Frontiers in Exposure Science

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Work supported by NIEHS
Nature versus nurture

- Epidemiologic evidence points to nurture (environment) as contributing at least 80-90% of attributable risk for cancer and degenerative diseases
  - Major diseases differ 5-fold to 100-fold across populations
  - When groups migrate, disease rates adapt to new environments
  - Disease rates change within countries over time
  - Modifying the ‘environment’ accounts for 70% of stroke and colon cancer, 80% of CHD, and 90% of adult onset diabetes
    - ‘Environment’ refers to diet, overweight, inactivity, and smoking

Note the broad definition of ‘environment’ - about 5% of cancer risk is attributable to air and water pollution
[Saracci and Vineis, *Environ Health*, 2007]
Air and water vs. dietary and endogenous sources of exposure

- Uptake of xenobiotic contaminants from air and water tend to produce fM – nM ($10^{-15}$ - $10^{-9}$ molar) blood levels (highest from occupational exposures)
- Reactive chemicals from dietary and endogenous sources tend to produce nM – mM ($10^{-9}$ - $10^{-3}$ molar) blood levels
  - Reactive oxygen species from metabolic and inflammatory processes (including stress)
  - Reactive carbonyl species from metabolism and lipid peroxidation (e.g. 100 μM formaldehyde in blood)
  - Reactive quinones from hormones (e.g., estrogens) and polyphenols (e.g., benzoquinone)
What is ‘exposure’?

• The epidemiologist’s view: something a person can tell you (location, diet, behavior, lifestyle, etc.)
  - Indirect, categorical surrogate for a predictor of disease risk

• The molecular epidemiologist’s view: something (biomarker) measured inside a person
  - Relates directly or indirectly to internal dose

• Exposure scientist’s view: something measured or predicted outside a person
  - External level(s) across media (air, water, dermal contact, etc.)
The exposure conundrum

Quantifying environmental risks of diseases is frustrated by conflicting views of ‘exposure’

- Categorical or continuous?
- Direct or indirect measure?
- Outside or inside the body?
- Exogenous or endogenous?

Bruegel’s “Little” Tower of Babel c. 1563
Putting the E into GxE

10% Genetic Risk

90% ‘Environmental’ Risk

Cancer and degenerative diseases

Exposure is dynamic

- Levels of both exogenous and endogenous chemicals vary within and between persons and across populations
  - The scale of variability ranges from 10-fold to 10,000-fold, depending upon the context
- Such variability makes it impossible to accurately predict exposure levels without empiric data
  - Need to measure something - repeatedly!
The exposome – a unifying concept for exposure assessment

Recognizing the disparity in current knowledge between genes and environmental exposures, Chris Wild defined the “exposome,” representing all environmental exposures (including those from diet, lifestyle, and endogenous sources) from conception onwards, as a quantity of critical interest to disease etiology.

Exposome

(Totality of exposure from air, water, diet, lifestyle, behavior, metabolism, inflammation, oxidative processes, etc. - during all stages of life)
The exposome shifts the paradigm

The exposome includes all chemicals - from all sources - all the time
Purpose of the workshop

- Examine the concept of the exposome and its importance to the etiologies of human diseases
- Discuss the roles of epidemiologists and laboratory scientists in elaborating and using the exposome
  - Conceptualization and finding a common language
  - Measurement challenges
- Discuss available and needed resources