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Evaluation of Methanol and Formate in Urine as Biological Exposure Indices of Methanol Exposure

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Biological monitoring of exposure to industrial chemicals commonly involves laboratory analyses of a toxicant or metabolites in urine. The American Conference of Governmental Industrial Hygienists has recommended biological exposure indices for methanol exposure based on methanol and formate in urine. The present study was designed primarily to evaluate methanol in urine and other potential biological determinants of methanol exposure. Volunteer subjects underwent controlled exposure to methanol vapor at different concentrations for approximately 8 hours to simulate a standard work shift. Urine was collected immediately prior to exposure sessions, during exposures, and immediately following cessation of exposures. Samples were analyzed for methanol, formate, specific gravity (SpGr), and creatinine. The following biological determinants were examined: total methanol excreted during the shift; mean concentration of methanol excreted during the shift (uncorrected, and corrected for SpGr and creatinine); and concentration of methanol and formate excreted in urine immediately following cessation of exposure (again uncorrected, and corrected for SpGr and creatinine). All methanol-based parameters were approximately linearly related to exposure concentration, but the results for formate related poorly to exposure. In addition, there was considerable interindividual variation in all measured parameters. Overall, measurement of formate in urine was not a useful indicator of individual or group methanol exposures in the range of the permissible exposure limit of 200 ppm. Because of large interindividual variation, methanol in urine (i.e., concentration at end of shift or mean concentration excreted across shift) would not appear suitable for quantitative assessment of individual exposures, but methanol in urine would appear useful as a semiquantitative or qualitative index of individual exposure, or to assess quantitatively the methanol exposure of a group. FRANZBLAU, A.; BATTERMAN, S.A.; ZHOU, N.; STEPIEN, C.J.; D'ARCY, J.B.; SARGENT, N.E.; GROSS, K.B.; SCHRECK, R.M.: EVALUATION OF METHANOL AND FORMATE IN URINE AS BIOLOGICAL EXPOSURE INDICES OF METHANOL EXPOSURE. APPL. OCCUP. ENVIRON. HYG. 12(5):367–374; 1997.

In the most recent edition of *Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices*,[1] the American Conference of Governmental Industrial Hygienists (ACGIH) recommends a number of biological exposure determinants as possible approaches to monitoring occupational methanol exposure. These strategies for biologically monitoring methanol exposure are all based on measurements performed on the urine of exposed workers. If methanol exposure prior to the end of the shift is known to be representative of the whole shift, then the concentration of methanol in urine collected at the end of a work shift is the biological determinant. The biological exposure index (BEI) is 15 mg/L.[2] If methanol exposure is unknown or likely to be nonuniform, then it is recommended that sampling be conducted over the whole shift (i.e., an 8-hour urine collection), and the mean concentration of methanol excreted in urine collected over the whole shift is the determinant.[2] The BEI for the latter is also 15 mg/L. An additional monitoring strategy is to measure formic acid and creatinine in urine collected prior to the shift at the end of the workweek, with the BEI set at 80 mg/g creatinine.[2] The formate-based determinant was dropped by ACGIH in the latest edition of *Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices*.

The methanol BEI carries notations "B" and "Ns." Chemicals listed with the B notation are "usually present in a significant amount in biological specimens collected from subjects who have not been occupationally exposed."[1] The notation Ns indicates that "the determinant is *non-specific*, since it is observed after exposure to some other chemicals."[1] The methanol determinant does not carry the notation "Sq." A notation of Sq implies that a "biological determinant is an indicator of exposure to the chemical, but the quantitative interpretation of the measurement is ambiguous" (i.e., it should be interpreted as a semiquantitative index of exposure).[1]

The ACGIH documentation and scientific support for these recommended values were most recently published in 1991. The methanol-based BEIs are based on data collected in both experimental[3,4] and field[5,6] investigations. Since 1991 a number of published studies have appeared which questioned the formic acid-based BEI,[7–9] and which presumably contributed to the decision to drop the formate-based determinant for biologically assessing methanol exposure.

