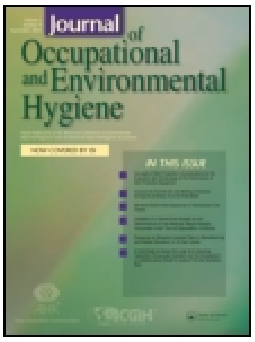

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Slow Curing of Aliphatic Polyisocyanate Paints in Automotive Refinishing: A Potential Source for Skin Exposure

Dhimiter Bello,[1] **Judy Sparer,**[2] **Carrie A. Redlich,**[2] **Karim Ibrahim,**[2]
Meredith H. Stowe,[2] **and Youcheng Liu**[2]

[1]Department of Work Environment, University of Massachusetts Lowell, Lowell, Massachusetts
[2]Occupational and Environmental Medicine Program, Yale University School of Medicine, New Haven, Connecticut

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Two-component, polyurethane paints containing aliphatic isocyanates are widely used in autobody spray painting. Such isocyanates can cause asthma, and skin exposure may be an important route of sensitization and may contribute to the development of isocyanate asthma. Autobody workers are frequently in contact with recently painted, dried auto parts. It is not known how fast the newly painted car surfaces are fully cured, that is, for how long unbound, isocyanate species remain on painted surfaces after initial drying. To address this question, scrap sections of auto bodies were painted and dried by autobody shop painters following regular practice. Routinely used paints were sprayed 23 different times on the parts. Drying was accomplished by baking the part in a paint spray booth by heating it with a heat lamp or air drying in the shop. The 23 sprayed surfaces were sampled at regular time intervals after drying to determine the presence of free NCO groups using the semiquantitative SWYPE technique. Quantitative isocyanate analysis was also performed on two sprayed parts using NIOSH method 5525. Geometric mean curing time of 23 painted surfaces was 56.4 hr (range: 0.8 hrs to 32 days). Unbound isocyanate species of similar composition to the original bulk material remained present on the majority of sampled painted surfaces for up to 120 hours for typical paint formulations and for 1 month for others. The actual curing of polyurethane paints in autobody refinishing can be a slow process. Unbound isocyanates may remain on the surface of painted car parts for prolonged periods (days to weeks) after dried. Such surfaces are an under-recognized potential source of skin exposure to autobody workers.

Keywords autobody shop, dermal exposure, hexamethylene diisocyanate, isocyanate, skin, spray paint

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Address correspondence to: Dhimiter Bello, University of Massachusetts Lowell, Department of Work Environment, Kitson Hall, Room 200 (UML North), 1 University Ave., Lowell, MA 01854; e-mail: dhimiter_bello@uml.edu.

INTRODUCTION

Isocyanates are a family of widely used reactive chemicals with the functional group N=C=O. Aliphatic isocyanates are used extensively in autobody refinishing, largely as blends of nonvolatile polymeric species of hexamethylene diisocyanate (pHDI) and isophorone diisocyanate (pIPDI), with $<1\%$ of the more volatile HDI and IPDI monomers.(1–3) There are about 35,500 autobody shops in the United States, with an estimated 205,000 workers.(4)

Autobody shop workers can have substantial inhalation exposures to aliphatic polyisocyanates,(3,5,6) which can cause isocyanate asthma.(7–10) Spray painters remain one of the highest risk occupations for developing isocyanate asthma.(11,12)

There is growing concern that skin exposure to isocyanates may contribute to the development of sensitization and asthma. Several animal models using HDI,(13) MDI,(14) and TDI(15–17) have employed skin exposure with subsequent inhalation challenge to produce an asthmatic response in the lungs. Limited clinical and field studies suggest that human isocyanate skin exposure may also contribute to the development of isocyanate sensitization and subsequently asthma.(18–20) It is therefore prudent to prevent skin exposure to isocyanates in the workplace, which in turn requires recognition of potential exposure sources.

