respiratory Protection	Asthma
1	Missile Craftsman	541330	*Paint, industrial*: Acute exposure from isocyanate spill in mix room. Otherwise assemble, disassemble and repair missiles.	Respirator used, type not specified.	NOA
2	Painter, industrial equipment	336612	*Paint, industrial*: Auto painting, heavy industrial equipment.	Had used APR. Began using a SAR at symptom onset.	NOA
3	Painter, concrete coating	238320	*Paint, industrial coating (MDI)*: Line inside of city sewer pipe with coating; Assistant to main sprayer.	Half mask, SAR used inconsistently -indirect exposure.	NOA
4	Painter, industrial journeyman	924110	*Paint, industrial coating*: Applied spray coatings in a construction setting.	'Full' PPE required when spraying product; injured worker felt exposure came from handling containers in storage area, when no PPE used.	NOA
5	Painter, industrial signs	238320	*Paint, signs:* Spray coat aluminum signs in spray booth with four to five other workers; spray large signs.	Dust mask	NOA
6	Painter and sign fabricator	339950	*Paint, signs*: Unknown process. Records state respirator was often removed to facilitate breathing	APR	WAA
7	Painter	325510	*Paint (polyurethane)*: Process not specified, various coating applications inside booth.	Half-face occasionally worn.	NOA
8	Forklift driver	313230	*Foam manufacture (TDI)*: Transport foam buns, using forklift, between cure and ship areas of manufacturing plant. Did not work directly with TDI.	None used - indirect exposure.	NOA
9	Equipment technician	325510	*Foam manufacture (MDI, TDI and HDI)*: Worker cleaned spray guns and performed other duties. Foam mfg. occurred inside spray booths.	Occasionally wears half face APR and PAPR - indirect exposure.	NOA
10	Assembler	326199	*Foam packing (MDI)*: Assemble small machines; spray packing foam around them for protection during shipment. Foam is applied inside a booth, but boxes cure on open floor.	Unknown	Unk
11	Aerospace assembler	332999	*Foam packing (TDI)*: Build and solder mechanical boxes; surround boxes with foam spray for protection during shipping.	Unknown	WAA
12	Assistant, residential foam insulator	238310	*Foam insulation (MDI)*: Assist application in small residential attic, no ventilation.	Dust mask at first SOB episode, APR at second episode. Indirect exposure.	RADS
13	Unknown	336411	*Adhesive*: Spray aircraft doors.	Unknown	NOA
14	Interiors mechanic	336411	*Adhesive*: Spray aircraft panels.	Unknown	NOA

(Continued on next page)

TABLE IV. Characterization of Isocyanate-Induced Asthma Cases Identified Through a Surveillance System *(Continued)*

ID	Job Title	NAICS	Process (Isocyanate)	Respiratory Protection	Asthma
15	Mgr. and Sprayer, truck bed linings	811121	*Truck bed liner (MDI)*: Mix and spray truck bed linings. Worker suspected that exposure while vehicle unmasking contributed to his exposure.	APRs and PAPR for 2.5 years, then SAR for the last 9 months.	NOA
16	Sprayer, truck bed linings	811121	*Truck bed liner (MDI)*: Mix and spray truck bed linings.	Full face SAR. Faulty air supply to respirator.	NOA
17	Sprayer; mold maker	327991	*Polyurethane resin and mold (MDI)*: Synthetic rock manufacturing. Process uses molds to form the rocks.	Unknown	WAA
18	Tire press operator	423990	*Polyurethane resin and mold (MDI)*: Worked in tire mounting and de-molding area. Urethane tire production involved injection of MDI product into hot molds.	None used - indirect exposure.	NOA
19	Production Worker	332321	*Sealant (MDI)*: Apply sealant to glass at insulated glass manufacturer.	Unknown	RADS
20	Painter and Stainer	336214	*Paint, automotive*: Paint campers and trailers.	Unknown	NOA
21	Firefighter, fire truck fabricator, painter	922160	*Paint, automotive (HDI, IPDI)*: Paint fire trucks and truck parts in unventilated wash bay.	Dust mask	NOA
22	Manager, automotive office	811121	*Paint, automotive*: Painting occurs on shop floor, outside of booth.	None used - indirect exposure.	NOA
23	Painter, automotive	811121	*Paint, automotive*: Paint autos.	Inconsistent use of APR and SAR	WAA
24	Painter, automotive	811121	*Paint, automotive (HDI, IPDI)*: Paint autos.	SAR used	NOA
25	Painter and Mgr., automotive	811121	*Paint, automotive*: Paint autos.	PPE not used 10 years ago.	NOA
26	Painter, automotive	811121	*Paint, automotive (HDI, IPDI)*: Paint autos and prep work.	Half-face APR at time of attack. Wore PAPR after attack.	WAA
27	Painter, automotive	811121	*Paint, automotive (HDI, IPDI)*: Paint autos.	Full face SAR used in paint booth.	NOA

