

# Too Hot to Handle: An Unusual Exposure of HDI in Specialty Painters

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**Background** Hexamethylene Diisocyanate (HDI) is a color stable aliphatic isocyanate that is used in specialty paints as a hardener. Due to the lower vapor pressure of its commercial biuret form, it is considered a relatively “safe” isocyanate from an exposure standpoint. This case series reports on an unusual toxic exposure to HDI. Between November 1993 and May 1994, seven specialty painters and one boiler maker who were working at three different power plants were examined at the Institute of Occupational and Environmental Health at West Virginia University. At their respective work sites, HDI was applied to the hot surfaces of boilers that were not shut down, and allowed sufficient time to cool. Consequently, these workers were exposed to volatile HDI and its thermal decomposition products.

**Methods** All of these workers underwent a complete physical examination, spirometry, and methacholine challenge testing.

**Results** All 8 workers complained of dyspnea, while 4 of the 8 also complained of rash. On examination 3 workers were methacholine challenge positive and 2 had persistent rash. At follow-up 4 years later, 5 workers still had to use inhalation medication and one had progressive asthma and dermatitis. All 8 workers, by the time of the follow-up, had gone through economic and occupational changes.

**Conclusions** This case series reports on an unusual exposure to HDI. It is unusual in that: 1) There were two simultaneous sentinel cases with two different Material Safety Data Sheets (MSDS) for the same product, 2) Exposure was to volatile HDI and its decomposition products and 3) Hazardous conditions of exposure occurred at three different sites. *Am. J. Ind. Med.* 37:431–437, 2000. © 2000 Wiley-Liss, Inc.

**KEY WORDS:** isocyanates; hexamethylene diisocyanate (HDI); asthma; dermatitis

## INTRODUCTION

Isocyanates are low molecular weight aromatic, aliphatic, or cycloaliphatic compounds characterized by a

highly reactive N=C=O group [Karol et al., 1986]. The most commonly used isocyanates are toluene diisocyanate (TDI), 4,4'-diphenylmethane diisocyanate (MDI) and 1,6-hexamethylene diisocyanate (HDI) [Banks et al., 1989].

Polyurethane foams were first produced in Germany during the Second World War, principally using toluene diisocyanate. Dr. Otto Bayer developed the initial technology in 1937 for their use as curing agents for polyurethane resins [Ulrich, 1983]. Reports appeared in the medical literature concerning their respiratory hazards by 1951 [Fuchs and Valade, 1951]. Today, isocyanates are increasingly used in the manufacture of various polyurethane products: elastic and rigid foams, paints, lacquers, adhesives, binding agents, synthetic rubbers, and elastomeric

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fibers [Brorson et al., 1990]. The worldwide production of isocyanates is estimated to be about 3 billion pounds annually with the potential for exposing over 280,000 U.S. workers [NIOSH, 1996].

This case series reports on 8 union specialty painters (and 1 boiler maker) from three facilities who were evaluated at the Institute of Occupational and Environmental Health (IOEH) at West Virginia University in 1993, and were exposed to a urethane hardener containing HDI. Since commercial grade HDI is in a pre-polymer form, it is considered relatively safer than TDI and most isocyanates from a toxic inhalation standpoint [Montanaro, 1992]. However, in this case report, certain generalized conditions of misuse caused it to be quite dangerous.

## MATERIALS AND METHODS

Clinical data and information were collected from both medical records and interviews with the patients. Spirometry and methacholine challenge testing were conducted using American Thoracic Society criteria guidelines and standards. A board certified neuropsychologist on staff at University of West Virginia Medical Center performed neuropsychologic testing according to standard clinical protocols.

### Sentinel Case Presentation

On November 16, 1993 a 33-year-old white male, specialty painter (Patient 1) was referred from a regional emergency room to the IOEH at West Virginia University. He was suffering from a severe rash on his face, hands, and feet, as well as dyspnea. He had been working as a union painter for a contractor at a nearby power plant. The job consisted of applying a two-component paint to a boiler at the plant using the brush and roll method. Due to technical reasons, relating in part to subcontractor incentives, the painting operation occurred shortly after the boiler ceased operation. The two-component paint was applied directly to the hot boiler surface in a poorly ventilated area. No respirators or other personal protective equipment were provided.

