

- What is toxicology?

- **Definition:** the study of adverse effects of chemicals and physical agents on biological systems.
- Notice that drugs have the potential to act as poisons and each drug can be toxic in some individuals (especially those with liver or renal diseases) at some doses.
- **Occupational toxicology:** it is the study of toxicity which arises from exposure of workers to toxins in their work environment.
- **Environmental toxicology:** it is the study of toxicity which arises from exposure to pollutants.

- Toxicity is classified according to duration of exposure to the toxin:

- **Acute toxicity:** resulting from short-term exposure to a toxin at a sufficient dose to cause a toxic effect.
- **Chronic toxicity:** resulting from repeated exposure to a toxin over a prolonged period of time at a dose sufficient to cause toxicity.



- What is an adverse effect?

- **Definition:** it is a response to a drug which is noxious (ضار ومؤيد) and unwanted and which occurs at doses normally used for prophylaxis, diagnosis or treatment of a disease or for a modification of a physiologic function.
- “There is no difference between a medicine and a poison... It is the dose which determines this issue” – Paracelsus (Father of Toxicology).

- Classification of adverse effects (based on the cause):

- **Type-A (Augmented):** it is dose-dependent and there is an extension of the normal effect of a drug. For example, insulin normally lowers blood sugar level but in high doses it results in hypoglycemia and coma!
- **Type-B (Bizarre):** represented by allergic reactions which are unpredictable and dose-dependent. Example: allergic reaction to penicillin.
- **Type-C (Continuous):** for example, osteoporosis resulting from prolonged use of steroids.
- **Type-D (Delayed):** effect appears after a long time of stopping the drug.
- **Type-E (End of dose):** which means something happens when stopping the drug. For example, stopping steroids after a long time of using them results in acute adrenal crisis!

- Factors affecting toxicity of a drug:

- **Dose:** with increased dose, there is an increased risk in producing adverse effects.
- **Route:** IV route of administration has more potential in causing harmful effects to the body because the drug will be introduced very rapidly to the systemic circulation.
- **Age:** especially in extremes of age (newborns and elderly).
- **Individual characteristics** (such as genetic makeup).
- **Species.**
- **Gender.**
- **Health.**
- **Environment.**

- Therapeutic index (ratio):

- **In humans:** median toxic dose (TD₅₀) divided by the median effective dose (ED₅₀).

$$\checkmark \text{ Therapeutic index} = \frac{TD_{50}}{ED_{50}}$$

- **In animals:** median lethal dose (LD₅₀) divided by the median effective dose (ED₅₀).

$$\checkmark \text{ Therapeutic index} = \frac{LD_{50}}{ED_{50}}$$

- **Therapeutic index has to be higher than (1) for the drug to be considered as being safe:**

✓ A drug with high therapeutic index is safe (example: penicillin).

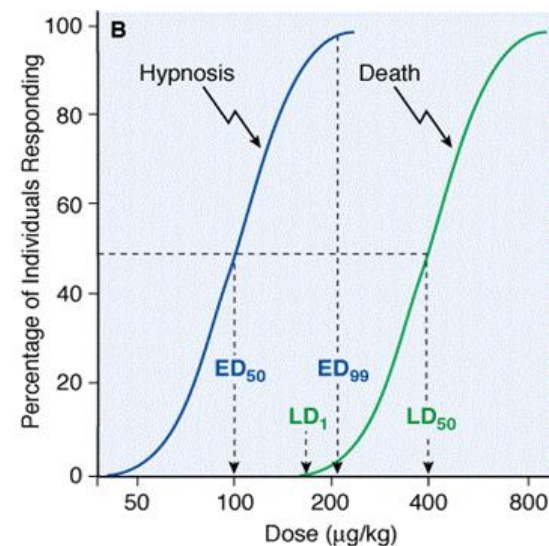
✓ A drug with low therapeutic index is dangerous (example: digoxin).

- Margin of safety:

- **Definition:** it is a measure of how close the lowest lethal dose is to the highest effective dose.
- It is mainly applied with humans because the median lethal dose cannot be calculated!
- **Margin of safety** = $\frac{LD_1 \text{ (lethal dose observed in one patient)}}{ED_{99}}$

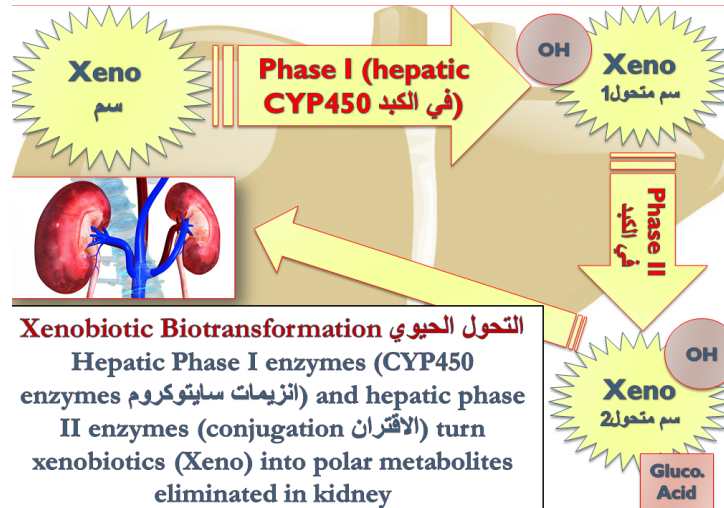
- Biotransformation of a drug (metabolism of a drug):

- **Biotransformation sites:** Liver, GIT, Lungs, skin, kidneys and brain.
- **Notice that the kidney is the main site for excretion.**





- **Why do we need biotransformation?**
 - ✓ Because polar, fully ionized drugs at physiologic pH are not reabsorbed while lipophilic unionized/partially ionized drugs at physiologic pH are reabsorbed.
- **Products of biotransformation may be:**
 - ✓ Inactive when compared to the original drug.
 - ✓ Less active than the original drug.
 - ✓ More active than the original drug:
 - ❖ This might be useful.
 - ❖ Or harmful!



- **What are prodrugs?**
 - ✓ They are pharmacologically inactive drugs which are converted to active molecules in the body through biotransformation.