

BIOMONITORING IN OCCUPATIONAL MEDICINE (REVIEW ARTICLE)

By

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Abstract

Introduction: Measuring of a chemical, its metabolite, or biochemical effect in a biological sample with the aim to identify exposure is known as biomonitoring. To determine the type and quantity of substances present in the body as a result of occupational and environmental exposures, biomonitoring is an essential technique. It has changed from being a tool for study to becoming a crucial aspect of exposure assessment. **Aim of Work:** to discuss the topic of biomonitoring in the occupational medicine so as to develop and evaluate biomarkers that represent particular exposures or are statistically related to unfavorable outcomes in humans to enable their use in risk prediction, assessment and management. **Conclusion:** The use of biomonitoring is beneficial for demonstrating adherence to exposure limits, occupational health research and surveillance, evaluating the efficacy of interventions, and assessing and managing risk. In order to aid in the evaluation of exposure and the characterization of exposure routes, biological and environmental monitoring are complementary to each other. Time of sampling and proper biomarker selection are both highly important. It is important to note that the majority of detected biomarker concentrations do not fundamentally correspond with clinical illness or disease risk. To produce reliable & significant results, laboratory conditions and interpersonal variability are essential. Any biomonitoring programme should also place a priority on ethical and social issues. According to Egypt's Labour Law No. 12/2003, the employer must take all necessary steps to guarantee worker health and safety, particularly with regard to potential mechanical, physical, chemical, and biological threats

Keywords: Biological monitoring; biomonitoring; biomarkers and occupational exposure

Introduction

In order to assess exposure, biological monitoring, also known as biomonitoring, entails measuring a chemical, its metabolite, or a biochemical consequence in a biological specimen. The type and quantity of substances in the body as a result of occupational and environmental exposures can be determined with the use of biomonitoring. It has shifted from being a research tool to becoming a vital aspect of exposure assessment. Although biomonitoring has long been used to monitor employees, it is increasingly being used in non-workplace settings, such as forensic medicine and drug research (Das, 2014).

Aim of Work

This review aims to discuss the topic of biomonitoring in the occupational medicine so as to develop and evaluate biomarkers that represent particular exposures or are statistically related to negative outcomes in humans to enable their use in risk prediction, assessment and management.

Biomonitoring versus environmental monitoring

Biomonitoring offers a more accurate way to evaluate the internal dose of a chemical than traditional exposure assessment, which depends on the measurement of chemicals in the external environment (air, water, soil, etc.). Environmental monitoring only offers data on exposure from the particular external source being measured. The amount of a chemical absorbed from all sources and routes of exposure (dermal absorption, inhalation, and/or ingestion) can be measured by biological monitoring, however individual variations in work habits, exercise levels, genetics, demographic traits (like age, gender, and ethnicity), and physical parameters (like body fat percentage) have an impact on a chemical's absorption, distribution, metabolism, and excretion. Biomonitoring should also take ethical concerns into account. The decision to carry out biomonitoring is complicated and dependent on a number of variables (Manno et al., 2010).

Table 1: Comparison of biological and workplace air monitoring (Manno et al., 2010).

	Biological monitoring	Workplace air monitoring
Quantifying	Internal dose	External dose
Absorption	All routes	Inhalation only
Confounders	Metabolic phenotype	Personal protective equipment, substances with similar structure/chemical properties
Standardisation	Difficult	Easy
Interpretation	Difficult	Moderately difficult
Measurement	Indirect (biomarkers)	Usually indirect (dangerous substance)
Ethical issues	Important	None
Variability	High	Usually low

Biological markers (biomarkers)

Biochemical, genetic, molecular, immunologic, or physiologic indications of events in biological systems are detected by biological markers, also known as biomarkers. A biomarker should be relevant, sensitive, specific, replicable, affordable, and readily available. Rarely does a biomarker fulfill all these requirements (Bodaghi et al., 2023).

As regards chemicals, biomarkers are classified as follows:

Biomarkers of exposure are chemicals, their metabolites, or a reaction product between a substance and a target molecule. For instance, blood lead accurately reflects recent lead exposure.

Biomarkers of effect are quantifiable

changes in an organism's biochemistry, physiology, behaviour, or other aspects that may have an impact on its susceptibility to certain diseases. For instance, when lead exposure impedes haemoglobin synthesis, the value of zinc protoporphyrin in blood increased.