An initial and more even severe episode had occurred a month earlier. Patient 1 gradually recovered until the second but milder episode occurred, following another paint application to a hot boiler. He observed that other painters at the job site were also ill. Following the second episode, he was seen at a local ER for dyspnea and rash and was treated with outpatient steroids, and referred to West Virginia University. His past medical history was significant for substance abuse problems and chronic mild hepatitis C. Medications included oral prednisone and topical steroids. His subsequent physical examination significantly showed a severe eczematous reaction involving areas of his face,

back, neck, forearms, and legs, with some peeling of skin. The lungs were clear to auscultation and percussion. The rest of the physical examination was normal.

The assessment included severe contact dermatitis, with secondary photoallergic sequelae, as well as possible respiratory disease (by history) due to an occupational chemical exposure, substance abuse, and hepatitis C. The plan included urine porphyrins (to rule out chemically induced porphyria), CBC, chemistry panel, liver function tests, hepatitis C, urine analysis, chest x-ray, spirometry/diffusing capacity (DLCO), methacholine challenge test, and GI consult. The patient was also counseled to seek help for his substance abuse problem and was kept on temporary total disability (TTD) status.

During a presentation concerning the index case at the Occupational Medicine Ground Rounds, it was brought forward that another patient (Patient 2), from the same union but painting at a different site, had also undergone examination by a different attending physician that same week. Curiously, the painters were presented with different material safety data sheets, featuring different primary ingredients, for an identically named paint product. After extensive discussion with both the manufacturers and other workers who were suffering with similar problems, it was determined that the index case had been provided an out-of-date Material Safety Data Sheet (MSDS). Patient 2's relevant exposures, and exposures of his colleagues seen later were likely due to the urethane hardener which contained 97% polymeric hexamethylene diisocyanate (HDI) and 3% monomeric HDI.

Follow-up examination of Patient 1 four months later revealed persistent rash, though it had become less severe in nature. He stated that exposure to perfumes and other skin irritants exacerbated his dermatitis. He also had new complaints of migraine/tension headaches. Follow-up laboratory data were normal except for hepatitis C antibody, with elevated ALT, AST, and GGT. The patient's physical and pulmonary laboratory examination remained normal. Due to his dermal sensitization he had been unable to resume work. On his final evaluation, he was advised not to work with isocyanate based specialty paints in the future.

### Other Case Presentations

During the 6 months following the examination of Patients 1 and 2, another 6 union painters who had worked at three power plants painting the boilers, as well as 1 boiler maker who worked in the proximity of the painters, were examined at the IOEH. Each of the power plants had been served by a similar subcontract mechanism for painting operations and paint was applied to hot boilers at each facility. Initial history and physical information (Tables I and II), pulmonary and radiographic data (Table III), and

**TABLE I.** Historical Data from Affected Specialty Painters

Patient	1	2	3	4	5	6	7	8
Age	33	35	28	33	38	32	29	38
Gender	M	M	M	M	M	M	M	M
Dyspnea	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Rash	Yes	No	Yes	No	Yes	No	Yes	No
Past med. hx	Hep.C				Crohns		Migraines	
Past hx. atopy/asthma	No	Asthma	No	No	No	No	No	No
Tobacco	Yes	No	No	No	Yes	Yes	Yes	No

**TABLE II.** Physical Examination Data: Initial Respiratory and Dermatologic Findings, HDI Exposed Specialty Painters

Patient	1	2	3	4	5	6	7	8
Respiratory	Normal	Rales	Normal	Normal	Normal	Normal	Normal	Normal
Dermatitis	Face/arms/legs	No	No	No	No	No	Chest	No

**TABLE III.** Pulmonary Function and Radiographic Data from Affected Specialty Painters

Patient	1	2	3	4	5	6	7	8
Spirometry	Normal	Normal	Normal Abnormal: 1997 <sup>a</sup>	Normal	Normal	Normal	Normal	Normal
Methacholine challenge: Date, Dose (mg/ml)	Normal	20 mg/ml	20 mg/ml Positive: 1997 0.2 mg/ml	Normal	5 mg/ml	10 mg/ml	25 mg/ml	Normal
Chest x-ray:	Normal	Normal	—	—	Normal	—	—	—

<sup>a</sup>Denotes 25% decline in FVC, FEV<sub>1</sub> from baseline (1993). Data are 1993-1994; unless otherwise indicated.

