

Biological monitoring at the Institute of Occupational Health

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Exposure to chemicals at the workplace is traditionally estimated from measurements of the chemical concentrations in the air (ie, by industrial hygiene). However, in some instances, notably when the chemical may be absorbed through the skin, this procedure can lead to erroneous results. Similarly, because of variations of the concentrations of the chemical in the air over time and in different locations and because of differences in work habits, the amount of a chemical absorbed from the air can differ significantly between individuals who are apparently under identical exposure. There are, therefore, instances when biological monitoring can be a better indicator of the absorbed amount of the chemical than an industrial hygiene measurement.

At the Institute of Occupational Health, some 40 different analyses of biological monitoring are performed in the Laboratory of Biochemistry and in the laboratories of the regional institutes. The analyses performed in these laboratories are listed in table 1.

Biological monitoring in its traditional form means measuring the concentration of a chemical or its metabolite in the blood or urine of an exposed worker. Recently, however, alternative methods have also been developed, chemically nonspecific methods for the biological monitoring of mutagenic or clastogenic compounds, on the basis of their biological effects. The Mutagenesis Laboratory of the Institute has extensively studied the feasibility and usefulness of urinary mutagenicity analyses, and analyses of chromosome damage (aberrations, sister chromatid exchange, micronuclei) in biological monitoring (eg, in exposure to cytostatics, styrene, tobacco smoke, welding fumes, and butadiene and in different industrial branches, such as the rubber and pharmaceutical industries). A further developing area is the measurement of specific chemical-induced adducts in deoxyribonucleic acid (DNA) or various plasma or blood proteins in exposed humans. The Laboratory of Toxicology has performed such studies, especially among people exposed to polycyclic aromatic hydrocarbons.

Another approach that has developed in recent years is in vivo measurement of the amount or concentration of cadmium in the liver and kidney or lead in the bone. Recently, my colleagues and I performed a study

(1) on the kinetics of lead in bone, in comparison with a history of lead exposure, on the basis of blood lead determinations. There was a relationship between the cumulative lead exposure and the concentration of lead in the tibia and calcaneus. The former reflected mainly long-term exposure, and the latter more recent exposure. As a follow-up, we have studied the relationship between bone lead concentrations, and psychophysical and neurophysiological performance in two groups of lead-exposed workers.

Levels of chemicals derived from occupational exposures in body fluids are, fortunately, usually rather low. Therefore, the analytical methods work close to their limits of detection. In addition, the biological matrices are variable and contain a variety of interfering

Table 1. Biological monitoring analyses performed in the Institute of Occupational Health (U = urine, B = blood)

Exposure	Analysis
Alkyl lead	U-lead
Aluminum	U-aluminium
Benzene	B-benzene
Cadmium	B-cadmium, U-cadmium
Carbon disulfide	U-thiothiazolidine
Carbon monoxide	B-hemoglobin-carbon monoxide
Chlorinated phenols	U-chlorophenols
Chromium	U-chromium
Cobalt	U-cobalt
Cyanides	U-thiocyanate
Dichloromethane	B-hemoglobin-carbon monoxide
Dimethylformamide	U-monomethylformamide
Fluorine, fluorides	U-fluoride
Formic acid	U-formic acid
Hexane	U-hexanediol
Lead	B-lead, B-protoporphyrin
Manganese	U-manganese
Mercury	U-mercury, B-mercury
Methanol	U-formic acid
Nickel	U-nickel
Nicotine	U-cotinine
Organophosphates	B-acetylcholinesterase, B-pseudocholinesterase
Polychlorinated biphenyl	S-polychlorinated biphenyl
Phenoxyacids	U-2,4-dichlorophenoxy acetic acid, U-dichloroprop, U-mechlorprop, U-2-(2-methyl-4-chlorophenoxy)- propionic acid
Phenol	U-phenol
Selenium	U-selenium
Styrene	U-mandelic acid
Tetrachloroethylene	B-tetrachloroethylene
Toluene	B-toluene
Trichloroethane	B-trichloroethane
Trichloroethylene	U-trichloroacetic acid
Vanadium	U-vanadium
Xylene	U-methylhippuric acid
Freon 113	B-freon 113

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chemicals. For these reasons, maintaining analytical quality is a major problem in biological monitoring. Recently, several external quality assurance schemes have become available. They assist in maintaining the accuracy and even precision of the analyses. The Laboratory of Biochemistry runs one such program, which concentrates on the metabolites of organic chemicals in the urine.

