BIOMARKERS, 1999, VOL. 4, NO. 2, 106–117

Detection of low level benzene exposure in supermarket wrappers by urinary muconic acid

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Received 1 October 1997, revised form accepted 22 August 1998

Women who use the 'hot wire' and 'cool rod' machines to wrap meat in supermarkets are potentially exposed to low levels of benzene and polycyclic aromatic hydrocarbons present in fumes emitted during the thermal decomposition of the plastic used to wrap meat. In order to evaluate whether the benzene metabolite *trans, trans*-muconic acid (MA) can be used to monitor these low levels, we collected urine samples from supermarket workers, and assayed the urine for MA. Geometric mean after-shift MA levels were highest for subjects who used the 'hot wire' machine, i.e. > 300 ng mg^{-1} creatinine (Cr). The corresponding levels for subjects who used the 'cool rod' machine were similar to those for subjects who did not use either type of machine, and were much lower. These results indicate that urinary muconic acid has some potential for use in monitoring benzene exposures of less than 1 part per million (ppm). The study detected very high background MA levels (exceeding 2000 ng mg^{-1} Cr) in some subjects, suggesting that individuals in the general population without occupational exposure to benzene may have urinary MA levels equivalent to exposure to up to 2 ppm benzene in ambient air. However, since non-benzene sources of the metabolite cannot be completely ruled out as partially responsible for these high levels, the public health significance of this finding is not known at the moment.

Keywords: benzene, muconic acid, biomarkers, supermarket, plastic wrap.

Introduction

Subjects who wrap meat, and other food products, in supermarkets can be exposed to fumes containing low levels of benzene. The fumes are given off when heat is electrically applied through a hot wire or cool rod in the wrapping machine to cut the required length of plastic film, or when ends of the film wrap are sealed by laying the film on a hot plate. Similar benzene exposure occurs when heat is used to activate the adhesive on price labels during labelling of the wrapped product. Polyvinyl chloride (PVC) plastic films are widely used throughout the industry, to wrap meat, and such wrapping and labelling of meat are activities predominantly carried out by women. Improper use of the wrapping and labelling machines at temperatures higher than those recommended results in scorching of the plastic film and fumes being given off from the burning plastic. Failure to regularly clean the hot wire or cool rod or the heating pad, or prolonged contact of the PVC film with the wire or rod, also predispose to generation of fumes (O'Mara 1970,

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1354–750X/99 $12.00

Vandervort and Brooks 1977). These fumes have been shown to cause an acute respiratory syndrome known as meatwrappers' asthma (Sokol *et al.* 1973). The fumes contain hydrogen chloride, hydrocarbons, most of which is *benzene* and also polycyclic aromatic hydrocarbons (PAH), plasticizers phthalates, adipates, and their breakdown products (O'Mara 1970, Vandervort and Brooks 1977, Boettner and Ball 1980).

Benzene concentrations of 0.02–0.04 parts per million (ppm), i.e. 0.06–0.14 mg m^{-3}), have been recorded in 8 h area air sampling in a room where the labelling machine was in use, and for a labeller using the machine, personal air concentrations of as much as 0.03–0.2 ppm (0.1–0.5 mg m^{-3}) were recorded (Frederick *et al.* 1981). Similar values when extrapolated over an 8 h shift were obtained in a simulated experiment in cutting PVC plastic films using the wrapping machine (Boettner and Ball 1980, Cook 1980). The amount of benzene emitted varied with the type of plastic used. We estimate that using the plastic film which gave the highest emission of benzene in the study by Boettner and Ball (1980) and Cook (1980), benzene exposure levels of 1 ppm in breathing zone air can be reached after 75 min of wrapping.

The compound *trans,trans*-muconic acid (MA) is a metabolite of benzene which has been suggested to be a reliable biomarker of low level benzene exposure when measured in urine. We therefore conducted a preliminary study to examine if urinary MA can be effectively used to detect the low levels of benzene which supermarket workers may be exposed to during wrapping.

