1411 BIOLOGICAL MONITORING OF THERMAL DEGRADATION PRODUCTS OF A 4,4'-METHYLENE-DIPHENYL DIISOCYANATE (MDI) ELASTOMER BY THE DETERMINATION OF 4,4'-METHYLENE-DIANILINE (MDA) IN HYDROLYSED URINE AND SERUM. G Skarping, M. Littorin and M Dalene. Department of Occupational and Environmental Medicine, University Hospital, Lund, Sweden. Sponsor: Y Alarie

A worker was blowing hot air on the surface of a MDI-based polyurethane polymer. He was struck with dyspnea, rhinoconjunctivitis and fever. The illness was suggestive of an MDI-associated illness, compatible with both an immediate hypersensitivity, and a complement-mediated immune complex reaction. MDI/MDA might be related to the worker's illness. The patient's blood and urine samples were hydrolyzed and analyzed for the presence of MDA. MDA was derivatized using pentafluoro-propionic acid anhydride (PFPA). GC-MS measurements were made using chemical ionisation with ammonia and monitoring the m/z = (M-20)-negative fragments from the MDA-PFPA and the ($^2H_2$) MDA-PFPA derivative. The concentration of MDA in the samples taken 22 h after the exposure was 2 µg/mmol creatinine in urine and 5.5 ng/ml in serum. The detection limit was below 0.1 µg/liter. The half-life ($t_{1/2}$) of MDA was 70-80 hrs in urine and about 21 days in serum, which suggests the presence of MDI/MDA protein adducts in the exposed worker. When estimating MDI exposure by urine analysis, the time after the exposure must be considered. By taking blood samples on a regular basis, a better estimate of individual exposure is achieved. This work was supported by the Swedish Work Environment Fund.

1412 2,4- AND 2,6-TOLUENEDIAMINE (TDA) IN HYDROLYSED URINE AND PLASMA AS BIOLOGICAL MARKERS OF EXPOSURE TO 2,4- AND 2,6-TOLUENE DIISOCYANATE (TDI). M Dalene, P Lind, L Hagmar and G Skarping. Department of Occupational and Environmental Medicine, University Hospital, Lund, Sweden. Sponsor: Y Alarie

Exposure to toluenediisocyanate was studied in a polyurethane (PUR) factory. Urine and plasma samples were collected from workers. Following hydrolysis, the corresponding amines 2,4-toluenediamine (2,4-TDA) and 2,6-toluenediamine (2,6-TDA), were determined as pentafluoropropionic anhydride (PFPA) derivatives by GC-MS using selected ion monitoring in the negative chemical ionisation mode. Trideuterium labeled TDA was used as an internal standard and the ions monitored were the molecular ions (M-20)- and (M-40)-. The detection limit was 1-5 fg, corresponding to less than 0.05 µg TDA/liter in human urine or plasma. The air concentration of TDI was in the 0.4 - 4 µg/m^3 range. The urinary elimination rate was related to TDI exposure. The concentration of 2,4- and 2,6-TDA in the workers plasma were virtually stable. No relation between the elimination rates of TDA in urine and plasma levels of TDA was observed. Five PUR workers showed plasma levels in the range of 1-8 ng per ml. Two white collar workers, present only occasionally in the factory, had 0.2-1 ng/ml plasma concentration. Two volunteers showed an increasing concentration of TDA in plasma over time. The present study indicates the possibility to monitor TDI exposure by the monitoring the urine or plasma levels of TDA following hydrolysis. This work was supported by The Swedish Work Environment Fund.

1413 METHODS FOR THE ANALYSIS OF BUTADIENE AND VOLATILE METABOLITES IN BLOOD. W E Bechtold, M R Strunk, R F Henderson. Inhalation Toxicology Research Institute, Albuquerque, NM.

Our laboratory is exploring the role of dose in understanding the marked species differences in the toxicity of 1,3-butadiene (BD). To do so, a new method was needed to quantify the levels of BD, butadiene monoxide (BDO), and butadiene dioxide (BDO_2) in blood. The method is based on cryogenic distillation of tissues followed by analysis using multidimensional gas chromatography/mass spectroscopy (GC/MS). Metabolites isolated from blood by vacuum distillation are condensed into a trap. BD and BDO are sampled from the trap vapor phase. BDO_2 is extracted from the co-distilled water phase using ethyl acetate. Samples are analyzed using a multidimensional GC. The method was validated by the addition and analysis of 40, 32, and 0.55 nmols of BD, BDO, and BDO_2, respectively, to 0.75 ml of control blood. The recoveries were 88 ± 8, 98 ± 4, and 98 ± 12%, respectively. Kinetic studies indicated minimal loss of BDO and BDO_2 in blood held at room temperature in closed containers for up to 1 hr. The method will be applied to blood samples from mice and rats exposed to 100 ppm BD for 4 hr. (Research supported by the CMA under FIA DE-FI04-19AL66351, under Contract No. DE-AC04-76EV01013 with the U.S DOE/OHER.)

1414 HAIR AS A TARGET TISSUE FOR PROTEIN-BOUND PYRROLES FOLLOWING SUBCHRONIC INTRA-PERITONEAL INJECTIONS OF 2,5-HEXANEDIONE. DJ Johnson, L Lack, SM Abdel-Rahman, and MB Abou-Donia. Dept. of Pharmacology, Duke Univ. Med. Cent., Durham, NC.

