

Toxicology vs Epidemiology

Toxicology:

- Uses lab experiments, typically on animals and with control groups.
- Role in risk analysis: identify dose-response relationship.

Epidemiology:

- Usually gathers and analyzes data from the real world.

High to Low Dose Extrapolation: Carcinogenesis

- High dose effects may produce carcinogenic mechanisms not found at low doses ~> overestimation of risk.
- Early, low-dose tumors are not identified as such ~> underestimate of risk.
- Tumors might have appeared after sacrifice ~> underestimate of risk
- Cumulative and sporadic doses may have different effects.
- Model selection may produce over or under estimation of risk.

Problems in Toxicological Modeling

- High to low dose extrapolation
- Species-to-species comparisons
- Exposure route comparisons (stomach, lungs, skin).
- Interactions among multiple toxins

Model Choice Affects Low to High Dose Extrapolation

- Threshold or not?
- Two-hit model? (production of oncogenes plus disabling of tumor suppressor gene - order of mutations not important)
- Multistage? e.g., initiation (reversible; oncogene or tumor suppressor disabling), promotion (proliferation), progression (spread to other locations).
- Different models may fit different types of cancer.

Species to Species Comparison

- Different body weights have different metabolisms, which may affect processing of toxins.
- Mechanisms and target organs or tissues may not be analogous.
- Use of homogeneous and highly susceptible test animals is necessary to obtain a detectable response and produce health-conservative risk estimates, but this may inflate cancer rates.

Reasons for High-Dose Toxicological Assessments

- Modeling provides information about possibilities. (e.g., if cost estimates for remediation vary by several orders of magnitude, but all are low, the choice of action is clear.)
- Modeling provides information about which assumptions are most important and highlights where more research can be most useful.
- Can address causality by using control groups.
- Experiments with small doses need large numbers of animals, which is prohibitively expensive. (High dose studies may cost \$1 - 5 million.)
- Experiments with humans are unethical.

Problems with Epidemiological Studies

1. Can not address cause and effect
 - No control group
 - Confounding variables (appropriate analysis helps somewhat)
2. Measurement error
 - Self-report may be necessary
 - Estimates, averages, or surrogates may be necessary.

Problems with Epidemiological Studies, Continued

3. Extrapolation
 - Population studied may have higher exposure than general population
 - Population studied may not be representative of general population (health, age, etc.)
4. Interpreting small effects (e.g., $RR < 2$)