

Dermal and Inhalation Exposure to Methylene Bisphenyl Isocyanate (MDI) in Iron Foundry Workers

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Diisocyanates are a group of chemically reactive agents, which are used in the production of coatings, adhesives, polyurethane foams, and parts for the automotive industry and as curing agents for cores in the foundry industry. Dermal and inhalation exposure to methylene bisphenyl isocyanate (MDI) is associated with respiratory sensitization and occupational asthma. However, limited research has been performed on the quantitative evaluation of dermal and inhalation exposure to MDI in occupationally exposed workers. The objective of this research was to quantify dermal and inhalation exposure levels in iron foundry workers. Workers involved in mechanized moulding and mechanized production of cores were monitored: 12 core makers, 2 core-sand preparers, and 5 core installers. Personal breathing-zone levels of MDI were measured using impregnated filter sampling. Dermal exposure to MDI was measured using a tape-strip technique. Three or five consecutive tape-strip samples were collected from five exposed skin areas (right and left forefingers, left and right wrists, and forehead). The average personal air concentration was $0.55 \mu\text{g m}^{-3}$, 50-fold lower than the Swedish occupational exposure limit of $30 \mu\text{g m}^{-3}$. The core makers had an average exposure of $0.77 \mu\text{g m}^{-3}$, which was not significantly different from core installers' and core-sand preparers' average exposure of $0.16 \mu\text{g m}^{-3}$ ($P = 0.059$). Three core makers had a 10-fold higher inhalation exposure than the other core makers. The core makers' mean dermal exposure at different skin sites varied from 0.13 to $0.34 \mu\text{g}$ while the two other groups' exposure ranged from 0.006 to $0.062 \mu\text{g}$. No significant difference was observed in the MDI levels between the skin sites in a pairwise comparison, except for left forefinger compared to left and right wrist ($P < 0.05$). In addition, quantifiable but decreasing levels of MDI were observed in the consecutive tape strip per site indicating MDI penetration into the skin. This study indicates that exposure to MDI can be quantified on workers' skin even if air levels are close to unquantifiable. Thus, the potential for uncured MDI to deposit on and penetrate into the skin is demonstrated. Therefore, dermal exposure along with inhalation exposure to MDI should be measured in the occupational settings where MDI is present in order to shed light on their roles in the development of occupational isocyanate asthma.

Keywords: dermal; diisocyanate; exposure; foundry workers; inhalation; methylene bisphenyl isocyanate (MDI)

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INTRODUCTION

Diisocyanates are a group of chemically reactive agents, which are extensively used in the production of coatings, adhesives, polyurethane foams, and parts for automotive industry. Diisocyanate formulations are also used for isolation of central heating pipes and tubes and as curing agents for cores in the foundry industry. The industrial use of diisocyanates increased drastically during 1990s [International Agency for Research on Cancer (IARC), 1999a,b]. The world production is estimated to be >4 billion tons annually and it is predicted to increase 10–15% per year (Turcot, 2000; Allport *et al.*, 2003). Production of diisocyanates in Sweden is 10 000 tons annually (Swedish Chemicals Agency, 2009).

Inhalation has long been considered to be the primary route for diisocyanate exposure. A number of studies describe occupational asthma and allergic contact dermatitis associated with diisocyanate exposure. Redlich and Herrick (2008) concluded in their review that the current scientific data indicate the important role of the skin in the development of occupational lung diseases. In animal models, the most commonly used diisocyanates, toluene diisocyanate (Karol *et al.*, 1981; Ban *et al.*, 2006), 1,6-hexamethylene diisocyanate (HDI) (Herrick *et al.*, 2002), and methylene bisphenyl isocyanate (MDI) (Rattray *et al.*, 1994), have been observed to induce airway hypersensitivity through dermal exposure route, which, in turn, with subsequent inhalation exposure could lead to asthma. Diisocyanate induced asthma and/or sensitization has also been reported in human case studies where workers applied MDI-containing orthopaedic casts and potential for dermal exposure was substantial (Sommer *et al.*, 2000; Donnelly, *et al.*, 2004). However, Larsen *et al.* (2001) observed mild and temporary skin symptoms among nursing staff of an orthopaedic outpatient clinic and suggested that diisocyanates are primarily irritants than sensitizers. Their conclusion was based on interviews and patch testing of 10 nurses and no relationship between exposure time and severity of symptoms was found. In a plant producing laminated wood products, new onset of asthma-like symptoms were documented in one-third of the individuals working with MDI or cleaning spills of liquid MDI. No environmental MDI sampling was conducted during the 2-year study but 7 months after the last health survey, personal breathing-zone samples and one wipe sample of dust from a worker's glove were collected. None of the air samples had detectable levels of MDI, but the glove wipe sample had a measurable quantity