Studies were carried out to ascertain the feasible use of body hair as a biological marker for chronic exposure to industrial neurotoxicants that yield the metabolite, 2,5-hexanedione (2,5-HD), i.e., *n*-hexane and methyl-*n*-butyl ketone. 2,5-HD is capable of forming N-substituted pyrroles by reacting with primary amines which include amino acids as well as the ε-amino groups of lysine-containing peptides. Male Sprague-Dawley rats were given daily ip. injections of 50 mg/kg 2,5-HD for 45 days. At intervals, hair samples distant from the site of injection of treated animals were taken and showed staining which was positive for the presence of pyrroles with Ehrlich's reagent (*p*-N,N-dimethylaminobenzaldehyde), whereas control animals were negative. In addition, proteins were solubilized from these samples. The protein solutions from the treated samples tested positive for the presence of pyrroles with Ehrlich's reagent and upon spectral analysis yielded an absorbance peak of 530 nm which is in the range characteristic of this type of pyrrole. The extent of positive staining for pyrroles in the vibrissae progressed linearly with time. These findings suggest the potential use of hair as an indicator for chronic exposure to this class of potential industrial neurotoxic chemicals and as a complement to the urinary analysis which is used to confirm recent exposure. (Supported by NIOSH Grant OHO 0823)

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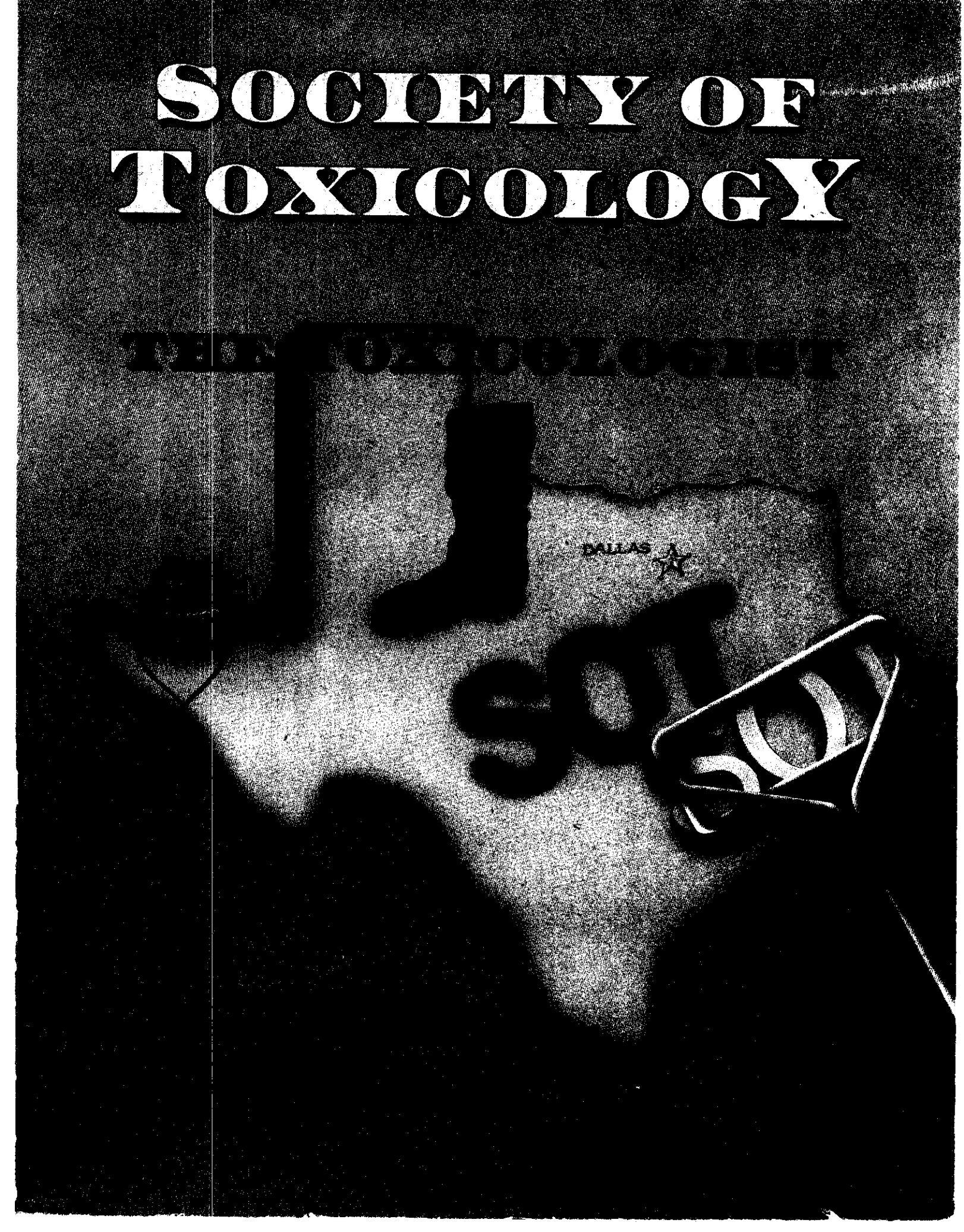

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Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, platform, poster/discussion, and poster sessions of the 33rd Annual Meeting of the Society of Toxicology, held at the Loews Anatole Hotel, Dallas, Texas, March 13-17, 1994.

An alphabetical Author Index, cross-referencing the corresponding abstract number(s), begins on page 439.

The issue also contains a Keyword Index (by subject or chemical) to the titles of all the presentations, beginning on page 467.

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