Exposure Assessment

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Measuring Human Exposure

Characteristics to Consider

• Magnitude/Intensity (How much)
• Frequency (How often)
• Duration (How long)
• Route of Exposure

• A complex combination involving the physical environment and the personal environment (both external and internal)

Source Emissions —— Health Effect

• Transport, Accumulation, Human Contact - all focused on the Physical Environment (air, water, soil, food)

• Human Contact and Potential Dose - route of exposure matters (inhaled, ingested, dermal absorption)

• From “Internal Dose” onwards – strong influence of individual characteristics such as age, genetics, nutritional and physiologic status

Levels of Personal Exposure Measurement

Total Personal Exposure

External exposure from environmental sources (levels in air, soil, food, water) considering the relative magnitude of routes of exposure (inhalation, ingestion, absorption)

Internal Dose

The amount of the substance that actually gets into the body. Often measured by blood/serum levels.

Body Burden

The amount of the substance that persists in the body.

Some organs or tissues act as “sinks”

Thyroid ----- radioactive iodine
Bone ----- lead
Fat tissue ----- PCBs, DDT, Dioxin
Kidney ----- Cadmium

Circulating levels (blood levels) are at equilibrium with the body burden levels, except under conditions of acute exposures.
Biologically Effective Dose
The amount of the substance that is reaching the critically sensitive or vulnerable target tissue, and is causing the health effect.

**Lead**
- External Dose - Air, Water, Food, Dirt, Dust Levels
- Internal Dose - Blood lead levels
- Body Burden - Bone lead concentrations
- Biologically Effect Dose - The lead levels reaching the CNS in young children

Other Exposure Parameters
- Intensity = Concentration
  - ppt = ng/kg and ng/L
  - ppb = ug/kg and ug/L
  - ppm = mg/kg and mg/L
- Frequency (per day/week/month/year)
- Duration
- Cumulative Exposure: a time integrated measure, usually intensity x duration
  - Pack-years = # packs/day x # years

Trying to choose the best exposure measure that is most relevant to the health outcome that is most likely and most detectable, or of greatest concern.
Consider:
1) The substance involved:
   - **Radiation**: Intensity is the critical exposure parameter. 
     - $^{131}I$: $t_{1/2} = 8$ days  sink = thyroid
   - **Dioxin**: Very persistent, accumulates in adipose tissue. Not mutagenic, but possible receptor-mediated; possible threshold.
     - Look at a cumulative exposure

2) The anticipated health effect

**Air Pollution**
- **Asthma Attacks** - an acute effect; look at the intensity of exposure (ambient air levels)
- **COPD, Lung Ca** - chronic effects; look at duration of exposure, the cumulative effects

Hierarchy of Exposure Data or Surrogates

<table>
<thead>
<tr>
<th>1) Quantified personal measurements</th>
<th>Accuracy</th>
<th>Cost</th>
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</thead>
<tbody>
<tr>
<td>2) Quantified area measurements</td>
<td>Best</td>
<td>High</td>
</tr>
<tr>
<td>3) Quantified surrogates (eg drinking water use)</td>
<td></td>
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<tr>
<td>4) Distance and duration</td>
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<tr>
<td>5) Distance or duration</td>
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<tr>
<td>6) Residence or employment in proximity where exposure can be assumed (Yes/No)</td>
<td></td>
<td></td>
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<tr>
<td>7) Residence or employment in a defined geographic area (Y/N)</td>
<td>Poor</td>
<td>Low</td>
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Surrogate Measures of Exposure
- No measure of a specific substance in the environment or in the individual.
- May incorporate some scaling of duration or exposure likelihood.

Typically Categorical
- Dichotomous: Yes/No, Ever/Never
- Ordinal: No/Low/Moderate/High
When using a surrogate measure of exposure always concerned about misclassification

- Some misclassification of study subjects with respect to disease and exposure status is virtually inevitable.

- Two types
  - Non-differential misclassification
  - Differential misclassification

Non-differential misclassification

- The probability of misclassification is the same for all of the groups being compared.

  - That is:
    - The likelihood of misclassification of exposure status is the same for diseased and non-diseased
    - The likelihood of misclassification of disease status is the same for the exposed and non-exposed

Result

- The measure of association is biased toward the null

- (Whatever the “true” odds ratio, the observed odds ratio will be closer to 1.0)

  “True” “Null” “True”
  0.6 1.0 4.5

  **** The observed association is a conservative estimate of the “true” association.

Differential Misclassification

- The probability of misclassification differs across groups.

  - That is:
    - The likelihood of misclassification of exposure depends on disease status.
    - The likelihood of misclassification of disease depends on exposure status.

  - Result: Unpredictable (either direction possible)

Can evaluate or reduce misclassification by:

1) Restricting the comparison:

   Levels: None Possible Probable Definite (compare None vs Def; None vs Probable+Def)

   Quartiles: Lowest (Ref) Highest

   Misclassification is most likely between contiguous categories; skipping a middle group reduces the error.

2) Validate exposure estimates in a subset of the study population.

   Pilot the surrogate measure, collecting some quantitative exposure measures using a “gold standard” and evaluate the accuracy of the surrogate.

   If the surrogate correlates well with the “gold standard” (High vs med vs low) than the surrogate might be good enough.

   Advantage: Lower cost = more subjects = more power
Conclusions:

- Surrogate measures of exposure are more readily available and less expensive than personal biological monitoring.

- Misclassification is more likely with surrogate measures.

- Negative studies of surrogate measures and health outcomes should be evaluated carefully, because of the possibility of nondifferential misclassification.