

Biological indicators of exposure in styrene polymerization workers

Styrene in blood and adipose tissue and mandelic and phenylglyoxylic acids in urine

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WOLFF, M. S., LILIS, R., LORIMER, W. V. and SELIKOFF, I. J. Biological indicators of exposure in styrene polymerization workers: Styrene in blood and adipose tissue and mandelic and phenylglyoxylic acids in urine. *Scand. j. work environ. & health* 4 (1978): suppl. 2, 114—118. The concentrations of mandelic and phenylglyoxylic acids, urinary metabolites of styrene, and styrene in blood were determined for 491 styrene polymerization workers. Styrene in subcutaneous fat was determined for 25 workers. The levels of styrene exposure were estimated to be less than 10 ppm, and urinary metabolite and blood styrene concentrations indicated that significant recent exposure (within 4 h) had occurred among workers in areas of styrene polymerization and styrene monomer production. Styrene analysis of subcutaneous fat suggested that the monomer may have been present for as long as 3 d after exposure, a time when urinary metabolites and blood styrene were almost invariably undetectable. All three biological parameters were correlated with recency of exposure and estimated intensity of exposure within job categories.

Styrene absorption among industrial workers exposed to ambient air levels near the threshold limit value (TLV 100 ppm) has been characterized mainly by urinary metabolite determinations. Excellent correlations have been found for controlled laboratory and industrial exposures to styrene between air concentrations and the urinary excretion of mandelic and phenylglyoxylic acid (1, 2, 4, 5, 6, 8, 10). Gas chromatographic measurement of these metabolites has provided a method sensitive to approximately 10 mg/l, depending on the technique of derivatization (9).

By extrapolation from previous studies, low level styrene exposures (1—10 ppm) would be expected to result in urinary metabolites in the range of 10—200 mg/l. Indeed, Thiess (12) reported such levels of urinary metabolites among 58 polymerization workers at exposures below 8 ppm. We had the opportunity to study urinary metabolites in 491 styrene polymerization workers, for whom the highest average exposure to styrene and ethylbenzene was reported to be in the range of 8—30 ppm (7, personal communication from the manufacturer). In this group measurements of blood styrene were also made (personal communication from Eisinger and Blumberg). Blood styrene determinations under experimental conditions have

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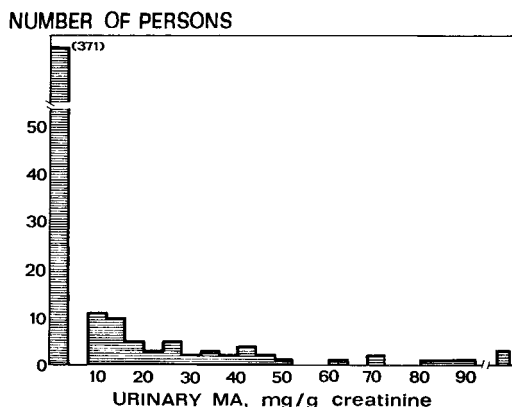


Fig. 1. Distribution of urinary mandelic acid (MA) concentrations among styrene polymerization workers.

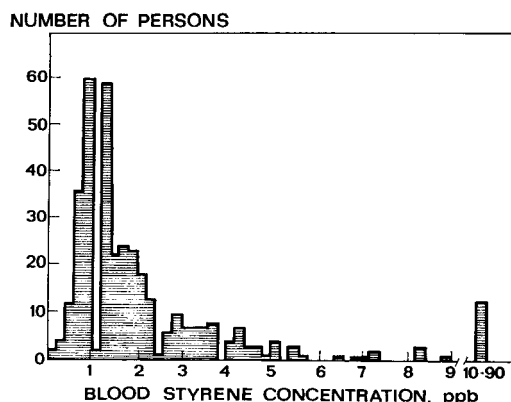


Fig. 2. Distribution of blood styrene concentrations among styrene polymerization workers.

been reported by Åstrand et al. (1) and Stewart et al. (11). Extrapolating from their data, at exposures below 10 ppm, one could expect the blood styrene concentrations to be in the lower range of less than 0.1 ppm.

Since styrene has a very high fat to blood partition, we attempted to measure styrene in the subcutaneous fat of 25 of these workers, as previously reported (14).

tection of urinary metabolites was approximately 10 mg/l.

Exposure assessment was made from an occupational history obtained during the clinical examination. The job category and the time of the last shift worked were recorded. The latter is hereafter referred to as "most recent exposure."