The focus has long been on isocyanate asthma, and exposure assessment and control efforts have focused largely on reducing respiratory exposures to reactive isocyanates. Skin exposure to isocyanates can also occur in such settings but has not been well documented. Limited studies to date(21,22) have focused primarily on isocyanate contamination of surfaces and skin exposure during activities such as painting and mixing. Autobody shop workers are also in contact with recently painted car parts that appear dry and polymerized, typically without use of personal protective equipment because risk of isocyanate exposure is presumed unlikely. Unmasking, wet or dry sanding, reassembly, buffing or compounding, and detailing are tasks that are done after some coating as soon as the paint is dry. These activities could result in isocyanate skin exposure if the paint is not fully cured.

The purpose of this study was to determine the curing time of newly painted car parts following shop drying, and the potential for skin exposure while in contact with such parts.

METHODS

Terminology

Technical bulletins on paint systems use the terms drying and curing synonymously to mean that the painted auto part is ready for the next step. In this article we use the term drying with that meaning, and we use curing to describe the consumption of NCO groups in polymerization reactions and cross-linking of isocyanate molecules into the polymeric network. Thus, full curing means there are no unbound isocyanate molecules on the painted surface, although there could still be unreacted NCO groups bound to the polymeric network. Although some polymerization occurs during drying, the extent of curing is not known nor the time until curing is complete.

Task Description

Autobody spray work involves paint mixing and spray painting with several coating layers. Isocyanates may be part of the hardener or activator component, which is mixed with polyols, solvents, pigments, and other additives to form a primer, sealer, basecoat, or clearcoat coating. The first layer, priming, is often done on the shop floor with air or infrared lamps as the drying mechanism. The remaining coatings (sealer, base, clearcoat) are usually applied in ventilated spray booths, which are typically equipped to perform a drying cycle at temperatures around 60°C. The sealer coating covers bare metal and may be used over primer or to seal the new factory parts. The next layer is base (or color) coats followed by the last layer—the top or clear coats. Isocyanate hardeners are components of primer, sealer, and clear paints but rarely of base coat paints.

The dry times, which vary by product type and drying method, range from over 5 min between coats to 2–4 hours for tasks such as sanding and can reach 9–16 hours for polishing after clear coating.

Semiquantitative Assessment

Twenty-three independent spray painting applications were executed by shop painters from five different shops using the paint products routinely used in their shops on five autobody parts, resulting in 16 spray applications on metal (fender, hood, door sections) and 7 on plastic (bumpers) surfaces. Each part was coated using 1 of 5 different paint brands of primer ($n = 7$ of 23) or clearcoat ($n = 16$) and dried by baking in a booth (13) heated with infrared lamps or air drying ($n = 7$). Weeks later these parts were recoated for another experiment after being completely cured. Parts that were heated and baked were dried side by side with actual work being done.

Typical drying conditions were: 0.5 hr at 54°C when baked, and at room temperature for 2–3 hr when air dried before further work and overnight (12 hr) before delivering the automobile to the customer. The air-dried coated parts were allowed to set for 20 min following spray painting/coating before sampling to prevent adherence of the qualitative pads onto the wet surface. Sampling for heat-dried parts was initiated 10 min after removal from the heat source, allowing the piece to cool. Typical environmental conditions during the curing period were: average temperature 14–29°C and relative humidity 21–41%.

SWYPE surface pads of 2.5 cm^2 from CLI (Colormetric Laboratories, Des Plaines, Ill.) were used according to manufacturer's specifications, as previously described by Liu et al.(21) The SWYPE is impregnated with a proprietary reagent, specific for the detection of aliphatic isocyanates, which changes color on contact with aliphatic isocyanates. Surfaces were not sprayed with mineral oil as suggested by CLI because of low surface porosity. Mineral oil is used to dissolve unbound isocyanates, which increases their recovery, especially on porous surfaces. Two to 3 min were allowed for color development. An orange to red color on the SWYPE indicated the presence of unbound aliphatic isocyanate species; that is, isocyanates physically transferred from the automobile surface to the SWYPE. Color intensity was rated on a 0 to 5 scale with 0 representing no color change, 1 (light orange), and 5 the highest color intensity, deep red. The color intensity scores from duplicate samples were averaged to obtain a mean score for each time point. All the SWYPE color intensity scores were rated by the same investigator. The investigator wore a pair of Supreno SE powder-free nitrile gloves (Microflex Manufacturing Company, Reno, Nev.) during the sampling and a clean pair after each positive sample.

