

Conducting biologically based exposure assessment for epidemiology

Instructors: TJ Smith, Harvard School of Public Health

The “right” choice of summary measure of exposure in epidemiologic studies has long been a dilemma for study design and data analysis in environmental and occupational epidemiology. We are proposing a new approach that offers a clear rationale and method for choosing a biologically appropriate exposure metric.

Our new approach is based on representing effects with two simple, directly observable dimensions of their dynamics: (1) Is the pathological effect reversible or irreversible across time i.e. is the effect repaired? And, (2) is the magnitude of the effect proportional to the exposure, or is it a discrete response triggered when a critical level of exposure is reached? Those two dimensions together define four distinct disease processes. Each type can be described by a temporal model. This model can be applied to repeated measure data on an effect and suspected exposure. The models are the basis for a new class of dynamic dose metrics calculated from each subject’s exposure time profiles. In their initial formulation, the models are simple, robust, and easily applied. More importantly, they also can be elaborately formulated using clinical and lab information about the mechanism of effects coupled with details about each subject’s physiological and genetic characteristics, such as toxicant uptake or metabolic formation rates.

The flexibility and detail possible with this new approach provides a framework for integrating new biological findings from genetics and molecular mechanism studies into epidemiologic studies of disease effects. Mechanistic hypotheses about human exposure-risk relationships can be tested with an appropriate disease model and dose metric.

The workshop will begin with background presentations on the approach. This will be followed by detailed presentations on the approach applied to four types of diseases: irreversible lung disease from silicon carbide exposure; reversible ocular effects from ammonia exposure; childhood asthma from ambient ozone exposure; and lung cancer from silica dust. Simulation of study data will illustrate dose metric formulation and testing.

The workshop will be based on “Biological Approach for Environmental Assessment and Epidemiology” by TJ Smith and D. Kriebel, published by Oxford University Press, 2010, which will be available at a discount for the participants.