METHODS

During a clinical field study of 491 styrene polymerization workers, samples of blood, urine and subcutaneous fat (the latter for 25 workers) were obtained. Styrene urinary metabolites were determined by the method of Buchet et al. (3). Blood styrene was measured by spectrofluorometric assay of a cyclohexane extract of whole, heparinized blood (personal communication from Eisinger and Blumberg). Determinations of styrene in fat have been previously reported (14). Urinary concentrations were expressed as milligrams per gram of urinary creatinine in an effort to adjust for individual variations of urinary concentration. The limit of de-

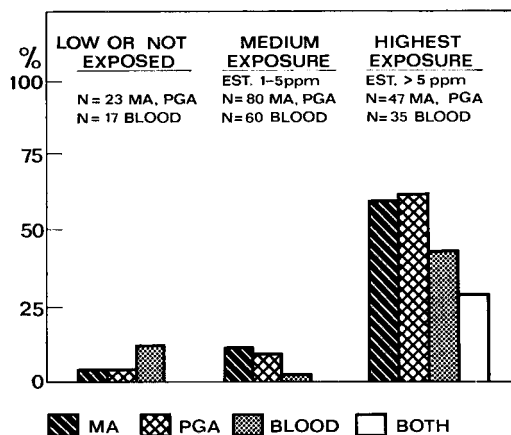


Fig. 3. Percentage of workers examined within 4 h of having worked and determined to have urinary metabolites mandelic acid (MA) and phenylglyoxylic acid (PGA) above 10 mg/g of creatinine, blood styrene above 5 ng/ml, or both blood styrene and urinary metabolites concomitantly elevated, according to level of exposure.

RESULTS AND DISCUSSION

Job categories were classified according to ambient air measurements reported by Maier and Ruba (7) and by the company (personal communication). Styrene polymerization, manufacturing, and purification

areas had the highest levels (mean styrene 8–35 ppm), maintenance, laboratory, and packaging operations were medium (detectable but less than 5 ppm), and areas with undetectable styrene in air were designated as low or no exposure.

Urinary metabolites were largely undetectable in this population (341/477) and most blood styrene concentrations were less than 2 ng/ml (244/364) (figs. 1 and 2). The highest blood styrene was 90 ng/ml, and the highest urinary mandelic acid 140 mg/g of creatinine. These levels were consistent with mean styrene exposure levels in the range of 10 ppm.

The highest prevalence of detectable levels and the highest concentrations of styrene in blood and of urinary metabolites occurred among styrene manufacturing, purification, and polymerization workers who had been exposed within 3 h of the sampling (fig. 3). In the low exposure group, tested soon after work (within 4 h) 1 of 23 workers had urinary metabolite concentrations and 2 of 17 workers had blood styrene concentrations above 10 mg/g of creatinine or 5 ng/ml, respectively. Two of 47 retirees had measurable urinary metabolites and none of 37 had elevated blood styrene.

The mean concentrations of urinary metabolites and blood styrene among those workers with urinary metabolite concen-

URINARY METABOLITE OR BLOOD STYRENE CONCENTRATION

(mg/g creatinine & ng/ml, respectively)

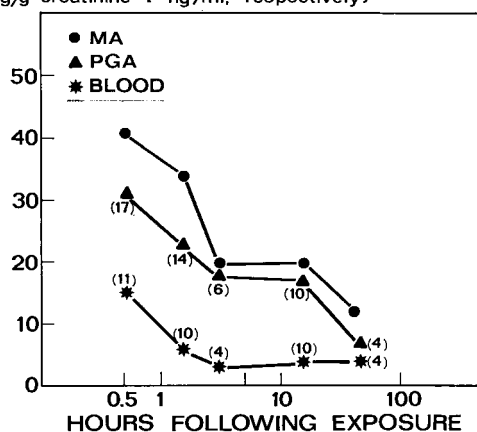


Fig. 4. Mean values of the observed elevated urinary metabolites mandelic acid (MA) and phenylglyoxylic acid (PGA) or blood styrene concentrations among workers as a function of the most recent exposure.

