The Science of Chemical Safety
Essential Toxicology - 4

Hazard and Risk

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IUPAC Educators' Resource Material

Hazard and Risk - 1

- Hazard is the potential of a substance to cause damage

  - Toxicity is the hazard of a substance which can cause poisoning

- Risk is a measure of the probability that harm will occur under defined conditions of exposure to a chemical

  - If there can be no exposure to a chemical, no matter how dangerous (hazardous) it may be, there is no risk of harm

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Hazard and Risk - 2

- The relation of risk to hazard may be expressed as;
    - $R = f(H \times E) = f(H \times D \times t)$
    - Where R is risk, f is function of, H is hazard, E is exposure, D is dose and t is time
- Thus, chemicals which pose only a small hazard but to which there is frequent or excessive exposure may pose as much risk as chemicals which have a high degree of hazard but to which only limited exposure occurs

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Reducing Risk

- Reducing risk is based on reducing exposure

- For example, some chemicals, such as pesticides, needed for food production may be fairly toxic, but their use may cause little or no risk to those who use them if exposure is kept low by using no more than is needed.

- However, many people have suffered illness as a result of careless use of pesticides

- All pesticides must be stored and handled with care and precautions taken to prevent exposure of people, pets, or animals that we do not wish to harm

Safe Exposure

- Control of exposure should ensure that exposure is kept below a "safe" level

- "Safe" exposure levels such as the Tolerable Daily Intake (TDI - see slide 10) are determined by establishing the dose-response curve, determining a <u>threshold dose</u> below which no harm occurs in an exposed population and extrapolating from this to a "safe" exposure by dividing by an uncertainty factor (UF), normally 100 or more.

- The <u>threshold dose</u> may be approximated by a NOAEL (No Observed Adverse Effect Level) or a LOAEL (Lowest Obseved Adverse Effect Level)

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Dose-Response Curve

- A dose response curve records the percentage of a population showing a given quantal (all or nothing) response such as death when each individual member of the population is subjected to the same dose of toxicant (reflecting a given exposure)

- The LD_{50} is the median dose associated with the death of 50% of the population

Dose-Response Curve
(for Ability To Cause Death)

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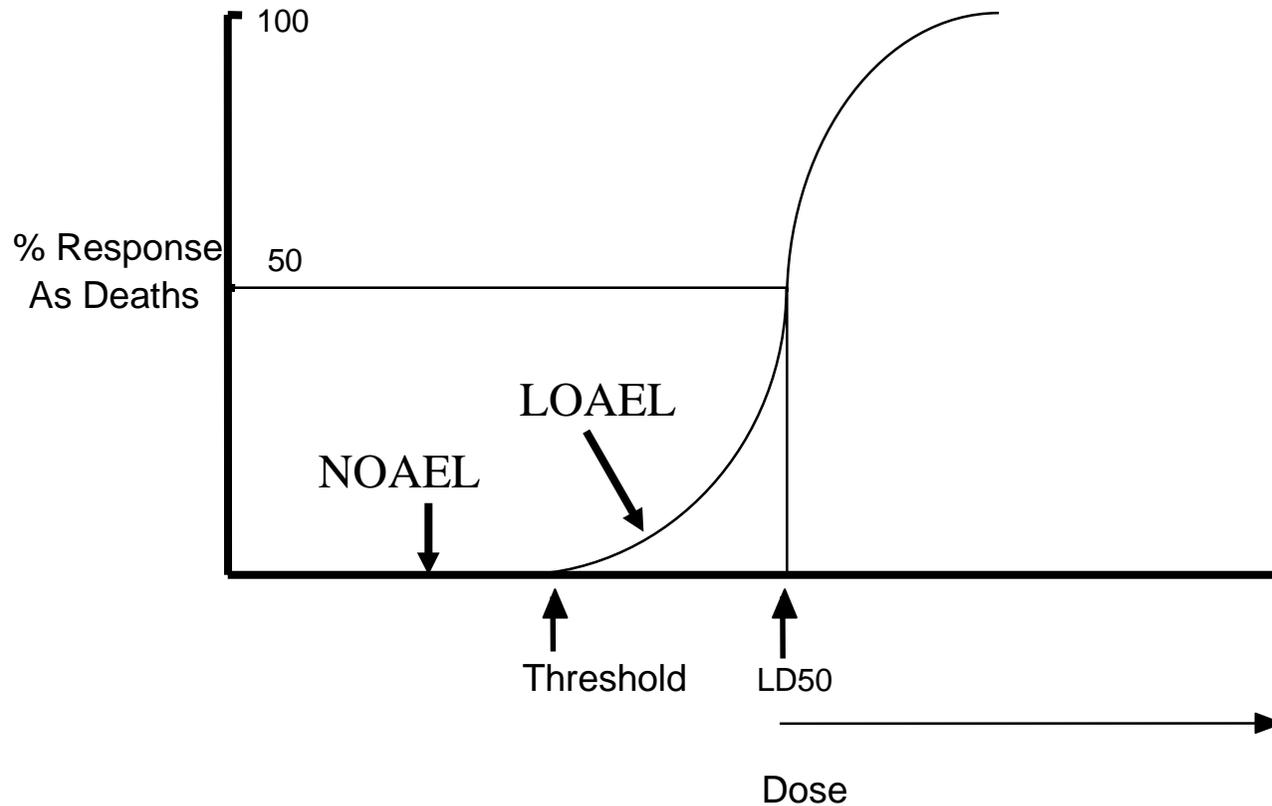
Dose-Effect Curves