Biomarkers of susceptibility are markers of inherited or acquired abilities to cope with the strain of chemical contact. An example of susceptibility biomarker is the gene that codes for 6-aminolevulinic acid dehydratase (ALAD) that is an enzyme linked to the toxic effect of lead that appears in two variants. Conventional biomonitoring does not typically utilize biomarkers of susceptibility (Ladeira and Viegas, 2016).

Biological matrix (medium)

Choosing a biomarker is frequently influenced by the biological media or matrix being utilised for biomonitoring. Although the most frequent samples for analysis are blood and urine, biomonitoring can be done on any biological matrix.

Since venipuncture is regarded as less invasive, whole blood may easily be collected and is the most frequent pathway for the majority of substances and their metabolites. Depending on the timing of sampling, there may be a significant difference in levels for volatile chemicals and other substances with short half-lives. Lead, mercury, and cadmium are just a few examples of the metals that could be examined in whole blood. Dioxins, furans, polychlorinated biphenyls (PCBs), and organochlorine insecticides are considered persistent organic compounds (POCs) that are lipid-soluble and they or their metabolites can be detected in serum. Whole blood must be managed for serum biomonitoring, including centrifugation, analysis, and lipid level adjustment (Dash et al., 2020).

The easiest sample to collect is urine because it can usually be found in large quantities and is well accepted by

participants. Biomonitoring of kidney-excreted molecules including non-lipid soluble (non-persistent) compounds like bisphenol A (BPA) and certain metals like arsenic, cadmium, and inorganic mercury is suited for urine. The most accurate way to measure exposure is with a 24-hour urine collection, however for practical purposes, only one sample is typically taken at a given time, called a spot urine sample. Spot urine samples should be corrected for urine specific gravity or urine creatinine because day-to-day dilutions can vary significantly. For people with advanced renal disease, urine monitoring may not be recommended (Balhara et al., 2023).

The ability to measure specific non-persistent pollutants, insecticides, and therapeutic medicine levels using saliva has been studied. The most suitable chemicals for measurements in exhaled air are volatile organic substances including benzene, methylene chloride, and toluene. Exhaled breath biomonitoring has the advantages of being noninvasively obtained and providing a direct comparison to data from air monitoring. Hair may be used to screen for heavy metals and is widely accessible. It has also been applied in studies to evaluate exposure

to persistent organic pollutants (POPs). The challenge with hair biomonitoring is that samples need to be cleaned to remove contamination from surface deposits to discern between internal and ambient exposure (WHO, 2015).

Breast milk is an excellent matrix to biomonitor levels of lipid-soluble POPs in the environment since it is simple to obtain and offers details on maternal and newborn exposures. Dichlorodiphenyltrichloroethane (DDT), hexachlorobenzene (HCB), polychlorinated biphenyls (PCBs), chlorpyrifos, and bisphenol A (BPA) were among the pollutants found in breast milk (Rovira et al., 2022).

Amniotic fluid, umbilical cord blood, meconium, nails, teeth, semen, sweat, and adipose tissue are other less popular matrices for biomonitoring (WHO, 2015).

Proper time of sample collection

Dioxins, PCBs and organochlorine pesticides are simply among the examples of persistent organic pollutants that are easily absorbed into the bloodstream and transported to fatty tissues and, in nursing women, breast milk. Persistent organic pollutants POP levels found in biological samples

denote cumulative exposures years before sample collection. POPs have very sluggish metabolic and excretory processes resulting in long half-lives in the body reaching years. The half-life of POPs is around 6 months in nursing women, who are an exception because lipid-soluble POPs accumulate in breast milk and are eliminated from the body during lactation. Contrary to persistent substances, non-persistent chemicals are more sensitive to the timing of collecting samples in relation to exposure. Non-persistent organic compounds are quickly metabolised and eliminated in the urine, including cholinesterase-inhibiting and pyrethroid insecticides, phthalates, and polycyclic aromatic hydrocarbons (PAHs). Unless samples are taken right away after exposure, these compounds and their metabolites have very short half-lives in blood, on the scale of hours to days, and their concentrations are often orders of magnitude lower than urine metabolite levels (Das, 2014).

Most people experience regular exposure to chemicals, either at work or in various areas of their lives. In the case of constant exposure to non-persistent chemicals that are rapidly metabolized, their concentrations vary significantly

during the day (Figure 1). That is why for these substances, a single sample could not accurately reflect typical exposure over time; alternatively, biomonitoring offers a moment in time snapshot of the concentrations of these substances in a specific tissue rather than a consistent indicator of “total body burden.” Given

this variation, biomonitoring of non-persistent chemicals may be especially useful for determining shift-related exposure in work environments where the time of collecting samples in relation to ambient substance concentrations is known (Fernández et al., 2020).

