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Perspective
Biological Monitoring as a Tool for Assessing Occupational Health-An Indian Perspective

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Abstract
Major occupational health problems in India or elsewhere include-industrial accidents, pesticide poisoning, farmers' lung, miners' lung, silicosis, asbestosis, byssinosis, metal fume fever, hearing loss and occupational cancer. The ATSDR has identified 275 chemicals, in its priority list, that cause morbidity in human population. The list includes heavy metals viz: Arsenic, lead, cadmium, chromium and nickel etc. and organic solvents i.e., benzene, xylene(s), alcohol(s) and trichloroethylene etc. They are being indiscriminately used in unorganized sector. Prolonged human exposure to them through work environment leads to serious health problems. Identification of exposure using reliable tools and techniques of biological monitoring has been found useful in the prevention of occupational diseases in developed countries. However, the concept is still to be promoted in countries like India. The results of some of the experiments done by us in the past, their comparison with international standards/values and application in occupational health risk assessment has been presented in this overview.

Key words: Biological monitoring, heavy metals, organic solvents, biomarkers, occupational health

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INTRODUCTION

International Labour Organization (ILO)/World Health Organization (WHO) defined occupational health," as the subject that aims at the promotion and maintenance of highest degree of physical, mental and social well being of workers in all occupations". From an ecological viewpoint, occupational health represents a dynamic equilibrium or adjustment between an industrial worker and his work environment. Whereas, an occupational disease is any chronic ailment that occurs as a result of study or occupational activity. Squamous -cell carcinoma of the scrotum was the first occupational disease identified in chimney sweep workers by Sir Percival Pott in 1775[1]. Later on, lung diseases like asbestosis, pneumoconiosis (black lung disease or miners lung), silicosis and byssinosis, occupational asthma and pesticide poisoning were also attributed to poor work environment. Several skin diseases viz: Contact dermatitis, eczema and urticaria have also been associated with occupational environment. History of occupational diseases includes classic examples viz: Phossy jaw among the London match girls, radiation sickness among workers of nuclear industry and radium dial painters[2].

Prevention of occupational diseases has been a matter of concern for health professionals all over the globe. The first paper on systemic assessment of occupational health after exposure to lead was published by Badham and Taylor[3]. Two important ILO conventions on occupational health and safety i.e., Radiation Protection Convention No. 115, (1960) and the Benzene Convention No.136 (1971) have been ratified (http://www.ilo.org). Japan was perhaps the first country to formulate labour standards in 1947 and Industrial Health Law was passed in 1972. Occupational Safety and Health Act also known as William -Steiger Act was signed by the President of United States in December, 1970. On May 1,1975, a special commission (Commission for the investigation of Health Hazards of Chemical Compounds in work area) was formed in Germany also known as Deutsche Forschungsgemeinschaft. In addition, several international agencies like Occupational Safety Health Association (OSHA), National Institute of Occupational Safety and Health (NIOSH), American Conference of Government and Industrial Hygienists (ACGIH), International Agency for Research on Cancer (IARC), United Nation Environmental Program (UNEP), Society of Toxicology (SOT) and International Union of Toxicology (IUTOX) and Agency for Toxic Substances and Disease Registry (ATSDR) do have a mandate to protect and safeguard human health from occupational hazards. Thus developed countries have framed sound policies to manage occupational health problems. Regulatory agencies strengthen their commitment with the support from legal provisions. However, in many developing countries the concept is yet to be introduced.

STATUS OF OCCUPATIONAL SAFETY AND HEALTH IN INDIA

Human population in India has crossed 1.21 billion according to the last government census carried out in 2011 (http://census india.gov.in). Of these, 833 million reside in rural areas and 377 million reside in urban areas. Those in working age group are estimated to be 63.60%. More than 90% work in the informal economy mainly agriculture and other services. Less than 10% have jobs in the organised sector. Major occupational health risks are industrial accidents, miners' lung, pesticide poisoning, silicosis, musculoskeletal injuries, chronic obstructive lung diseases, asbestosis, byssinosis, noise effects and effects of workplace agents/chemicals. According to the Director General of the Factory Advisory Services and Labour Institute (DG-FASLI), 1509 fatal and 33093 non fatal injuries were reported in 2009.

Research reports indicated that the real figure of fatalities/injuries may be much higher than these official numbers.

Although, there are 16 laws, major legal provisions for the protection of health and safety are contained in two acts, the Factories Act ,1948[4] and Mines Act ,1952[5]. The Factories Act was amended in 1987. It makes periodic medical examination and monitoring of the work environment mandatory for those industries defined as hazardous. There are other legal provisions for protection of special groups of workers ie., those working in plantations (Plantation Labour Act,1951) Dock Workers (Safety Health and Welfare) Act, 1986, buildings and construction workers (Regulation and the Employment and Conditions of Service) Act, 1996, the beedi and Cigar Workers (Conditions of Employment Act, 1966, child labour (Prohibition and Regulation) Act and the Insecticides Act, 1968.

