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Risk Assessment's New Era:

part 2: Evolving Methods and Future Directions

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For more than three decades, health practitioners and regulatory agencies have used risk assessment methods to characterize health risks. Risk assessment is the process of determining the likelihood and severity of health risk to an individual or population from exposure to a chemical or other stressor.[1,2] Evolving methods and advances in science and technology offer several opportunities for improving risk assessment and its application to occupational settings.

Cumulative Risk Assessment (CRA)

Broader in scope than traditional chemical risk assessments, CRAs determine which chemicals, stressors or other risk factors are affecting certain populations. They address multiple chemical and non-chemical stressors, aggregate exposures and risks (that is, exposure to a single stressor by multiple routes), and combined risks for common health end points by chemical or stressor groupings.[3,4]

The EPA framework for conducting CRAs involves planning, scoping and problem formulation; analysis; and interpretation and risk characterization.[5,6] This framework has been applied to CRAs of chemicals, such as organophosphate pesticides and phthalates. In addition, EPA has developed various models and web-based tools to assess aggregate and cumulative exposures and risks.[7,8]

The greatest strength of CRAs is their emphasis on multiple exposures (stressors) and health effects in varied populations. But it's challenging to identify common groups and develop common metrics to evaluate dissimilar risks, and because of gaps in data and methodological limitations, CRAs have yet to include non-chemical stressors or focus on occupational exposures.

Editor's note: This article is the second in a series sponsored by the AIHA Risk Assessment Committee intended to highlight research and policy initiatives that are shaping the future of risk assessment in the industrial hygiene profession. Part 1 appeared in the April 2012 issue.

Biomonitoring

Biomonitoring assesses human exposure by measuring chemicals or their metabolites in human tissues or fluids (blood and urine, for example). This method quantifies the amount of a chemical that has been absorbed into the body from all potential sources. Biomonitoring data are discussed in terms of biomarkers, which are commonly divided into three categories: biomarkers of exposure, biomarkers of effect and biomarkers of susceptibility.[9] But the collection of bio monitoring data-which involves selecting a target population, identifying chemicals and biomarkers, collecting and analyzing samples, and interpreting the results-can be challenging.

Many population-based biomonitoring efforts are under way. For example, a national survey conducted by the CDC measures numerous chemicals and their metabolites in a representative sample of the U.S. population. The findings are published periodically and represent one of the largest publicly available biomonitoring datasets.[10]

Biomonitoring data integrates exposures from multiple sources and pathways to provide a direct measure of total exposure and is, therefore, a powerful tool for assessing aggregate exposure and risk. This data can be used to assess trends in exposures over time, evaluate the effectiveness of exposure-reduction policies, provide direction for future research and help medical professionals diagnose people who have potentially been exposed to excessive amounts of chemicals. Collecting and analyzing biomonitoring data requires significant resources, so only a limited number of people, compounds and body fluids have been studied to date. Also, these data provide no information on exposure conditions, such as frequency, duration, magnitude of exposures or the exposure routes that contributed to the total measured body burden.

Reach

The European Union's Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) legislation requires all chemicals manufactured, imported and used in the EU to be assessed for safety. Its underlying principle is that the use of chemicals under “reasonably foreseeable conditions” should not adversely affect human health and the environment. REACH places responsibility for demonstrating the safety of chemicals on industry. Companies must identify, manage and communicate the risks that chemicals may pose to human health and the environment.

REACH has the potential to generate a large volume of technical data that may be useful in assessing occupational exposures to chemicals. For example, companies must submit a Technical Dossier for chemicals manufactured or imported in quantities greater than 1 tonne per year, and a Chemical Safety Assessment (CSA) for chemicals manufactured or imported in quantities greater than 10 tonnes per year.[11] The Technical Dossier contains summary information on the manufacture and use of the chemical along with guidance on its safe use, while the CSA contains more detailed information on hazard, exposure and risk characterizations. The hazard assessment classifies chemicals according to their physical, human health and environmental hazards and includes Derived No-Effect Levels (DNELs)-exposure levels below which adverse effects are not expected. Companies are expected to

establish separate DNELs for different population groups (general population, workers), exposure routes (inhalation, dermal) and types of effects (acute, chronic).