of MDI (Petsonk *et al.*, 2000). Although the mechanistic pathway is unknown, there is increasing toxicological and epidemiological evidence that dermal exposure to diisocyanates plays a role in the development of respiratory sensitization and occupational asthma.

While preventive measures and use of less volatile forms of diisocyanates (e.g. MDI) have reduced the potential for respiratory exposure, development of occupational asthma is still observed in workers whose respiratory exposure is low or non-detectable, prompting us to focus more on the skin as a route of exposure (Bello *et al.*, 2007). It is unlikely that respiratory exposure to diisocyanates alone would occur (i.e. no potential for dermal exposure) in work settings where diisocyanates are used. MDI exposure as a cause for sensitization and asthma was demonstrated among foundry workers (Zammit-Tabona *et al.*, 1983; Liss *et al.*, 1988). Furthermore, Sennbro *et al.* (2006) reported a poor association between air and biomarker levels for MDI (correlation coefficients in the range of 0.51–0.65) with a large individual variation.

In the occupational setting reported here, MDI is used as a component of a binder while using the Cold Box method for core production (Archibald and Smith, 1988). Previously, we conducted a pilot study to identify the skin sites potentially exposed to MDI in this occupational setting. Six workers performing different job tasks (core-sand preparer, core maker, core installer, moulder, caster, and model workshop mechanics) were selected to participate. Five different body sites (i.e. calf, right forefinger, right wrist, neck, and forehead) were sampled by collecting one tape strip per site. We observed quantifiable amounts of MDI in tape samples collected in three body locations (right forefinger, volar side of the right wrist, and the middle of the forehead) in core-sand preparers, core makers, and core installers (I. Liljelind, C. Norberg, L. Egelrud, H. Westberg, K. Eriksson, L. A. Nylander-French, unpublished data). These results indicate potential dermal exposure to MDI in this worker population and, thus, this study was undertaken to quantify dermal and inhalation exposure levels in iron foundry workers performing different work tasks.

MATERIALS AND METHODS

Study population

Our study was carried out in minor section of a large iron foundry with 279 blue- and 53 white-collar workers. The foundry production is 28 000 metric

tons of cast annually, mainly nodular iron (75%) and grey-iron (25%). Most of the products, such as houses for gearboxes and rear shafts, hubs, brake discs, and structural elements in the chassis as well as in the vehicle body, are used in the manufacturing of trucks and wheel loaders. The sand used for moulding was mostly green sand (75% silica, 6% carbon black, 5–6% bentonite, and 13–14% water). Cores were produced based on a phenol–formaldehyde resin (ISOCURE 300 EP 3644, Beijer G&L, Malmö, Sweden) and the curing resin based on a polyol (ISOCURE 600 EP 3642, Beijer G&L). The activator (ACTIVATOR SAR 2, Beijer G&L) was a commercial mixture containing 80–85% homologues and isomers, mainly of 4,4-MDI (product CAS no. 9016-87-9), 10–15% of aromatic solvent-based naphtha, and traces of phosphorous oxichloride. The catalytic agent (GH3, Beijer G&L) was dimethylethylamine.

Workers for this study were selected based on our observations when conducting pilot measurements that covered all job titles in the foundry. Workers involved in core handling, and most potential for dermal exposure, were monitored in this study. The core makers' duties include overseeing the mechanized function of core machines in which the actual core is produced, cleaning the machines by using compressed air, removing damaged cores to a waste bin, and removing the newly baked cores for storage. During core making, frequent dermal contact occurs with newly baked and uncured polyurethane resin. Core-sand preparation comprises handling of the barrels containing polyurethane resins and gaseous catalyst, overseeing the transportation system in which resin is introduced into the core machine, and cleaning the systems and machines. After the core making process, the cores are manually placed in the moulds in a mechanical moulding line. In all, 19 workers were included: 12 core makers, 5 core installers, and 2 core-sand preparers; each work shift included six core makers, two or three core installers, and one core-sand preparer. The workers were usually provided cotton gloves to protect themselves from injuries.

