

Occupational Exposure to *N,N*-Dimethylformamide in the Summer and Winter

Hiroyuki MIYAUCHI^{1*}, Yoko TSUDA⁴, Aoi MINOZOE¹, Shigeru TANAKA², Heihachiro ARITO³, Teruomi TSUKAHARA⁴ and Tetsuo NOMIYAMA⁴

¹The Association of Industrial Health, Japan

²Department of Public Health, Graduate School of Human Life Science, Jumonji University, Japan

³Occupational Health Research and Development Center, Japan Industrial Safety and Health Association, Japan

⁴Department of Preventive Medicine and Public Health, Shinshu University School of Medicine, Japan

Received March 25, 2014 and accepted July 16, 2014

Published online in J-STAGE September 13, 2014

Abstract: We evaluated total body burden of *N,N*-dimethylformamide (DMF) taken through the lung and skin by personal exposure of workers to DMF and urinalysis of *N*-methylformamide (NMF) and *N*-acetyl-*S*(*N*-methylcarbamoyl)-cysteine (AMCC). A total of 270 workers were engaged in four different jobs in a workplace distant from main production lines emanating high levels of DMF. They were not required to wear any personal protective equipment including respirators or gloves. We found that log-transformed urinary levels of NMF and AMCC increased with an increase in log-transformed concentrations of exposure to DMF. Urinary levels of NMF and AMCC were significantly higher in the summer than the winter, although there was no significant seasonal difference in the concentrations of exposure to DMF. Our findings suggested that the increased urinary levels of NMF and AMCC in the summer resulted in increased skin absorption of DMF due to an increased amount of DMF absorbed by the moisturized skin under humid and hot conditions. Seasonal changes in the relative internal exposure index confirmed the present finding of enhanced summertime skin absorption of DMF. AMCC is thought to be a useful biomarker for assessments of cumulative exposure to DMF over a workweek and for evaluations of workers' health effects.

Key words: *N,N*-Dimethylformamide, *N*-Methylformamide, *N*-Acetyl-*S*(*N*-methylcarbamoyl) cysteine, Biological monitoring, Seasonal variation

Introduction

N,N-Dimethylformamide (DMF) is an excellent solvent for dissolving synthetic resins and polar polymers in chemical applications¹. Since DMF is highly permeable through the skin, workers may be exposed to DMF vapor through the skin and lungs. Experimental studies^{2–5}) on

the exposure of human volunteers to DMF vapor showed that the proportion of skin absorption to total body burden through the lungs and skin ranges from 13 to 70%. Workers exposed excessively to DMF were reported to suffer from hepatic disorders^{6–9}), pancreatic disorders¹⁰) and intolerance to alcohol^{11, 12}).

For the protection of workers from excessive exposure to DMF, the American Conference of Governmental Industrial Hygienists (ACGIH)¹³) and the Japan Society for Occupational Health (JSOH)¹⁴) recommended an occupational exposure limit (OEL) of 10 ppm. A MAK (Maximale Arbeitsplatz Konzentration) value of 5 ppm for

*To whom correspondence should be addressed.

E-mail: miyauchi-hiroyuki@k6.dion.ne.jp

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the OEL of DMF was recommended by Deutsche Forschungsgemeinschaft (DFG)^{15, 16}. Both of these OEL values were designated with “skin” notation^{13–16}. The ACGIH¹⁷ has also recommended the biological exposure index (BEI) values of 15 mg *N*-methylformamide (NMF)/l and 40 mg *N*-acetyl-*S*(*N*-methylcarbamoyl)-cysteine (AMCC)/l in a worker’s urine collected at the end and at the beginning of the last shift of the workweek, respectively. In 2002, the DFG changed the BEI value of 15 mg NMF/l of worker’s urine to 35 mg/l¹⁸.