- The relationship between dose and effect illustrates what happens in an individual as dose increases

- The curves are similar to dose-response curves

- Note the curve for an essential nutrient
  - For such substances there is an optimum range of dose required for good health

- Note the curve for no threshold toxicants
  - Carcinogens are believed to have no safe threshold of exposure

Dose-Effect Curves

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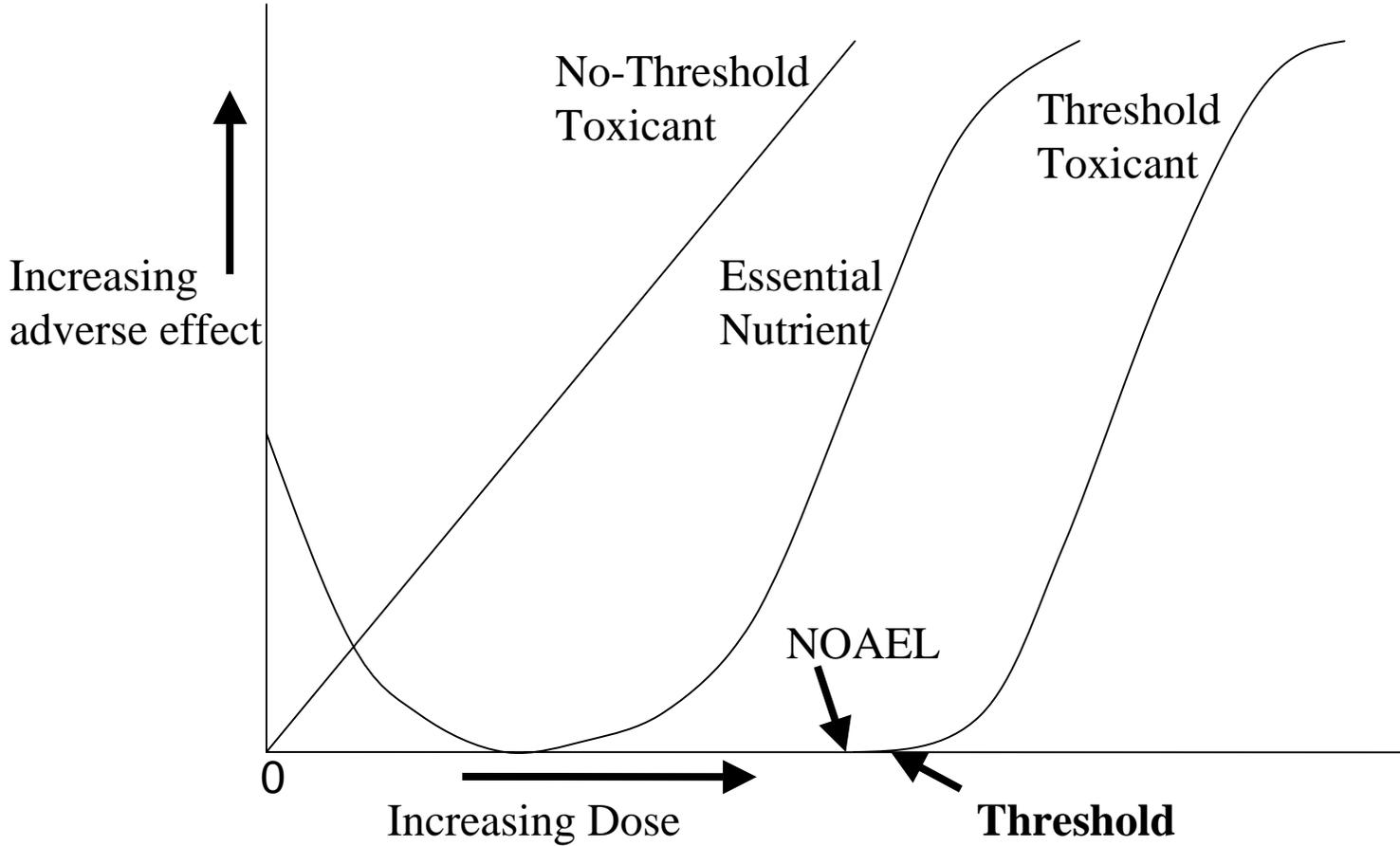
"Safe" Exposure Levels - 1