The study was performed on 1 day in November 2006 and on 1 day in May 2007, each day covering a whole work shift. The study was approved by Umeå University Ethics Committee (approval No. EPN dnr 06-026M).

Air measurements

Personal breathing-zone measurements of MDI were conducted using a personal pump (Escort ELF, MSA, Pittsburgh, PA, USA or Air check 2000, SKC Inc., Pittsburgh, PA, USA) operating at 1 l min^{-1} and connected to a 1-(2-methoxyphen-

yl)-piperazine (2-MP)-impregnated mixed cellulose ester filter in a 25-mm Millipore cassette (Sennbro *et al.*, 2004). This sampling method has been described by the Health and Safety Laboratory (1999). Immediately after the sampling, the filter was transferred to glass vials containing 2-MP reagent in toluene. This filter technique enabled us to sample MDI aerosols and vapours. Sample collection was started at the beginning of the work shift and stopped when dermal tape-strip sample collection began. The average sampling time was 370 min (range 191–532 min). Two air samples per a typical work shift (8 h) were collected from each worker.

Dermal exposure measurements

Levels of MDI in the skin were measured using a tape-strip technique for collection of diisocyanates from the skin as described elsewhere (Fent *et al.*, 2006) and modified the analytical technique to be suitable for quantification of MDI in the tape-strip samples as described below (see 'Chemical analysis' and 'Recovery of MDI'). Tape strip ($2.5 \times 4\text{ cm}^2$, Fixomull®, BSN medical GmbH & Co., Hamburg, Germany) were applied to five exposed skin sites (right and left forefingers, volar sides of the left and right wrists, and middle of the forehead) after the work shift. After collection, each tape was placed in a clean glass vial containing dibutylamine (DBA) [0.01 M, Merck FS (for synthesis)] dissolved in 10 ml toluene (Fisher Scientific, High Performance Liquid Chromatography grade) and closed with a screw-tight lid. During each sampling occasion, one field blank for each worker was prepared. Samples were stored at room temperature until analysed within 10 days.

Three to five consecutive tape-strip samples were collected from each site. Our original plan was to collect five tape strip per site from each. However, due to time constraints experienced during one sampling occasion, we had to limit tape stripping to three successive tapes on nine workers (see Table 2). No data on demographic determinants such as hand washing behaviour, usage of protective equipment (e.g. glove usage and changes) and production measures were collected.

Chemical analysis

The analysis of the air filter samples was performed using liquid chromatography mass spectrometry (LC–MS/MS) as described elsewhere (Östin *et al.*, 2002). The tape samples were analysed for MDI with LC–MS (Tinnerberg *et al.*, 1997; Karlsson

et al., 1998; Östin *et al.*, 2002). This method was evaluated to be suitable for the analysis of MDI in tape-strip samples. The limit of detection (LOD) was determined to be 0.01 µg per filter and 0.003 µg per tape and the limit of quantification (LOQ) 0.03 µg per filter and 0.005 µg per tape. The analysis in air using 2-MP was performed by the Department of Occupational and Environmental Medicine at Lund University Hospital, and the corresponding analysis of the tapes was performed at the Department of Occupational and Environmental Medicine at Örebro University Hospital. The laboratory in Örebro is accredited by the Swedish Board for Accreditation and Conformity Assessment.

Recovery of MDI from tape and Teflon® surface

The tape-strip method was evaluated by adding MDI (CAS 101-68-8, 98%, Aldrich Chemical Company Inc., Milwaukee, Wisconsin, USA) to clean tape strip and to a Teflon® surface, respectively. To a set of 12 tapes, 0.004 µg of MDI dissolved in 2 µl of toluene was applied while 0.1 µg in 2 µl toluene was applied to another set of six tapes each. In addition, to examine the removable capacity of the tape, 0.015, 0.15, and 0.75 µg of MDI dissolved in 2 µl toluene was evenly applied to six 10-cm² areas on a cleaned Teflon® plate, respectively. All sites were tape stripped two times immediately thereafter. Simultaneously, 2 µl of each of the above mentioned solutions of MDI was added directly to the DBA solution (10 ml). Since the MDI-DBA reaction is complete (100%), the recovery was based on the amount observed in this sample. The tapes were analysed as described above and used for both the recovery and the method evaluation. Regarding the recovery, the deposited amount of MDI on the tape strip and Teflon® surfaces was based on our findings in the pilot study, thus ensuring realistic levels of MDI for the recovery tests.