Methods

The study population consisted of 45 subjects who were employed in several supermarkets in Albuqerque, New Mexico. Complete muconic acid data for both days of sampling were not available for three individuals. These subjects were retained in the analyses when they had the required information for that particular section. Spot urine samples were collected from each individual immediately before the start of a shift between 07:00 and 08:00 hours, and immediately after the end of the shift between 17:00 and 18:00 hours, on two consecutive days, making a total of four samples from each subject. Information on the number of cigarettes smoked during the past 24 h preceeding the shift, and during the shift, was also collected. Data were collected on whether the individual used the wrapping machine during the shift, as well as the specific job the individual performed. Most of the study subjects wrapped meat, bakery products, or produce (wrappers), or were meatcutters, a few were checkers and one was a meatstocker. Measurements of creatinine, nicotine and cotinine in the urine were also performed on each urine sample. Creatinine was measured by the IL Test Creatinine with a Monarch Instrument (Amherst, N.H.) centrifugal chemical analyser. The method is based on the reaction of creatinine with picric acid under alkaline conditions. The resulting red-coloured complex is determined colorimetrically. The reproducibility of the assay was assessed by making duplicate determinations of several urine samples over a concentration range of 51 to 166 mg dl^{-1}. The reproducibility, defined as the mean of the percent differences, was 17 %. Nicotine and cotinine were measured in urine by radioimmunoassay as previously described (Langone *et al.* 1973). Muconic acid was measured by a gas chromatography/mass spectroscopy (GC/MS) method using a Hewlett Packard 5890 gas chromatograph interfaced with a Hewlett Packard 5970B mass selective detector. The GC was equipped with a Hewlett Packard Ultra–1 fused silica capillary column, 25 m (length) ×0.25 mm (internal diameter) with a 0.5 μm film thickness (Bechtold *et al.* 1991).

Each subject had four measurements of urinary MA concentration, viz. before-shift (baseline) and after-shift for Day 1 and Day 2. The creatinine-corrected MA values were used. The four measurements of MA were not normally distributed. Accordingly, the log-transformed MA values were used. Means and standard deviations of the log MA, and the mean difference between after-shift and before-shift log MA concentrations, were computed. Extreme Studentized Deviate (ESD) statistics by Rosner (1995) were computed to identify any outliers in the logarithmic muconic acid baseline values for Day 1 and Day 2. Where appropriate, paired or independent *t*-tests were used to compare within (before shift/after shift changes in a group), and between group differences, in mean log urinary muconic acid, respectively (Fleiss 1981).

Results

The distribution of job-titles was as follows: of the total of 35 women, 30 were wrappers, four were checkers and one was a stocker; of the nine men, eight were meatcutters amd one was a checker. Subjects with the job-title of wrapper are the primary users of the wrapping machine. Checkers and meatstockers do not normally use the wrapping machine, and did not in this study. On the other hand, meatcutters primarily cut meat as their main job, but when demand for wrapping is excessive, they could be called upon to wrap. This did happen during the study. Also, some wrappers did not use the wrapping machine on the days sampling was done. Therefore, to avoid misclassification of exposure through the use of job-title, benzene-exposed subjects were instead defined as those who actually used the hot-wire or cool-rod wrapping machine on the day urine samples were taken, and unexposed subjects as those who did not use any type of wrapping machine.

Before-shift MA concentrations are supposed to reflect background levels of MA. However, one subject who used the hot wire machine on Day 1 had a before-shift MA concentration of 2716.9 ng mg^{-1} Cr, which turned out to be the highest MA value recorded in the entire study. This was also the only value identified by the ESD statistic by Rosner (1995) as an outlier for the two days of sampling. Accordingly, because of this abnormally high background value, this subject was excluded from all Day 1 results in the tables below.

In table 1, it is seen that in all groups on both days of sampling, the log-transformed mean after-shift MA levels were consistently higher than the corresponding before-shift levels, but none of the differences was statistically significant. The highest after-shift log-transformed mean MA values of 5.76 on Day 1 and 5.80 on Day 2, were both consistently recorded for subjects who used the hot wire machine. These values correspond to geometric mean MA values of 317.3 ng mg^{-1} Cr and 330.3 ng mg^{-1} Cr in the original scale, respectively, but were not statistically significantly different from the corresponding Day 1 and Day 2 log-transformed means of 5.53 (252.1 ng mg^{-1} Cr) and 5.24 (188.7 ng mg^{-1} Cr) for control subjects who did not use any wrapping machine on the day of sampling. Log-transformed after-shift mean MA values on both days of sampling for subjects

Table 1. Mean and standard deviation (s.d.) of creatinine-corrected urinary muconic acid concentration (on a log-transformed scale) by day.

