EOH 2504
Lecture 4
Exposure Assessment Definitions Continued

Conrad Daniel Volz, DrPH, MPH

Department of Environmental and Occupational Health, Graduate School of Public Health, University of Pittsburgh

Co –Director for Exposure Assessment, University of Pittsburgh Cancer Institute, Center for Environmental Oncology

Scientific Director, Center for Healthy Environments and Communities, cdv5@pitt.edu

Exposure and Dose Differences

- Concentration (mg/M^3, ppm {volume or weight}, mg/L, mg/kg) and time (minutes, hours, days, weeks ,months, years, lifetime) are used to depict exposure.
- Amount/Mass (mg, µg, ρg) and time (minutes, hours, days, weeks ,months, years, lifetime) characterize Dose.

Exposure

$$E = \int_{t_1}^{t_2} C(t)\ dt$$

E is the magnitude of exposure, C(t) is the exposure concentration as a function of time, and t is time, t2 - t1 being the exposure duration (ED).

Exposure	Contact of chemical with outer boundary of a person	concentration x time	**Dermal**--(mg chem/L water) • (hrs of contact) (mg chem/kg soil) • (hrs of contact) **Respiratory** -(ppm chem in air) • (hrs of contact) or (µg/m3 air) • (days of contact) **Oral**--(mg chem/L water) • (min of contact) (mg chem/kg food) • (min of contact)

Exposure estimation by integration and averaging

- A minimal description of exposure for a particular route must include exposure concentration and the duration of contact. If the exposure concentration is integrated over the duration of contact, the area under the resulting curve is the magnitude of the exposure in units of concentration multiplied by time (e.g., mg/litre-day, mg/kg-day, µg/m3-h). This is the method of choice to describe and estimate short-term doses, where integration times are of the order of minutes, hours or days.

Integrated Exposures vs. Exposure Profiles

- Integrated exposures are useful when a total exposure for a particular route (i.e., the total for various pathways leading to exposure via the same route) is needed.
- An exposure profile (a picture of exposure concentration over time) contains more information than an integrated exposure (a number), including the duration and periodicity of exposure, the peak exposure, and the shape of the area under the time-concentration curve.

Time Weighted Averages

- Time-weighted averages are widely used in exposure assessments, especially as part of a carcinogen risk assessment. Time-weighted average exposure concentration (units of concentration) is the integrated exposure divided by the period where exposure occurs.
- Time-weighted average dose rate is the total dose divided by the time period of dosing, usually expressed in units of mass per unit time, or mass/time normalized to body weight (e.g., mg/kg/day). Time-weighted average dose rates such as the lifetime average daily dose (LADD) are often used in dose-response equations to estimate effects or risk.

Potential Dose

Potential Dose	Amount of a chemical contained in material ingested, air breathed, or bulk material applied to the skin. The concept of potential dose is straightforward for inhalation and ingestion, where it is analogous to the dose administered in a dose-response experiment. For the dermal route, however, it is important to keep in mind that potential (or administered) dose refers to the amount of the agent, whether in pure form or as part of a carrier medium, that is applied to the surface of the skin.	mass of the chemical Dose rate is mass of the chemical/time; the dose rate is sometimes normalized to body weight: mass of chemical/unit body weight • time	**Dermal**---(mg chem/kg soil) • (kg soil on skin) = mg chem in soil applied to skin **Respiratory**---(µg chem/m3 air) • (m3 air breathed/min) • (min exposed) = µg chemical in air breathed **Oral**---(mg chem/L water) • (L water consumed/day) • days exposed = mg chemical ingested in water **(also dose rate: mg/day)**

Most Common Dose Measure Average Daily Dose (ADD)

ADD= C * IR * B* D/ BW* AT

ADD= Potential average daily dose.

BW= Body weight (kg).