The urinary metabolites of DMF are considered to serve as a marker for assessments of the total body burden of DMF when an individual worker is exposed to DMF through respiration and dermal contact. In addition, urinary AMCC was reported to be a good indicator for the assessment of cumulative exposure to DMF over a workweek^{19, 20}, since the elimination half-life for AMCC was reported to be 22.1 h²¹ or 23 h²². Simultaneous measurements of personal exposure to DMF and the urinary levels of NMF and AMCC could be used to evaluate the contribution of the skin absorption of DMF to total DMF exposure through the lung and skin.

Our previous study²³ showed that workers’ urinary levels of NMF and AMCC were significantly higher in the summer than in the winter, suggesting increased skin absorption of DMF due to the summertime increase in room temperature and relative humidity²³. Drexler *et al.*²⁴ demonstrated workers’ increased internal exposure to carbon disulfide (CS₂) resulting from more intensive skin contact and physical work. To do so, they used a quotient of the urinary concentration of a CS₂ metabolite, 2-thiothiazolidine-4-carboxylic acid (TTCA), obtained by determining the concentration of inhalation exposure to CS₂ vapor, and they referred to the quotient as a relative internal exposure (RIE) index.

We conducted the present study to further examine our hypothesis²³ that the skin absorption of DMF vapor was enhanced in the summer compared to the uptake of DMF vapor through the lungs, due to the summertime increase in room temperature and relative humidity. For this examination, we recruited another group of workers who were working without respiratory protective masks (in contrast to the previously reported respirator-wearing workers directly handling DMF in the same resin-product manufacturing factory)²³, and we used the same RIE index for DMF-exposed workers as that demonstrated for CS₂-exposed workers by Drexler *et al.*²⁴.

Materials and Methods

Study subjects

The present survey was conducted over a period of 9 yr spanning from August 2000 to February 2008. A total of 270 workers, 79 males and 191 females (aged 46.9 ± 11.5 [mean ± SD] yr) with 14.1 ± 7.4 yr of work duration at the start of their participation were recruited as the subjects. The room temperature and relative humidity in the workplace ranged from 23.1° to 29.5 °C and 66.3 to 96.0% in the summer, and from 15.3° to 22.7 °C and 15.3 to 68.0% in the winter, respectively.

The workers all engaged in one or more of four different jobs: the formulation of resin products, finishing the formulated product, inspection of the manufactured products, and packing of the final products for marketing. Their workrooms were located in a different place distant from the main production lines which emanated relatively high levels of DMF, as described in our previous study²³. Their workload was regarded as light work without discernible perspiration. They did not wear respirators or gloves during the entire 8-h workshift.

This study was approved by the Ethics Review Committee of the Shinshu University School of Medicine. All of the subjects gave written informed consent to participate, and the individual results of exposure concentrations of DMF and urinary levels of NMF and AMCC were returned to each subject.

Sampling of DMF vapor in workplace air and workers’ urine

Simultaneous measurements of the concentrations of personal exposure to DMF and the urinary levels of NMF and AMCC were carried out for 128 workers in August (summer) and for 142 workers in February and March (winter). The subjects were asked not to drink alcohol on the days before the urine sampling. We performed sampling of the personal breathing zone of DMF in the workplace air, using the diffusive passive sampler (LiPS) developed by Tanaka *et al.*²⁵. This personal sampler (containing distilled water as an absorbent) was worn by each worker on the collar of his or her workdress.

Each worker’s breathing-zone DMF vapor in the workplace air was collected by the passive sampler during the entire last 8-h workshift of the workweek in the summer or winter. After the workplace air at the breathing zone was collected by the personal sampler, the absorbent was transferred to a glass vial and it was stored at 3 °C until analysis. The workers’ urine was sampled at the beginning

of the last 8-h shift for the AMCC analysis and at the end of the 8-h last workshift for the NMF analysis on the same day that their specimens of breathing-zone DMF vapor were collected. The urine was collected in individual plastic bottles and stored at -20°C until analysis. The timings of the urine collections for the NMF and AMCC analyses were those recommended by the ACGIH¹⁷⁾.