Some recent studies on the biological monitoring of different chemical exposures

In an effort to improve the possibilities of biologically monitoring exposure to low levels of benzene, volunteers were exposed to benzene in a dynamic exposure chamber, and the levels of benzene in exhaled air and blood, as well as the levels of phenol in the urine, were followed (2). Benzene was analyzed by gas chromatography with photoionization detection. Benzene in blood and exhaled air could easily be followed after a 4-h exposure to 10 ppm until the next morning, and also after exposure to 1.7 ppm for 4 h, the benzene level the morning after the exposure differed from the values observed in unexposed subjects. It was concluded that, at high (5–10 ppm) levels of benzene, samples taken 16 h after the cessation of exposure reflect the body burden of benzene, while at low exposure (<1 ppm) sampling 1 h after exposure gives an estimate of exposure over the preceding few hours. Smoking was confirmed as an important potential source of error. The analysis of exhaled air specimens is more sensitive than the analysis of blood. The sample collection apparatus using the head-space vials that recently became available makes exhaled air sampling an appealing alternative to blood sample collection in the biological monitoring of benzene.

In a study (3) on the biological monitoring of exposure to carbon disulfide (CS_2), urinary levels of thiothiazolidine carboxylic acid (TTCA) were analyzed for workers exposed to CS_2 in a viscose rayon fiber factory and a viscose sheeting factory. The CS_2 concentration in the air was analyzed with capillary gas chromatography (4), and the TTCA in urine by a modification of the high-performance liquid chromatography method of van Doorn et al (5). An excellent correlation was observed between the exposure (time-weighted average concentration of CS_2 in breathing-zone air) and the end-of-shift urinary concentration of TTCA. Even at low levels of exposure, the concentrations of TTCA could be analyzed accurately and repeatably. The relationship between urinary TTCA levels and CS_2 in the air were very similar to those observed in the study of Campbell et al (6).

Exposure to styrene has traditionally been monitored through the analysis of the amounts of mandelic acid in postshift urine samples (7). However, because of the short half-time of styrene immediately after exposure, this procedure may not always be optimal. In order

to determine the optimal method for the biological monitoring of styrene, my co-workers and I studied (8) the urinary excretion of styrene itself, and of mandelic, phenylglyoxylic, and p-hydroxymandelic acids, in 205 workers in 32 different factories working with reinforced plastics. It was concluded that an optimal method for biological monitoring was the determination of the sum of mandelic and phenylglyoxylic acids in the urine on the morning following the exposure. At this time, the sum of $1.2 \text{ mmol} \cdot \text{l}^{-1}$ corresponds to 8-h exposure at the Finnish occupational exposure limit of $85 \text{ mg} \cdot \text{m}^{-3}$.

Exposure to chromium, especially to hexavalent chromium, and its biological monitoring were studied in a large industrial complex, which includes an open pit mine of chromite ore and the production of ferrochromium and stainless steel (Huvinen et al, unpublished results). Exposure to hexavalent chromium was low everywhere, the highest measured concentration in the breathing zone being $6.6 \text{ } \mu\text{g} \cdot \text{m}^{-3}$. Total airborne chromium was highest in the ferrochromium smelter (median $248 \text{ } \mu\text{g} \cdot \text{m}^{-3}$). The average blood and urinary chromium levels were higher than in an unexposed population, but they were still rather low (maximal urinary and blood chromium levels measured 0.34 and $0.03 \text{ } \mu\text{mol} \cdot \text{l}^{-1}$, respectively). Although several exposed workers exhibited an exposure-related variation of their urinary chromium levels, no consistent relationship was observed between the exposure and urinary (or blood) chromium levels. It was concluded that, at the exposure levels encountered in this factory, biological monitoring was not very useful.