B= Bioavailability

D= Duration

IR= Ingestion Rate

C= Mean exposure concentration

AT= time period over which the dose is averaged (days)

Example ADD Calculation non-carcinogens

- **Assume the quantity of lettuce ingested is 1.5kg week/daily maximum 0.4 kg. Aldrin pesticide is 4 ppm. Calculate the ADD of Aldrin for the maximum week, assuming the bioavailability is 90%.**
- ADD= C * IR * B* D/ BW* AT

- **C= 4mg/kg Aldrin**
- **BW= 70 kg**
- **AT= 7 days**
- **IR= 1.5kg**
- **B= 0.9**

So ADD= (4mg/kg Aldrin)(1.5kg)(0.9) (1 week)/ (70 kg) (7 days/week)

ADD=.0.011 mg/kg-day

Lifetime Average Daily Dose (LADD) carcinogens

LADD=C* IR*B*D/BW*LT

BW= Body weight (kg).

B= Bioavailability

D= Duration

IR= Ingestion Rate

C= Mean exposure concentration

LT= Life time-70 year or 25,550 days

Applied Dose

$$D_{applied} = \alpha \int_{t_1}^{t_2} C(t)\, IR(t)\, dt$$

E, magnitude of exposure; t_2 t_1, exposure duration; α, availability factor; C(t), exposure concentration as a function of time; IR, ingestion or inhalation rate; f(t), nonlinear absorption function (Sexton et al., 1995a)

Applied Dose	Amount of chemical in contact with the primary absorption boundaries (e.g., skin, lungs, gastrointestinal tract) and available for absorption **Information is rarely available on applied dose, so it is calculated from potential dose based on factors such as bioavailability**	mass of the chemical Dose rate is mass of the chemical/time; the dose rate is sometimes normalized to body weight: mass of chemical/unit body weight • time	**Dermal**----(mg chem/kg soil) • (kg soil directly touching skin) • (% of chem in soil actually touching skin) = mg chem actually touching skin **Respiratory**-- (µg chem/ m3 air) • (m3 air directly touching lung) • (% of chemical actually touching lung) = mg chemical actually touching lung absorption barrier **Oral**-- (mg chem/kg food) • (kg food consumed/day) • (% of chemical touching g.i. tract) = mg chemical actually touching g.i. tract absorption barrier **(also absorbed dose rate: mg/day)** **chemical available to organ or cell**

Internal (Absorbed) Dose

Internal dose

$$D_{\text{internal}} = D_{\text{applied}} \int_{t_1}^{t_2} f(t)\,\mathrm{d}t$$

E, magnitude of exposure; t_2 t_1, exposure duration; α, availability factor; C(t), exposure concentration as a function of time; IR, ingestion or inhalation rate; f(t), nonlinear absorption function (Sexton et al., 1995a)

Internal (Absorbed) Dose	The amount of a chemical penetrating across an absorption barrier or exchange boundary via either physical or biological processes.	mass of the chemical Dose rate is mass of the chemical/time; the dose rate is sometimes normalized to body weight: mass of chemical/unit body weight • time	**Dermal**-mg chemical absorbed through skin **Respiratory**- mg chemical absorbed via lung **Oral**--mg chemical absorbed via g.i. tract **(dose rate: mg chemical absorbed/day or mg/kg • day)**

Delivered Dose-Organ or Cell

Delivered Dose	Amount of chemical available for interaction with any particular organ or cell. **The delivered dose is the portion of the internal (absorbed) dose that reaches a tissue of interest.**	mass of the chemical Dose rate is mass of the chemical/time; the dose rate is sometimes normalized to body weight: mass of chemical/unit body weight • time	mg chemical available to organ or cell (dose rate: mg chemical available to organ/day)

Biologically effective (target) dose.

- The biologically effective dose is the portion of the delivered dose that reaches the site or sites of toxic action.

Relationship Between Target Dose and Disease

- The link, if any, between biologically effective (target) dose and subsequent disease or illness depends on:
- the relationship between dose and response (e.g., shape of the dose-response curve)
- underlying pharmacodynamic mechanisms (e.g., compensation, damage, repair)
- and important susceptibility factors (e.g., health status, nutrition, stress, genetic predisposition).

Biological effect

- . A measurable response to dose in a molecule, cell or tissue is termed a biological effect. The significance of a biological effect, whether it is an indicator or a precursor for subsequent adverse health effects, may not be known.

Adverse effect

- A biological effect that causes change in morphology, physiology, growth, development or life span which results in impairment of functional capacity to compensate for additional stress or increase in susceptibility to the harmful effects of other environmental influences (IPCS, 1994).