Analyses of DMF and urinary NMF and AMCC

The analytical methods used in the present study were as described²³⁾. Briefly, DMF vapor collected in the diffusive passive sampler was analyzed with a combined gas chromatograph-mass spectrometer (GC-MS) equipped with an HP-WAX capillary column (30-m-long, 1- μm -thick film, cross-linked polyethylene; Hewlett Packard, Palo Alto, CA, USA) and with an automatic liquid sample injector (7683 Series Injector, Agilent Technologies, Santa Clara, CA, USA). The limit of quantitation (LOQ) for the present DMF analysis method with the passive sampler and GC-MS was estimated to be $0.039\ \mu\text{g}/\text{sample}$, which is equivalent to $0.053\ \text{ppm}$ DMF for an 8-h collection of workplace air.

Urinary NMF was analyzed according to the methods of Kawai *et al.*²⁶⁾ and Nomiyama *et al.*²⁷⁾, and urinary AMCC was analyzed according to the method of Mraz²⁸⁾. The precision of the determination of NMF (expressed as mean/ $\text{SD} \times 100$) with standard solutions of 0.1 and 15 mg NMF/l was 8.5% and 1.1%, respectively. The corresponding accuracy, expressed as mean/(concentration of standard NMF solution) $\times 100$, was 98.0 and 97.7%, respectively.

For the determination of urinary AMCC at 0.1 and 40 mg/l, the precision was 9.5% and 0.5%, respectively, and the corresponding accuracy was 88.0% and 98.1%. The urinary levels of NMF and AMCC are expressed as the urine volume-based (mg/l) concentrations. We also used the urinary creatinine-adjusted (mg/g-Cr) concentrations of NMF and AMCC to compare the urine concentrations between summer and winter and between the beginning and the end of the 8-h shift.

Chemicals

NMF and DMF were obtained from Tokyo Kasei Kogyo (Tokyo). Ethanol, diethylformamide, quinoline and anhydrous potassium carbonate were purchased from Wako Pure Chemical Industry (Osaka, Japan). AMCC was synthesized by the method of Mraz and Turecek²⁹⁾.

Data analysis

We examined the concentrations of exposure to DMF

and the urinary levels of NMF and AMCC for logarithmic normal distribution by the Shapiro-Wilk test. It was found that all of these data followed a logarithmic normal distribution. Thus, we examined the relationship between the logarithmic concentrations of exposure to DMF and the logarithmic urinary levels of the metabolites by conducting a linear regression using the least square method, and we tested the correlation coefficient (r) and the slope (a) for statistical significance using Pearson's product-moment coefficient. We also examined the relationship between the urinary levels of NMF or AMCC and the breathing-zone concentrations of DMF in the summer and winter according to a quartile analysis.

We examined the trend of NMF or AMCC levels to be increased with the concentrations of exposure to DMF using the Jonckheere-Terpstra test. Significant differences in the mean urinary levels of NMF or AMCC among the four quartile groups in each season were tested by Dunnett's multicomparison. The seasonal differences in the concentrations of exposure to DMF and the urinary levels of NMF and AMCC were tested by Wilcoxon signed rank test. We calculated the urinary level of NMF or AMCC corresponding to the ACGIH's or JSOH's OEL value of 10 ppm for each worker by dividing the urinary NMF or AMCC level by the concentration of personal exposure to DMF and then multiplying the dividend by 10 ppm.

The RIE index was calculated by dividing the urinary NMF level expressed by mg/l by the concentration of inhalation exposure to DMF vapor expressed as mg/m^3 for each DMF-exposed worker in the summer and the winter, and the seasonal difference in the RIE index was tested for statistical significance. All reported p -values were one-tailed ($p < 0.05$). All of the statistical analyses were performed using SAS 15.03 software (SAS Institute, Cary, NC, USA).

Results

As shown in Fig. 1, the log-transformed NMF levels in the workers' urine collected at the end of the last shift of the workweek were found to increase significantly with the increase in the log-transformed concentrations of exposure to DMF in both the summer and winter. The slope of the regression line for the summer was steeper than that for the winter. Notably, the log-transformed urinary levels of NMF were significantly higher in the summer than in the winter.