The present study was designed primarily to assess the methanol-based BEIs for occupational methanol exposure and other potential determinants of exposure. Specifically, we exposed volunteer subjects to various concentrations of methanol

in air, both at rest and with exercise to simulate light industrial work. Urine specimens were collected prior to exposures, during exposures, and immediately following cessation of exposures. The time of each voided specimen was recorded, and the following measurements were performed: volume, methanol concentration, formate concentration, specific gravity (SpGr), and creatinine concentration. The results were analyzed with the goal of assessing some of the factors that bear on the validity and proper interpretation of the different BEIs with respect to documented airborne exposures to methanol.

Methods

Methanol Exposures

Subjects were exposed to vapor concentrations of 0, 100, 200, and 400 ppm during separate 8-hour sessions. Subjects repeated each exposure twice: once while sedentary and once while performing light, intermittent exercise on a bicycle ergometer. Except for a 15-minute interruption after 6 hours, exposures lasted 8 hours. Urine samples were obtained before exposure and immediately following cessation of exposure after 8 hours, and all urine was collected during exposure sessions.

The exercise protocol was designed to increase mean minute ventilation 50 percent over baseline sedentary ventilation. During each exposure session, two subjects alternated every 30 minutes on a bicycle ergometer. Minute ventilation was first measured at rest. Subjects then began cycling on the ergometer. After subjects accommodated to using the ventilation test equipment while cycling (about 5 or 10 minutes), cycling work load was adjusted to achieve a minute ventilation rate that was 100 percent over baseline. Ventilatory monitoring was continued for the duration of the first exercise period only. During subsequent 30-minute exercise periods, subjects exercised at the previously determined work load on the ergometer. No direct measurements of minute ventilation were performed after the first period of exercise because of the discomfort associated with breathing through a mouthpiece for prolonged periods. Once set, the ergometer automatically maintains the set work load regardless of cycling speed. Since subjects alternated periods of rest (baseline ventilation) with equal periods of exercise (ventilation 100 percent over baseline), the overall mean ventilation rate during exposure sessions with exercise was estimated to be 50 percent over baseline.

Inhalation Chamber

Human exposures to methanol vapor were conducted in a 3.7 × 3.7 × 2.7-m stainless steel Rochester-type exposure chamber with 45° tetrahedral top and bottom cones, a suspended floor and ceiling, a restroom, and an airlock for entry and exit. The chamber had a total volume of 47 m^3 and a ventilation rate of 14.2 m^3/min (18 chamber volumes/hour) using high efficiency particulate air-filtered, dehumidified air. Air contaminants such as nitrogen oxides, sulfur dioxide and other sulfur compounds, ammonia, carbon monoxide, unsaturated hydrocarbons, and particulate matter were removed by a series of adsorbent beds, catalytic beds, and filters. Temperature was controlled at 22° ± 2°C, and relative humidity was maintained at 50 ± 5 percent by rehumidification of the inlet air. Vaporization and delivery of methanol vapor to the chamber took place in two steps. The methanol was pumped from a reservoir into the 80°C vaporization section of the generator by an explosion-proof metering pump. The vaporizer had a continuous flow of 190 L/min of filtered, compressed air, producing a methanol concentration of approximately 15,000 ppm. The diluted methanol vapor stream was metered into the inhalation chamber air flow through a mass flow controller to achieve the desired concentration.

Exposure Chamber Air Monitoring

The concentration of methanol in the chamber was monitored using a MIRAN 1-A (The Foxboro Co., Foxboro, Massachusetts) infrared analyzer equipped with a closed-loop calibrator. The MIRAN was set at a wavelength of 9.55 μm (1047 cm^{-1}), absorbance scale of 1.0, and path lengths of 7.75, 3.10, and 1.95 m for 100, 200, and 400 ppm, respectively. The output was recorded continuously using a Keithley data acquisition system (model 575; LABTECH, Taunton, Massachusetts) and analyzed with LABTECH notebook software. Calibration was performed using direct injection of methanol liquid into the calibration loop. The limit of detection was approximately 1 ppm, and the coefficient of variation for calibration of the instrument was 3 percent.

