

# **Toxicology**

**Introduction in the practical of toxicology**

**Lab. 1**

**4<sup>th</sup> stage**

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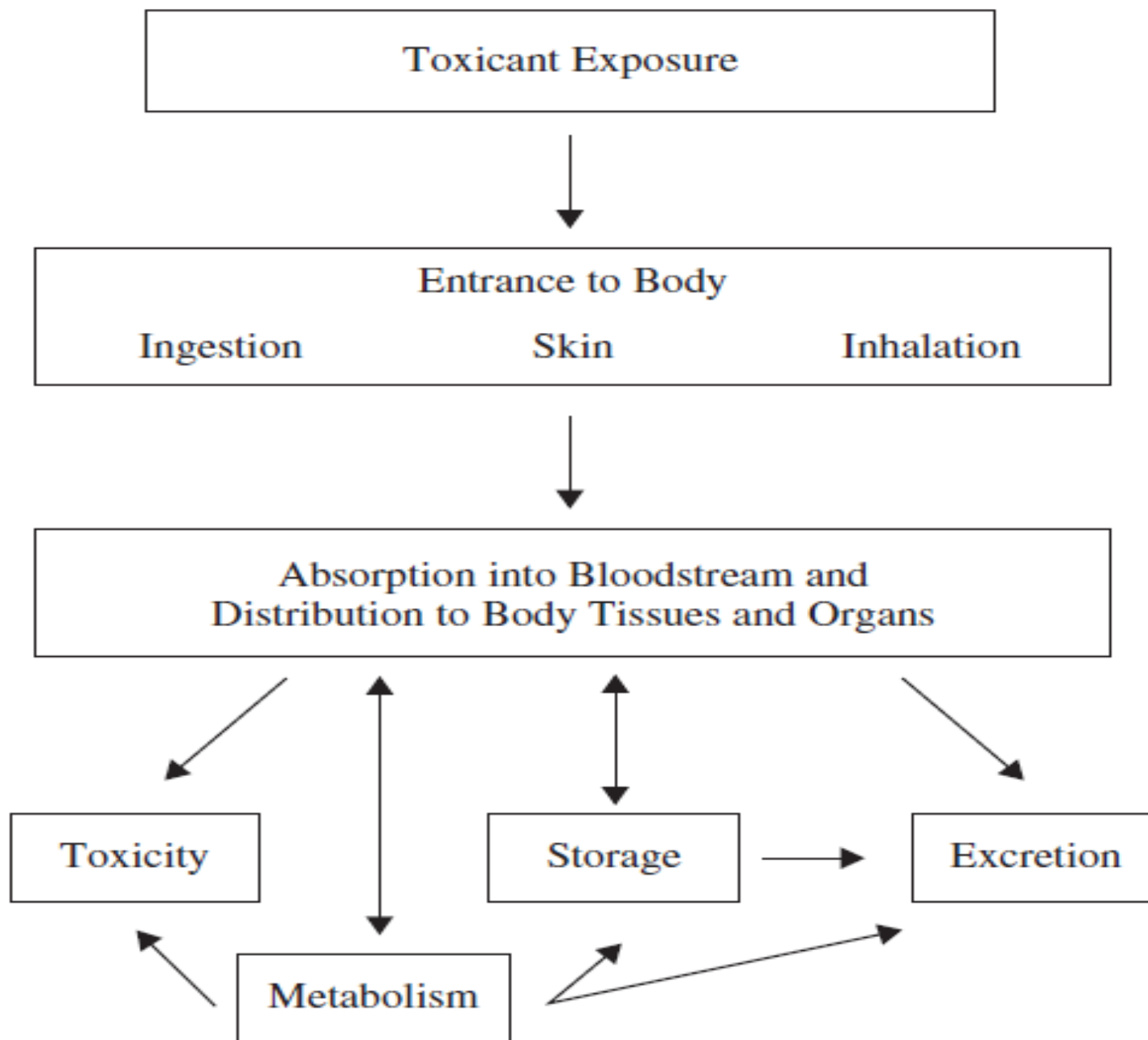
# Introduction to Toxicology

- **Toxicology** can be defined as that **branch** of science that **deals with poisons**.
- **poison** can be defined as **any substance** that causes a **harmful effect** when *administered*, **either** by **accident** or by **design**, to **a living organism**.
- By convention, toxicology also includes the study of harmful effects caused by **physical phenomena**, such as **radiation** of various kinds, **noise**, and so on.
- **Broader definitions of toxicology**, such as “ the study of the **detection**, **occurrence**, **properties**, **effects**, and **regulation of toxic substances**, ”

□ Toxicity is a cascade of events starting with:-

➤ exposure, proceeding through distribution and metabolism, and ending with interaction with cellular macromolecules (usually DNA or protein) and the expression of a toxic endpoint.