Figure 2 shows that log-transformed urinary levels of AMCC significantly increased with the increase in the log-transformed concentrations of exposure to DMF in both

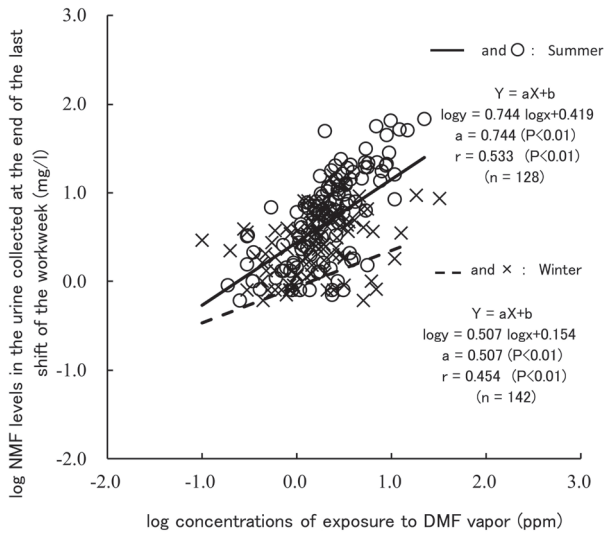


Fig. 1. Relationship between log-transformed NMF levels in workers' urine collected at the end of the last shift of the workweek and the log-transformed concentrations of exposure to DMF collected over the 8-h workshift on the same day. The solid line indicates the linear regression for the summer data (circles). The dotted line indicates the linear regression for the winter data (crosses).

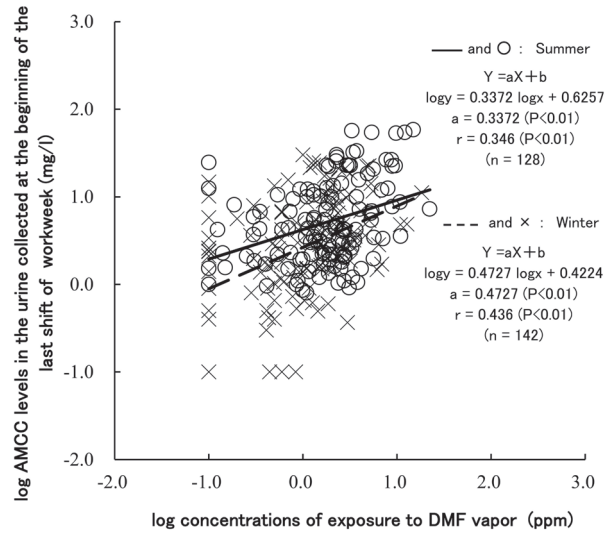


Fig. 2. Relationship between the log-transformed AMCC levels in the workers' urine collected at the beginning of the last shift of the workweek and the log-transformed concentrations of exposure to DMF during the workshift on the same day. Solid line: the linear regression for the summer data (circles). Dotted line: the linear regression for the winter data (crosses).

seasons. In contrast to the two regression lines for NMF, the seasonal difference in the urinary levels of AMCC tended to decrease with the increase in the concentrations of exposure to DMF. A comparison of Figs. 1 and 2 reveals that the slopes of the two regression lines in each of the two seasons were less steep for AMCC than for NMF. Notably, the log-transformed urinary levels of AMCC were less correlated with the log-transformed concentrations of exposure to DMF in both seasons compared to the higher correlations of urinary NMF levels.