Statistical analysis

The amount of MDI collected from each site on the skin was determined by summing the levels collected with three or five consecutive tape strip. Prior to statistical analysis, levels of MDI below LOQ ≤ 0.005 µg were assigned a value of LOD/2 (i.e. 0.0015 µg). In order to satisfy the assumption of normal distribution, log-transformation of the data was performed before the statistical analysis. Note, untransformed data are presented in Tables 2 and 3 (i.e. amounts below LOQ are denoted as ≤ 0.005 µg). The levels of MDI in the tape samples collected from the workers were not corrected for the recovery from the spiked tapes or

from the tape experiments using the Teflon® surface because the observed lower than expected recoveries which were observed may be attributed to a number of issues, e.g. potential reaction of MDI with some components in the tape or Teflon® surface, polymerization of MDI, or reaction with moist in the air or on the surface. Field blank tape samples values were subtracted from the MDI levels measured in the tape samples collected from the exposed workers, where 50% of the blanks had values close to LOQ or just above LOQ and 50% of the blank samples had values below LOQ. Amounts < 0.005 µg (≤ LOQ) were not added to the sum of MDI reported in the results. Differences between exposure groups were evaluated using univariate (two-tailed) Student's *t*-test while differences between skin sites were evaluated using pairwise univariate Student's *t*-test at significance level of $\alpha = 0.05$ (Microsoft® Office Excel 2003).

RESULTS

Recovery of MDI from tape and Teflon® surface

The average recovery and the coefficient of variation (CV) from the tape was 84 ± 2.7% for 0.10 µg MDI and 72 ± 34% for 0.0040 µg MDI (Table 1). The average recovery and CV from the Teflon® surface was 58 ± 38%. The recovery from the Teflon® surface for the highest applied amount of 0.75 µg was twice the recovery of the lowest applied amount of 0.015 µg (Table 1) while the CV was almost seven times greater for the lowest amount compared to the two highest amounts. The removal capacity for the first tape strip was ≥ 75% of the total recovered amount (data not shown).

Air sampling

The average measured air concentration of MDI was 0.55 µg m⁻³, 50-fold times lower than the

Table 1. Recovery of MDI from tape strip and from two consecutive tape strip on a Teflon® surface

Sample type	Number of samples	Applied amount (µg)	Mean recovery (%) (mean first; second tape strip)	CV ^a (%)
Tape strip	12	0.0040	72	34
Tape strip	6	0.10	84	2.7
Teflon® surface ^b	6	0.015	34 (27; 7)	69
Teflon® surface ^b	6	0.15	63 (50; 13)	11
Teflon® surface ^b	6	0.75	78 (69; 9)	11

^aCoefficient of variance.

^bThe sum of two consecutive tape strip.

Swedish occupational exposure limit (OEL) of $30 \mu\text{g m}^{-3}$ (Swedish Work Environment Authority, 2005) (Table 2). The core makers had an average exposure of $0.77 \mu\text{g m}^{-3}$ [geometric mean (GM) $0.35 \mu\text{g m}^{-3}$], which was not significantly different from core installers' and core-sand preparers' average exposure of $0.16 \mu\text{g m}^{-3}$ (GM $0.14 \mu\text{g m}^{-3}$; $P = 0.059$). This non-significance remained even when the two core-sand preparers (who had different work tasks than core installers) were excluded from the analysis. Three core makers had a 10-fold higher inhalation exposure than the other core makers (Table 2).

