PD_{50}, ED_{50}, LD_{50}

Effective Dose (ED)

- In pharmacology, an **effective dose** (**ED**) or **effective concentration** (**EC**) is the minimum dose or concentration of a drug that produces a biological response.
- The term "effective dose" is used when measurements are taken *in vivo*, while "effective concentration" is used when the measurements are taken *in vitro*.
- It has been stated that any substance can be toxic at a high enough dose.
- The line between efficacy and toxicity is dependent upon the particular patient, although the dose administered by a physician should fall into the predetermined therapeutic window of the drug.

Median effective dose (ED_{50})

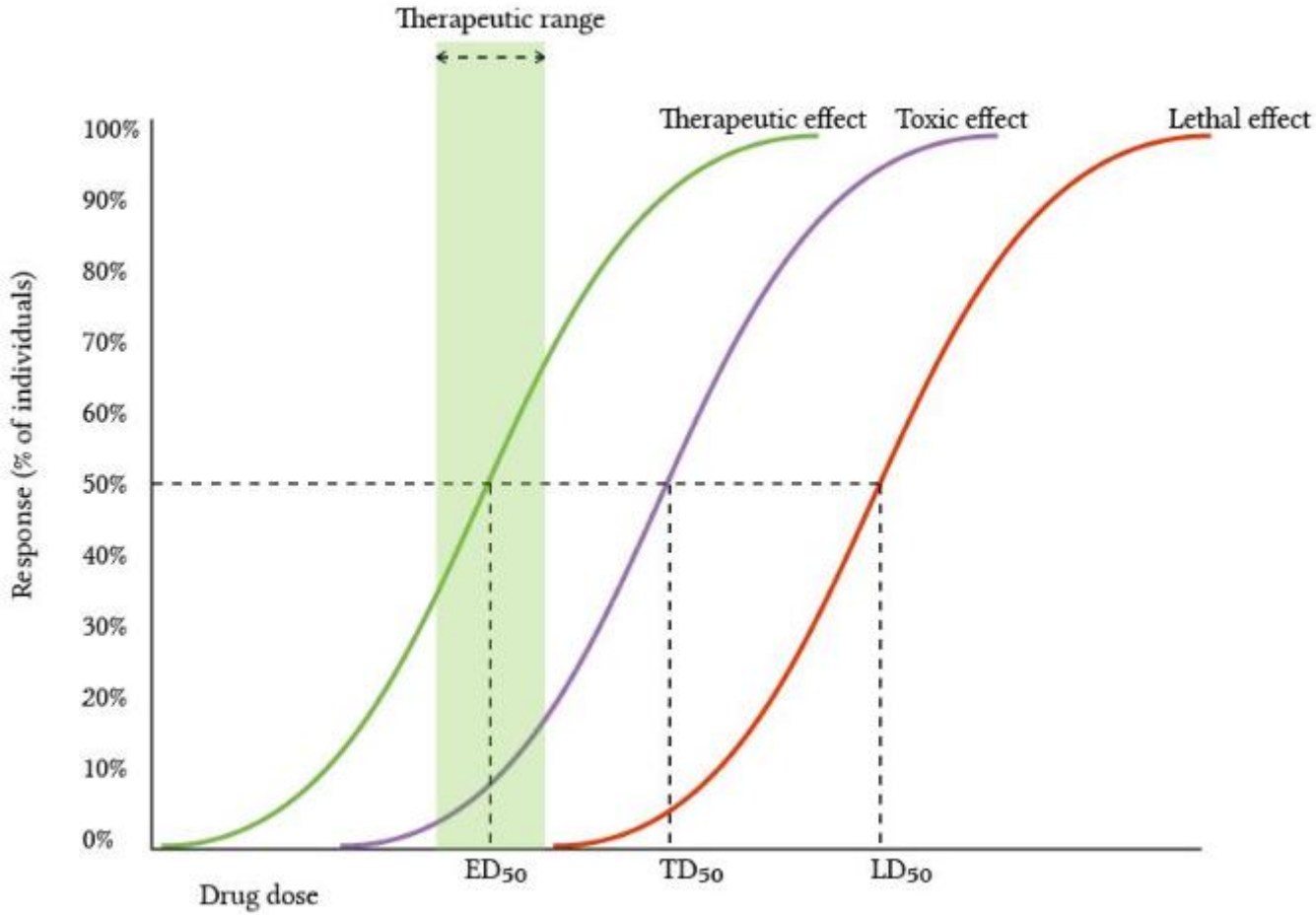
- *In quantal dose-response curves, the Katzung textbook defines ED_{50} as "the dose at which 50% of individuals exhibit the specified quantal effect"*
- The International Union of Pharmacology Committee on Receptor Nomenclature and Drug Classification (Neubig et al, 2003) give an "official" definition as *"the dose of a drug that produces, on average, a specified all-or-none response in 50% of a test population*" It is also sometimes abbreviated as the ED_{50}, meaning "effective dose for 50% of the population".
- The ED50 is commonly used as a measure of the reasonable expectancy of a drug effect, but does not necessarily represent the dose that a clinician might use.
- Ideally, the effective dose would be substantially less than either the toxic or lethal dose for a drug to be therapeutically relevant.