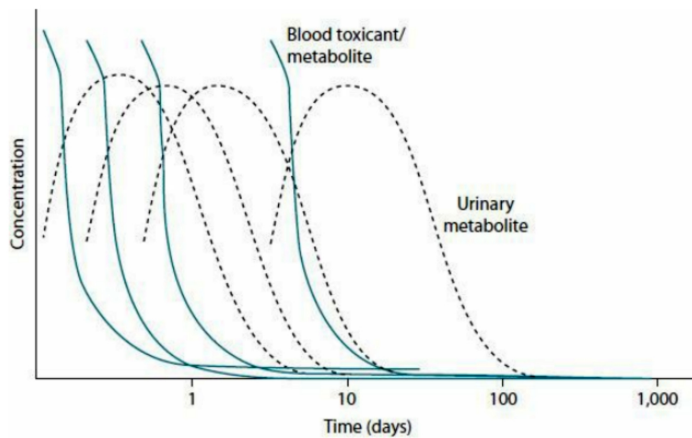


Figure 1: Theoretical fluctuation in levels of a non-persistent compound following repeated, long-term exposure in the blood and urine (Das, 2014).

For short half-live biomarkers, sampling generally takes place at the shift end; while for short half-live biomarkers exhibiting a tendency to accumulate, sampling is recommended at the completion of the workweek; whereas for highly accumulating lengthy half-lived biomarkers, sampling typically occurs at any time (Fiserova-Bergerova and Vlach, 1997).

Does an exposure mean a disease?

Measuring concentrations for the majority of chemicals used in biomonitoring today do not consistently reflect the presence of actual illness or the chance probability of disease occurrence (Paustenbach and Galbraith, 2006). The toxic nature of the substance, its quantity taken into the body, a person’s pharmacokinetics

(absorption, distribution, metabolism, and excretion), and their particular sensitivity affect the progression from exposure to the resultant health outcome. These include genetics, environmental and behavioural stresses, dietary habits, general well-being status, and associated various other exposures. Demographic factors (such as age and ethnicity) are also included. The elderly, kids, newborns, and women who are either pregnant or of childbearing age are among the particular populations thought to be at intensified risk for the negative consequences of chemical exposure. Although biomonitoring may not be able to anticipate harmful health impacts with any degree of accuracy, results may be interpreted using one of two comparison approaches: health-based values or reference ranges (Vogel et al., 2019).

Health-Based Values

Chemical concentrations at which a person would not be anticipated to experience negative health impacts, such as symptoms, signs, or abnormal clinical laboratory tests, are known as health-based values. These standards are frequently used in occupational settings, are based on both published and unpublished scientific material

and may take safety considerations into account. In order to assess the possibility of negative impacts, requirements like medical assessment and heightened environmental and biological monitoring are often triggered when health-based values are exceeded (SCOEL, 2014).

The American Conference of Governmental Industrial Hygienists' (ACGIH) proprietary biological exposure indices (BEIs) are the most often used health-based biomonitoring recommendation values for occupational exposures in the United States. These estimates are based on a comprehensive analysis of the literature and studies that were submitted for review, with a focus on research that address levels of adverse health effects preferably in exposed humans and to a minor extent on animals that are scarcely existing. Over 40 chemicals have BEIs, which typically represent exposure levels in healthy workers at ACGIH threshold limit values (TLVs) and denote concentrations below which detrimental health consequences are not anticipated (ACGIH, 2015).

Reference Ranges

The 95th percentile, or the level below which 95% of the reported

values fall, is frequently used to define reference ranges, which are measures that have been observed for a given population. Exceedance of these limits indicates that the concentration determined in a person is statistically greater than the general population's range but does not suggest that exposure will likely have any negative impact on one's health. Reference values must be collected from a comparison group with matching demographic and socioeconomic factors that might affect biomonitoring results-(Nakayama et al., 2023).

Differentiating occupational from non-occupational exposures is a tough procedure since biomonitoring represents all sources and routes of exposure. The interpretation of biomonitoring results can be aided by the use of exposure questionnaires, environmental monitoring, and consultation with an industrial hygienist. Cigarette smoking is a common "lifestyle" component that may affect occupational biomonitoring. Smokers may have high blood and breath cadmium concentrations. Regular consumption of seafood may result in high levels of organic mercury, and eating shellfish may induce high levels

of urinary arsenic, as it contains an inorganic arsenic metabolite. Also there are elevated arsenic concentrations in some underground water supplies in the United States and to a greater extent in other nations (such as Bangladesh, Chile, and India) (Bevan et al., 2013).

