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REVIEW PAPERS

BIOMARKERS USED FOR THE ASSESSMENT OF HEALTH HAZARDS IN POPULATIONS LIVING IN THE VICINITY OF COMMUNAL AND INDUSTRIAL WASTE DUMP SITES*

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Abstract: The measure of individual hazard from exposure to environmental toxicants are the biomarkers which are indicies of abnormalities within different biological systems that may be induced by hazardous agents of various chemical or biological nature. The biomarkers make it possible to "monitor" the processes within the organism from the moment of toxic agent penetration to the development of clinical symptoms. Biomarkers offer the possibility of early detection of phenomena which tend to be arranged in the sequence of pathogenic changes, usually not detectable by the conventional methods. Depending on the type of processes which accompany the effect of a specified harmful environmental agent on the human organism it may be determined with the aid of the biomarkers, which are then classified as exposure, health effect, and individual susceptibility. By integrating such concepts as exposure, health effect, and individual susceptibility, enhanced analysis of the problem of health risk in people exposed to environmental toxic agents has become possible.

Every day large quantities of domestic and industrial chemical wastes are produced and stored in the vicinity of human dwellings. The chemical wastes penetrate soil and drinking water and are dispersed by the wind. Owing to their ubiquity in environmental components, the chemicals also enter the human organism, either directly in drinking water or indirectly by the digestion of plant and animal product from contaminated areas. Regrettably, the institutions

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responsible for surveillance of chemical safety do not employ methods that would allow a reliable assessment of health hazard from environmental toxicants.

Toxic environmental chemicals are diverse with respect to their structure and physicochemical properties, toxic potential and the effect on the different biological systems of the human organism. This is a major hindrance to the activities related to health risk assessment. Unlike industrial exposure, where one is usually capable to determine which occupational chemicals bring about the health effects observed in the exposed populations, environmental waste chemicals are rarely subject to health risk assessment. This comes not only from their low concentrations penetrating the system, but also from the fact that they may be components of a mixture of several dozen, if not thousand, chemical substances with unknown chemical structures or toxic potential. If examined separately, they may not produce any toxic effects; however, they may induce toxicity when combined in a chemical mixture (2, 3, 5).

In view of the fact that we cannot carry out a complete analysis of environmental chemicals entering the system or determine their toxic potential, it seems reasonable to undertake measurement of the resulting health effects in exposed individuals along with routine evaluation of exposure based on measuring the toxic agent concentration. Complicated and costly as it is, the performance of health effect assessment seems highly justified from the point of view of social and economic needs. In many a case, the excessive expenditure connected with the relocation of inhabitants of the hazardous territories can thus be avoided. This may also help to prevent the panic among the population of contaminated areas. Moreover, the development of methods for the evaluation of actual exposure as well as the resulting health effects may form the grounds for undertaking relevant preventive measures. The latter, in turn, increase the probability that the health effects of exposure when detected early will still be reversible and the discontinuation of exposure and the appropriate treatment will inhibit their transformation into irreversible clinical effects (4).

An essential aspect to be considered when evaluating the exposure and health effects of environmental chemicals is an individual susceptibility to their toxic effects. For many years, it has been known that people differ with respect to their reaction to the toxic properties of particular chemicals, including environmental contaminants. Omitting this aspect in the evaluation of exposure and related health effects may lead to a misinterpretation of any results obtained (1).

Over the last few years a considerable progress has been made in the investigation of the effects of environmental contamination on a population's health. It has been found that the progressive environmental degradation resulting from the heavy industrialization of human life exert negative health effects both with respect to specific health effects and increased incidence of the so-called "common illnesses" (6).