Median effective dose (ED_{50})

- **It depends entirely on the definition of the quantal response.** When studying an antibiotic, is the endpoint complete elimination of bacteria from the blood, or is it clinical resolution of infection, or is it the inhibition of bacterial growth? Reported ED_{50}s are therefore potentially completely different among published investigators.
- **It does not necessarily represent a clinically relevant dose**, which is the dose you actually prescribe. That might be higher or lower. For instance, when looking at cardiovascular mortality prevention as the end-point for quantal effect, one might discover that one is occasionally prescribing candesartan in doses which are 32 times the ED_{50} (Dimmitt et al, 2017).
- **It may not be the clinical outcome of interest.** To have 50% of one's patients anaesthetised would be a pretty low bar to clear. For this reason, some may prefer to use ED_{95} (effective dose for 95% of the population).

Median Lethal dose, LD_{50}

- This is the dose required to kill 50% of a test subject population. LD_{50} is identical in definition to TD_{50}, except the toxic effect is death.
- There are some problems with the usefulness of LD_{50} as a means of comparing drugs. For example:
- **Death may not represent a useful endpoint:** toxicity is a continuum, and functionally for the purposes of the clinician there is only a trivial practical distinction between the states of "dead from cocaine" and "almost dead from cocaine".
- **Pharmacokinetics change the LD_{50}:** the rapid administration of phenytoin may be fatal, whereas the same dose administered slowly may have no toxic effects whatsoever. Nonlinear pharmacokinetics (eg. where increasing the dose also increases or decreases the clearance) factors into this.
- As a measure of toxicity, LD_{50} is somewhat unreliable and results may vary greatly between testing facilities due to factors such as the genetic characteristics of the sample population, animal species tested, environmental factors and mode of administration.
- There can be wide variability between species as well; what is relatively safe for rats may very well be extremely toxic for humans (*cf.* paracetamol toxicity), and vice versa. For example, chocolate, comparatively harmless to humans, is known to be toxic to many animals. When used to test venom from venomous creatures, such as snakes, LD_{50} results may be misleading due to the physiological differences between mice, rats, and humans.


Therapeutic range
Therapeutic effect
Toxic effect
Lethal effect
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Response (% of individuals)
ED50
TD50
LD50
Drug dose

50% protective doses (PD_{50})

- A vaccine's potency is a measure of the number of protective doses (PD) in a vaccine estimated from the resistance to infectious virus challenge of animal groups immunized with different amounts of a vaccine.
- One 50% protective dose (PD50) represents the dose of vaccine that will protect 50% of vaccinated animals against clinical disease.
- The quantity of PD_{50} doses present in a standard dose is its PD_{50} value.
- A PD_{50} of greater than or equal to 3 is classed as acceptable for routine vaccination, while a PD_{50} of greater than or equal to 6 is suitable for emergency vaccination.