Considerations for laboratories

Since biomonitoring uses sophisticated and delicate tools to quantify small amounts of compounds that could be present in the environment, laboratory factors are vital for obtaining precise, meaningful findings. It will be less likely for mistakes to be made when interpreting the results if laboratory experts are involved in the design of biomonitoring research. Before beginning a biomonitoring programme in collaboration with a laboratory, some factors should be taken into account that include risk of contamination, specimen management, quality assurance (QA), and quality control (QC).

Contamination

Compared to other clinical laboratory procedures, sample contamination is a far more significant issue for biomonitoring investigations. Specimen collecting tools (such as lead in needles or glass tubes and phthalates

in urine containers) and materials used in the lab (such as triclosan in hand soaps) are examples of common sources of contamination. Also, we should consider the ambient air pollutants, in the laboratory or collecting facility (such as dust polluted with polybrominated dibrominated ethers, or PBDEs) and the outside air (such as pesticide degradation products entrained through inadequate ventilation) (Abraham and Silambarasan, 2016).

Utilizing the proper containers, screening specimen collecting tools beforehand, acquiring field blanks to account for background contamination, and performing analysis in clean rooms are some ways to reduce and control contamination. Further prevention of contamination can be provided by creating comprehensive collection and processing operations, training clinical and laboratory staff on proper implementation. To avoid obtaining suspicious findings, it is crucial to record specimen collecting information, including the date, time, and location of collection (NRC, 2006).

Specimen Management

To prevent the deterioration of compounds of interest, proper specimen management is required. Common

mistakes include, for instance:

- Improper mixing of withdrawn blood in collection tubes containing the anticoagulant EDTA that may result in forming blood clots that can trap heavy metals and cause falsely low levels.
- Delaying centrifuging blood and processing serum for too long; the ensuing blood clot affects analysis by trapping both lipids and chemicals.
- Using too high or too low of storage or transportation temperatures, which causes hemolysis of whole blood.

Errors during this stage can be reduced by following precise and stringent processing, storage, and shipping protocols. Both the clinic where the specimen collection takes place and the laboratory doing the analysis must keep and share records and methods for collecting, storing, and transporting specimens (CDC, 2018).

Quality Assurance (QA) & Quality Control (QC)

It is crucial to confirm that the addressed laboratory conform with a quality management system before beginning a biomonitoring programme. A quality management system ensures

the validity of the samples, the analytic method, and the data produced. For reliable and significant results, laboratories must follow rigorous QA and QC guidelines (López et al., 2021). Quality assurance covers the whole laboratory operation, which should include proficiency testing programmes that compare measured results with benchmarks or standards from other laboratories. Internal accuracy and precision evaluation is part of quality control, and it includes daily equipment calibration and analysis of control samples used in conjunction with study samples. Written standard operating procedures (SOPs) are intended to outline sample processing, analysis, quality control; and appropriate chemist training, as well as specimen collecting, handling; and transport (Schaller et al., 2002).

Implementing biological monitoring programmes:

Multidisciplinary cooperation is crucial for biomonitoring programmes, regardless of the environment. During the planning stages of any biomonitoring initiative or programme, clinicians, laboratories personnel, toxicologists, epidemiologists, industrial hygienists, and ethicists are among the key partners

to be involved. Projects or programmes involving biomonitoring must be examined and approved by Institutional Review Boards (IRBs) for the protection of the participants, unless they are obviously related to an emergent public health action. Participants should be treated ethically and fully informed of the risks and advantages of the study, including the potential incapacity to determine the therapeutic implications of the results and, if applicable, the intention to keep samples for future studies, according to the protocols (Schulte and DeBord, 2000).

Biomonitoring of Workers

In the workplace, biological monitoring may be an optional or necessary part of both normal medical surveillance and worker monitoring during and after emergency response. Individual clinical worker evaluations, which may include obtaining a thorough occupational and environmental history to verify all potential sources of exposure and biomonitoring, may be triggered during routine surveillance when environmental monitoring identifies exceedance of a specified standard (such as cadmium, lead). The logistics and viability of conducting biomonitoring of personnel as part of

emergency or disaster response play a significant role in the selection (Decker et al., 2013).

