

Toxicology of “The Big Four” (Pb, Hg, As, and Cd)

What is considered safe? For a mother the only safe level of a toxic substance in anything ingested would be “zero.” However, we all know, “absolute” zero is a problem for quantitative science. Toxicity is influenced by many factors including age, weight, exposure route, organic compounds and forms of heavy metals (such as As) as well as metabolic differences.

Current Inputs for Assessing Acceptable Exposure for Metals:

- 1.) Human and animal toxicity data associated with exposure to the metal (human data is of course, preferred).
- 2.) Likelihood of the presence of the metal in the article to be tested.
- 3.) Level and pattern of use or consumption of the article or product.
- 4.) Level of exposure to the metal
- 5.) Other sources of exposure to the metal
- 6.) Other factors that may affect toxicity (e.g., co-exposure to other metals)
- 7.) Data quality and individual variability
- 8.) Special populations at increased risk for toxicity.

Quantifying Toxicity:

- 1.) Impact the development or functioning of the whole body or specific organs.
- 2.) “Toxicity threshold” – The dose below which adverse health effects are not expected to occur.
- 3.) Potential for adverse effects increasing as dose increases above toxicity threshold (dose response).

Dose Levels and Toxicity:

- 1.) NOEL: No-Observed Effect Level.
- 2.) NOAEL: No-Observed-Adverse Effect Level.
- 3.) LOAEL: Lowest-Observed-Adverse Effect level.
- 4.) MTD: Maximum Tolerated Dose.
- 5.) LD(50): Lethal Dose to 50% of the population.

Reference Dose (RfD):

- 1.) An estimate of the daily dose of a chemical that will avoid toxic effects other than cancer.
- 2.) NOAEL or LOAEL is adjusted by uncertainty factors (UF) to allow for differences in sensitivity to chemicals:
 - a. Human data UF = 10
 - b. Animal data UF =
 - i. 100 (NOAEL)
 - ii. 1000 (LOAEL)
 - iii. 1000 (NOAEL, less data)

3.) The Reference Dose (RfD) is used to calculate the Permissible Daily Exposure (PDE): $\text{RfD} \times \text{weight} = \text{PDE}$.

Some Sources of toxicity Information:

- 1.) IRIS – Integrated Risk Information Service.
- 2.) EPA Criteria Documents.
- 3.) HEAST – Health Effects Assessment Summary Tables.
- 4.) ATSDR – Agency for Toxic Substances and Disease Registry.
- 5.) Food and Drug Administration.
- 6.) Peer-Review literature.