Exposure to cobalt and its biological monitoring were studied in a large factory refining metallic cobalt and producing several cobalt chemicals, in powder metallurgical production of hard metal products, and in the welding, grinding and polishing of hard metal products (Kiilunen et al, unpublished results). The urinary and blood concentrations of cobalt were elevated in workers exposed to cobalt in different forms. It was therefore possible to identify exposed people, and this ability might be of importance in light of the possible carcinogenicity of cobalt to humans. There was a very marked variation in the relationship of air and urinary cobalt concentrations between different individuals, which could partly be due to a different body burden of cobalt. The interindividual differences obscured possible differences between exposures to different cobalt species and made it difficult to evaluate accurately the exposure of individuals, and even groups of workers, to cobalt from urinary cobalt levels. Exposure to cobalt was very low in hard metal metallurgy, where the process was well encapsulated, intermediate in cobalt refining and in the manufacture of cobalt compounds, but high in the powder metallurgy of hard metal products.

Creosote oil is a very complex mixture containing many different polycyclic hydrocarbons. Creosote oils are used for wood preservation, and in several stages

workers can be exposed to creosote fumes, and to the oils through skin contact. A study was made to investigate the feasibility of urinary alpha-naphthol (Luotamo et al, unpublished results) and 1-hydroxypyrene (9) analyses as means of biologically monitoring exposure to creosotes. The main volatile component of creosote was naphthalene. There was an increase in the concentration of alpha-naphthol in the urine during a workday, and also during the workweek (measured in morning samples). The correlation between the airborne concentrations of naphthalene and the concentration of naphthol in the urine was reasonably good (0.66). The determination of alpha-naphthol is thus a promising approach for the biological monitoring of creosote. The main objection against the use of alpha-naphthol for this purpose is that the toxicologically most important components of creosote, the carcinogenic polycyclic aromatic hydrocarbons, do not necessarily behave similarly to naphthalene. It is, for example, clear that their proportion in the air is much lower (as compared with their proportion in the oil). Therefore, my colleagues and I also studied the excretion of 1-hydroxypyrene in urine among creosote-exposed workers and investigated the relationship between airborne pyrene and urinary 1-hydroxypyrene. An exposure-related variation was observed in the urinary concentrations of 1-hydroxypyrene, with an accumulation during the workweek. The correlation between the airborne concentrations of pyrene and urinary concentrations of 1-hydroxypyrene in the individual workers was low. This was an expected finding because the exposure probably occurs mainly through the skin (the volatility of pyrene is low) and does not mean that urinary concentrations cannot be used for monitoring the uptake of pyrene — and creosote oil — but shows that these measurements cannot be used for verifying compliance with occupational exposure limits for workplace air.

Recently, several dry-cleaning shops have replaced tetrachloroethylene by chlorofluoro hydrocarbons such as trichlorofluoromethane (CFC 11) and 1,2,2-trichloro-2,1,1-trifluoroethane (CFC 113). My co-workers and I followed the kinetics of these CFC compounds in volunteers during and after exposure to 200 ppm of the CFC compounds, with intermittent peaks of 1000 ppm by CFC analyses from the blood and exhaled breath (Pekari et al, unpublished results). The purpose of the study was to develop a biological monitoring method for the CFC compounds. We also

analyzed the number of ventricular arrhythmias in the volunteers. Later, measurements of exposure were also performed in a dry-cleaning shop. No relationship was observed between ventricular arrhythmias and exposure to the CFC compounds. The disappearance of both CFC compounds from the body followed biphasic kinetics, with half-times of about 1 and 5 h. It was calculated that exposure at the level of the occupational exposure limit in Finland (1000 ppm) leads to blood concentrations of 0.2 and 0.1 $\mu\text{mol} \cdot \text{l}^{-1}$ of CFC 11 and CFC 113, respectively, in a specimen collected 16 h after the cessation of the exposure (ie, in a next morning sample). Measurements of these CFC compounds in exhaled air can also be used for biological monitoring purposes.

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