A grid template was used to avoid sampling identical areas of the auto part and to standardize the sampled surface area to 5 cm × 5 cm. The sampled area was wiped three times in concentric circles starting from the periphery, which took on average 1 min to perform. Two parallel SWYPE samples were collected from adjacent grids for each time point at approximately 0, 1, 2, 3, 5, 7, 12, and 24 hr and every 24 hr thereafter until a negative test (no color change) was observed. A sampling form was used to record the material of the car part, paint brand and quantities used, coating and drying type, and results of each evaluation.

Quantitative Assessment

Quantitative assessment was performed to confirm the SWYPE test results and to evaluate the chemical composition and quantity of unbound isocyanate species on two clearcoat-painted metal parts (Parts 22 and 23) using 4 cm × 4 cm wipe pads, impregnated lightly by CLI with polypropylene glycol (PPG, no. 202304, Aldrich, St. Louis, Mo.) and the quantitative wipe samples were paired side by side with SWYPE samples. PPG-impregnated wipes provide good recovery of unbound isocyanates from the surface.(23) The sampled surface area, wiping technique, frequency, and precautionary measures (gloves and grid template) were similar to the SWYPE and were performed by the same investigator.

Both Parts 22 and 23 were heat dried in a downdraft spray booth. Wipes were collected in duplicates or triplicates at 0.5, 3, 4, 50.5, and 273 hr postdrying for Part 22 and similar intervals for Part 23. The wipe was transferred immediately post-sampling into a scintillation vial containing 10 mL 2.5×10^{-4} M 1-(9-anthracenylmethyl)piperazine derivatizing reagent in methylene chloride and shipped in cooled containers to the laboratory for chemical analysis. Samples were processed through solid phase extraction (SPE) for solvent exchange and purification using LC-Si Supelclean 6 mL (0.5 g) from Supelco (Bellefonte, Pa.) based on the NIOSH method 5525 protocol for total isocyanates in air.(24) Samples were acetylated with 5 μL acetic anhydride after the SPE step, one night before injection into the HPLC. Sample analysis was performed using high-performance liquid chromatography with fluorescence and ultraviolet detection (HPLC/FLD/UV) as previously described.(25) Recovery of HDI monomer and pHDI was near 100%, whereas that of pIPDI was 76–89% over a range of concentrations.(25) The analytical assay does not measure IPDI monomer in the presence of HDI-polyisocyanates due to its co-elution with HDI-derived species.

Statistical Analysis

All statistical analyses including tests for normality, descriptive statistics, and t-tests were performed with SAS version 8 (SAS Institute, Cary, N.C.).

RESULTS

Semiquantitative Assessment

Free NCO groups on unbound isocyanate species remained present on heat- or air-dried auto parts after prolonged periods. The curing time varied considerably by paint brand, coating type, and drying method. The curing times were approximately lognormally distributed. Summary statistics for curing times are provided in Table I. The geometric mean (GM) curing time was 56.4 hr (GSD = 6.9; range = 0.8–768.7) across all 23 tested parts. The GM time (GSD) by curing type (heat vs. air dry) was 58.5 (9.1) vs. 52.0 (3.5) hr, and by coating type (clearcoat vs. primer) was 67.2 (9.4) vs. 37.9 (2.6), respectively. The differences for both comparisons were not statistically significant (Table I). The curing times for clear coated parts (n = 16) as a function of drying method had a GM = 200.5 (range = 120.2–334.5) for air dried (n = 2), and 57.5 (0.8–768.7) for heat dried (n = 14). The formulation with the longest curing time (768.7 hr) was a clearcoat, which was heat dried at 54°C for 20 min. The small number of air-dried parts did not allow for meaningful comparisons with the heat-dried parts.