No measurements of methanol distribution within the chamber were made during these studies. However, in earlier studies using ozone in the same chamber, the concentration distribution on a 4-ft grid at floor level, breathing zone height (5 ft), and ceiling level (8 ft) did not vary by more than 5 percent from the concentration measured simultaneously at the inlet valve just below the top of the chamber.[10] From these data with a very reactive gas at 0.4 ppm we are confident that the concentration of methanol vapor did not vary by more than 5 percent of the measured value at any location within the chamber during these studies.

Urine Sampling and Analysis

All voided specimens were collected by subjects in standard hospital collection containers. The volume of each void was measured immediately, and the specific gravity determined by refractometry. A 15-ml aliquot was then stored in a labeled sterile specimen container and placed on wet ice or refrigerated at 4°C for later analyses for methanol, formic acid, and creatinine.

Samples were analyzed using head space gas chromatography for methanol and formate, the latter via formic acid methylester according to Ogata and Iwamoto.[11] Using an autopipetter, 1 ml of urine and 20 μL isopropanol standard [1000 mg/L, high performance liquid chromatography (HPLC)-grade] were placed in a clean, previously labeled 20-ml vial. The vial was immediately sealed with a butyl-rubber septum-equipped crimp cap and well mixed. Vials were then loaded onto the carousel of a Tekmar 7050/7000 (Cincinnati, Ohio) automated head space sampler with a 50-sample capacity. After a 30-minute incubation at 60°C and 2 minutes of mixing, a 1-ml head space sample was injected into a 2 m × 0.125 inch packed column containing 5 percent Carbowax 20M 60/80 Carbopack B (Supelco Inc., Bellefonte, Pennsylvania) of a Varian 3700 gas chromatograph (San Fernando, California). The column was operated isothermally at 90°C. Eluting methanol was detected by flame ionization. The de-

tector output was collected on a personal computer data acquisition system and processed for baseline correction and peak integration.

All urine analyses were performed within 7 days of sample collection. A previous study has documented that with refrigeration at 4°C this amount of delay between sample collection and laboratory analysis results in negligible loss of analyte.[12]

Five- to seven-point calibration curves for methanol were obtained for each set of analyses. Standards (0 to 60 mg/L, depending on exposure levels) were prepared using HPLC-grade methanol, distilled water, and an internal standard, isopropanol. In addition, each carousel included at least two blanks (distilled water) and five quality control (QC) standards. All standards and samples included the internal isopropanol standard. Methanol concentrations calculated by integrating the methanol peak on the chromatogram were verified by methanol:isopropanol ratios. Acceptable analyses achieved QC accuracies and precisions better than 10 and 5 percent, respectively. The limits of detection for methanol and formate (based on six to ten times the noise level in the chromatogram) in urine were less than 0.5 mg/L in all cases. The coefficient of variation for calibrations was typically 3 to 5 percent.

Human Subjects

Subjects had to be at least 18 years old, and less than 65. Subjects were permitted to eat and drink freely during the experiment, even while in the exposure chamber, with the caveat that they had to abstain from alcoholic (ethanol-containing) beverages during experimental sessions and during the 24-hour period preceding each experimental session. Although a potential source of exogenous methanol, consumption of foods sweetened with aspartame was not restricted or monitored since the contribution of this source has been shown to be small or negligible.[13] There was only one subject who smoked, and this individual was not permitted to smoke cigarettes during experimental sessions. None of the subjects had known occupational or avocational exposure to methanol, formic acid, or formaldehyde.

Because of limited animal data suggesting possible developmental toxicity of methanol exposure during pregnancy,[14] all potential female subjects who suspected they might be pregnant were excluded from participation. In addition, a urine pregnancy test was performed on the first voided specimen of premenopausal female participants during each experimental session. None were positive.

All subjects provided written informed consent. The consent forms and research protocols had been approved by the Human Subjects Review Committees of the University of Michigan School of Public Health and the General Motors Research & Development Center.

Results

Twenty-two subjects participated in at least one exposure session, and most were male (64%) and white (95%). Ages ranged from 20 to 63 years, with a mean of 36.4 years. The total number of subjects exceeds the number of participants in any single experiment since not all subjects participated in all experimental sessions. However, there was a core group which completed all exposure and exercise combinations (7 men, 3 women, age range 22 to 54, mean age 36.1), so most of the data represent comparisons among the same individuals. Some variation may be attributed to the different composition of the groups. The means and standard deviations of methanol concentrations shown in Tables 1 and 2 for all subjects were compared with similar statistics computed for the ten core subjects. For the various methanol measures, the percent differences between the two groups were small, typically a few percent, and no systematic biases were observed.