	Day 1*			Day 2	
	N	Before mean (s.d.)	After mean (s.d.)	*N*	Before mean (s.d.)	After mean (s.d.)
All	43	4.81 (0.86)	5.33 (0.83)	42	4.63 (0.77)	5.33 (0.87)
Used Hot Wire	4	5.03 (0.90)	5.76 (0.80)	7	4.61 (0.59)	5.80 (0.78)
Used Cool Rod	28	4.78 (0.82)	5.19 (0.82)	24	4.60 (0.80)	5.24 (0.88)[a]
No use of any wrap machine	11	4.80 (1.01)	5.53 (0.84)	11	4.71 (0.86)	5.24 (0.89)
Smokers	12	5.10 (0.70)	5.48 (0.72)	11	5.06 (0.87)	5.37 (0.98)
Non-Smokers	31	4.70 (0.89)	5.28 (0.86)	31	4.48 (0.69)	5.31 (0.85)

[a] n = 26.

* Subject with abnormal background MA value of 2716.9 ng mg^{-1} Cr on Day 1 excluded from the Day 1 results only.

who used the cool rod machine were similar to those for control subjects who did not use any wrapping machine that day, especially on Day 2. Smokers had higher before- and after-shift MA concentrations than non-smokers on both days of sampling, but these differences were also not statistically significant.

In table 2, similar comparisons as above were made by smoking status, and the findings were also similar. The results for smokers were much clearer and consistent than those for non-smokers. Among smokers on both days of sampling, a distinct gradient was observed, with the highest mean values obtained for subjects who used the hot wire machine, followed by those who used the cool rod machine, with the lowest value being recorded for those who did not use any wrapping machine. The after-shift mean MA value of 4.76 for subjects who did not use the machine, was actually lower than the before-shift value of 5.53.

For non-smokers also, the mean after-shift MA concentration was highest for subjects who used the hot wire machine on Day 2. However, the mean after-shift Day 1 MA concentration for subjects who did not use any wrapping machine was surprisingly slightly higher than that for subjects who used the hot wire machine. As before, none of the differences (before shift versus after shift, or hot wire versus no use, or cold rod versus no use) in table 2 was statistically significant. In general, for each group, smokers had higher mean MA values than non-smokers, except that for Day 1 only, the reverse was observed for subjects who did not use the machine.

In tables 3 and 4 are the results of comparisons of the means of the differences of log-transformed MA values between before- and after-shift, and for the different groups. The findings correspond to those in tables 1 and 2 as would be expected, and none of the results was statistically significant.

In table 5, detailed descriptive data are given for the 12 individuals in the study

Table 2. Mean and standard deviation (s.d.) on a log-scale of creatinine-corrected urinary muconic acid concentration by wrapping machine and by smoking status.

	Day 1*			Day 2		
	N	Before mean (s.d.)	After mean (s.d.)	*N*	Before mean (s.d.)	After mean (s.d.)
Smokers						
All	12	5.10 (0.70)	5.48 (0.72)	11	5.06 (0.87)	5.37 (0.98)
Used hot wire	1	5.06 (–)	5.98 (-)	2	5.01 (0.66)	5.74 (0.13)
Used cool rod	8	5.28 (0.78)	5.67 (0.67)	7	4.93 (0.79)	5.45 (1.15)
No use of any wrap machine	3	4.64 (0.42)	4.83 (0.59)	2	5.53 (1.67)	4.76 (0.78)
Non-Smokers						
All	31	4.70 (0.89)	5.28 (0.86)	31	4.48 (0.69)	5.31 (0.85)
Used hot wire	3	5.03 (1.10)	5.69 (0.96)	5	4.45 (0.56)	5.83 (0.95)
Used cool rod	20	4.58 (0.76)	5.00 (0.81)	17	4.46 (0.79)	5.16 (0.78)[a]
No use of any wrap machine	8	4.86 (1.18)	5.79 (0.79)	9	4.53 (0.61)	5.35 (0.92)

[a] n = 19.