TABLE I. Statistics of Curing Times for 23 Coats on Autobody Parts

Factor	N	GM[A] (hr)	GSD[B]	Range[C] (hr)	Test for Differences
Curing[D]					
Heat	16	58.5	9.1	0.8–768.7	Not significant
Air	7	52.0	3.5	18.6–334.5	p-value = 0.90
Coating					
Clearcoat	16	67.2	9.4	0.8–768.7	Not significant
Primer	7	37.9	2.6	18.6–166.9	p-value = 0.40

[A] GM = geometric mean.
[B] GSD = geometric standard deviation.
[C] The maximum value of 768.7 hr was with clearcoat, heat dried at 54°C for 20 min.
[D] Fourteen of 16 heat-dried parts were clearcoated; 5 of 7 air-dried parts were primed.

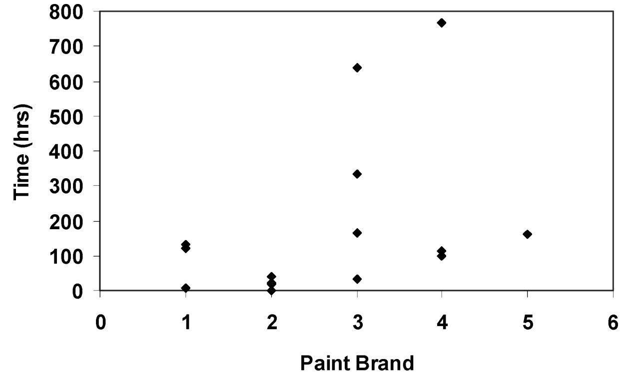

FIGURE 1. Curing times of shop-dried automotive paints as a function of the isocyanate paint brand. Each data point represents an independent test.

Variable curing rates were found for the different paint brands (Figure 1). The GM (GSD) curing times for each isocyanate paint brand were as follows: Brand 1, 32.1 (4.8); Brand 2, 10.5 (5.3); Brand 3, 262.4 (2.76); Brand 4, 205.7 (4.3); Brand 5 consisted of only one sample with a curing time of 162.7 hr. The small sample size for each paint brand did not allow for meaningful statistical comparisons of curing times between them.

The mean initial SWYPE color intensity score was 2.0 for the 23 samples; 30% had an initial color intensity score of <1 (no or marginal color change), 35% had 1 to <3 (definitive color change), and 35% had a score of 3 or higher (intense color change). Unbound isocyanate species were present on the majority of sampled auto part surfaces for up to one week (120 hr) for typical paint formulations and nearly a month for other formulations. The amount of unbound isocyanates on the surface typically followed an exponential decay curve over time, with large amounts coming off in the first few hours and diminishing quickly afterward (Figure 2).

Quantitative Assessment

An average of 12 quantitative wipes were collected on the two auto parts used for quantitative analysis. Two bulk materials were also analyzed for comparison purposes. Both bulks (Brands 4 and 5) were a mixture of pHDI (isocyanurate) and pIPDI (isocyanurate). The chromatograms for each bulk

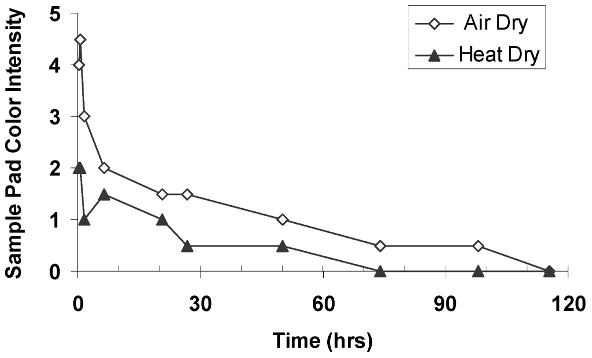

FIGURE 2. Decay curve of the unbound isocyanates on the surface of a clearcoat layer as a function of the drying method (for paint brand 4 shown in Figure 1), as measured by the SWYPE method.

sample and the respective wipe part samples were quite similar, as shown in Figure 3 (for Part 22). These chromatograms confirm that wipes removed unbound isocyanate species with similar composition to the original mix, even many hours after apparent drying, and suggest that the time needed to achieve full polymerization can be quite long.