**TABLE IV.** Clinical Work Follow-Up Data: Exposed Specialty Painters

Patient	1	2	3	4	5	6	7	8
Dyspnea	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Rash	Yes	No	Yes	No	No	No	No	No
Asthma Med usage	No	Yes	Yes	Yes	Yes	Yes	No	No
Job status Date	Lost F/U 1994 <sup>a</sup>	Painter 1998	Unable to work 1998	Painter 1998	Painter 1998	Not working 1996	Painter 1998	Dry waller 1998

<sup>a</sup>Dates are most recent follow-up.

follow-up data and information (Table IV) are presented for the eight painters.

Table I shows that all 8 patients had complaints of dyspnea, while 4 patients also complained of rash. Only 1 patient had a previous history of asthma. The most significant initial physical findings were dermatological. Two of the four patients with dermatitis continued to complain of persistent rash when examined some 4 to 10 months after their initial examination. This included Patient

1 who exhibited a severe, extensive rash some 4 months after his initial examination at our clinic.

Pulmonary function data (Table III) is significant for the methacholine challenge test results. Initially, all the 8 patients had normal spirometry results. Of the 8 patients who had a methacholine challenge test, 3 tested positive and 2 were borderline. Patient 3 initially had normal spirometry and a borderline methacholine challenge. At follow-up 4 years later he continued to have exacerbation of his asthma

and dermatitis. Repeat spirometry and methacholine challenge performed in 1997 revealed a severe response to the methacholine challenge and a 25% decline in both FVC and FEV1 on spirometry.

Table IV presents follow-up information concerning persistent complaints, including the need for continued medication usage and the occupational impact of the exposure. Approximately 4 years after the initial exposure, 7 of the 8 patients still complained of intermittent dyspnea. Five of these patients still used inhalation medication to control their respiratory disease. Patient 3 continued to experience worsening respiratory disease and dermatitis. Follow-up occupational data in 1999 showed that 7 patients (Patient 1 was lost to follow-up) had job status changes. Three patients were general painters, with only 1 patient continuing as a specialty painter. Others had left this work environment due to sensitization. Patient 3 was unable to work due to progressive occupational asthma and dermatitis. All the patients described marked economic impact due to this exposure. Those who continued to work as painters were in much lower paying jobs.

## DISCUSSION

HDI is a color stable aliphatic isocyanate [Banks et al., 1986], unlike the aromatic isocyanates MDI and TDI. Because of this characteristic, HDI is used in paints as an activating agent and is suited for coatings and external finishes. The vapor pressure of the monomer form is 0.05 mm Hg at room temperature [ATSDR, 1998], which is similar to TDI. When HDI exists in the biuret form, (i.e., three molecules of HDI bound together) which is the usual commercial form, the vapor pressure significantly reduces to  $7.5 \times 10^{-5}$  mm Hg. When employed in the biuret form in HDI paints, the risk of respiratory disease also reduces. Most of the case reports of HDI toxicity occur during applications which produce aerosols of HDI [Alexandersson et al., 1987; Parmeggiani, 1983].

