

2.3: Dose Estimates of Toxic Effects

Dose Estimates

Dose-response curves are used to derive dose estimates of chemical substances.

Historically, **LD50** (Lethal Dose 50%) has been a common dose estimate for acute toxicity. It is a **statistically derived maximum dose** at which 50% of the group of organisms (rat, mouse, or other species) would be expected to die. LD50 testing is no longer the recommended method for assessing toxicity because of the ethics of using large numbers of animals, the variability of responses in animals and humans, and the use of mortality as the only endpoint. Regulatory agencies use LD50 only if it is justified by scientific necessity and ethical considerations.

The Three Rs

The current practice for estimating acute toxicity emphasizes the following approaches, known as the Three Rs:

1. **Replacing** animals in science by *in vitro*, *in silico*, and other approaches.
2. **Reducing** the number of animals used. For example, the oral LD50 approach has been replaced in some circumstances by an **up-and-down method** in which animals are dosed one at a time.
3. **Refining** care and procedures to minimize pain and distress.

Other dose estimates also may be used.

Lethal Doses/Concentrations

- **Lethal Dose 0% (LD0)** — represents the dose at which no individuals are expected to die. This is just below the threshold for lethality.
- **Lethal Dose 10% (LD10)** — refers to the dose at which 10% of the individuals will die.
- **Lethal Concentration 50% (LC50)** — for inhalation toxicity, air concentrations are used for exposure values. The LC50 refers to the calculated concentration of a gas lethal to 50% of a group. Occasionally LC0 and LC10 are also used.

Effective Doses (EDs)

Effective Doses (EDs) are used to indicate the effectiveness of a substance. Normally, effective dose refers to a beneficial effect such as relief of pain. It may also stand for a harmful effect such as paralysis. Thus, the specific endpoint must be indicated. The usual terms are:

Term	Effective for this percentage of the population
ED0	0%
ED10	10%
ED50	50%
ED90	90%

Table 2.3.1. Typical terms for describing effective doses

Toxic Doses (TDs)

Toxic Doses (TDs) are used to indicate doses that cause adverse toxic effects. The usual dose estimates include:

Term	Toxic to this percentage of the population
TD0	0%
TD10	10%
TD50	50%
TD90	90%

Table 2.3.2. Typical terms for describing toxic doses

Determining the Relative Safety of Pharmaceuticals

Toxicologists, pharmacologists, and others use **effective** and **toxic dose** levels to determine the relative safety of pharmaceuticals. As shown in Figure 1, two dose-response curves are presented for the same drug, one for effectiveness and the other for toxicity. In this case, a dose that is 50% to 75% effective does not cause toxicity. However, a 90% effective dose may result in a small amount of toxicity.

Graph of two dose-response curves for the same drug - one for effectiveness and one for toxicity. ED10, ED50, ED90, TD10, TD50, TD90 are marked on the graph. A 50-75% effective dose does not cause toxicity in this example, but a 90% effective dose could result in a small amount of toxicity.

Figure 2.3.1. Dose-response curves representing effective dose and toxic dose for the same drug
(Image Source: NLM)

It should be noted that a desired effect in a drug is often an undesired effect with an environmental chemical.

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