Dermal exposure

The sum of MDI levels measured on the tape-strip samples collected from each skin site are presented in Table 2. The core makers' mean dermal

exposure at different skin sites varied from 0.13 to $0.34 \mu\text{g}$ per tape (GM 0.076 – $0.15 \mu\text{g}$ per tape) while the two other groups' exposures ranged from 0.006 to $0.062 \mu\text{g}$ per tape (GM 0.0035 – $0.062 \mu\text{g}$ per tape). There was a significant difference ($P < 0.05$) in dermal MDI levels for each sample site between core installers and core-sand preparers (as one group) and core makers, except for the forehead ($P = 0.093$). However, when the two core-sand preparers were excluded and only core installers were compared to core makers, a significant difference ($P = 0.024$) was observed in the forehead as well.

No significant difference was observed in a pairwise t -test of the sum of the MDI levels measured with consecutive tape strip for each of the skin sites in any of the exposed groups (e.g. comparing right

Table 2. The sum of MDI (μg) measured on three^(I) or five^(II) tape strip in each skin site (area 10 cm^2) and breathing-zone concentrations of MDI for each worker

Job title	Worker ID	Skin site (μg)					Breathing-zone ($\mu\text{g m}^{-3}$)
		Forehead	Right forefinger	Left forefinger ^{a,b}	Right wrist ^a	Left wrist ^b	
Core maker	CM1 ^{II}	0.028	0.12	0.11	0.090	0.11	0.062
	CM2 ^I	0.019	0.037	0.030	0.049	0.13	0.55
	CM3 ^{II}	0.013	0.066	0.044	0.021	0.012	0.084
	CM4 ^I	0.202	0.029	0.031	0.076	0.068	0.21
	CM5 ^I	0.032	0.065	0.046	0.12	0.26	0.58
	CM6 ^{II}	0.55	0.15	0.37	0.43	0.54	1.6
	CM7 ^{II}	0.97	0.32	0.44	2.3	1.0	3.5
	CM8 ^{II}	0.12	0.16	0.15	0.23	0.23	0.74
	CM9 ^{II}	<0.005	0.16	0.11	0.24	0.30	0.088
	CM10 ^{II}	<0.005	0.010	0.0083	0.040	0.024	0.12
	CM11 ^{II}	0.042	0.31	0.083	0.15	0.11	0.15
	CM12 ^{II}	0.48	0.28	0.10	0.42	0.20	1.6
Group arithmetic mean (GM)		0.20 (0.047)	0.14* (0.095)	0.13* (0.076)	0.34 (0.15)	0.25* (0.14)	0.77 (0.35)
Core installer	CI1 ^I	<0.005	0.0098	<0.005	<0.005	<0.005	0.32
	CI2 ^I	0.010	0.021	0.015	0.016	0.015	0.044
	CI3 ^I	<0.005	<0.005	<0.005	<0.005	<0.005	0.072
	CI4 ^I	<0.005	<0.005	<0.005	<0.005	<0.005	0.16
	CI5 ^I	0.042	0.015	0.0079	0.015	0.044	0.14
Group arithmetic mean (GM)		0.011 (0.0043)	0.0098 (0.0059)	0.0056 (0.0033)	0.0060 (0.0035)	0.013 (0.0047)	0.15 (0.12)
Core-sand preparer	CSP1 ^I	0.046	0.034	0.044	0.027	0.032	0.20
	CSP2 ^{II}	0.077	0.043	0.051	0.056	0.062	0.20
Group arithmetic mean (GM)		0.062 (0.060)	0.038 (0.038)	0.047 (0.047)	0.042 (0.040)	0.047 (0.045)	0.20 (0.20)

LOD $0.01 \mu\text{g}$ per filter for the breathing-zone samples and $0.003 \mu\text{g}$ per tape for dermal samples. Prior to statistical analysis, levels of MDI below LOQ $\leq 0.005 \mu\text{g}$ were assigned a value of LOD/2 (i.e. $0.0015 \mu\text{g}$).

^aSignificantly different ($P < 0.05$) from the core installers' and core-sand preparers' mean exposure at each site.

^aSignificant difference in the pairwise comparisons between left forefinger and right wrist ($P = 0.015$).