Although REACH requires safety assessments prior to the use of a chemical in commerce, it may prove difficult to determine all foreseeable uses and exposure scenarios. Relevant environmental monitoring data are often lacking. Available exposure models are also based on limited data and typically contain many conservative default values. In addition, DNELs are not yet available for many substances, population groups, exposure routes or effects, and the values derived using default calculations often differ significantly from health guidelines derived using a weight-of-evidence approach.[12]

Toxicity Testing in the 21st Century

The groundbreaking report “Toxicity Testing in the 21st Century: A Vision and a Strategy,” published in 2007 by the National Research Council (NRC), outlined how chemical health risks should be evaluated in the future.[13] The report proposed using advances in science and technology to assess chemical hazards and prioritize chemicals for more in-depth toxicity testing.

NRC's proposed toxicity testing system would rely mainly on understanding toxicity pathways (that is, the cellular response pathways that can result in adverse health effects when sufficiently perturbed). Toxicity testing would shift from high-dose, whole-animal testing to new rapid assays and high-throughput techniques designed to evaluate biologically significant alterations in exposed cells, tissues or organisms. Targeted testing of some chemicals in animals would clarify and refine information from toxicity pathway tests and ensure the adequate evaluation of chemicals. Coupled with other exposure and risk assessment components, this information could enable the translation of cellular tests to whole human systems.

NRC's proposed approach could make toxicity testing quicker, less expensive and more directly relevant to human exposure concentrations, which would help industrial hygienists better explain how chemical exposures lead to certain health effects. But implementing this system will require coordinated research over a long time horizon and a cultural shift in how health professionals collect, interpret and use toxicity testing data.

Exposome

The exposome is the measure of all exposures, both internal and external, that an individual receives over his or her lifetime and how those exposures relate to disease.[14] The underlying premise of the exposome is that an individual's exposure begins before birth and includes insults from environmental and occupational sources. However, little is known about environmental determinants of chronic diseases and gene-environment interactions. Exposome studies seek to understand how exposures from the environment, infections, diet, lifestyle and other sources interact with an individual's genetics, physiology and epigenetic makeup to cause disease.

Two strategies for characterizing an individual's exposome have been proposed: measuring chemicals in air, water and food; and measuring chemicals in blood or other human fluids or

tissue.[15] The first approach would identify potentially important external exposures and their sources but would miss sources of internal exposure (such as those from products of normal metabolism). The second approach would identify all potentially important exposures but would provide no information about the original sources of exposure, making it less useful for designing risk management options. Integrating these approaches will likely be necessary to identify how environmental factors affect human disease.

In the future, people could potentially monitor their exposome and take preventive strategies based on observed changes. The effort to characterize total exposures, encompassing all life stages, for individuals may help identify vulnerabilities in certain populations. But the exposome is highly variable and dynamic, and it evolves throughout a lifetime. Mapping an entire exposome will be very challenging, and appropriate measurement techniques are lacking. Common metrics are needed to make meaningful comparisons between different exposures.

Opportunities for Industrial Hygienists

Advancements in science and technology are changing the practice of risk assessment. The application of new tools and methods in public health initiatives and chemical health risk regulations opens several possible roles for industrial hygienists:

- identifying target populations, activities and stressors (akin to similar exposure groups) within the CRA framework and quantifying cumulative exposures and risks
- correlating biomonitoring data with environmental and occupational data to link aggregate exposure to risk management opportunities
- helping develop and validate exposure models under REACH and as part of the toolkits for CRA
- using novel (in vitro) toxicity testing data to refine occupational risk assessments and worker hazard identification and labeling needs, and to develop hazard bands and occupational exposure limits
- providing key information regarding occupational exposures for use in exposome studies as part of total worker health protection initiatives[16]

The contribution of industrial hygiene to these developing areas will demonstrate the value of our profession as a critical component in the broader public health team.

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