As shown in Fig. 3, we examined the seasonal variation of NMF levels in the workers' urine collected at the end of the last shift of workweek by conducting a quartile analysis, classifying the concentrations of exposure to DMF into four quartile groups in the summer and the winter. The urinary levels of NMF tended to positively increase with the increase in the concentrations of exposure to DMF in the summer and the winter, as evidenced by a significant positive trend by Jonckheere-Terpstra test at $p < 0.01$. In the summer, the urinary level of NMF was significantly higher in the 4th quartile group than in the 1st quartile group by Dunnett's multicomparison test, while in the winter the urinary levels of NMF in the 3rd and 4th quartile groups were significantly higher than that in the 1st quartile group. Our further examination of the workers in the 4th quartile group revealed that there were 22 workers (69%) in the summer whose urinary levels of

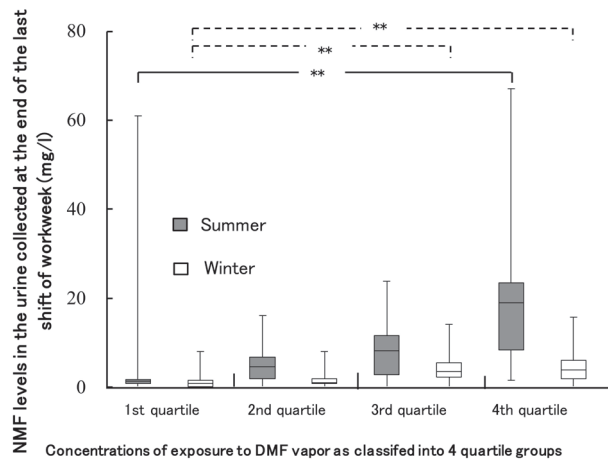


Fig. 3. Urinary levels of NMF collected in the summer and winter for workers whose concentrations of exposure to DMF were classified into four quartile groups. The 1st, 2nd, 3rd and 4th quartiles span 0.1 to 1.1 ppm, 1.2 to 1.9 ppm, 2.0 to 3.4 ppm and 3.5 to 22.3 ppm in the summer, and 0.1 to 0.5 ppm, 0.6 to 1.3 ppm, 1.4 to 2.3 ppm and 2.4 to 32.3 ppm in the winter, respectively. The double asterisk (**) with solid and dotted lines indicates significantly higher levels of NMF in the summer and winter, respectively, compared to the urinary level of NMF in the 1st quartile group at $p < 0.01$.

NMF exceeded the ACGIH's BEI of 15 mg/l, although their average concentrations of exposure to DMF were below the ACGIH/JSOH 10-ppm OEL. In contrast, there

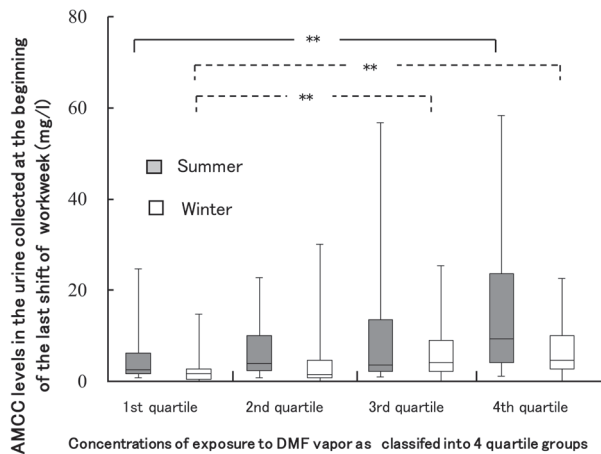


Fig. 4. Urinary levels of AMCC in the summer and winter for workers whose concentrations of exposure to DMF were classified into four quartile groups. The spans of the 1st to 4th quartiles are the same as that described in Fig. 3. The double asterisk (**) with solid and dotted lines indicates significantly higher levels of AMCC in the summer and winter, respectively, compared to the urinary level of AMCC in the 1st quartile group at $p < 0.01$.

was only one worker (3%) in the winter whose level of NMF exceeded 15 mg/l, and his concentration of exposure to DMF was below 10 ppm.