* Subject with the abnormal background MA value of 2716.9 ng mg^{-1} Cr on Day 1 excluded from the Day 1 results only.

Table 3. Comparison of the means of the differences in before/after shift creatinine-corrected urinary muconic acid levels by use of wrapping machine and smoking status.

	Day 1* Difference (After – Before)		Day 2 Difference (After – Before)	
	N	Mean (s.d.)	*N*	Mean (s.d.)
All	43	0.52 (1.01)	42	0.70 (1.06)
Used hot wire	4	0.73 (0.45)	7	1.18 (1.08)
Used cool rod	28	0.41 (1.06)	24	0.63 (1.00)
No use of any wrap machine	11	0.73 (1.05)	11	0.53 (1.17)
Smokers	12	0.38 (0.82)	11	0.32 (0.95)
Non-smokers	31	0.58 (1.08)	31	0.84 (1.08)

* Subject with the abnormal background MA value of 2716.9 ng/mg Cr on Day 1 excluded from the Day 1 results only.

Table 4. Comparison of the means of the differences in before/after shift creatinine-corrected urinary muconic acid levels by use of wrapping machine for smokers and non-smokers.

	Day 1* Difference (After – Before)		Day 2 Difference (After – Before)	
	N	Mean (s.d.)	*N*	Mean (s.d.)
Smokers				
All	12	0.38 (0.82)	11	0.32 (0.95)
Used hot wire	1	0.92 (-)	2	0.73 (0.54)
Used cool rod	8	0.39 (0.98)	7	0.51 (0.91)
No use of any wrap machine	3	0.19 (0.40)	2	-0.78 (0.88)
Non-smokers				
All	31	0.58 (1.08)	31	0.84 (1.08)
Used hot wire	3	0.67 (0.49)	5	1.37 (1.23)
Used cool rod	20	0.42 (1.12)	17	0.68 (1.06)
No use of any wrap machine	8	0.94 (1.16)	9	0.83 (1.04)

* Subject with the abnormal background MA value of 2716.9 ng mg^{-1} Cr on Day 1 excluded from the Day 1 results only.

whose untransformed urinary MA concentration was 700 ng mg^{-1} Cr or higher. (The cut-off point of 700 ng mg^{-1} Cr was used because published studies indicate that the highest urinary MA concentration among unexposed smokers is usually less than this value (Ducos *et al.* 1990, Ghittori *et al.* 1996).) Both the urinary nicotine and cotinine values closely agree with the reported amount of cigarettes smoked. As noted before, the highest *before-shift* (background) MA concentration of 2716.9 ng mg^{-1} Cr was recorded in a non-smoker. Similarly, the highest after-shift MA concentration of 1567.8 ng mg^{-1} Cr was recorded in a non-smoker who

Table 5. Descriptive data for subjects with urinary muconic acid (MA) levels of 700 ng/mg Cr of higher, by job title, smoking status and use of wrapping machine.

Subject	Job title	No. of cigarettes smoked during the past 24 h before Shift	Before shift			Type of wrapping machine used during shift	No. of cigarettes smoked during shift	After shift		
			Nicotine in ng mg^{-1} Cr	Cotinine in ng mg^{-1} Cr	MA in ng mg^{-1} Cr			Nicotine in ng mg^{-1} Cr	Cotinene in ng mg^{-1} Cr	MA in ng mg^{-1} Cr
8	Wrapper	0	65.4	24.6	77.0	Hot wire	0	3.3	5.5	1234.2
9	Wrapper	25	20714.3	3219.3	822.8	Did not use	6	16666.5	5170.0	202.2
16	Cutter	0	2.3	8.9	118.2	Cold rod	0	9.4	34.0	1060.0
17	Cutter	0	14.2	4.6	343.4	Hot wire	0	10.9	6.7	822.5
20	Wrapper	5	31.3	4125.0	1040.0	Hot wire	2	316.7	4833.3	201.1
20	Wrapper	5	581.8	9010.9	204.6	Hot wire	2	807.7	2923.1	1265.2
24	Wrapper	0	37.5	25.5	2716.9	Hot wire	0	64.4	17.4	244.1
25	Checker	0	5.3	3.6	745.0	Did not use	0	16.3	12.22	287.9
32	Wrapper	20	6687.1	21634.8	300.2	Cold rod	16	12753.3	11306.7	905.5
32	Wrapper	30	1911.8	4862.8	441.0	Cold rod	18	4166.7	10000.0	871.7
40	Checker	0	58.5	118.0	528.5	Did not use	0	42.6	72.8	1567.8
44	Wrapper	0	66.7	13.0	53.1	Did not use	0	4.5	10.4	845.4