- Important regulatory "safe" exposure levels are those for food of which the Tolerable Daily Intake (TDI) is typical

- The Tolerable Daily Intake is an estimate of the daily intake of a chemical contaminant which can occur over a lifetime without appreciable health risk. The concept of a "TDI" generally applies to unavoidable and undesirable contaminants of food or water which have no useful purpose. The term "tolerable" is intended to signify permissibility rather than acceptability

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"Safe" Exposure Levels - 2

- In the United States, the "Reference Dose (RfD)" has a very similar definition to that of the Tolerable Daily Intake

- Exposures above the TDI or RfD are not necessarily dangerous because a large margin of safety is allowed in their calculation but every effort should be made to keep below these values

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Chemicals That Can Cause Cancer

- In the absence of data in humans to the contrary, chemicals which can induce cancer in experimental animals are regulated as if they could induce cancer in humans

- There is a generally held assumption that there is no threshold for safe exposure to substances which may cause cancer by mutation of the genetic information in DNA. This may not be the case but it ensures that regulatory levels are set very far below those which might carry a significant risk.

Regulation of Agents that Can Cause Cancer

- Regulatory permitted levels of agents that can cause cancer (for which no safety threshold of exposure can be established) are based on calculations of lifetime risk

  - It is generally considered that exposure levels corresponding to a calculated increased lifetime risk of 1 in a million are acceptable since an increased incidence of cancer at this level would be undetectable with current epidemiological methods; calculations are based on the worst possible case and the true increase is likely to be much less

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Environmental Exposure Guidelines

- Guideline values developed by international agencies for chemical contaminants in environmental media are intended to provide guidance for the protection of the "general" population

- Such guidelines are not legally enforceable but guide regulatory authorities in establishing legal standards

- Guidelines are set well below exposure levels thought likely to cause harm BUT

- These guidelines may not always protect specially sensitive subsets of the population although they are designed to do so.

- For example, the guidelines may not apply to babies, small children and those with genetic enzyme deficiencies

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Self Assessment - 4.1
True or false?

- Risk is a measure of probability of exposure to a chemical hazard - see slide 2

- "Safe" regulatory values such as T DI and RfD (slide 10) are related to "threshold" values on dose-response curves divided by uncertainty factors based on the quality of available data -see slide 5

- It is assumed that there are no safe "thresholds" of exposure for substances causing cancer - see slide 8

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Self Assessment - 4.2
True or false?

- "Guidelines", TDI's and RfD's are chosen to protect human populations at risk with a large safety margin - see slides 10, 11, 12, 13 and 14

- For substances causing cancer, "safe" exposure levels may cause cancer in one person in a hundred thousand - see slides 12 and 13

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Self Assessment - 4.1 Checklist

- Risk is a measure of probability of exposure to a chemical hazard - False

  – N.B. It is a measure of probability <u>of harm</u> following exposure

- "Safe" regulatory values such as TDI's and RfD are related to "threshold" values on dose-response curves divided by uncertainty factors based on the quality of available data - True

- It is assumed that there are no safe "thresholds" of exposure for substances causing cancer - True

Self Assessment - 4.2 Checklist

- "Guidelines", TDI's and RfD's are chosen to protect the human populations at risk with a large safety margin- True
  - But note that there may be highly susceptible subpopulations or individuals who need special attention
- For substances causing cancer, "safe" exposure levels may cause cancer in one person in a hundred thousand - False
  - Rarely, exposure levels at this level of probability may be permitted for industrial circumstances where the process is regarded as essential in the national interest and lower levels of exposure are impossible to attain