Notes: NAICS, North American Industry Classification System; when specifically known, the isocyanates are given for the process. TDI, toluene diisocyanate; MDI, methylene diphenyl diisocyanate; HDI, hexamethylene diisocyanate, IPDI, isophorone diisocyanate. Information in the claim records was not sufficient to distinguish between monomeric or oligomeric isocyanate forms. APR, air purifying respirator; PAPR, powered-air purifying respirator; SAR, supplied air respirator; PPE, personal protective equipment; WAA, work-aggravated asthma; NOA, new-onset asthma; RADS, reactive airways dysfunction syndrome (a type of NOA)

painted.[41] The highest exposures to HDI polyisocyanates (HDI_p) were documented during spray painting of large objects such as coaches (buses), boats, and horse trailers.[41] The geometric means (GM) for HDI_p during large-object spraying ranged from 2 to 16 mg/m^3 with a peak of 30 mg/m^3; this exceeds the Oregon Occupational Safety and Health Administration (OSHA) short-term exposure limit (STEL) of 1 mg/m^3 for HDI_p by a large margin. Two contributing factors in the high exposures documented by Janko et al. are: a) the inherent difficulty in ventilating large or outdoor objects and b) team spraying, in which more than one painter is simultaneously generating isocyanate exposure.[41] Fifty percent (n = 9) of the respiratory disease cases presented here for painting and coating processes were associated with large, awkward, or fixed outdoor objects that are difficult to ventilate. The propensity of illness described here is in agreement with Janko et al.'s documentation of high airborne isocyanate exposures from the painting of large and awkward-shaped objects.[41]

Second, six cases document new-onset asthma to isocyanates from indirect exposure. Three of the cases involve

TABLE V. SENSOR Asthma Classification for Isocyanate-Induced Asthma Cases Compared to "All Other" Asthma Cases

	Asthma cases from isocyanates 1999 – 2010	Asthma cases from "all other" agents 2001 – 2010
Total # Cases	27	1438
-Males (%)	24 (89)	590 (38)
# Classified with Diagnosis	26	571
New Onset Asthma (%)	21 (81)	301 (52)
-RADS (%)	*2 (8)*	*62 (11)*
Work-Aggravated Asthma (%)	5 (19)	270 (47)

Notes: SENSOR, Sentinel Event Notification System for Occupational Risk; Two cases of isocyanate-induced asthma were identified between 1999 and 2001, before formal institution of the surveillance system; RADS, Reactive Airways Dysfunction Syndrome

injured workers who typically might not be enrolled in an employer's respiratory protection program such as forklift driver, equipment technician, and automotive office manager. Two additional cases occurred in workers who were not spraying isocyanate product directly, but were indirectly exposed while assisting lead sprayers. Half of the indirect-exposure cases occurred from exposure to MDI associated with the manufacturing of MDI-based foam. The observation of indirect exposure underscores the importance of: a) isocyanate source control, particularly for MDI-based manufacturing processes and b) the use of ventilation and respiratory protection for assistants working in close proximity to an isocyanate application.