This case series report demonstrates how multiple risk factors can combine to produce a toxic outcome. The urethane hardener was a 97% biuret form of HDI. The application process used either hand- or roller-painting only. In normal circumstances, the risk of vapor or aerosols toxicity would be minimal. However, exposure and resultant toxicity were due to the following factors. The painting process involved application to a very large, confined surface area with poor ventilation. This was compounded by the fact that the painting surface was quite hot since the boilers were not turned off and allowed to cool. Normal operations call for the boiler to be cold before initiating painting and the boiler cooling process normally requires several days. These procedures were circumvented. Contractors' and subcontractors' economic incentives or ignorance may have been the underlying factors. Tempera-

ture readings taken off painted surfaces by a consulting industrial hygienist were reported at 470°F. Actual temperatures at times of application may have deviated above and below this reading. The painters also stated that at times their brushes would flame when painting the boiler surface. We suspect that this report represents an observation of lower ignition temperatures of off-gassing breakdown products of the biuret form of HDI, or of residual solvents used to clean or thin brush paints. Actual ignition of the brushes is also possible, but seems less likely. In addition, personal protective equipment was not issued or used. (There was also no documentation of any industrial hygiene monitoring data to confirm the HDI or HDI breakdown product exposure levels). The outcome of these combined factors, we believe, was significant vaporization of HDI, HDI decomposition products, and worker dermal and inhalation exposure.

The decomposition of polyurethanes by fire results in the release of potentially harmful fumes, such as hydrocarbons, carbon monoxide, hydrogen cyanide, nitrogen oxides, and nitriles, which may have caused an acute toxic exposure [Marks and Metcalfe, 1996]. The chronic effects experienced by the painters are most likely due to the decomposition of HDI biuret at the elevated temperatures. Out of the several forms of pre-polymers, the biuret form of isocyanates is the least thermally stable [Ravey and Pearce, 1997]. By 340°F, HDI biuret completely dissociates to give volatile monomeric units containing isocyanate, urea, and/or amine functional groups [Ravey and Pearce, 1997; Lattimer et al., 1998]. Also, these monomeric units have been shown to recombine in the vapor phase to form aerosols [Ravey and Pearce, 1997]. Finally, the biological potency of HDI is due to its high reactivity with nucleophilic organic functional groups present in proteins, nucleic acids (RNA and DNA), and polysaccharides. It reacts readily with water, alcohols, phenols, thiols, carboxylic acids, and amines to give stable, covalently-bound structures [Von Burg, 1993] resulting in cellular malfunction.

The respiratory and dermatological systems are the major target organs of HDI toxicity. Both human and animal studies demonstrate respiratory tract disease that range from mucosal irritation to asthma or occasionally hypersensitivity pneumonitis [Musk, 1988]. It has been stated that 5–10% of workers, chronically exposed to isocyanates, will develop asthma [Diller, 1988]. Both the monomer and polymeric forms of HDI have been shown to cause asthma [Belin et al., 1981; Cockcroft and Mink, 1979; Grammer et al., 1988; Janko et al., 1992; Usui et al., 1992; Vandenplas et al., 1993; Ferguson et al., 1987], but the polymer form does so infrequently. The frequency of illness in this case series appears to be due to problems related to high temperature applications.

The natural history of isocyanate asthma has classically been thought of as resolution. Increasing number of reports

suggest persistent asthma and spirometry changes once the worker has been removed from possible exposure. Some of the studies [Lozewicz et al., 1987; Fabri et al., 1988; Moller et al., 1984; Paggiaro et al., 1984] suggest that up to 50% of the workers can still have persistent asthma upon follow-up examination and provocative testing. Five of our 8 patients still needed medication to control their respiratory disease 4 years after their initial exposure, and one of these progressed to worsening asthma after cessation. None of these cases were severe. The possible main determinants [Pisati et al., 1993; Rosenberg et al., 1987; Hudson et al., 1985; Mapp et al., 1988; Lozewicz et al., 1987; Moller et al., 1986] of an unfavorable outcome of asthma cited in the literature after cessation of work include: long duration of exposure before the onset of asthma, long duration of symptoms before diagnosis, persistence of exposure after diagnosis, more severe airway obstruction, and a dual or late response on inhalation challenge testing. Moreover, cross-sensitization between different isocyanates can occur [Malo et al., 1983; O'Brien et al., 1979], and other nonspecific irritants can induce allergic reactions once sensitization has occurred. Thus, a conservative strategy once isocyanate sensitization has occurred is permanent removal of the worker from isocyanate exposure.

