Toxicity assessment

- Determining the relationship between the exposure to a contaminant and the increased likelihood of the occurrence or severity of adverse effects

1. Hazard identification

   determines whether exposure to a contaminant causes increased adverse effects

2. Dose-response evaluation

   describes how the adverse effects are related to the dose provided to humans

Toxicity assessment

2. Dose-response evaluation (continued)

– dose: the mass of chemical received by an exposed individual (mg contaminant / kg body mass)

– response: can be any adverse effects such as reduced body weight, reduced fertility, tumor formation, and death

http://www.dailymail.co.uk

“The dose makes the poison”

- All chemicals can be toxic if too much is eaten, drunk, or absorbed

Q: All chemical can be non-toxic if very little is eaten, drunk, or absorbed?

Strange but True: Drinking Too Much Water Can Kill

In a hydration-obsessed culture, people can and do drink themselves to death.

Jun 21, 2007 | By Coco Ballantyne

Liquid H_2O is the sine qua non of life. Making up about 66 percent of the human body, water runs through the blood, inhabits the cells, and lurks in the spaces between. At every moment water escapes the body through sweat, urination, defecation or exhaled breath, among other routes. Replacing these lost stores is essential but rehydration can be overdone. There is such a thing as a fatal water overdose.

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Earlier this year, a 28-year-old California woman died after competing in a radio station's on-air water-drinking contest. After downing some six liters of water in three hours in the "Hold Your Wee for a Wii" (Nintendo game console) contest, Jennifer Strange vomited, went home with a splitting headache, and died from so-called water intoxication.

Toxicity assessment: terminologies

- **Acute toxicity**: an adverse effect that has a rapid onset, short course, and pronounced symptoms

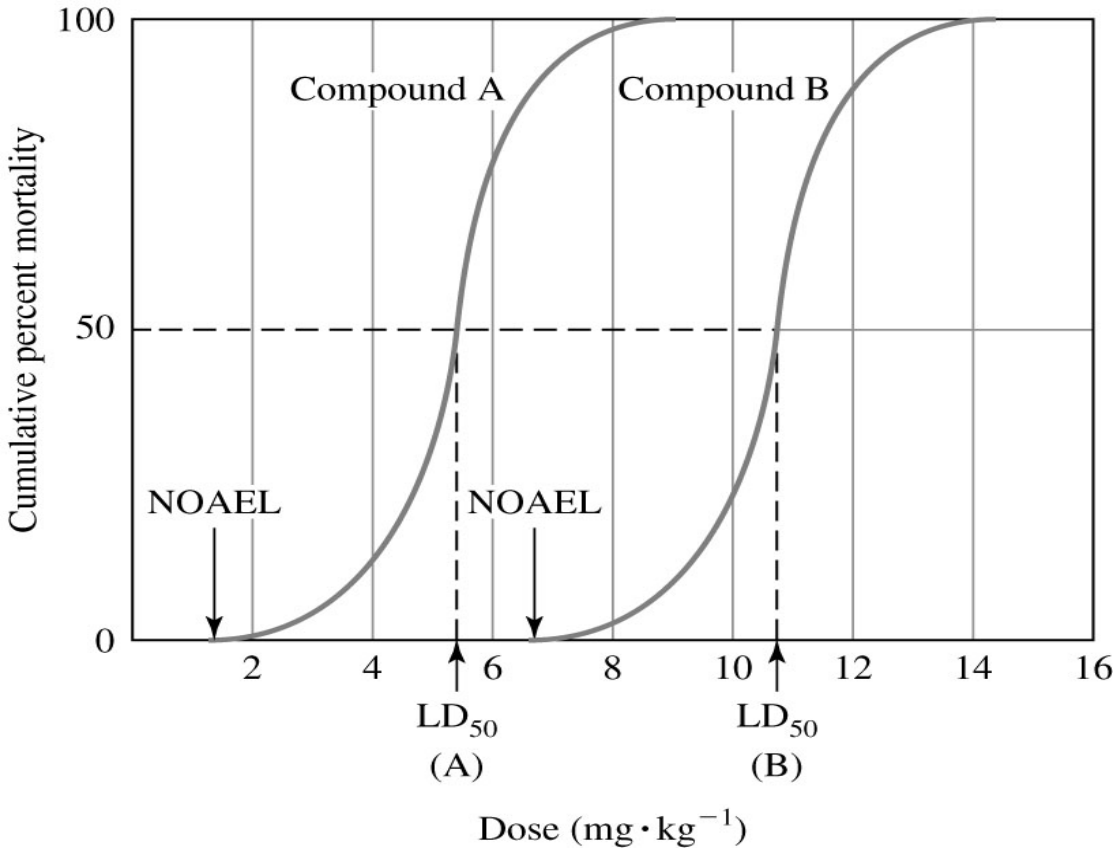
- **Chronic toxicity**: an adverse effect that frequently takes a long time to run its course and initial onset of symptoms may go undetected (ex: carcinogenesis)