The third observation relates to two cases presented here in which injured workers were exposed to isocyanates during secondary tasks (such as cleanup) and reported dermal exposure as contributing to their symptoms. There is evidence from animal toxicity studies[23,24,42] as well as limited human data,[19,21,22] that dermal exposure to isocyanates can lead to systemic respiratory sensitization. In a few limited epidemiological studies, isocyanate skin exposure[27,28] and not wearing gloves when handling isocyanates[26] have been associated with asthma symptoms in some workers. Petsonk et al. described an association between skin exposure during spill cleanup and the cleanup of an MDI blender in a wood products plant and asthma-like symptoms in the workers performing those tasks.[27] Petsonk et al.'s observations are similar to the cleanup tasks reported here for handling empty storage containers and unmasking of vehicles after spray painting.[27] Heederick et al. conducted a comprehensive literature search on primary prevention for occupational asthma and concluded that published case reports and cross-sectional studies provide "limited" evidence that skin exposure contributes to the onset of occupational sensitization and asthma.[20]

Limiting dermal exposure to isocyanates is a prudent approach in the prevention isocyanate-induced asthma.[19,20] The surveillance cases presented here highlight a challenge for limiting dermal exposure: while employers may recognize and control isocyanate exposures during the primary task,

TABLE VI. Workers' Compensation Cost and Time Loss for Isocyanate-Induced Asthma Cases Compared to All Other Asthma Cases

Cost	Isocyanate-induced asthma cases 1999–2010	All other asthma cases 2001–2010	
Total # All Cases	n = 22	n = 839	
Total cost ($)	1,723,867	10,765,746	
Median ($)	22,885	520	
Medical-only ($)	n = 8	n = 584	
Median	1,173	398	$p < 0.08$
Q1–Q3	1,099–1,247	154–881	
Max	88,229	75,894	
Compensable ($)	n = 14	n = 255	
Median	48,112	3,366	$p < 0.0006$
Q1 – Q3	17,632–82,213	719–19,546	
Max	593,032	554,944	
Time loss (days)	n = 14	n = 255	
Median	367	39	$p < 0.0005$
Q1 – Q3	56–954	0–80	
Max	2,375	3,788	

Notes: Cost data available only for medical claims covered by Washington's state insurance system; Compensable claim costs include payment for time lost from work, medical costs, disability awards, and pension costs; all reported *p*-values are Kruskal-Wallis rank test; Two cases of isocyanate-induced asthma were identified between 1999 and 2001, before formal institution of the surveillance system

exposure during secondary tasks may be under-recognized and the importance of dermal protection throughout all tasks needs to be stressed. Selecting appropriate dermal protection in the workplace can be difficult, however, because most glove and coverall manufactures do not provide information specific to protection from isocyanates. The U.S. Environmental Protection Agency (EPA) recommends nitrile gloves when handling isocyanates.[43] Ceballos et al. have shown that while latex is not protective, butyl rubber and thicker (>8 ml) nitrile materials do provide some protection from the isocyanates present in automotive paint formulations.[44]

Characterization of Asthma Cases and Two Notable Work Processes

Two cases reported here involve work processes not commonly associated with occupational asthma. The first involved the use of an MDI-based sealant in insulated glass manufacturing. The production worker (case 19), who had 31 years experience at the facility, experienced respiratory irritation within 30 days of using the MDI-based sealant during window production. The worker's respiratory symptoms resolved when the worker was retrained into the facility's service department. The second processes (case 3) involved the application of an MDI-based protection liner (similar to truck bed liners) inside a city sewer pipe. The worker developed new-onset asthma from indirect exposure as a line tender working inside the pipe during the liner application. The purpose of installing the isocyanate-based liner was to prevent corrosion and to extend the service life of the sewer pipe.