Polymeric pHDI and pIPDI species were quantified in all 12 samples obtained from Part 22 after drying. The average total NCO amount on the wipe declined as follows: from 4.82 μg total NCO (pHDI + pIPDI) at 0.5 hr to 2.15 at 3 hr, to 0.62 at ~4 hr, to 0.42 at 50.5 hr and was still quantifiable as 0.025 μg NCO at ~273 hr after drying. A similar decay curve was observed for Part 23; from 2.26 μg total NCO at 0.5 hr to 0.47 μg at ~163 hr. HDI monomer was found only in Part 22 at 0.5 hr at 15–33 ng NCO/wipe.

Although IPDI monomer was not measured in these samples, our analytical experience with pIPDI bulks and pIPDI air samples from the autobody shops suggests that IPDI monomer is expected in such samples in comparable levels to HDI monomer, both of which were very low compared with pIPDI and pHDI. Both monomers contribute ~1% of the total NCO group in these paints.[3,25] Thus, free NCO groups in unbound isocyanate species that are not crosslinked with the main polymeric backbone remain present on these surfaces for prolonged periods of time.

The semiquantitative SWYPE method was comparable to the quantitative (HPLC) method for both tests, as illustrated in Figure 4 for Part 22. The SWYPE method thus provides reasonably reliable information on the availability of free NCO groups.

DISCUSSION

To our knowledge this is the first study to evaluate curing time of freshly painted autobody parts. The results demonstrate the presence of uncured, unbound isocyanate species on the paint surface for prolonged periods, typically from hours to 1 week, and in some circumstances for up to a month, contrary to the common belief that such surfaces contain no unbound isocyanates. Quantifiable amounts of free polyisocyanates of pHDI and pIPDI were detected at all time points in wipes obtained from the two parts used for quantitative analysis. The chemical composition of these wipe samples was almost identical to the original bulk materials, suggesting that the rate of polymerization of isocyanate paints in body shops after baking or air drying can be slow, and that isocyanate species, unbound to the polymeric backbone, can be removed from the paint surface on contact.

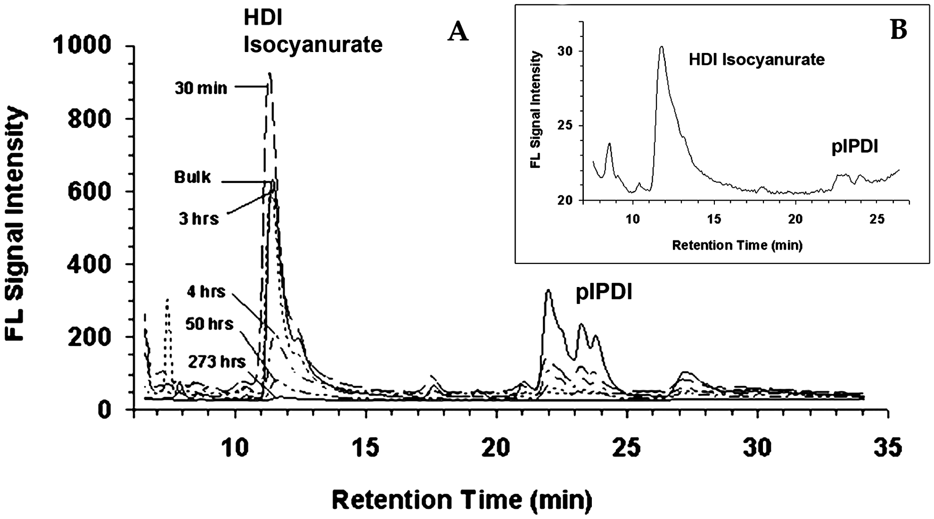

FIGURE 3. (A) Chromatograms (FL = fluorescence detector) of wipe samples for Part 22 over the time period sampled (at 0.5, 3, 4, 50.5 and 273 hr after shop drying) are similar to the bulk paint sample, indicating that some amounts of the original isocyanate material have not cross-linked/polymerized and can be removed from the surface. (B) Enlarged chromatogram of the sample collected at 273 hr also contains the same major peaks as the bulk paint sample.

