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Identifying important life stages for monitoring and assessing risks from exposures to environmental contaminants: Results of a World Health Organization review ☆,☆☆

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ABSTRACT

In this paper, we summarize exposure-related issues to consider in determining the most appropriate age ranges and life stages for risk assessment. We then propose a harmonized set of age bins for monitoring and assessing risks from exposures to chemicals for global use. The focus is on preconception through adolescence, though the approach should be applicable to additional life stages. A two-tiered set of early life age groups is recommended. The first tier involves the adoption of guidance similar to the childhood age groups recommended by the U.S. Environmental Protection Agency, whereas the second tier consolidates some of those age groups to reduce the burden of developing age-specific exposure factors for different regions. While there is no single "correct" means of choosing a common set of age groups to use internationally in assessing early life exposure and risk, use of a set of defined age groups is recommended to facilitate comparisons of potential exposures and risks around the globe, the collection of data and analyses of aggregate exposure and cumulative risk. Application of these age groups for robust assessment of exposure and risk for specific populations will require region-specific exposure factors as well as local environmental monitoring data.

1. Introduction

A significant challenge associated with monitoring and assessing individual- and population-level exposure to and risk from exposure to environmental chemicals is associated with the need to rigorously consider changes in behavior and physiology that are related to age and life stage. Age- and life stage-related differences will determine windows of highest exposure as well as the appropriate distribution of exposure factors required to address specific exposure scenarios. Age and life stage differences in how people interact with the environment may be a major determinant for identifying the individual or population most vulnerable to risks from particular exposures to environmental contaminants. Identifying the most vulnerable age range or life stage for a particular population and exposure scenario requires a better scientific basis. Currently available approaches are limited in scope and potentially in applicability to the full range of geographic, social, cultural and economic diversity in populations worldwide. In addition, there is a need to better link or coordinate hazard and exposure assessment (the need to identify the most vulnerable based on windows of greatest susceptibility as well as windows of highest exposure, and then to incorporate that knowledge in a population-based risk assessment). Therefore, the World Health

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Organization (WHO) convened a group of experts to review these issues and provide guidance on how to better identify critical life stages for use in exposure and risk assessment.

The objective of this exercise was to propose a fit-for-purpose set of life stages independent of exposure context and exposure scenario. In this context, the group considered the following steps towards development and application of common life stages for exposure assessment:

- Define age bins by carefully identifying the particular characteristics that distinguish them.
- Decide how finely the overall life stage of childhood should be divided into age bins.
- Describe how additional factors, such as sex, culture and geography, might modify the significance of standard age bins.
- Recognize that there may be cases in which a specific factor (e.g. mouthing behavior) is a more significant indicator of exposure than age.
- Identify the most pressing gaps in the base of scientific knowledge that would justify standard age bins and in the exposure factor data required to use the age bins for risk assessment.

In this paper, we summarize important exposure-related issues to consider in determining the most appropriate age ranges and life stages for risk assessment. We then propose a harmonized set of age bins for monitoring and assessing risks from exposures to chemicals for use globally. The focus is on preconception through adolescence, though the approach should be applicable to addressing additional life stages. Information collated here was developed as follows. A review of previous efforts to establish standardized age bins was conducted, and previously proposed bins were used as a starting point for harmonization. Important developmental changes underpinning extant binning approaches were identified. A literature review was conducted to identify potential modifying factors and impacts on development, exposure and vulnerability to risk. The influence of social structure and geography on exposure factors was considered, and proposed age bins were evaluated based on important contextual elements.

2. Background

According to the United Nations Convention on the Rights of the Child, which has been ratified by 192 countries and is a legally binding international instrument, a "child means every human being below the age of eighteen years unless under the law applicable to the child, majority is attained earlier".

Life stage is defined as "a distinguishable timeframe in an individual's life characterized by unique and relatively stable behavioral and/or physiological characteristics that are associated with development and growth" (Firestone et al., 2007). The evolution of the use of a life stage-specific approach to assessing risks associated with the exposure of children to environmental contaminants is noted in a number of publications that relate mainly to the development of specific age categories to determine what the most critical "windows" of exposure are for particular health outcomes, such as cardiovascular disease, chronic diseases and cancers (Adams et al., 2000; Armstrong et al., 2000; Barr et al., 2000; Brown et al., 2008; Daston et al., 2004; Faustman et al., 2000; Makris et al., 2008; Olshan et al., 2000; Pohl and Abadin, 2008; Selevan et al., 2000; Stevens, 2006; Weiss and Bellinger, 2006; West, 2002). This approach views childhood as a sequence of life stages, from conception through fetal development, infancy and adolescence, rather than characterizing children as a population subgroup.

Life stages can be defined by referring to specific characteristics related to changes in anatomy, physiology, metabolism and behavior that can lead to differences in potential for exposure and/or risk—i.e. children may experience higher exposures to chemicals and greater risks from those exposures compared with adults. Table 1 illustrates different aspects of toxic substance exposure as described by Sexton et al. (1995). Again, the focus on children or childhood is highlighted in this paper because of their potential vulnerabilities (Bruckner, 2000; Graeter and Mortensen, 1996; Makri et al., 2004; Schwenk et al., 2003; Walker, 2005).

"Although there is no single 'correct' set of age groups, adopting a common convention for defining age groups will enable scientists to better understand differences in exposure and risk across life stages and the factors that may account for such differences, such as nutritional status, prevalence of certain diseases, ethnic/cultural norms regarding activity or behavior patterns, population genetic characteristics, meteorological conditions, geography, and social stress" (Firestone, 2010). This improved understanding will facilitate health-protective decisions and policy.

Harmonizing exposure and risk assessment approaches and tools requires consideration of a range of life stage-specific issues. Relevant issues include:

- identification of the relevant changes in behavior and physiology;
- guidance on use of available data to identify the age range at which important behavioral and physiological changes occur;
- approaches for incorporating factors influencing age- or life stage-related differences in behavior, physiology and exposures (e.g. nutritional status and endemic disease) for a given population and in different geographic regions, and the influence of social structure on these parameters;
- approaches for determining age ranges to conduct exposure assessment when data are limited or unavailable;
- approaches for determining age ranges to conduct hazard assessment when data are limited or unavailable;
- selection of important age ranges to consider in designing and conducting exposure and health studies;
- approaches for coordinating windows of highest exposure with windows of greatest susceptibility to hazardous effects.

The WHO group began by reviewing existing standardized age groups used by other organizations, including those developed recently by the U.S. Environmental Protection Agency (US EPA). The issues delineated above were among those considered when the US EPA undertook a significant effort to develop a consistent set of age groups for assessing childhood exposure to and potential dose of environmental contaminants (Firestone et al., 2007). This effort consisted of integrating scientific knowledge in disparate fields through a series of workshops and extensive input from a variety of experts in pediatric development, exposure assessment and risk assessment. It was undertaken in part to aid the US EPA in implementing regulatory initiatives requiring federal agencies to ensure that standards take into account special risks to children. The US EPA pediatric life stage categories as well as those of other national and international agencies are summarized in Table 2. These and some other childhood integrated life stages are mapped and presented in Fig. 1 (NCS, 2011).

3. Developmental changes in children

Children's physiology changes over time in ways that can impact both their exposures to environmental contaminants and their susceptibility to certain health effects. Children's behavior also changes over time in ways that can have an important impact on exposure to environmental contaminants. These developmental changes occur as a continuum that contributes to an exposure function over all ages. However, typically existing information is not adequate to construct an exposure function that reflects con-