The majority of cases reported here are for exposure to processes that are similar to other cases previously reported. The most common work process presented here is exposure to automotive paints, a process that is well known to cause respiratory disease,[8,45,46] and that has been associated with two fatalities.[33,34] One of the indirect exposures presented here was for an automotive manager in a collision repair setting, and the case is similar to an indirectly exposed automotive secretary with hypersensitivity pneumonitis (HP), reported by Schreiber et al.[9] High airborne exposure to MDI during truck bed lining application has been previously reported in Washington and we report two cases of asthma in truck bed applicators.[47]

Exposure to isocyanates during foam manufacturing is well known to be associated with respiratory illness,[10,12,48], and one fatality[30]; we present two cases of asthma in foam manufacturing here. Two additional foam cases are presented, both associated with spray foam used as a stabilizer in the shipment of mechanical instruments. The development of asthma by two home occupants (non-occupational exposure) following the installation of spray polyurethane foam insulation in a residential attic has been recently reported,[49] and we document occupational asthma in a foam insulation assistant here. An MDI-based resin system for making molds in the manufacture of synthetic rocks is also reported here, similar to a fatality reported by Carino et al. for a MDI-exposed worker in a steel foundry using mold and core processing.[29]

Regarding isocyanate exposure in workplaces overall, there are industrial processes associated with isocyanate-induced respiratory illness that are not reported here. In the wood products industry for example, isocyanate exposure in woodchip board manufacturing[15] and in composite and synthetic wood product manufacturing[27,50] is associated with respiratory illness. In health care, isocyanate asthma has been reported in a nurse handling plaster casts and isocyanates as irritants have been reported in orthopedic nurses working with soft casts.[16,51] While these industries have reported non-isocyanate (i.e., cleaning chemicals, mold, and so on) asthma into Washington's asthma surveillance program,[7] no cases of isocyanate-induced asthma were reported from these industries to date, but cases could be reported in the future.

Respiratory Protection and Isocyanate Exposure

Isocyanate-exposed workers reported using all types of respiratory protection, from dust masks through supplied air systems (Table III). The value of the respiratory protection documented in workers' compensation claims is limited because the respirator's Assigned Protection Factor (APF), cartridge type, and consistency of use cannot be discerned with sufficient detail. Nonetheless, review of these cases raises two useful observations. The first observation concerns laborers assisting lead sprayers in enclosed spaces, such as attics and sewer pipes (cases 12 and 3). In both of these cases, the assistants were not provided the same level of respiratory protection as the leads, despite working in very close proximity to the exposure. To prevent these types of cases elsewhere, product vendors and employers need education on the potential toxicity not just to the spray operator, but for all workers in the vicinity of product application, particularly in enclosed spaces.

The second observation is tied to the association of asthma from exposure to painting large objects that are difficult to ventilate. While there is evidence that respiratory protection can reduce isocyanate exposure in spray operations,[52–54] unfortunately there is little direct evidence in the literature on respirator effectiveness in the primary prevention of respiratory disease.[20] Several of the exposure scenarios presented here are outside of the manufacturing setting, are difficult to effectively ventilate, and therefore rely on effective respiratory protection programs. The effectiveness of respiratory protection programs to prevent asthma in these settings is currently not well understood, and this is an opportunity for further research.

The substitution of isocyanates with less hazardous chemicals could reduce the risk of respiratory illness and is the preferred hierarchy of control. The development, testing, and adoption of isocyanate-free formulations is currently limited and varies among the many processes and products that utilize isocyanates. Toxicity testing and health evaluation of isocyanate-free products are needed to establish the safety of new chemical formulations; this is an area in need of further research and development.

LIMITATIONS

It is probable that the 27 cases reported here do not fully reflect the full burden of occupational asthma caused by isocyanates in the workplace. Work-related asthma is generally thought to be under-recognized, under-reported, and poorly evaluated in the general medical community,[55] and these dynamics are relevant to the identification of isocyanate asthma. Workers who successfully seek alternative employment away from their asthma-causing source are not likely to obtain medical help or to file a worker's compensation claim if their symptoms resolve. For example, an automotive spray painter can successfully transfer away from spray painting into the position of insurance estimator (no exposure) without seeking medical help or filing a claim. Some workers may not relate their symptoms to being caused by exposure in the workplace. Others may know their symptoms to be work-related but chose not to report them for a variety of reasons, including fear of discrimination, job security, or concern over creating an economic burden on their employer.

