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Biological monitoring today and tomorrow.

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these methods are applied, a matched group of unexposed people has to be studied concurrently.

It is difficult to interpret cytogenetic changes, although several carcinogens induce chromosome damage. There is suggestive evidence that groups of people with chromosome damage may have an increased risk of cancer (97), and such a relationship is apparent after exposure to ionizing radiation. However, after exposure to chemicals, it is not known whether the persons who show the highest frequencies of chromosome aberrations, micronuclei, or sister-chromatid exchanges are at a higher risk than the average person. Even on a group basis, no quantitative estimate of the cancer risk can be made. Neither can the kind of cancer to be expected be predicted (ie, the validation of cytogenetic monitoring as far as the health outcome is concerned is still lacking). On the other hand, observed cytogenetic damage gives no clue of the type of chemical exposure, and cytogenetic changes cannot be assessed in quantitative exposure terms. Thus the only way of estimating the results of cytogenetic monitoring results is to compare the results observed in similar industries — and even such data are scant. At present, cytogenetic examinations are best suitable for ad hoc studies, rather than for routine monitoring programs.

Quality management

Many studies have shown that the quality of biological monitoring analyses is often mediocre (98—105). What is positive is that, in continuously running external quality assessment schemes, improved analytical quality has often been observed (13, 98—100, 106, 107). The other positive development is that several international quality assessment schemes are currently available, in addition to the schemes limited to blood lead, such as those of the United States Public Health Services (Centers for Disease Control), the State of New York Department of Health, the Commonwealth of Pennsylvania Department of Health, the College of American Pathologists, the United States Public Health Service (Health Care Financing Administration), the United States Occupational Safety and Health Administration, the Commission of the European Communities, and the Chinese Academy of Preventive Medicine (108, 109).

The German Society of Occupational Medicine has offered intercomparison programs for toxic chemicals in blood or serum since 1982. The program consists of one annual round, and the number of participants is approximately 90 (12, 99). In the rounds in 1991 and 1992, the program was expanded to include four chlorinated solvents in blood, six polychlorinated biphenyl isomers, and six other chlorinated environmental contaminants.

The Centre de Toxicologie du Québec has operated an interlaboratory comparison program for cadmium and lead in blood; aluminum, selenium, copper, and zinc in serum; and arsenic, fluoride, mercury, cadmium, and chromium in urine (106).

In Japan, an industrial health regulation obliges the employers to monitor biologically all workers exposed to lead, toluene, xylene, trichloroethylene, tetrachloroethylene, 1,1,1-trichloroethane, styrene, dimethylformamide, or n-hexane. Since 1980, the Japan Federation of Occupational Health Organization has conducted an annual quality assurance round among the laboratories performing such analyses. In 1991, 36 to 67 laboratories participated in 10 types of such analyses (lead in blood; free protoporphyrin in blood; aminolevulinic acid, hippuric acid, methylhippuric acid, total trichloro compounds, trichloroacetic acid, and mandelic acid in urine; monomethylformamide; and 2,5-hexanedione) (13, 100, 110).

The Occupational Medicine and Hygiene Laboratories of the Health and Safety Executive in the United Kingdom has run an external quality assurance scheme for the analysis of mercury in urine since 1983; the number of participating laboratories is 15—20 (111). As a part of this external quality assessment scheme, a program for the quality assurance of lead in blood was started in 1973. Currently, some 80 laboratories take part in these analyses, and about 40 laboratories participate in the blood cadmium analyses (98).

The Robens Institute of Health and Safety runs an external quality assurance scheme for copper, zinc, gold, aluminum, and selenium in serum; lead and cadmium in blood; and mercury and cadmium in urine. The number of participating laboratories is 20—110 for different elements (98, 107, 112).

The Finnish Institute of Occupational Health has arranged a quality assurance scheme for metabolites of organic solvents in urine. Currently, four sets of specimens are sent annually for the analysis of methylhippuric acids, hexanedione, trichloroacetic acid, mandelic acid, and phenol (102).

Thus, at present, an external quality assessment scheme is available for most important analytes. (Volatile solvents in blood and aluminum, nickel and speciated arsenic analysis in urine are still exceptions.) [Note added to proof: From 1994 on, the German quality assurance scheme also includes samples for the analysis of some volatile organic solvents in blood (K-H Schaller, personal communication).] Therefore, no laboratory should do biological monitoring without external quality assessment — and it is foreseeable that the analytical performance in biological monitoring will improve.

In the early 1980s, the Organisation for Economic Cooperation and Development (OECD) established principles of good laboratory practice in order to facilitate mutual acceptance of test data on the harmful effects of chemicals, and thus to limit unnecessary duplicate testing, with the aim of avoiding technical barriers to free international trade. The principles are concerned with the organizational process

and the conditions under which laboratory studies are planned, performed, monitored, recorded, and reported (113). These principles then developed into recommendations on quality systems (ie, organizational structure, responsibilities, procedures, processes, and resources for implementing quality management) that are generally applicable to laboratories doing analyses, chemical or other (114, 115). These recommendations were recently adapted for use in clinical chemistry laboratories (116), whose functions closely resemble those of biological monitoring laboratories. It is thus apparent that quality systems will be required from biological monitoring laboratories also. This requirement will probably assist in improving analytical performance by drawing the attention of personnel to quality. One should, however, be aware that the quality system is, in principle, a framework that guarantees only that the laboratory can achieve acceptable results, not that it does so. The actual achievement can only be attained through functioning quality assurance, in other words, a thorough investigation of the performance of every new analytical method and continuous follow-up of all methods through internal quality control and external quality assessment to ascertain that the adopted methods continuously perform in an acceptable way.

Analytical methods in biological monitoring

In biological monitoring, several different approaches and analytical methods may be selected that are widely different as to practicability and cost. Often, more accurate results are obtained when more expensive methodology and instrumentation are selected. Especially, the limit of detection is dependent on the cost involved. The selection of approach and methodology must be made according to the requirements of the user of the results, that is, occupational health care. The methods chosen must be accurate enough, but must not involve unnecessary detectability, accuracy, sophistication, or cost.

It is thus apparent that while, for example, flameless atomic absorption spectrometry and gas and liquid chromatographic methods are the mainstream in biological monitoring, there is still space for colorimetric methods where levels of exposure is high.

On the other hand, it is likely that mass spectrometric analysis, combined with gas and liquid chromatographic separation, will gain further use in biological monitoring. There are also indications that, as in clinical pharmacology — which in scope is very similar to biological monitoring — immunologic methods will become routine in biological monitoring. Immunologic methods have already been published for the analysis of cotinine, some pesticides, and even mercury (68, 117—119).

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