^bSignificant difference in the pairwise comparisons between left forefinger and left wrist ($P = 0.014$).

forefinger and forehead, a total of 10 possible comparisons), except when left forefinger was compared to the left ($P = 0.014$) and right wrist ($P = 0.015$), respectively (Table 2). Neither was a significant difference ($P = 0.236$) observed in the total amount of MDI measured in the skin of core makers (i.e. the sum of MDI levels measured from all skin sites) with three consecutive tape strip per site (three workers) and five consecutive tape strip per site (nine workers). The results indicate that the use of three repeated tape strip per site is sufficient for estimating dermal exposure to MDI in this worker population. However, the number of samples is low and we do not know the amount of MDI, if any, left in the skin when three tape strip were collected. Therefore, these results need to be interpreted with caution.

Quantifiable (MDI levels above LOQ) but decreasing levels of MDI were observed in the consecutive tape strip per site indicating MDI penetration into the skin (Fig. 1). The gradient was observed for at least one of the five skin sites in seven (of nine) workers with three repeated tape strip and for eight (of 10) workers with five repeated tape strip. One worker with three repeated tape strips per site and four workers with five repeated tape strip per site had quantifiable gradients of MDI levels in all dermal sites (data not shown).

DISCUSSION

Recovery of MDI from tape strip and Teflon® surface

Recovery of the larger applied amounts of MDI from tape strip and from the Teflon® surface was precise but much lower (72–84%) compared to the

reported recovery of HDI from the tape (99.3%; 95% confidence interval 97.1–102%) as reported previously for the Fixomull tape (Fent *et al.*, 2006). In addition, the recovery of the MDI at levels close to LOQ was imprecise (CV 34% and 96% for tape strip and Teflon® surface, respectively). Teflon® was chosen because it is considered to have a smooth and inert surface. The incomplete recovery with the first tape (at least 75% of the total recovered amount) may be attributed to potential reaction of MDI with some components in the tape or Teflon® surface, polymerization of MDI, or reaction with moist in the air or on the surface. The amounts applied to the Teflon® surface were in the same range as we expect to observe in the samples collected in the occupational exposure setting. Because neither the tape nor the Teflon® surface is representative of the human skin and because the recovery of MDI from the tape and Teflon® surface was lower than expected, we opted not to adjust the MDI levels measured in the dermal tape strip samples with the recovery of MDI from the tape. A skin recovery study using human volunteers is warranted and impending in our laboratory. The values reported here are by no means absolute values. For some workers (Table 2), the exposure levels were much higher than what was included in the method evaluation. This adds an additional degree of uncertainty in the exposure values reported here.

Air sampling

The measured air levels were very low compared to the Swedish OEL value of $30 \mu\text{g m}^{-3}$. However, as expected, these levels were similar to earlier reported measurements ranging from 0.1 to $0.2 \mu\text{g m}^{-3}$ (Westberg *et al.*, 2001). In a study that included companies which used diisocyanates to produce moulded polyurethane products, insulation material, and those involved in industrial painting, only 30% of the samples showed air concentrations $>0.001 \text{ mg m}^{-3}$ (the LOQ for the used analytical method) (Creely *et al.*, 2006). These samples were collected from four different workplaces and were predominately related to spray applications. Fent *et al.* (2006) observed 10-fold higher HDI levels (mean $20.2 \mu\text{g m}^{-3}$) and, consequently, less non-detectable HDI levels (21%; $n = 34$) in the air samples collected from automotive spray painters. However, these levels may reflect the higher vapour pressure of HDI compared to MDI as well as the differences in the processes in which these two diisocyanates were monitored. With the current air sampling and analytical tools, it is likely that diisocyanates may

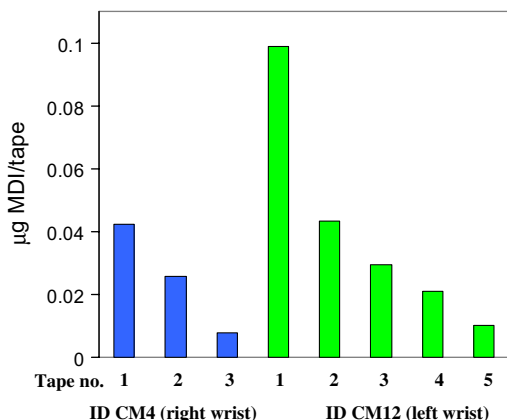


Fig. 1. Quantifiable amounts in the gradient of MDI levels in the tape strip collected from two core makers. Three or five consecutive tape strip were used on the right and the left wrist, respectively.

have to be aerosolized in order to be measurable in the environmental air.