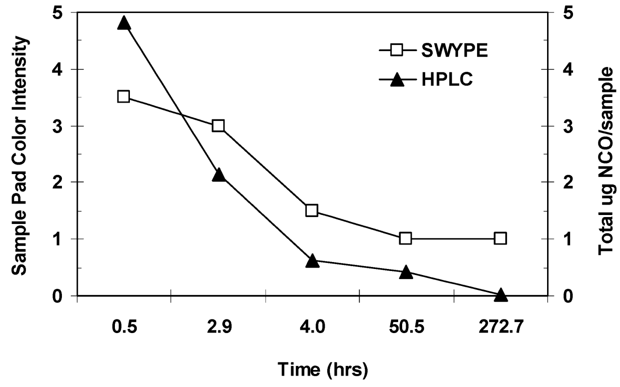

FIGURE 4. Side by side comparison of the curing kinetics for the quantitative (HPLC) and semiquantitative (SWYPE) technique for one auto part (Part 22). Data points are an average of two to three independent measurements. Similar kinetics were observed for the other auto part. The last sample point at ~273 hr on the HPLC curve (Figure 3B) contained 0.025 μg NCO and is therefore a positive sample despite its appearance as nondetectable.

Several aspects of this study support these findings: duplicates on all SWYPE tests; kinetic studies over prolonged periods documenting the decay of unbound isocyanate species; all sampling and scoring tests performed by a single person; and, importantly, the correlation of SWYPE results with the quantitative HPLC analysis for two painted parts. The SWYPE is less sensitive compared with HPLC analysis; thus, a negative SWYPE test does not preclude the possibility of unbound isocyanates on the tested surface. The fact that 70% of all SWYPE tests in this investigation had a definitive color change demonstrates the presence of unbound isocyanate species in car paints for some time following shop or booth drying. Similar observations for the two common coating layers, primer and clearcoat, and curing method (heat, infrared lamp, vs. air) implies this is a common phenomenon.

PPG-impregnated pads were used for quantitative wipes because PPG provides good recovery of unbound isocyanates from skin and surfaces.(23,26) Although PPG may have had a small effect on the amount of unbound isocyanates recovered, it is unlikely that PPG has produced false positive results. SWYPE samples, which in essence are the equivalent dry pad, were positive and their color intensity paralleled the quantitative wipes in side-by-side tests. The similarity in chemical composition between bulks and quantitative wipes further substantiate the presence of unbound isocyanates on these surfaces.

The availability of unbound isocyanate species on recently painted surfaces, largely as polyisocyanates, indicates potential for skin exposure to workers who contact these parts during tasks such as sanding, buffing, untaping, and polishing of such surfaces. These are tasks where isocyanate exposure traditionally has not been considered to occur and where workers are less likely to wear gloves, compared with paint mixing and spraying.

Whether these surfaces result in human skin exposure is unclear. The transfer rate of isocyanates from such surfaces to skin is not known, neither is the uptake rate of polyisocyanates from the skin into the body. It is possible that skin uptake of polyisocyanates may be modified by co-exposure, such as solvents and/or compromised stratum corneum, such as cuts, abrasion from mechanical forces, hand washing, and other scenarios.

To date, attention has focused primarily on isocyanate respiratory exposures during use of unpolymerized isocyanate products such as fresh paints, uncured foams, and adhesives, with little attention to skin exposure or to the time needed to achieve full curing. Our field studies, observations, and interactions with autobody workers corroborate an overall low awareness of isocyanate skin exposure, whereas isocyanate surface and skin contamination is common. Paint manufacturers in their technical bulletins provide information on dry times of auto parts prior to performing subsequent tasks, such as applying the next coating or sanding, and generic recommendations on reducing inhalation exposure during spray painting. However, there is no mention of the potential for skin and inhalation exposure to isocyanates or solvents following the recommended drying time.

Workers should be advised to avoid direct skin contact with recently painted uncured surfaces. Impermeable gloves should be worn when performing downstream tasks such as untaping, wet sanding, buffing, and detailing. Recently painted autobody parts should be kept in a well-ventilated area following coating or drying.