MEASURING EXPOSURE TO STUDY PLACE CHEMICALS

As of August 2011, Registry of Toxic Effects of Chemical Substances (RTES) contained 1,60,000 chemical entries with some toxic effect. ATSDR has registered 275 chemicals in its priority list of hazardous substances till March, 2017. Many of them are extensively used in agriculture, industry and commerce. These include inorganic as well as organic substances. ACGIH periodically issues safety guidelines on a few of them including arsenic, benzene, cadmium, carbon disulfide, chromium, carbon monoxide, ethyl benzene, fluorides, n-hexane, lead, organo phosphorus cholinesterase inhibitors, parathion, phenol, styrene, toluene, trichloroethylene and xylenes. These guidelines are based on the study and recommendations of laboratories engaged in health surveillance/risk assessment projects through- out the world. Decades of their sincere and sustained efforts have helped in developing the concept of biological monitoring (BM), biological effect monitoring (BEM) and recently the concept of biomarkers or molecular markers.

BIOLOGICAL MONITORING

Biological monitoring by definition is measurement and assessment of workplace agents or their metabolites either in tissues, secreta, excreta or any combination of these to evaluate the exposure and health risks compared to an appropriate reference[6]. Biological monitoring should be considered in the total context of control and prevention of work related diseases[7]. The ACGIH acknowledged and endorsed the concept of biological monitoring in 1973 by introducing Biological Limit Values (BLVs) in the preface of Threshold Limit Values (TLVs). In the fall of 1982, the Biological Exposure Indices (BEI) Committee was formed as a technical Committee of ACGIH. Germany was the first country to introduce this concept and develop biological standards essentially as means of controlling worker's health. Biological Tolerance Values for working materials (BAT-Werte) were published in the list of occupational standards in 1981[8]. The MAK values aim at protecting groups of workers whereas BAT values are aimed at surveying the health of individuals and at establishing appropriate protective devices. The primary objectives of BM are:

- To prevent disease by detecting meaningful exposure before the occurrence of a significant health effect
- To assist in the assessment of health risk(s)
- To evaluate the effectiveness of environmental controls

Research on biological monitoring by the scientists of developed countries and the efforts of OSHA, NIOSH, ASTDR, ACGIH have been appreciated by occupational health professionals. Biological monitoring groups in Japan[9], in European communities[10], Germany[11], USA[12] continue to practise biological monitoring. US-Japan Cooperative Seminar on Biological Monitoring was held in Hawaii in 1989 under the leadership of Professor Masana Ogata and Professor Fiserova-Bergerova. Another activity was the International Symposium on Biological Monitoring and Industrial Medicine in Asia, held at Kurashiki (Japan) in 1991. However, concept of BM still remains to be introduced in India and other developing countries[13].

Biological monitoring of exposure to heavy metals: Exposure to heavy metals viz: Lead, cadmium, chromium, copper, nickel and arsenic etc through work environment can cause serious health problems in man. Several excellent reviews have described their health effects in the past[14]. However, very few reports are available from India. At Toxicology Laboratory of Ch. Charan Singh University, Meerut analysed the urine samples of petrol pump operators, pottery makers, workers engaged in glass and bangle industries, battery makers and traffic policemen for delta-amino levulinic acid as a biomarker of lead exposure and recorded very high values in comparison to ACGIH BEI[15-17]. Periodic measurement of ALAU in urine and lead in blood has been legally enforced in Japan amongst workers exposed to lead. India needs such a legal step with immediate effect.

Another study made by us in a population exposed to cadmium through work environment i.e., goldsmiths, welding operators, scissor makers showed very high values for Cd in their urine samples reaching upto 307 $\mu g\ g^{-1}$ creatinine[18], whereas, BEI adopted for Cd by ACGIH is 10 $\mu g\ g^{-1}$ creatinine. Cd concentration in the urine samples of a healthy population ranges from 0.5-2 $\mu g\ L^{-1}$ [19]. Exposure to cadmium in unorganised sector in India remains to be a serious public health problem.

Occupational exposure to chromium may occur through mining, industrial coolants, chromium plating and leather tanning. In our laboratory, exposure to chromium was studied in electroplating workers and those working in leather industries[20]. Our observations on urinary Cr showed values ranging from 22.23-42.85 $\mu g\ g^{-1}$ creatinine in electroplating workers. In the leather industry workers, comparatively lower values (3.6-12.8 $\mu g\ g^{-1}$ creatinine) were registered. According to ACGIH standards, the urine concentration of Cr should not exceed 10 $\mu g\ g^{-1}$ creatinine. These results are alarming and the workers face the risk of Cr poisoning.

Similarly, in healthy adults urinary excretion of copper is generally between 30-60 μg Cu/day[21]. Normal level of nickel in unexposed adults are expected be in the range of 0.5-4.0 mg g^{-1} creatinine . Well validated biomarkers of Ni exposure besides direct measure of Ni in serum or urine are still needed.