To evaluate the environmental contamination due to the emission of toxic chemicals or their release from waste dump sites, the measurements of chemical concentration in three basic environmental media — water, soil and ambient air — are carried out. The data obtained, however, is relatively difficult to correlate with the level of hazard for exposed populations as such essential aspects as the rate of penetration of environmental contaminants into the human organism or the individual susceptibility to toxic effects of chemicals are not considered. It is presently assumed that the evaluation of individual contamination with environmental chemicals and the resulting health effects is superior to the determination of the level of general environmental contamination. The method allows to prevent the misinterpretation of results when the same person is simultaneously exposed to occupational and communal contaminants and the lifestyle factors (e.g. cigarette smoking). The evaluation of the health status of the exposed population, or the possible health hazard becomes top priority, while estimating the conditions of external contamination remains in the background of the problem (11).

The measures of individual hazard from esposure to environmental toxicants are biomarkers, which are indices of abnormalities within different biological systems (at the level of the whole body or of particular organs, tissues and cells) that may be induced by hazardous agents of various chemical or biological nature. The biomarkers make it possible to "monitor" the processes within the organism from the moment of toxic agent penetration to the development of clinical symptoms. Biomarkers can be compared to "windows" which allow us to look into a "black box" and track the fate of the toxic agent and the effects it produces in the exposed organism. It is worth pointing out, however, that the very notion of "biomarker" refers not only to the data on the particular laboratory test results, e.g. toxic agent concentration or enzymatic activity, but also to the fact that it may provide tentative information about the possible concentration of the agent or the enzymatic activity within those tissues which are inaccessible for testing. Biomarkers can supply measurable data on the rate of absorption of the environmental contaminant and the answer whether the critical dose leading to eventual molecular, subcellular and cellular changes has reached the critical organ. The nature of these abnormalities is determined both by the type of the toxic agent and the quantity that penetrates the target organ as well as the actual duration of exposure (8).

Biomarkers offer the possibility of early detection of phenomena which tend to be arranged in a sequence of pathogenic changes, usually not detectable by conventional methods (5).

Depending on the type of processes which accompany the effect of a specified harmful environmental agent on the human organism it may be determined with the aid of the biomarkers, which are then classified as exposure (dose), effect (response), and susceptibility biomarkers (2).

Exposure biomarkers indicate the dose absorbed by quantitatively determining the toxic agent (or its metabolites) absorbed, or the products of its interaction with endogenic substances (such as DNA and proteins). These are measurable indicators which appear in the organism after exposure to environmental toxins. It should be noted here that their presence in the organism can also be detected in the case of no detectable health response. One of the main problems in the use of biomarkers as environmental toxin exposure indicators consists of finding biomarkers with a given specificity for a given toxic agent, and identifying where the biological test material is relatively easily available. The biomarkers which can be determined in urine, saliva, blood or exhaled air are especially interesting. The biomarkers which are particularly important and may be applied in the biological monitoring of the populations inhabiting chemically-polluted areas, include those which are "specific" for specified substances only, e.g. for benzene, trichloroethylene, acrylonitrile, styrene, nicotine, lead, cadmium, as well as those which are indicators of substance classes, e.g. of dioxines, biphenyls, or polycyclic aromatic hydrocarbons. The group of exposure biomarkers includes a large proportion of "non-specific" biomarkers, which may be used to determine indirectly the level of exposure or may serve as an indicator confirming the occurrence of exposure to such an agent. The determination of enzyme activity changes resulting from the inhibiting action of the toxic agent is an example of such biomarkers. In many instances, enzyme activity inhibition is proportional to the quantity of the toxic agent which penetrates into the organism from the chemically polluted environment (10).

Health effect biomarkers are indicators which provide information on the changes in the organism which took place as a result of exposure to an environmental toxic agent. This biomarker group includes, in a measurable way, those phenomena which constitute either the individual stages of the pathogenic process or the manifestations of the disease itself. The biological response of the organism to environmental toxic agents includes a relatively wide range of changes, from temporary and reversible which do not produce any noticeable health effects to permanent changes associated with increased disease incidence and mortality. This wide spectrum of changes may be arbitrarily divided into several categories: a) metabolic disturbances which remain within the physiological limits; b) physiological dysfunctions not accompanied by any detectable morphological changes in tissues; c) pathological changes in tissues, but not accompanied by overt manifestations of disease; d) clinically overt pathology. Environmental medicine is interested primarily in these biomarkers which enable the detection of changes occurring in the organism which are classified to the first three categories. These biomarkers are referred to as pre-clinical, or early health effect biomarkers (5).