Table 1 summarizes results of analyses for methanol in urine collected at the end of exposures. The concentrations of methanol in urine (uncorrected for SpGr or creatinine) collected at the end of exposures were strongly linearly correlated with exposures (see Figure 1; $r = 0.78$), but it is obvious from Figure 1 that there was considerable interindividual variation. Adjustment for SpGr and creatinine did not improve the correlation (data not shown). The mean concentration of methanol in urine among sedentary subjects exposed to 200 ppm for approximately 8 hours was 17.9 mg/L, and the corresponding value with exercise was 22.5 mg/L. The current recommended BEI for methanol in urine collected at the end of a shift is 15 mg/L.[1]

The mean concentrations of methanol in urine (uncorrected for SpGr or creatinine) collected following exercise were consistently higher than the corresponding sedentary values for nonzero exposures (see Table 1). However, since it is believed that methanol absorption is linearly related to ventilation rate,[4] and most of the same subjects participated in all exposure sessions (thus largely controlling for interindividual biological differences among subjects studied in each session), we anticipated that the values with exercise would be 50 percent above the corresponding sedentary values. The actual mean results with exercise were generally in the range of 50 percent over corresponding sedentary results (76.7 percent for 100 ppm, 25.7 percent for 200 ppm, and 51.8 percent for 400 ppm), suggesting that subjects maintained roughly their target cycling speeds and ventilation rates when exercising.

Table 1 also displays the percentage of all subjects in each session (and the percentage among the ten core subjects) whose end-of-shift urine concentration of methanol exceeded 15 mg/L (uncorrected for SpGr or creatinine), the current methanol-based threshold recommended by ACGIH.[1] These percentages increase with exposure concentration, and, as expected, also demonstrate a consistent increase with exercise. With 100 ppm exposure [half the threshold limit value (TLV)], the concentration of methanol in urine collected at the end of the shift exceeded 15 mg/L in 25.0 and 18.2 percent of all subjects with and without exercise, respectively. With exposures at the TLV (i.e., 200 ppm), the concentration of methanol in urine collected at the end of the shift exceeded 15 mg/L in 72.7 and 53.3 percent of all subjects with and without exercise, respectively. All subjects exceeded 15 mg/L following exposures at 400 ppm. The corresponding results for the ten subjects who completed all exposure sessions were very similar to results shown for all subjects for each experimental condition (see Table 1).

Overall, the results illustrate that, with 15 mg/L as a cutoff for methanol in urine collected at the end of the shift, there is considerable misclassification of the overexposure and underexposure status of subjects relative to the actual vapor concentration. The choice of cutoff is not the source of the misclas-

TABLE 1. Concentration of Methanol in Urine Collected at the End of 8-Hour Exposures

Exposure	0 ppm	0 ppm	100 ppm	100 ppm	200 ppm	200 ppm	400 ppm	400 ppm
Exercise	No	Yes	No	Yes	No	Yes	No	Yes
No. of subjects	15	11	11	12	15	11	11	11
Mean (SD) uncorrected (mg/L)	1.5 (1.2)	1.2 (0.7)	8.6 (5.7)	15.2 (14.2)	17.9 (7.9)	22.5 (15.1)	30.3 (7.2)	46.0 (17.7)
Mean (SD) (mg/L, corrected to SpGr = 1.015)	1.6 (1.3)	1.4 (0.8)	8.5 (4.0)	15.2 (8.8)	21.7 (13.3)	22.8 (9.6)	34.1 (16.8)	48.0 (22.9)
Mean (SD) (mg/g creatinine, corrected for creatinine)	3.4 (3.6)	2.0 (1.4)	15.7 (10.2)	19.1 (9.6)	27.7 (17.6)	25.7 (13.9)	51.7 (25.8)	68.9 (33.4)
% > 15 mg/L uncorrected (all subjects)	0.0	0.0	18.2	25.0	53.3	72.7	100.0	100.0
% > 15 mg/L uncorrected (core subjects only)	0.0	0.0	20.0	30.0	40.0	70.0	100	100