The filter air monitoring method used was selected due to the fact that this technique is established (Health and Safety Laboratory, 1999, MDHS 25/3), it is more practical to use for personal air sampling in these work conditions than the impinger-based DBA method (Karlsson *et al.*, 1998), and we attempted to monitor MDI concentrations over a full work shift (Sennbro *et al.*, 2004). The impinger method is only suitable for short-term sampling (5–15 min sampling). Further, in comparison, the quantitative and qualitative analytical performances of these methods are equal.

The core makers had a higher average inhalation exposure to MDI than the core installers and core-sand preparers. This may be explained by evaporation of MDI from the cores. The cores were heat cured and still warm when leaving oven and handled by the core makers. Because of the large variability in the MDI air levels among the core makers and the small number of workers in each group, the difference in the exposure levels was not statistically significant.

Dermal exposure

We are not aware of any published studies where dermal exposure to MDI was quantified in an occupational setting. Fent *et al.* (2008) quantified dermal exposure on 13 automotive spray painters performing 35 different paint tasks. They observed detectable levels of HDI in 71% of the tasks and a mean HDI dermal concentration of 48.5 ng mm^{-3} . They assumed that triplicate tape strip collect $\sim 1 \text{ mm}^3$ of skin (10-cm^2 area $\times 1 \text{ mm}$ thickness). In our study, quantifiable levels of MDI were observed in the skin of all the workers, except in two core installers (Table 2). The corresponding mean concentrations observed at the five different dermal sites (calculated from the first three tape strip for all workers, data not shown) for core installers varied from 5.6 to 13 ng mm^{-3} , for the core-sand preparers from 38 to 53 ng mm^{-3} , and for the core makers from 113 to 306 ng mm^{-3} (data not shown). Indeed, core makers were the predominantly exposed workers in this industry because they directly handled (lift and move) the cores. However, high dermal exposure was consistent in all core makers and the average dermal exposure was significantly higher for core makers than the other two groups at all skin sites. In our previous study, a tape sample (area 10 cm^2) collected from a freshly made core showed a MDI amount of $1.4 \text{ }\mu\text{g}$. Thus, uncured MDI may be present on the surface of the material the workers handle and, hence, opportunity for dermal exposure exists despite the use of cotton gloves to protect the work-

ers from injuries. The thin cotton gloves do not protect the workers from MDI exposure since small molecules and dust will easily penetrate this type of gloves. Unfortunately, we did not record the frequency of glove use during the workday and, therefore, we cannot comment on a possible glove effect among the workers.

The MDI levels observed in the different dermal sites were comparable. We did not observe any overall significant difference between the 5 dermal sites and 10 possible comparisons, except when left forefinger was compared to the wrists. Thus, when the hands were contaminated, the forehead was also contaminated within the same magnitude. This implies that the workers probably spread MDI contamination by touching their face or forehead with their hands and fingers. However, this relationship is probably more complicated because the workers are supposed to wash their hands a couple of times during the day but that does not necessarily include washing their face. Another explanation for the contamination of the face may be due to the deposition of MDI-containing dust immediately before tape stripping. Contamination of the skin that occurred well before (e.g. several hours) tape stripping may not be measurable due to reaction of MDI with the moist in the air or with the skin and its components. This could also be the reason for no quantifiable exposure observed for two core installers (Table 2). Further, although a significant correlation was observed between dermal and breathing-zone levels ($R^2 = 0.92$), this correlation was dramatically affected by the three highest breathing-zone concentrations. When these three highest measurements were excluded from the analysis, no correlation between the breathing-zone and dermal exposure was observed ($R^2 = 0.19$). Therefore, our results indicate that all the dermal sites monitored in our study should also be included, along with any other potentially exposed skin sites, e.g. upper arm, neck, chin, nose, or chest (under the clothes), in the measurement strategy in the future dermal exposure studies involving MDI.