Biological monitoring of exposure to arsenic has been reviewed by Mandal and Suzuki[22], who documented human arsenic exposure throughout the world. Arsenic concentration in urine can be used as an index of exposure, however, a number of factors such as diet, specially sea food can influence the results.

Biological monitoring of exposure to organic solvents: Aromatic hydrocarbons have been widely used as organic solvents and chemical intermediates. Biological monitoring of workers exposed to organic solvents has been conducted in Japan since 1962[23]. Other countries are lagging behind in this effort for health risk assessment. However, exposure to toluene in painters was monitored in our laboratory. We monitored exposure to toluene in Indian shoe makers[24,25].

Biological monitoring of exposure to benzene has been performed in several countries as component of health surveillance program[26,27]. In India, our group only has monitored the exposure to benzene in petrol pump workers and dry cleaners[28], traffic policemen[29] and tyre retreaders[30].

Since there is no other data available from other laboratories in India, the comparison with the data generated by workers from other countries and that compiled by other agencies need to be validated by ACGIH who issues reliable guidelines for human safety against these industrial chemicals.

Biological monitoring after exposure to mixtures of industrial chemicals: It has been reported by several studies that in the workplace, exposure to mixtures of chemicals is more common than exposure to a single compound. For example, thinners used in paints usually contain toluene, xylenes, ethylbenzene, methyl ethyl ketone and acetone. Commercial xylene is a mixture of o,m and para xylenes and ethyl benzene. Co-exposure to styrene and acetone is common in plastic industry. Coal fly ash contains arsenic, lead, cadmium, manganese and other toxic metals. Therefore, both toxicokinetic and toxicodynamic effects must be considered while making biological monitoring data.

Further, other confounding factors like gender, age, nutritional status and social habits like alcohol intake, tobacco smoking and chewing also need to be considered.

Ethics in bio-monitoring: All those who use the biological monitoring data are expected to follow certain ethical obligations. These include knowledge on sample collection, interpretation of biological monitoring, responsible communication of the results, use of individual data exclusively for the benefit of the worker and his colleagues and prompt action for the improvement of the workplace environment. The laboratory that performs these experiments is also to observe ethics i.e., good demonstrated analytical quality, provision of up to date and accurate reference values, maintaining confidentiality of data, knowledge on the limitations of bio monitoring methods and continuous education and training of the target group.

ROLE OF BIOMARKERS IN OCCUPATIONAL HEALTH

Concept of biomarkers is yet to be applied in occupational safety and health. National Institute of Health (NIH) defines a biomarker as a, "characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes or pharmacological responses to a therapeutic intervention". U.S. National Academy of Sciences Committee on biological markers classifies biomarkers into three types:

- Biomarkers of exposure
- Biomarkers of response
- Biomarkers of susceptibility

Toxicity of a drug or chemical can be assessed by different types of biomarkers which include a large variety of biological endpoints. Biomarkers may be invasive or non invasive. Ideally to determine the exposure, non invasive, specific, diagnostic, sensitive and easy to measure methods can be applied. Concept of molecular markers i.e., toxicogenomics or proteomics are yet to be developed for human health risk problems posed by study environment. Rana[31] deliberated on the role of molecular markers in environmental health risk assessment at the International Conference of Toxicogenomics, held at Incheon, South Korea on 1-2 November, 2007. Possibilities of using molecular markers in health risk assessment after exposure to heavy metals and industrial solvents have also been reviewed[32-34].

STATUS OF RESEARCH AND EDUCATION ON OCCUPATIONAL HEALTH IN INDIA

In India, health issues of workers/labour are primarily the concern of Ministry of Health joined by the Ministry of Labour. Indian Council of Medical Research supervises all activities concerned with occupational health. There are apex National Institutes with state of art facilities and skilled man power. These include, National Institute of Occupational Health (ICMR), Ahmedabad, Indian Institute of Toxicology Research, (CSIR), Lucknow, Central Labour Institute, (Ministry of Labour) Mumbai and All India Institute of Hygiene and Public Health , Kolkata. In addition, several Universities also conduct occupational and environment health research and undertake educational activities. These include Department of Environmental Health at Sri Ramachandra Medical College and Research Institute, Chennai, Centre for Occupational and Environmental Health at Lok Nayak Hospital, Delhi and

Department of Toxicology at Ch. Charan Singh University, Meerut. Indian Association of Occupational Health holds annual conference to discuss and disseminate knowledge on all issues concerned with occupational health.

CONCLUSION

Results on biological monitoring of human exposure to metallic compounds and organic solvents described in above paragraphs and their comparison with international standards clearly show poor status of occupational health in India. To prevent occupational health risks, practice of BM should be made mandatory for organized as well as un-organized industrial sectors. Education and awareness programs on occupational safety need to be promoted. Enforcement of available regulatory measures is also required.

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