SD = standard deviation.

sification since the mean concentration of methanol in urine following exposure at 200 ppm (the TLV) is approximately the cutoff value of 15 mg/L. Misclassification is related to interindividual (and possibly intraindividual) variation in end-of-shift urine methanol concentrations; in addition, exertion (i.e., ventilation rate) also has a noticeable effect. The variation observed in the current data exists despite ideal exposure conditions (i.e., constant vapor concentrations without opportunity for dermal exposure). Correction for SpGr or creatinine does not reduce the variation observed in uncorrected values (i.e., coefficients of variation for nonzero exposures remain large despite correction for SpGr or creatinine).

Other possible biological determinants of methanol exposure are total methanol excreted during a work shift and mean concentration of methanol excreted over a shift. Table 2 displays these results for each exposure level with and without exercise. As with methanol concentration in urine collected at the end of the shift, there is an almost linear increase in the mean total methanol excretion in relation to airborne concentration. There is also a consistent increase in the total methanol excretion with exercise relative to total excretion while sedentary at each level of nonzero exposure. However, the standard deviations are relatively large in relation to the means, which reflects the large degree of interindividual variation. Another way of illustrating the magnitude of variability is that the maximum cross-shift excretion of methanol among subjects exposed at 100 ppm exceeded the minimum cross-shift excretion of methanol of subjects exposed at 400 ppm (data not shown). Therefore, any cutoff for total methanol excretion will invariably result in considerable misclassification of subjects in this range of exposures. The percentage of the ten core subjects who exceeded the 15 mg/L BEI under each experimental condition is also listed in Table 2, and there is no significant difference from results based on data from all subjects.

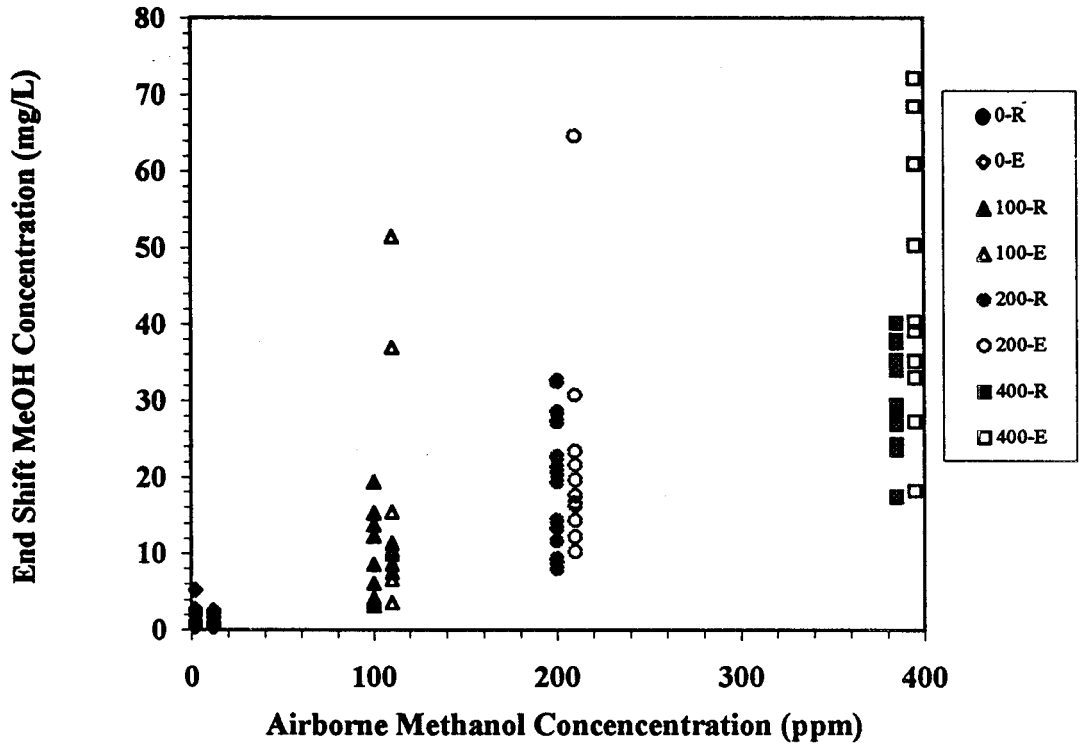
The total methanol excreted during exposures may also be expressed as a (volume-weighted) mean concentration for each individual (i.e., the total methanol excreted in milligrams divided by the total volume of urine excreted during the shift). These results are also displayed in Table 2. The pattern of results is similar to methanol concentration at the end of the shift—a strong linear trend of the group means with exposure, but with considerable interindividual variation.