The quartile analysis (Fig. 4) also revealed the essentially similar relationships between the urinary levels of AMCC and the concentrations of exposure to DMF compared to those for the urinary levels of NMF. The urinary levels of AMCC tended to positively increase with the increase in the concentrations of exposure to DMF in the summer and the winter, as evidenced by the significant positive trend by Jonckheere-Terpstra test at $p < 0.01$. In the summer, the urinary level of AMCC was significantly higher in the 4th quartile group than in the 1st quartile group by Dunnett's multicomparison test, whereas in the winter the urinary levels of AMCC in the 3rd and 4th quartile groups were significantly higher than that in the 1st quartile group. Our further examination of the workers in the 4th quartile group revealed that there were three workers (9%) in the summer whose AMCC levels exceeded the ACGIH's BEI of 40 mg/l although their average concentrations of exposure to DMF were below the ACGIH/JSOH 10-ppm OEL. There was no such worker in the winter (whose AMCC levels exceeded 40 mg AMCC/l with an exposure concentration below 10 ppm DMF).

Table 1 summarizes the seasonal differences in the concentrations of exposure to DMF during the 8-h workshift and the levels of AMCC and NMF in the workers' urine. The mean concentration of exposure to DMF tended to

increase in the summer compared to that in the winter, but this seasonal difference was not significant. In contrast, both the urine volume-based levels (mg/l) of AMCC and NMF were found to be significantly increased in the summer compared to those in the winter.

The concentrations (mean \pm SD) of creatinine in the workers' urine collected at the beginning and at the end of the 8-h shift were 1.12 ± 0.89 g/l and 1.55 ± 0.84 g/l in the summer and 0.72 ± 0.57 g/l and 0.87 ± 0.62 g/l in the winter, suggesting that the urine was more concentrated in the summer than in the winter, and more concentrated at the end of the shift than at the beginning of the shift. However, there was no alteration in the significant seasonal difference in the urinary levels of AMCC and NMF, even after the correction of the urine volume-based concentrations of AMCC and NMF by urinary creatinine. Notably, the urinary level of NMF corresponding to the ACGIH/JSOH 10-ppm OEL for DMF was significantly higher in the summer than in the winter, and the mean urinary NMF level (22.5 mg NMF/l) exceeded the ACGIH's BEI value of 15 mg NMF/l.

However, the urinary levels of AMCC corresponding to the ACGIH/JSOH 10-ppm OEL for DMF in the summer and winter were below the ACGIH's BEI value of 40 mg AMCC/l. Unlike the NMF level, there was no seasonal difference in the urinary AMCC level corresponding to the OEL value of 10 ppm for DMF. Notably, the RIE index was significantly increased (by 4.8-fold) in the summer compared to that in the winter, suggesting that the relative uptake of DMF through the skin with reference to the unit concentration (1 mg/m^3) of inhalation exposure to DMF vapor was significantly increased in the summer.

As shown in Fig. 5, the urinary levels of NMF and RIE indices in the summer increased unambiguously in comparison with those in the winter throughout the 9-yr period, although such a clear trend was not observed for the seasonal difference in the concentrations of exposure to DMF.

Discussion

In the present study, we found that the log-transformed urinary levels of NMF and AMCC were significantly increased with the increase in log-transformed concentrations of exposure to DMF. We also found that the urinary levels of NMF and AMCC were higher in the summer than in the winter, although there was no significant seasonal difference in the concentrations of exposure to DMF. The mean urinary level of NMF corresponding to the ACGIH/

Table 1. Concentrations of exposure to DMF vapor during the 8-h shift and levels of NMF and AMCC in the urines of workers in the summer and winter. The urines were collected at the beginning (BS) or at the end of the last shift of workweek (ES). The urinary levels of NMF and AMCC were expressed as the urine-volume based (mg/l) and urinary creatinine-adjusted concentrations (mg/g · Cr)