CONCENTRATION URINARY MA, PGA OR BLOOD STYRENE

(mg/g creatinine) (ng/ml)

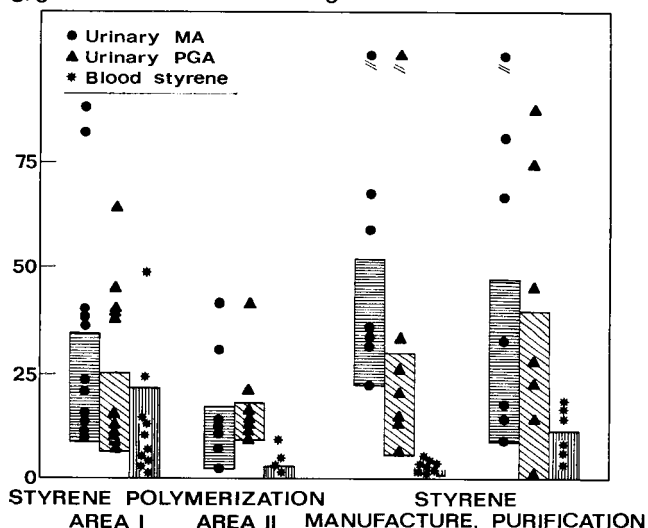


Fig. 5. Observed elevated mandelic acid (MA), phenylglyoxylic acid (PGA) and blood styrene concentrations among workers with urinary mandelic acid > 10 mg/g of creatinine who worked in high exposure jobs. Shaded area depicts mean value and lower range.

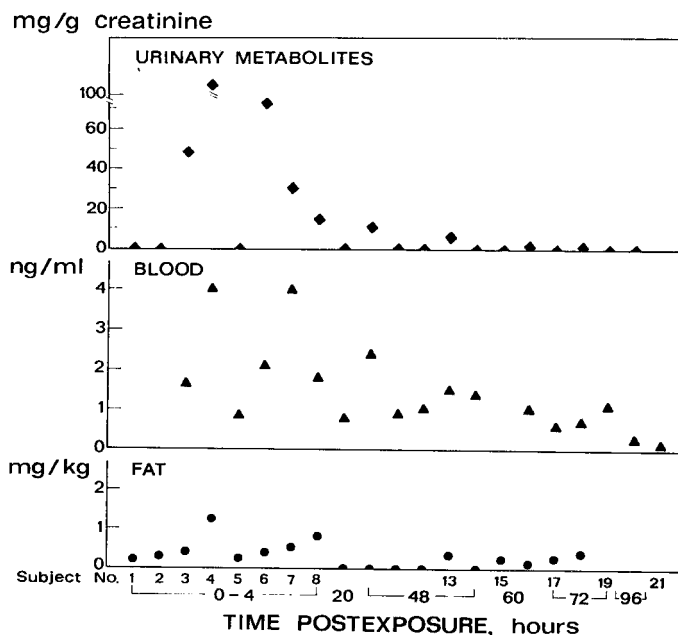


Fig. 6. Urinary mandelic acid, blood styrene and fat styrene concentrations of two subjects. Time since last exposure was within specified range.

trations greater than 10 mg/g of creatinine declined with time from the last exposure (fig. 4). The highest concentrations of both urinary metabolites and blood styrene occurred among workers who had arrived from work within the past hour. Mean concentrations of urinary metabolites among workers recently exposed in the high exposure category were the highest for styrene manufacturing and purification workers (fig. 5). Blood styrene concentrations were the highest for recently exposed polymerization workers in an area designated as Polystyrene I. Among styrene manufacturing workers, there was a significantly higher ratio of mandelic acid to phenylglyoxylic acid than among polymerization or purification workers (fig. 5). This finding may be related to ethylbenzene exposure, which was highest in this area [mean of 8 measurements, 3 ppm (7)]. Mandelic and phenylglyoxylic acids have also been reported as urinary metabolites of ethylbenzene (2).

We have previously reported the detection of styrene in subcutaneous fat of these workers as long as 3 d after the most recent exposure (14). These data, combined with blood styrene and urinary metabolite concentrations (fig. 6), suggest the presence of styrene in fat at a time when urinary

metabolites and blood styrene are no longer detectable or significantly elevated. The data in fig. 6 suggest a correlation between fat, blood, and urinary metabolite determination, e.g., subjects 4, 6, 8, 10, and 13 had simultaneously elevated values. However, although the correlations for fat with blood ($r = 0.78$, $N = 10$) and blood with urinary mandelic acid ($r = 0.66$) were statistically significant in the group in which fat styrene levels were determined (fig. 6), in the larger group the correlation between blood styrene and urinary mandelic acid was poor ($r = 0.12$, $N = 42$). This latter result is consistent with the metabolic model for styrene, which would predict a sharp exponential drop in blood styrene (1, 13) shortly after exposure, the concentrations of urinary metabolites increasing during 8–12 h after exposure and becoming undetectable after 16–24 h (2, 8).

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