Figure 2 illustrates the relationship between the mean concentration of methanol in urine collected at the end of the shift and the mean concentration of methanol excreted across the entire shift. The correlation between these two parameters is high ($r = 0.90$). The correlations between the concentrations of methanol in urine (end of shift or entire shift) and total methanol excreted across the shift are weaker, since the latter is greatly dependent on volume and timing of voids[4] (data not shown).

Table 3 displays results for formate in urine collected at the end of exposures for all subjects. The mean concentrations of formate in urine (uncorrected) collected at the end of exposures were essentially indistinguishable for exposures at 0, 100, and 200 ppm, regardless of exercise. There was a modest increase in formate concentrations at the end of exposures at 400 ppm, although the variation was large. Correction for SpGr and creatinine did not substantially alter these patterns. Differences between statistics in formate concentrations for all subjects (Table 3) and the core group of ten subjects were larger than those seen for methanol concentrations, although the differences were generally below 20 percent (one value did reach 37 percent). The relationship between exposure and formate concentrations was not improved, however, when the analysis was restricted to the core subjects. Thus, the pattern of results for formate concentration in urine suggests that this would be a poor indicator for methanol exposure in this range.

Discussion

The current study was designed to assess different strategies for biologically monitoring occupational methanol exposures using various urinary determinants (methanol concentration at end of shift, total methanol excreted across shift, mean concentration of methanol excreted across shift, and formate concentration at end of shift). The study design allowed for examination of the effects of differing levels of exposure and ventilation rates using a complete block design. Because ten of



Regression Statistics:

Multiple R	0.78
R Square	0.61
Adjusted	0.61
Observations	97

Regression Model:

	Coefficient	Stand. Error	t Statistic	p-value
Intercept	0.9821	1.7085	0.5748	0.567
X variable	0.0954	0.0078	12.28	2.6E-21

FIGURE 1. Scatter plot and correlation between concentration of methanol in urine (uncorrected for SpGr or creatinine) collected at the end of shift and methanol vapor concentration.

the subjects completed all exposure/exercise sessions, and they comprise most of the subjects in each session, the study also controlled for interindividual variation.

As noted above, the execution of the exercise protocol appeared to achieve roughly the desired goal of increasing mean minute ventilation approximately 50 percent over baseline. The results are consistent with previous observations that methanol excretion in urine is, in part, a function of ventilation rate during airborne exposure.[4] Possibly more importantly, in a real-world work setting, actual ventilation rates of exposed workers are almost never known precisely, so it is important that any proposed biological index of exposure must be robust enough to remain valid despite substantial variation in ventilation rates.

The protocol for this study was not designed to fully evaluate the formic acid BEI which had been recommended by ACGIH, but which was subsequently withdrawn. In particular, methanol exposures in the present study consisted of only one shift, rather than an entire work week. The justification of the formic acid BEI for methanol is based on a single field study.[6] However, the present results are consistent with previously published experimental data which suggest that there is no accumulation of formate in urine following methanol exposures in the range of the TLV.[7–9] A related study has also

TABLE 2. Total and Mean Concentration of Methanol Excreted During 8-Hour Exposures

