The Importance of Rigorous Analytical Strategies for Elucidating Cumulative Risk Burdens and Disproportionate Effects

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The history of cumulative assessment of effects from exposures to harmful agents in the environment dates back at least several decades, and these assessments were notably complex and combined multiple chemical classes and modes of action with a range of plausible health effects (NRC, 2009). The legacy of these efforts can be seen in the recent Menzie et al. (2007) summary of practical approaches to cumulative assessment. Under the rubric of vulnerability, differentiation among subpopulations at risk extends beyond epidemiologic notions of susceptibility and resilience to include nonchemical stressors as important factors in how risk cumulates in community settings. Much less is known about how the effects of these stressors actually accumulate or whether some process analogous to interaction occurs. It is not surprising then that, as a 2009 NRC report notes, no cumulative risk assessment by the U.S. Environmental Protection Agency has formally employed non-chemical stressors (NRC, 2009).

What do we currently know about aggregate and cumulative health impacts, and how do we apply this knowledge to cumulative risk assessment? The peer-reviewed science tells us that there is clear and convincing scientific evidence that either simultaneous or sequential exposure to multiple environmental agents, including biological, chemical, physical, and psychosocial stressors, can, under the right circumstances, modify the toxic effects of these same agents acting alone. A diversity of biologic mechanisms that occur inside the body may alter toxicity from concurrent exposure to two or more environmental agents so that their combined adverse health effects are either greater than or less than the sum of adverse effects from each individual agent acting separately. There is also no question that people are routinely exposed during their everyday activities to a diverse and ever-changing concoction of multiple environmental stressors.

Assessment of cumulative risk from exposure to environmental mixtures is hindered in most cases by lack of information on the magnitude, duration, frequency, and timing of exposure to multiple stressors; insufficient data on whether mixture-related effects are antagonistic, synergistic, or additive at real-world exposure levels; and inadequate knowledge and understanding about interactive mechanisms of toxicity among mixture components. As complicated as it is to evaluate interactive effects of chemical mixtures, even simple ones, the degree of difficulty increases dramatically when we attempt to include non-chemical stressors in our analysis.

The models and analytical frameworks for understanding biological mechanisms are simply more developed and offer firmer guidance for empirical investigations than the frameworks currently applied to social and contextual factors that are proposed under EPA's current cumulative risk paradigm. Any given theory may be equally compatible with a wide range of empirical results; and conversely, the same data may support rival theories. In practice this means that one's commitment to a given set of theoretical assumptions, or to the selection of a particular model, cannot depend exclusively on empirical evidence. Other forms of justification and analysis are also required. Similarly, when a model or framework is deployed to make sense of empirical results, underlying concepts and assumptions should be scrutinized in judging its adequacy and appropriateness. We adopt this perspective in the subsequent comparison and assessment of approaches to cumulating non-chemical and chemical stressors.

Although the peer-reviewed science tells us that cumulative impacts will occur from exposure to multiple stressors, and available data bases tell us that these impacts will lead to disproportionate health effects in many cases, the practice of cumulative risk assessment in communities (i.e., how to interpret the data and reach conclusions) is a nascent science. There is as yet no widely accepted single conceptual framework for community cumulative risk assessment. This leaves us currently with the situation that the framework chosen will make a difference in how data are generated and interpreted, and how conclusions from the assessment can be drawn and interpreted. This situation leaves us with the following "take home messages":

- There are at least three frameworks relevant to understanding and measuring cumulative risk.
- Each is relatively well developed and supported by empirical findings.
- They share many of the same measurement indicators, but:
- Pathways, causal ordering, inferences, and interpretations are distinctive to each.
- The researcher's chosen (or default) framework matters for how empirical results are generated and interpreted.
- The framework in use should be acknowledged explicitly and subject to some accountability criteria.
- A framework should be subject to revision and possible rejection on both empirical and conceptual grounds.
- The estimation and understanding of cumulative risk has to begin with an evaluative consideration of frameworks.