Whenever abnormal biomonitoring findings are obtained, it is important to repeat the measurement on the sample and gather further samples in order to confirm the results. To help identify potential exposure sources and evaluate necessary control measures, such as engineering controls, modified work practices, appropriate respiratory protection, or removal from the workplace, environmental monitoring must be conducted concurrently with biomonitoring and compared to appropriate standards. Clinical protocols must be defined in order to guarantee results confidentiality, voluntary involvement rather than mandated participation, and responsible results transmission. Clinicians have to be accessible to explain any inquiries concerning test results and their consequences on patient's health. All medical data and biomonitoring findings should be kept on file for at least 30 years, if not extended retention periods (Bauer, 2008).

The Art of Communicating Results in the Workplace

Both employers and employees must

be informed if the levels of biomonitoring in the workplace exceed occupational guidelines or if possible health impacts from exposure are suspected. Based on this information, measures to lower exposures or conduct health checks may be conducted to lower the risks of morbidity and mortality. Materials used to communicate results should mention the possibility that non-occupational factors could affect biomonitoring outcomes. If it is possible, monitoring for industrial hygiene regulations and additional details on exposure sources should be used to distinguish between different sources of exposure (Viegas et al., 2020).

Workplace biomonitoring raises unique confidentiality and liability issues. Employees can worry that biomonitoring violates their privacy and that their employers would treat them unfairly based on the results. Employers could be reluctant to agree to biomonitoring unless it is mandated because they are concerned that the results of the monitoring could result in workers' compensation claims even when the health implications are unclear. Employers shouldn't be informed of specific results; biomonitoring results should be treated as confidential health

information similar to other types of medical data. Instead of mentioning personal information, employer notifications should talk about detected deviations from permitted levels or other health standards together with suggested workplace adjustment to minimize exposure. It is important to distinguish between required workplace biomonitoring and research. Research study protocols and informed permission forms should make it clear that identifying data from biomonitoring carried out for research purposes in workplace settings will be confidential and kept apart from employee health and other medical records (Manno et al., 2010).

Biomonitoring of workers in Egypt

According to Egypt's Labour Law No. 12/2003, the employer must take all necessary steps to guarantee workplace safety and health, particularly with regard to potential mechanical, physical, chemical, and biological dangers. The Social Insurance Law No. 79/1975 and amendments' annexe, Article 219, instructs additional requirements for workers, including pre-employment medical examinations, first aid procedures, medical attention

and treatment, and periodic medical examinations for those who are at risk of occupational diseases. Employees must be provided with personal protective equipment and informed of the risks they face if safety precautions are not followed by their employers (articles 208 to 215).

To receive the required service, employees can apply in person or through the facility/enterprise physician at the closest Health Insurance Organisation (HIO) Centre/office. The HIO center/office will then review and investigate the case, analyse how it relates to employment in the event that compensation is sought, decide and define the rating for physical and/or functional impairment, and determine the level of disability giving rise to compensation in accordance with certain tables appended to Law 79 of 1975. Such health impairments are also started on therapy by the HIO.

According to Law 79/ 1975 and Law 12/ 2003 (article 216), HIO is also obligated to conduct pre-placement and periodic health checks in addition to evaluating disabilities. Each year, the HIO typically conducts 400–450 thousand periodic medical check-ups and 125–150 thousand pre-placement

medical examinations. The ministerial decrees no. 218/ 1977 and 133/ 1983, respectively, govern the periodic medical checkups and pre-placement medical examinations, respectively (Abo El-Ata and Nahmias, 2005; Abo El-Ata, 2014).

For each occupational exposure and/or disease covered in the current (2013) Egyptian Schedule, the necessary investigations and their recommended frequency are identified.

Conclusion and Recommendations

Biomonitoring is a useful technique for risk assessment and management, demonstration of compliance with exposure limits, and occupational health research and surveillance. The assessment of exposure and characterization of exposure pathways are made possible by the complementary nature of biological and environmental monitoring, which also serves as a component of risk identification and health surveillance. It's crucial to decide which biomarker (exposure or effect biomarker) is more appropriate to the study's stated objectives, as well as significance of sample timing.

Measurable concentrations for

the majority of chemicals that are biomonitoring now do not fundamentally correspond with clinical illness or the chance of disease. It's crucial to take into account interpersonal variation in relation to traits like behaviour and demographics, among other variables.

For precise and valuable results, laboratory components are essential. Improved data quality and outcomes that are easy to understand will be provided via written standard operating procedures and a quality assurance program. Programs for biomonitoring also require multidisciplinary teamwork.

Any biomonitoring procedure should prioritize ethical and social concerns to protect the confidentiality of information.

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