Exposure	0 ppm	0 ppm	100 ppm	100 ppm	200 ppm	200 ppm	400 ppm	400 ppm
Exercise	No	Yes	No	Yes	No	Yes	No	Yes
No. of subjects	15	11	11	12	15	11	11	11
Total methanol mg (SD)	1.4	1.1	6.9	8.1	11.4	14.1	25.9	31.4
	(1.2)	(0.9)	(2.7)	(3.9)	(4.7)	(6.7)	(10.4)	(12.9)
Mean (SD) uncorrected (mg/L)	1.1	0.9	5.2	8.7	11.0	13.3	19.3	29.6
	(0.7)	(0.4)	(2.3)	(3.2)	(4.8)	(6.4)	(7.1)	(8.6)
Mean (SD) (mg/L, corrected to SpGr = 1.015)	1.5	1.3	7.5	10.3	17.1	16.1	27.9	33.5
	(1.0)	(0.8)	(2.6)	(3.8)	(11.7)	(4.5)	(12.9)	(13.8)
Mean (SD) (mg/g creatinine, corrected for creatinine)	3.1	1.9	12.3	13.8	23.0	19.3	41.1	59.3
	2.9	(1.3)	(4.9)	(6.2)	(12.1)	(8.0)	(20.9)	(38.6)
% > 15 mg/L uncorrected (all subjects)	0.0	0.0	0.0	8.3	26.7	27.2	72.7	100.0
% > 15 mg/L uncorrected (core subjects only)	0.0	0.0	0.0	10.0	20.0	30.0	70.0	100

SD = standard deviation.

demonstrated an absence of formate accumulation in blood following exposure at the TLV.[15] In addition, the present data indicate that the interindividual variability of formate in urine is considerable, thus further weakening the potential usefulness of formic acid as a biological determinant of methanol exposure in the range of the TLV. Large interindividual variation in formic acid levels in urine was also found in a previous study.[5]

In a field study Heinrich and Angerer[5] studied methanol in urine as a possible index of exposure among 20 male workers. The methanol concentrations in air ranged from 22 to 139 ppm, with a geometric mean of 56 ppm. Ventilation rates were not monitored. Methanol concentrations in urine collected over the last 4 hours of the work shift ranged from <0.6 to 57.3 mg/L, with mean = 21.8 mg/L and standard deviation = 20.0 mg/L. Although as a group the methanol-exposed workers were clearly distinguishable from unexposed controls, there were large interindividual differences. The authors concluded that, "When considering the possible application of these parameters for biological monitoring, difficulties were encountered, especially for the individual case from the overlapping range in the concentrations of exposed and unexposed persons for each of the applied parameters."[5]

In an experimental study, Šedivec *et al.*[4] exposed four subjects (at rest) to methanol vapor at 78, 157, and 229 ppm for 8 hours.[4] The ranges of values of methanol in urine collected at the end of exposures did not overlap among the three exposures (e.g., the minimum urine concentration following exposure at 229 ppm exceeded the maximum urine concentration following exposure at 157 ppm), and were also clearly distinguishable from preexposure values. Based on these results, it was suggested that the concentration of methanol in urine collected at the end of the shift could be used as a quantitative index of personal exposure. In addition, they exposed three sedentary subjects to approximately the same concentration of methanol vapor for 8 hours per day on four consecutive days (237, 257, 242, and 227 ppm). Again, the means and ranges of measured values appeared to be similar and very small, respectively. Overall, in this study the interindividual variability appeared to be quite low even though the exposure protocols were similar to the present study. However, less variability would be expected with a smaller sample size (n = 3 or 4 versus n = 11 to 15). The present study also included a broad range of ages and both genders, which may have also contributed to the greater observed interindividual variability.