➤ This sequence may be mitigated by excretion and repair.



**Figure 1.1** Fate and effect of toxicants in the body.

# Poison

□ quantitative

□ qualitative

## □ quantitative

- almost **any substance** being **harmful at some doses** but, at the same time, being **without harmful effect** at **some lower dose**.
- Between these two limits, there is a range of **possible effects**, from subtle long – term chronic toxicity **to immediate lethality**.
- Vinyl chloride may be taken *as an example*:
  - It is a **potent hepatotoxicant** at high doses,
  - **a carcinogen** with a long latent period at lower doses,
  - and apparently **without effect** at very low doses.

➤ Clinical drugs are even more poignant examples because:-

▪ although therapeutic and highly beneficial at some doses, they are not without deleterious side effects and may be lethal at higher doses.

❖ Aspirin (acetylsalicylic acid), for example:

✓ is a relatively safe drug at recommended doses and is taken by millions of people worldwide.

✓ At the same time, chronic use can cause deleterious effects on the gastric mucosa,

✓ it is **fatal** at a dose of about 0.2 – 0.5 g/kg.

✓ Approximately 15% of reported accidental deaths from poisoning in children result from ingestion of salicylates, particularly aspirin.

➤ The **importance of dose** is well illustrated by **metals** that are **essential in the diet** **but** are **toxic** at higher doses.

• Thus, **iron, copper, magnesium, cobalt, manganese, and zinc**

✓ can be present in the diet **at too low** a level (**deficiency**),

✓ at an **appropriate** level (**maintenance**),

✓ or **at too high** a level (**toxic**).

# qualitative

□ a poison, or toxicant, also involves a qualitative biological aspect because:

➤ a compound, toxic to one species or genetic strain, may be relatively harmless to another.

➤ For example, carbon tetrachloride, a potent hepatotoxicant in many species, is relatively harmless to the chicken.

□ Compounds may be toxic under some circumstances **but not** others or, perhaps, **toxic in combination with another compound** **but nontoxic alone.**

✓ The **methylenedioxyphenyl insecticide synergists**, such as **piperonyl butoxide**, are of *low toxicity* to **both insects** and *mammals* when **administered alone**, **but** are, by virtue of their ability to **inhibit xenobiotic - metabolizing enzymes**, **capable of** causing dramatic increases in the toxicity **of other compounds.**

# measurement of toxicity

- The measurement of toxicity is also complex.
- Toxicity may be acute or chronic
- and may vary from one organ to another
- as well as with *age, genetics, gender, diet, physiological condition,* or the *health status of the organism.*

- As opposed to experimental animals, which are highly inbred, genetic variation is a most important factor in human toxicity since *the human population is highly outbred and shows extensive genetic variation.*
- Even the simplest measure of toxicity, the LD 50 (lethal dose ; the dose required to kill 50% of a population under stated conditions) is highly dependent on the extent to which the above variables are controlled.
- LD 50 values, as a result, vary markedly from one laboratory to another.

# Exposure

□ Exposure of humans and other organisms to toxicants

may result from many activities:

- intentional ingestion, occupational exposure, environmental exposure, as well as accidental and intentional (suicidal or homicidal) poisoning.

- ❖ The **toxicity** of a **particular compound** may vary with the portal of entry into the body, whether through the **alimentary canal**, the **lungs**, or the **skin**.
- ❖ **Experimental methods of administration** such as **injection** may also give highly variable results;
- the **toxicity from** intravenous (IV), intraperitoneal (IP), intramuscular (IM), or **subcutaneous (SC) injection** of a given compound may be quite different.

❖ **Thus**, toxicity may vary as much as 10 - fold with the route of administration.

❖ Following exposure, there are multiple possible routes of metabolism, both detoxifying and activating, and multiple possible toxic end points

# Factors affecting the toxicity of toxic agents:

1. The **concentration**, **duration** and **frequency** of **exposure**.
2. The **route** of *administration* of the **toxic agent**.
3. The **physical** and **chemical properties** of the **toxic agent**.
4. **Toxicokinetic** and **toxicodynamic** factors ( **absorption**, **distribution**, **metabolism**, **excretion**, and the **presence of other chemicals**).
5. Other **factors** such as: **age**, **sex** , **nutritional status** ....etc.