The primary purpose of this study was to document the availability of unbound isocyanate species on freshly painted surfaces and curing time. Whether such exposures result in skin exposure and contribute to isocyanate sensitization and asthma are important questions that are difficult to address and beyond the scope of this study. For prevention purposes, it would be desirable to identify major determinants of unbound free isocyanate species on painted surfaces, such as humidity, paint amount used, or paint composition, and investigate their influence on the curing rate during actual workplace application. Manpower limited the sample size for evaluating the above determinants in this study. Cost considerations also limited the use of HPLC analysis to two painted car parts; quantitative measurements on other parts may have provided additional useful information. As noted above, this study did not address the question of transferability of unbound isocyanate species to human skin following contact with freshly painted parts, an important area of future study.

CONCLUSION

This study documents an under-recognized source of potential skin exposure to isocyanates in autobody shops: freshly painted dry autobody parts. Free isocyanate groups in unbound isocyanate species were measured in 23 painted surfaces, using five different isocyanate paint brands for priming and clearcoating. The chemical composition of unbound isocyanates transferred on wipes for two car parts, as revealed by HPLC analysis, was strikingly similar to that of the original isocyanate bulk, 2–11 days later, and was composed of polyisocyanate species. Curing proceeds at a much slower rate than originally thought, and unbound isocyanate species can remain on dry painted surfaces for prolonged periods, providing opportunity for skin exposure. Autobody shop workers should be made aware of this exposure potential and take adequate precautions to avoid skin exposure.