	GM (GSD)	GM (GSD)	Ratio
	Summer	Winter	Summer/Winter
Number of workers examined	128	142	
DMF (ppm)	1.7 (3.2)	1.0 (3.5)	1.7
ES NMF (mg/l)	4.1* (4.8)	1.4 (4.1)	2.9
ES NMF (mg/g · Cr)	3.1* (4.7)	2.1 (4.7)	1.5
ES NMF (mg/l) corresponding to 10 ppm DMF ^{§1}	22.5* (3.9)	14.3 (4.1)	1.6
ES RIE index (NMF (mg/l)/DMF (mg/m ³)) ^{§2}	5.8* ± 34.3	1.2 ± 2.6	4.8
BS AMCC (mg/l)	5.2* (3.0)	2.7 (3.8)	1.9
BS AMCC (mg/g · Cr)	6.7* (3.6)	4.9 (4.7)	1.5
BS AMCC (mg/l) corresponding to 10 ppm DMF ^{§1}	28.9 (3.6)	26.7 (3.9)	1.1

Concentrations were expressed as geometric means (GM) and geometric standard deviations (GSD) except for the RIE index. Asterisk * indicates that the values were significantly higher in the summer than in the winter at $p < 0.05$. ^{§1}: The calculation method was given in Data Analysis. ^{§2}: RIE (relative internal exposure) index, expressed as arithmetic mean ± SD in each season, is a quotient of the urinary NMF level by the concentration of inhalation exposure to DMF vapor.

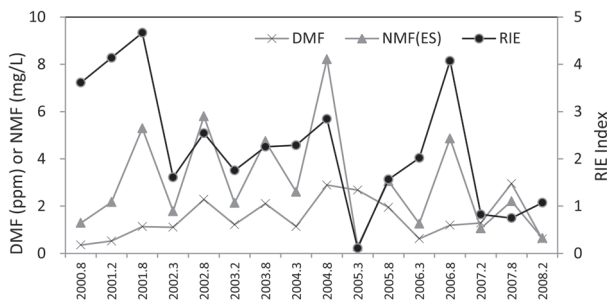


Fig. 5. Seasonal changes in the concentrations of exposure to DMF, the urinary levels of NMF, and the RIE indices for a total of 270 DMF-exposed workers during a 9-yr study period from August 2000 (2000.8) to February 2008 (2008.2).

JSOH 10-ppm OEL for DMF was found to exceed the ACGIH’s BEI value of 15 mg NMF/l in the summer but not in the winter. The urinary level of AMCC corresponding to the 10-ppm OEL for DMF did not exceed the ACGIH’s BEI value of 40 mg AMCC/l in either the summer or the winter.

Notably, there were 22 workers (69%) whose urinary levels of NMF in the summer exceeded the ACGIH’s BEI value of 15 mg/l although their concentrations of exposure to DMF were below the ACGIH/JSOH 10-ppm OEL. There were three workers (9%) whose urinary levels of AMCC in the summer exceeded the ACGIH’s BEI of 40 mg AMCC/l, even though their DMF exposure concen-

trations were below the ACGIH/JSOH 10-ppm OEL.

The significantly increased RIE index in the summer compared to that in the winter is compatible with a clear yearly trend of summertime enhancement of the RIE indices throughout the 9-yr study period. It is possible that the skin absorption of DMF contributed to a greater extent to the total uptake of DMF through the lung and skin in the summer than in the winter. Consistently, Drexler *et al.*²⁴⁾ attributed the increased RIE index of TTCA/CS₂ to the enhanced skin penetration of CS₂ among CS₂-handling workers with skin diseases. CS₂ is reported to penetrate the skin at a high rate, designated as “Skin Notation” by the ACGIH¹³⁾.

However, another possibility should not be ruled out: concentrated urine due to increased perspiration. Elkins *et al.*³⁰⁾ reported that a correction of the urine volume-based concentration by creatinine is needed when the urine of smelter workers exposed to lead is very concentrated. However, all of the workers participating in the present study were engaged in light work without discernible perspiration. Notably, there was no alteration in the statistical significance of any seasonal difference even after the creatinine adjustment, although the mean urinary concentrations of creatinine were higher in the summer than in the winter.