Susceptibility biomarkers are indicators capable of indicating whether, in the case of a specified person or population, health effects may be expected at a lower, or a higher exposure. They affect the probability of disease development as a result of exposure to environmental toxins. They may be used as measurable indicators of those biological factors of the organism which are present before exposure and are genetically-related or display the features of acquired traits. The latter may result from diseases suffered in the past or from previous exposure to harmful (chemical, physical or biological) agents (1).

It may be now stated that the introduction of the biomarker concept in the assessment of the effect of environmental factors on the human organism enables a much better survey of the population to be studied and permits to find out whether the level of the environmental exposure is sufficient to be assessed by measurable health effects. Biomarkers enable individuals with high or low exposure to the harmful agent from the studied population to be more accurately selected. This in turn increases the power of statistical inference of the detected relationships between exposure and pathological effect. Research costs can thereby be reduced by limiting the number of test subjects to those who are indeed exposed to harmful environmental agents. Biomarkers can also greatly reduce the number of errors which may result from the misclassification of a given individual, or individuals, to the exposed population when the classification is based on the environmental determinations only. Such errors are possible particularly when a population is exposed to small doses of harmful agents for a relatively long period of time. In such cases, biomarkers which cumulatively reflect prolonged exposure are particularly valuable. It is worth noting that biomarkers permit an integrated assessment of exposure effects regardless of the penetration route and origin of the harmful agent. As a result, the assessment of the environmental concentration of each potential source of those harmful agents and the examination of the probable effects of the harmful agent penetration route on the observed pathological consequences are no longer necessary. By the application of biomarkers, it is possible to provide the conditions necessary to determine which biomarker, or a group of biomarkers out of many harmful agents present in the environment is responsible for specified pathological symptoms (7, 11).

The introduction of biomarkers able to record the very early health effects produced by harmful environmental agents makes it possible to assess the risk of incidence of a disease at a very early stage in its development. Of course, there are some limits to this assessment. It is known that early-response biomarkers, e.g. DNA or protein adducts, occur more frequently under conditions of exposure to carcinogens, and that the number of people in whom those adducts are detected is much greater than the number of people who may develop the neoplastic disease. Not everyone of these people in whom DNA adducts have been detected will develop cancer in the future. On the other hand, the failure to detect adducts does not mean that the person in question will not develop cancer. However, in many instances, the likelihood of correct assessment of increased cancer risk on the basis of DNA or protein adduct determination can be augmented by the simultaneous determination of other biomarkers, for example the presence of oncogenes, or their protein products, oncoproteins, in the cells. A greater number of positive biomarker determination results significantly increases the risk of the disease. However, the determination of a large number of biomarkers noticeably increases the cost of the research; this may be essential in epidemiologic studies conducted on large populations. Therefore, before selecting such a biomarker set, the biomarkers should be carefully examined, and those which supply similar information, or those which are not related to the investigated pathologic process or harmful factor – should be eliminated (3, 9, 10).

To sum up the above discussion, it may be stated that biomarker-based biological monitoring is the most efficient measure capable of assessing the risk to an individual organism resulting from exposure to external harmful agents. According to the biomarker concept, environmental effects on the human organism can be assessed by the determination of exposure, health effect, and susceptibility biomarkers. By integrating such concepts as exposure, health effect, and individual susceptibility, an enhanced analysis of the problem of health risk in people exposed to environmental toxic agents has become possible. The assessments performed directly in the organism contribute to the elimination of uncertainties inherent in epidemiological studies.

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