did not use the machine on the day of sampling. The only other known source of muconic acid is sorbic acid (Ducos *et al.* 1990). It has been shown that ingestion of 200 mg of sorbic acid which is supposed to exceed the daily intake in the diet for the average person, resulted in an increase of urinary muconic acid concentration to less than 700 ng mg^{-1} Cr. Thus the cut-off point of 700 ng mg^{-1} Cr will also serve to indicate urinary MA concentrations that exceed those associated with normal dietary intake of sorbic acid or background levels.

Discussion

Before-shift MA levels which reflect non-occupational or background levels were comparable in all groups, especially on Day 2, as would be expected. The highest geometric mean after-shift MA concentrations of greater than 300 ng mg^{-1} Cr were observed consistently on both days in the exposed group of workers who used the hot-wire machine, and the same pattern was observed separately in smokers and to a lesser extent in non-smokers. The reason for the less consistent results with non-smokers is probably related to the not too infrequent occurrences of abnormally high background MA–for example in table 5, four subjects had before-shift MA values of >700 ng mg^{-1} Cr, and two others who were non-smokers who did not use any wrapping machine on the day of sampling also had after-shift MA levels of >700 ng mg^{-1} Cr. We will comment on this further below. The association of the highest mean MA levels with the hot wire machine is consistent with the notion that use of the hot wire machine is associated with higher than background exposure to benzene. As mentioned, benzene concentrations of up to 0.2 ppm have been recorded in personal air measurements of subjects using the hot wire wrapping and labelling machines (Boettner and Ball 1980, Cook 1980, Frederick *et al.* 1981,) and it has been estimated that exposures of 1 ppm benzene in ambient air are possible after 75 min of wrapping. The highest after-shift MA concentration of 1234 ng mg^{-1} Cr in a worker who used the hot wire machine on Day 2 is compatible with exposure to at least 1 ppm benzene in ambient air as estimated from data by Inoue *et al.* (1989) and Lauwerys *et al.* (1994).

The hot wire wrapping machine has been in use since the early 1950s when plastic films were first used to wrap meat in supermarkets. Because of the health problem (meatwrappers' asthma) associated with fumes from this machine, in 1975 the cool rod was substituted in place of the hot wire in these machines. This resulted in substantial reduction of emission of fumes from the wrapping machine and the virtual disappearance of meatwrappers' asthma, since the cool rod had more mass than the hot wire, and was operated at lower temperatures. Thus the observation in this study that mean levels of MA in subjects who used the cool rod machines were similar to those in unexposed subjects who did not use the wrapping machine, is consistent with the known reduction in exposure to fumes associated with use of the cool rod machine. Interestingly on both days of sampling, the 90th percentile MA values of 653.5 and 662.7 ng mg^{-1} Cr for workers who used the cool rod machine were nevertheless higher than the levels of 482.4 and 371.3 respectively observed for workers who were not exposed (data not shown). This could mean that occasionally workers who used the cool rod machine can be exposed to above background levels of benzene. It has been reported that incorrect use of the cool rod machine at temperatures above those recommended can result in significant amount of fumes being emitted. Actual field measurements in

supermarkets indicate that 10 % of the time the cool rod was as hot as the hot wire (D.H. Wegman, unpublished data). Furthermore, it has been reported by Smith *et al.* (1983) that operating the the cool rod cutter at temperatures of 210 °C or more results in emissions that exceed those obtained with a poor practice hot wire technique.