An estimate of MDI exposure to a defined skin surface was made by using the observed MDI exposure levels. For example, the average skin surface area of the face is estimated to be 1300 cm^2 , for both palms of the hands 420 cm^2 , and for both left and right wrist 120 cm^2 (Organisation for Economic Co-operation and Development, 1997). The total dermal MDI exposure, as calculated by multiplying the sum of MDI with the surface area per worker, is shown in Table 3. No apparent distribution pattern was seen in the groups based on job title. Five workers had MDI exposure predominantly observed on their hands,

Table 3. The total dermal MDI exposure (μg) measured with the consecutive tape strip and based on the estimated dermal areas (both palms of the hands, both the left and right wrists, and face), and the distribution of the estimated MDI exposure in the three exposed dermal areas

Job title	Worker ID	MDI (μg)	Distribution (%)		
			Hands	Wrists	Face
Core maker	CM1	9.56	50	13	37
	CM2	4.96	28	22	50
	CM3	4.14	55	5	40
	CM4	28.4	4	3	93
	CM5	8.78	26	26	48
	CM6	87.9	12	7	81
	CM7	162	10	12	78
	CM8	24.4	27	11	62
	CM9	8.87	63	37	0
	CM10	0.77	50	50	0
	CM11	15.1	54	10	36
	CM12	73.7	11	5	84
Core installer	CI1	0.256	93	7	0
	CI2	2.26	34	8	58
	CI3	<0.005	0	0	0
	CI4	<0.005	0	0	0
	CI5	6.24	8	5	87
Core-sand preparer	CSP1	8.02	20	5	75
	CSP2	12.8	15	6	79

while in 11 workers the face was observed to have the highest MDI exposure. The wrists had the lowest MDI exposure levels and, therefore, contributed the least to the total dermal exposure. Hence, the face can be an important but sometimes overlooked area, which should be included in the dermal exposure measurement strategy, especially when dermal exposure potentially contributes to the total body burden (e.g. pesticide applicators and spray painters). Assuming a dermal uptake of 1% (very conservative estimate by Riihimäki and Pfäffli, 1978) and a breath volume of 10 m^3 ($20 \text{ l min}^{-1} \times 60 \text{ min} \times 8 \text{ h} = 10 \text{ m}^3$) for 8-h work shift (Holmes, 1994) and 70% uptake from the breathed air (estimate based on organic volatiles by Nomiyama and Nomiyama, 1974, Lin *et al.* 2001, Xu and Weisel, 2005), the contribution to the body burden from dermal exposure would be in the magnitude of 20 times less than for inhalation in the exposure scenarios described here [e.g. 1% of the amount for worker CM8 (Table 3) is $0.24 \mu\text{g}$ and 70% from 10 m^3 breathed air with $0.74 \mu\text{g m}^{-3}$ (Table 2) is $5.2 \mu\text{g}$]. However, the variability between workers is huge very large and these kinds of approximations are questionable but, nevertheless, usable to provide an understanding of the potential exposure in

relation to the exposed skin area. This type of reasoning may be useful in risk management and implementations of protective measurements.

The tape-strip method provides information about the penetration pattern of contaminant into the skin (Cullander *et al.*, 2001; Hostynek *et al.*, 2001). This was recently shown among spray painters exposed to HDI (Fent *et al.*, 2006) and among workers dermally exposed to resin acids during production of wood pellets (Eriksson *et al.*, 2008). We observed quantifiable amounts of MDI monomer on the fifth tape strip in eight workers indicating penetration of MDI into the skin (Fig. 1). A possibility exists that the amounts detected in the fourth and fifth tape strip were due to contamination of the tape during sampling even though clean gloves were used for each application and removal of tape. However, we believe that most likely the overall exposure assessment may have been somewhat biased due to the collection of too few tape strip (undetected exposure) instead of overestimation of exposure due to contamination of tape strip.

Even when we observed quantifiable amounts of MDI in the skin, there are too few reports on cases of dermatitis caused due to exposure to diisocyanates (Sommer *et al.*, 2000; Larsen *et al.*, 2001; Donnelly *et al.*, 2004). Frick-Engfeldt (2007) suggests that the reasons for the low frequency of dermatitis observed in diisocyanate-exposed workers are inadequate patch test diagnostics, instability of patch test allergens, and/or lack of late reading of the patch tests. With this developed tape-strip technique to measure dermal exposure to diisocyanates, the potential exists for development of strategies to prevent exposure as well as for development of improved diagnostic techniques for diisocyanate-induced sensitization.

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