- **Carcinogenesis**: creation of cancer (transformation of normal cells into cancer cells)

- **Carcinogen**: a cancer-producing substance

Toxicity assessment

- Dose-response curve



NOAEL:

No **O**bserved **A**dverse **E**ffect **L**evel

LD50:

Lethal **D**ose for **50**% of the population

Toxicity assessment

- Non-carcinogenic vs. carcinogenic risk

  – Non-carcinogenic risk: It is believed that there is a safe dose (*NOAEL* exists), i.e., the body can repair itself. From the *NOAEL* of a dose-response relationship, reference dose (*RfD*) is estimated:

$$RfD = NOAEL/10^{x},$$

  ($1 \le x \le 3$; safety factors for animal/human differences & variation within humans)

  –Carcinogenic risk: Assume no safe dose (no *NOAEL*). At low doses, the slope of the dose-response curve is represented by a ***slope factor*** (SF).

Exposure assessment

- Estimate the magnitude of exposure to chemicals of potential concern
- The exposure concentrations are predicted, then the pathway-specific intakes are calculated as:

$$CDI = C\left[\frac{CR \times EFD}{BW}\right] \times \frac{1}{AT}$$

* for different exposure pathways, see Table 6-6.

CDI = chronic daily intake (mg/kg body weight/day)
C = chemical concentration (ex: mg/L water);
CR = contact rate (ex: L/day)
EFD = exposure frequency and duration (= EF x ED)
EF = exposure frequency (days/year)
ED = exposure duration (years)
BW = body weight (kg)
AT = averaging time (days)

Exposure assessment

Q: Estimate the lifetime average chronic daily intake of benzene from exposure to a city water supply that contains a benzene concentration of 0.005 mg/L. Assume the exposed individual is an adult male who drinks 2 L of water every day for 63 years and ingestion of benzene in drinking water is the only exposure pathway. The averaging time (AT) is 75 years (=27375 days).

Risk characterization

- For **carcinogenic risk** (risk below 0.01),

  Risk = (intake)(slope factor)

  For multiple substances and multiple pathways,

  Total exposure risk = $\sum \text{Risk}_{ij}$

  i = compounds; j = pathways

* Goal: ensure risk < 10^{-4} to 10^{-6}

Risk characterization

- For non-carcinogenic risk,

  calculate Hazard Index (HI):

  $HI = (\text{intake})/(RfD)$

  For multiple substances and multiple pathways,

  $HI_T = \sum HI_{ij}$ i = compounds; j = pathways

* Goal: ensure $HI_T < 1$

Risk characterization

Q: Using the previous example, estimate the carcinogenic risk by ingestion of benzene in drinking water.

(benzene slope factor for oral ingestion = 0.015 kg·day/mg)

Risk management

- Based on the risk assessment, action is taken/not taken to reduce the existing risk to an acceptable level

- Strategies to reduce risk
  - change the environment

    ex) apply engineering techniques to reduce the contaminant concentration

  - modify the exposure

    ex) restrict public access to a contaminated site

  - compensate for the effects

    ex) provide a free health screening program

Reading assignment

- Textbook Ch6 p. 236-249