After-shift MA values were higher than before-shift values in all groups including subjects who did not use the wrapping machine. One possible explanation is that increased benzene exposure other than through direct use of the wrapping machine occurred within the supermarkets. For example, it is possible that benzene emitted from the machines could spread from the room where wrapping is carried out to other areas in the supermarket, thus exposing everyone in the building, although to a much lesser degree than occurs in the wrapping room. This is supported by the findings of James (1975) that in the breathing zone of workers operating the machine, the average concentration of hydrogen chloride (which is one of the constituents in these fumes) while the hot wire machine was in use was 0.57 ppm as compared with 0.03 ppm while the cool rod cutter was in use. Similarly, background levels of hydrogen chloride in the rest of the store varied from 0.12 to 0.16 ppm while the hot wire machine was in use, as compared with 0 to 0.04 ppm when the cool rod was in use.

In table 5, the highest *background* MA levels of 2716.9 ng mg^{-1} Cr measured in a sample obtained *before* the start of a shift and the highest after-shift level of 1567.8 ng mg^{-1} Cr measured in a subject who did not use the wrapping machine, warrant special comments. Both individuals were non-smokers as confirmed not only by their smoking history, but also by their urinary nicotine and cotinine levels. As mentioned above, four other subjects without occupational exposure to benzene had MA levels of >700 ng mg^{-1} Cr (before-shift of 822.8, 1040, and 745, and after shift of 845.4 ng mg^{-1} Cr–table 5). We first called attention to the fact that in some areas in some countries, certain members of the general population without known exposure to benzene seem to have benzene metabolite levels in their urine compatible with exposure to up to greater than 1 ppm benzene in ambient air (Johnson and Lucier 1992). Our concern has been validated in several reports. Virtually all the studies published to date have reported urinary metabolite levels equivalent to exposure to at least 0.3–0.5 ppm benzene in ambient air in a proportion of subjects, while the majority of subjects had very low levels equivalent to ambient air exposure in the parts per billion range (Inoue *et al.* 1988,1989, Stommel *et al.* 1989, Ducos *et al.* 1990,1992, Bechtold *et al.* 1991, Lee *et al.* 1993, Melikian *et al.* 1993, van Sittert *et al.* 1993, Lauwerys *et al.* 1994). Additionally, as mentioned, some of the studies reported that some subjects in the general population have metabolite levels equivalent to having being exposed to more than 1 ppm benzene in ambient air (Inoue *et al.* 1988, Stommel *et al.* 1989, Bechtold *et al.* 1991, Johnson and Lucier 1992, Melikian *et al.* 1993). In some of these studies, the highest concentrations were observed in non-smokers (Bechtold *et al.* 1991, Lauwerys *et al.* 1994). This was most vividly illustrated in the study in Baltimore in which urinary MA levels of well over 2500 ng mg^{-1} Cr were recorded in 4-year old children (Weaver *et al.* 1996). Our findings here which were partly alluded to in our earlier paper (Johnson and Lucier 1992) add to this body of evidence. We reiterate that there is an urgent need to ascertain whether these high metabolite levels are primarily indicative of benzene exposure and, if so, whether these exposures in the general population are sporadic or chronic. If the latter