Mraz and Nohova³⁾ demonstrated with DMF vapor-exposed volunteers that the urinary level of *N*-hydroxymethyl-*N*-methylformamide (HMMF) was markedly

enhanced with an increase in room temperature and relative humidity after a 4-h percutaneous exposure to DMF vapor, and they concluded that humidity of the skin as well as temperature appears to play a decisive role in the increased skin absorption of DMF vapor³⁾. A considerable influence of the skin moisture level on dermal absorption of the pesticide propoxur was also observed in a study with human volunteers³¹⁾. Moisture and temperature are thought to affect both skin morphological structures such as the stratum corneum, microcirculation and sweat ducts and several barrier-functioning physicochemical properties of the horny layer such as diffusivity, as well as physical properties of DMF such as water and lipid-solubility³²⁾.

Taking these reports into consideration, it can be inferred that the increased urinary levels of NMF and AMCC in the summer result from the increased skin absorption of DMF vapor rather than from concentrated urine due to increased perspiration. The increased skin absorption of DMF in the summer might be causally related to an increased amount of water- and lipid-soluble DMF absorbed by moisturized skin, leading to the increased penetration of DMF molecules through the warm skin into the microcirculation. On the basis of the present findings, therefore, we recommend that the prevention of the increased skin absorption of DMF vapor should be implemented by having workers wear protective clothing, gloves or aprons in the summer, with a further reduction of DMF vapor in the workplace air by the use of a local exhaust ventilation system.

We found that the log-transformed levels of AMCC in the workers' urine collected at the beginning of the last 8-h shift of the workweek were less correlated with the log-transformed concentrations of exposure to DMF collected during the last 8-h shift in comparison with the high correlation of the urinary NMF level. This finding is consistent with that of Sakai *et al.*³³⁾, who reported the highest correlation of NMF levels in the urine collected at the end of the workshift with the personal exposure concentrations of DMF compared to a lower correlation of urinary AMCC levels with DMF. The ACGIH¹⁷⁾ designated the BEI of AMCC as an Sq (semi-quantitative) notation, indicating that due to the variability in the reported data, this BEI can be used as a screening test for exposure to DMF.

The lower correlation of the urinary AMCC levels with the DMF exposure concentrations compared to that of the urinary NMF levels can be attributed to the long elimination half-life of 22–23 h for AMCC^{21, 22)} versus the short half-life of 2.2–4.8 h for NMF⁵⁾. The AMCC levels in the workers' urine collected at the beginning of the last shift of

the workweek (Friday) would have been more highly correlated with the DMF exposure concentrations averaged over four consecutive days (Monday through Thursday) compared to the single-day DMF exposure concentration collected only during the last 8-h shift of the workweek (Friday).

The lower correlation of the urinary AMCC levels with the personal exposure concentration of DMF found in the present study seems to reflect the day-to-day variation of the personal exposure concentrations of DMF, depending on both the job handling DMF-containing material or not and the time period spent for the job. Although a total of 270 workers were recruited over the 9-yr period, 22 workers participated six times or more in the present study. This might pose a limitation of the present study, because we could not separate intra- and inter-individual variations of the urinary levels of NMF and AMCC and the exposure concentrations of DMF vapor.

In conclusion, the log-transformed urinary levels of NMF and AMCC significantly increased with the increase in the log-transformed concentrations of exposure to DMF. The urinary levels of these two metabolites were higher in the summer than in the winter, suggesting the increased skin absorption of DMF in the summer. Although the urinary levels of AMCC were less correlated with the concentrations of exposure to DMF vapor, AMCC is considered a useful biomarker for assessments of cumulative whole-body exposure to DMF over a workweek and for evaluations of workers' health effects (including liver impairments). Therefore, simultaneous measurements of both the DMF exposure concentrations and urinary levels of AMCC and NMF are recommended for occupational health practices, to protect workers from excessive exposure to DMF through the lung and skin and from adverse health effects under the working conditions of high temperature and humidity, where the control of DMF exposure relies primarily on respiratory protection.

Acknowledgement

The authors are deeply indebted to Dr. Haruhiko Sakurai, Professor Emeritus of Keio University, for his fruitful discussion and encouragement throughout the present study and for his editing of the English manuscript.

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