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REFERENCES

1. **Bello, D., S.R. Woskie, R.P. Streicher, et al.:** Polyisocyanates in occupational environments: A critical review of exposure limits and metrics. *Am. J. Ind. Med. 46*:480–491 (2004).
2. **Sparer, J., M.H. Stowe, D. Bello, et al.:** Isocyanate exposures in autobody shop work: The SPRAY study. *J. Occup. Environ. Hyg. 1*:570–581 (2004).
3. **Woskie, S.R., J. Sparer, R.J. Gore, et al.:** Determinants of isocyanate exposures in auto body repair and refinishing shops. *Ann. Occup. Hyg. 48*:393–403 (2004).
4. **U.S. Bureau of the Census:** North American Industry Classification System (NAICS) Code 811121, "Automotive Body, Paint, and Interior Repair and Maintenance," In *2002 Economic Census*, Vol. 2006.
5. **Janko, M., K. McCarthy, M. Fajer, and J. van Raalte:** Occupational exposure to 1,6-hexamethylene diisocyanate-based polyisocyanates in the state of Oregon, 1980–1990. *Am. Ind. Hyg. Assoc. J. 53*:331–338 (1992).
6. **Pronk, A., E. Tielemans, G. Skarping, et al.:** Inhalation exposure to isocyanates of car body repair shop workers and industrial spray painters. *Ann. Occup. Hyg. 50*:1–14 (2006).
7. **Randolph, B.W., U.G. Lalloo, E. Gouws, and M.S. Colvin:** An evaluation of the respiratory health status of automotive spray-painters exposed to paints containing hexamethylene di-isocyanates in the greater Durban area. *S. Afr. Med. J. 87*:318–323 (1997).
8. **Redlich, C.A., M.H. Stowe, A.V. Wisnewski, et al.:** Subclinical immunologic and physiologic responses in hexamethylene diisocyanate-exposed auto body shop workers. *Am. J. Ind. Med. 39*:587–597 (2001).
9. **Tornling, G., R. Alexandersson, G. Hedenstierna, and N. Plato:** Decreased lung function and exposure to diisocyanates (HDI and HDI-BT) in car repair painters: Observations on re-examination 6 years after initial study. *Am. J. Ind. Med. 17*:299–310 (1990).
10. **Vandenplas, O., A. Cartier, J. Lesage, et al.:** Prepolymers of hexamethylene diisocyanate as a cause of occupational asthma. *J. Allergy Clin. Immunol. 91*:850–861 (1993).
11. **Di Stefano, F., S. Siriruttanapruk, J. McCoach, M. Di Gioacchino, and P.S. Burge:** Occupational asthma in a highly industrialized region of UK: Report from a local surveillance scheme. *Allerg. Immunol. (Paris) 36*:56–62 (2004).
12. **Ameille, J., G. Pauli, A. Calastreng-Crinquand, et al.:** Reported incidence of occupational asthma in France, 1996–99: The ONAP programme. *Occup. Environ. Med. 60*:136–141 (2003).
13. **Herrick, C. A., L. Xu, A. V. Wisnewski, J. Das, C. A. Redlich and K. Bottomly:** A novel mouse model of diisocyanate-induced asthma showing allergic-type inflammation in the lung after inhaled antigen challenge. *J Allergy Clin. Immunol. 109*:873–878 (2002).
14. **Rattray, N.J., P.A. Botham, P.M. Hext, et al.:** Induction of respiratory hypersensitivity to diphenylmethane-4,4′-diisocyanate (MDI) in guinea pigs. Influence of route of exposure. *Toxicology 88*:15–30 (1994).
15. **Karol, M.H., B.A. Hauth, E.J. Riley, and C. M. Magreni:** Dermal contact with toluene diisocyanate (TDI) produces respiratory tract hypersensitivity in guinea pigs. *Toxicol. Appl. Pharmacol. 58*:221–230 (1981).
16. **Vanoirbeek, J.A., M. Tarkowski, J.L. Ceuppens, E.K. Verbeken, B. Nemery, and P. H. Hoet:** Respiratory response to toluene diisocyanate depends on prior frequency and concentration of dermal sensitization in mice. *Toxicol. Sci. 80*:310–321 (2004).
17. **Ban, M., G. Morel, I. Langonne, N. Huguet, E. Pepin, and S. Binet:** TDI can induce respiratory allergy with Th2-dominated response in mice. *Toxicology 218*:39–47 (2006).
18. **Donnelly, R., J.B. Buick, and J. Macmahon:** Occupational asthma after exposure to plaster casts containing methylene diphenyl diisocyanate. *Occup. Med. (Lond.) 54*:432–434 (2004).
19. **Petsonk, E.L., M.L. Wang, D.M. Lewis, P.D. Siegel, and B.J. Husberg:** Asthma-like symptoms in wood product plant workers exposed to methylene diphenyl diisocyanate. *Chest. 118*:1183–1193 (2000).
20. **Stowe, M., Y. Liu, A. Wisnewski, et al.:** Cross-sectional study of auto body workers exposed to diisocyanates: Does dermal exposure contribute to sensitization? In *Proceedings of the American Thoracic Society*, San Diego, Calif., April 2006.
21. **Liu, Y., J. Sparer, S.R. Woskie, et al.:** Qualitative assessment of isocyanate skin exposure in auto body shops: A pilot study. *Am. J. Ind. Med. 37*:265–274 (2000).
22. **Pronk, A., F. Yu, J. Vlaanderen, E. Tielemans, L. Preller, I. Bobeldijk, et al.:** Dermal, inhalation, and internal exposure to 1,6-HDI and its oligomers in car body repair shop workers and industrial spray painters. *Occup. Environ. Med. 63*:624–631 (2006).
23. **Bello, D., S. R. Woskie, R. P. Streicher, et al.:** A laboratory investigation of the effectiveness of various skin and surface decontaminants for aliphatic polyisocyanates. *J. Environ. Monit. 7*:716–721 (2005).
24. **National Institute for Occupational Safety and Health (NIOSH):** Method 5525, Isocyanates, total (MAP). In *NIOSH Manual of Analytical Methods (NMAM)* 4th Edition, 3rd Suppl., P.C. Schlecht and P.F. O'Connor (eds.). Cincinnati, Ohio: NIOSH, 2003.
25. **Bello, D., R.P. Streicher, and S. R. Woskie:** Evaluation of the NIOSH draft method 5525 for determination of the total reactive isocyanate group (TRIG) for aliphatic isocyanates in autobody repair shops. *J. Environ. Monit. 4*:351–360 (2002).
26. **Wester, R.C., X. Hui, T. Landry, and H. I. Maibach:** In vivo skin decontamination of methylene bisphenyl isocyanate (MDI): soap and water ineffective compared to polypropylene glycol, polyglycol-based cleanser, and corn oil. *Toxicol. Sci. 48*:1–4 (1999).