Conclusion

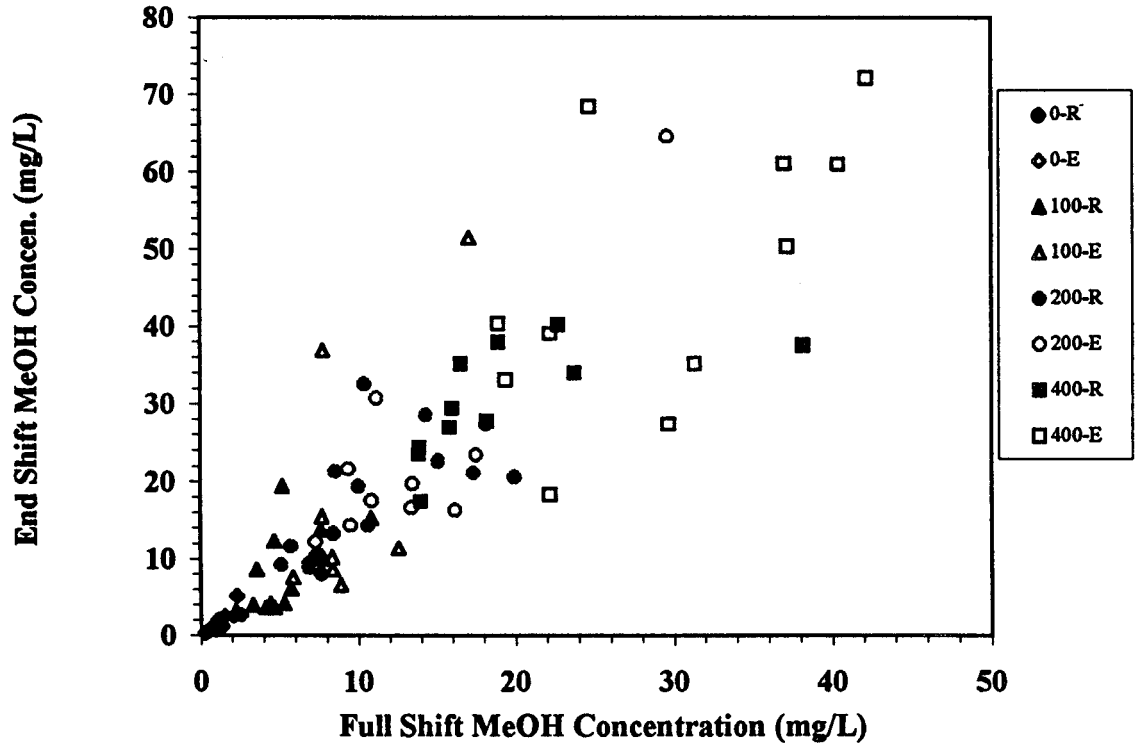
The use of formic acid in urine as a biological determinant of methanol exposure is not supported by the present data, or most previously published studies. In our opinion, formic acid should not be used as an index of exposure to methanol vapor in the range of the TLV, and the formate-based BEI was withdrawn by ACGIH in 1994.

The biological determinants of methanol exposure based on methanol in urine (concentration at end of shift or mean

TABLE 3. Concentration of Formate in Urine Collected at the End of 8-Hour Exposures

Exposure	0 ppm	0 ppm	100 ppm	100 ppm	200 ppm	200 ppm	400 ppm	400 ppm
Exercise	No	Yes	No	Yes	No	Yes	No	Yes
No. of subjects	15	11	11	12	15	11	11	11
Mean (SD) uncorrected (mg/L)	7.7	11.7	12.9	10.0	13.2	10.0	19.8	27.8
	(9.3)	(10.5)	(8.4)	(8.4)	(9.8)	(7.6)	(12.3)	(21.2)
Mean (SD) (mg/L, corrected to SpGr = 1.015)	7.6	11.3	11.3	9.3	14.6	9.1	18.2	24.0
	(6.2)	(9.0)	(4.2)	(4.6)	(9.3)	(5.7)	(4.9)	(9.7)
Mean (SD) (mg/g creatinine, corrected for creatinine)	12.1	12.9	16.8	12.7	15.2	9.9	28.2	30.4
	(11.5)	(9.2)	(5.0)	(8.2)	(8.7)	(6.3)	(13.6)	(12.3)

SD = standard deviation.



Regression Statistics:

Multiple R	0.90
R Square	0.80
Adjusted	0.80
Observations	98

Regression Model:

	Coefficient	Stand. Error	t Statistic	p-value
Intercept	0.9206	1.1164	0.8246	0.4117
X variable	1.5209	0.0766	19.86	9.2E-36

FIGURE 2. Scatter plot and correlation between mean concentration of methanol in urine collected at the end of shift and mean concentration of methanol excreted across the entire shift.

concentration excreted across shift) appear to have considerable interindividual variability, and are related to ventilation rates. They appear to be useful as qualitative or semiquantitative indices of individuals' possible exposure to methanol vapor in the range of the TLV. In addition, it would appear that either of these indices could be used as quantitative indices of exposure of groups of workers that share the same exposure environment.

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