From a logistical perspective, there are limitations to identifying cases that have been filed and bringing them into the surveillance system. The surveillance system relies on a text word search for the word "asthma" (including misspellings) on the claim form jointly filed by the injured worker, employer, and health care provider to initiate the workers' compensation claim. Therefore claims with no (blank) text information or for which asthma is not recognized at the time of claim initiation are not brought into the surveillance system. Workers employed by a self-insured employer may not be brought into the surveillance system because those claim records are often incomplete.

The medical record review that was done to identify trends (such as direct vs. indirect isocyanate handling) is based on information such as employer-provided job descriptions or statements made from injured workers to their doctor. This information was not validated independently by the authors. Additionally, for indirectly exposed workers, the information does not explicitly rule out the possibility of direct handling at some point in their past work history.

No attempt was made to differentiate between the monomeric and oligomeric forms of isocyanates associated with illness, as this requires product MSDS sheets (not always available) to ascribe this level of detail on a case-by-case basis. The differentiation between the monomeric and oligomeric isocyanate forms is relevant to exposure assessment and in the application of United States-based occupational exposure levels (OELs). This differentiation is not critical when using the United Kingdom's OEL for all isocyanates which is based on the total reactive isocyanate group (TRIG) and does not differentiate between isocyanate forms.

It is important to note that isocyanate exposure from automotive paints is predominantly for exposure to the oligomeric, not the monomeric form, of HDI and IPDI isocyanate.[56–58] Seven (26%) of the 27 cases here involve exposure to automotive paints and subsequently to isocyanates in their oligomeric form. In terms of prevention, this is challenging in the United States because there is no national enforcement (i.e., OSHA permissible exposure levels [PELs]) or guidance (i.e., threshold limit values [TLV®s] or recommended exposure levels [RELs]) for exposure to isocyanate oligomers. Beyond the national level, the state of Oregon has adopted the Bayer Manufacturer Guideline for HDI oligomers (referred to as polyisocyanates).[41]

PREVENTION GUIDANCE AND SUMMARY STATEMENTS

The following summary statements and prevention guidance are based on key observations and trends made following the in-depth review of asthma cases:

1. Spray application on large objects is associated with isocyanate-induced asthma. Half of the asthma cases associated with spray application occurred during application to large or awkward-shaped objects; exposures can be high because the process is inherently difficult to ventilate effectively. Source control through spray gun technology, maximum paint-transfer efficiency, roller application (vs. spray gun), or other means should be explored for these applications. When source control is difficult to achieve, the protection afforded through administrative controls and PPE is essential to protect the worker. Occupational health professionals could take object size into consideration when targeting interventions or when prioritizing resources for airborne exposure monitoring.
2. Workers who are indirectly exposed to isocyanates can develop new-onset asthma. While it is understood that source control is required to minimize exposure for employees directly handling isocyanate products, the cases presented here underscore the role that these measures critically provide for employees who are indirectly exposed, such as forklift drivers, maintenance technicians, or others who may enter areas where isocyanates are being used. Employers can and should factor indirect isocyanate exposure into job hazard analyses.
3. The self-reported information collected through this surveillance system supports the prudent approach to emphasize dermal protection for workers handling isocyanates. The emphasis for dermal protection should include the main isocyanate-based process, but also secondary tasks outside of the main process, such as handling spent containers or for repeated contact—e.g., vehicle unmasking—with uncured isocyanates.
4. Isocyanate-induced asthma is a burden for both employees and employers and was associated here with lost days from work, disability awards, and workers' compensation costs comprising 14% ($1.7 million) of the total cost for all asthma claims.

CONCLUSION

Occupational health surveillance data were used to identify exposure characteristics and to make useful observations for the prevention of isocyanate-induced asthma. Injured worker interviews, coupled with medical record data, were rich sources of information with which to characterize the industries, processes, and circumstances associated with isocyanate exposure.

ACKNOWLEDGMENTS

The authors thank Randy Clark, Diana Ceballos, Don Lofgren, and Todd Schoonover for manuscript review. Thanks to Nick Morris for workers' compensation claim review. This work was supported in part by CDC-NIOSH, grant number 5U60OH008487. This article is solely the responsibility of the authors and does not necessarily represent the official views of CDC-NIOSH.

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