HDI is also a potent dermal sensitizer. Dermal aspects of isocyanate sensitization may be insufficiently emphasized in health discussions. In animal studies HDI was more potent as a sensitizer than was TDI [Thorne et al., 1987]. The dose required to cause sensitization to HDI was approximately one-tenth the dose required for TDI sensitization. Dermal cross-sensitization among the different isocyanates has also been demonstrated in these studies. In our series, 4 of the 8 patients complained of a rash at their initial examination at our clinic. Two patients demonstrated severe and extensive dermatitis at their initial office visit, which was 4–6 months after their initial exposure. At follow-up 4 years later, one patient still had recurrent exacerbations of his dermatitis and was receiving intermittent oral prednisone and evaluation for immunotherapy.

Previous literature concerning HDI toxicity does not usually feature human neurotoxicity. In our study, 6 patients complained of neurologic symptoms ranging from short-term memory loss to problems with concentration. Seven of the 8 patients underwent neuropsychological testing. Four patients had abnormal results potentially consistent with neurotoxin exposure, and 3 had equivocal results. Assessing causation in small populations is difficult, especially for continuous variables such as human intellectual performance. These painters worked with many different neurotoxic chemicals including solvents and heavy metals. We cannot be certain whether isocyanates, as well as the breakdown products of HDI, or some combination of workplace chemicals common to painters and the social setting are the etiology of their neurologic symptoms.

Important lessons of this case series revolve around the sentinel, MSDS, materials handling, and human aspects. In this case series, there were two almost simultaneous sentinel cases of a similar misuse at two separate facilities. Each of these sentinel cases presented with a different MSDS for the same product, thereby masking the similarity of the problem. After extensive research, it was determined that HDI in the urethane hardener was the cause for the exposure. The accuracy of the material safety data sheet is a critical element in worker protection. We do not know what combination of manufacturer, facility, and contractor activities led to the provision of identically named MSDS describing fundamentally different materials. This points to the need for accurate, up-to-date MSDS information. It also points to a need for provider-diligence in making sure that a complete analysis is performed in order to define etiologic agents, processes, procedures, and consequences. Sentinel cases serve as warnings [Rutstein et al., 1983; Shy et al., 1994]. The need to search for additional victims is apparent in this case series. After initial presentation of two patients, ultimately determined to have the same procedural exposure, six additional symptomatic patients were discovered in our immediate region. The three power plant facilities where exposure occurred are all in or adjacent to Northern West Virginia. Whether there is a national scope to this problem is, as yet, unknown.

An essential public health purpose of this report is to point out the inappropriateness of handling procedures. There were several levels of error and inadequate oversight, which led to a toxic outcome. Management had clear procedures for cooling boilers before application of hazardous materials, which were subverted by a subcontract mechanism and incentives for “timely” job completion that affected subcontract operations and worker health outcomes. Application of epoxy materials to hot surfaces is clearly inappropriate. Establishing the exact characteristics of the exposures in this case series would have clear value. A thorough occupational hygiene assessment, safely modeling the conditions of exposure with industrial hygiene chemistry analysis of products, would resolve unanswered questions about the precise agents in these episodes. Preventing the exposure is a simpler and effective public health endeavor. There is a clear need for owner-contractor communication so that an adequate hazmat plan is created for these kinds of applications.

There were also several areas of social losses for these workers which have compensation and employment system implications. Seven of the patients still had complaints of dyspnea, with 5 of them also requiring intermittent medication to control their respiratory symptoms 4 years after exposure. One patient was still having progressive exacerbations of both his asthma and dermatitis. Yet, an independent medical review for impairment ratings under workers compensation led to maximum ratings of 10

percent impairment. In the state where these illnesses occurred, no permanent benefits accrue at this rating. This reflects the inability of impairment ratings to adequately compensate a disease that is neither stable nor predictable in nature [Moscato et al., 1999], as well as the possible difference between impairment and disability when the impairment impacts more directly on employment than on other quality of life issues.

The majority of these painters can no longer be professionally related to applications of specialty paints, which is a de facto functional requirement for continued success in the union painter environment. Some of the men are now working as general non-union paint contractors at much lower salary rates. Others have chosen from a narrowed spectrum of job opportunities, unrelated to painting operations, that are also much lower paying.

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