these levels of exposure could be associated with the development of cancer (Rinsky *et al.* 1987, Wong 1987). It is of interest that cohort mortality studies we have conducted in the meat industry have observed excess risk of leukaemia, lymphomas and lung cancer in women who wrap meat in supermarkets, but not in meatcutters who work in the same room as these women and only infrequently wrap meat (Johnson *et al.* 1986, Johnson 1994, Metayer *et al.* 1998). Benzene and PAHs are present in fumes from the wrapping machine (Vandervort and Brooks 1977). Benzene is leukaemogenic in humans (Rinsky *et al.* 1987) and induces tumours in multiple sites including the lung in animals (International Agency for Research on Cancer 1982). PAHs have also been reported to induce leukaemia in animals (Rigdon *et al.* 1967, Sugiyama *et al.* 1967, Rigdon and Neal 1969) and are well known lung carcinogens in humans and animals (International Agency for Research on Cancer 1973, 1985), and excess leukaemia has been reported in workers exposed to PAHs (International Agency for Research on Cancer 1985). Our findings of these high levels also have important implications. They indicate that neither cigarette smoking nor sorbic acid can account for these levels. For a start, urinary concentrations of other benzene metabolites such as *S*-phenylmercapturic acid compatible with exposure to more than 1 ppm benzene in ambient air have also been recorded in general population subjects without known exposure to benzene (Stommel *et al.* 1989). Also, as mentioned above, the MA concentration associated with the highest intake of tobacco smoke or sorbic acid is less than 700 ng mg^{-1} Cr. For example, in the two studies by Ducos *et al.* (1990, 1992), the highest MA concentration observed was 500 ng ml^{-1} and 660 ng ml^{-1} respectively, in unexposed members of the general population (smokers and nonsmokers not distinguished). Also, in the study by Melikian *et al.* (1993), smokers had a *mean* urinary MA concentration of 290 ng mg^{-1} Cr which was three times that of 90 ng mg^{-1} Cr found in non-smokers; the upper bound of the 99 % confidence limits for smokers was 410 ng mg^{-1} Cr and for non-smokers it was 150 ng mg^{-1} Cr. Also a recent study reported that mean MA levels in unexposed persons smoking more than 20 cigarettes a day was 207 ng mg^{-1} Cr (range 93 to 604 ng mg^{-1} Cr) (Ghittori *et al.* 1996). Furthermore, smoking cannot possibly account for MA concentrations of over 2500 ng mg^{-1} Cr observed in 4-year old children in Baltimore (Weaver *et al.* 1996). This would mean therefore that the generally accepted belief that tobacco smoking is the most important source of benzene exposure in the general population (Wallace 1989, Hricko 1994) may be inaccurate.

It is also likely at this time that benzene exposure is not the primary source of these high levels in the general population. If this is so, then factors other than tobacco smoking and sorbic acid need to be considered to explain these levels. For example, individuals with these high levels could simply represent subjects who are genetically extremely efficient at converting benzene into its metabolites, or subjects with increased metabolic activity resulting from increased physical activity (none of the studies of benzene metabolites considered physical activity). Alternatively, it is possible that apart from sorbic acid there are also as yet other unidentified sources of muconic acid, and other unidentified sources of *S*-phenylmercapturic acid, in the diet or in the environment, which are responsible.

In conclusion, this preliminary study provides some evidence that urinary muconic acid may have potential use in monitoring very low benzene exposures (below 1 ppm) not only in the occupational setting but also in the general

population. The findings indicate an urgent need for studies to determine the reasons for the very high levels of urinary benzene metabolites in certain individuals in the general population (including children) which may or may not be due to benzene. If they are primarily due to benzene, the public health significance will depend on whether these are occasional sporadic exposures which may be of no significance, or whether they are chronic, in which case they may have significant public health implications. Thus studies will be needed also, to delineate the temporality of these exposures.

The study also provides some evidence to support previous reports (Boettner and Ball 1980, Cook 1980, Frederick *et al.* 1981) that women who use the hot-wire machine to wrap meat and other food products in food establishments, are occupationally exposed to low levels of benzene. The possibility exists that for women with long-term employment in this capacity, this chronic exposure may have public health implications. However, because of the small sample size, and the fact that benzene exposure was not concomitantly measured in this study by personal air sampling, and the unexplained high background levels of MA in some subjects, caution should be exercised in interpreting the findings. The results should simply be regarded as preliminary evidence indicating the urgent need for more rigorous studies in this area.

Although use of the 'cool rod' machine in supermarkets has definitely resulted in substantially reduced exposure to fumes, two points are to be noted:

(1) The 'hot wire' machine is still being used in some supermarkets, and in other areas of the meat industry such as meatpacking/processing plants (Frederick *et al.* 1981, personal observation). Thus the potential for exposure to these fumes though significantly reduced has not been completely eliminated in the meat industry.
(2) Variants of the hot wire machines are widely employed not only in other food industries such as bakery and confectionery, but also in many diverse industries such as pesticides manufacture where plastic films are used as wraps or packages. In many of these industries, these activities are predominantly carried out by women. Apart from our mortality studies in the meat industry, any chronic effects resulting from exposure to these fumes have not been investigated.

Acknowledgements

This study was funded by the National Institute of Environmental Health Sciences. Our thanks to Eddie Eyer, President of UFCW Local 1564 in Albuquerque, New Mexico, and his staff, and to the UFCW International in Washington, DC for their full support without which the study would not have been possible.

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