Toxicology

Introduction in the toxicology

Lec. 1

4th stage

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Principles of Toxicology

❖INTRODUCTION TO TOXICOLOGY

❑**Toxicology** is the study of the **adverse effects** of *chemical*, *biological,* or *physical agents* ***(toxicant)*** on **living organisms and the environment** **including** the **prevention** and **amelioration** of ***such adverse effects.***

❖ In more details

❑ ***Toxicology studies the <u>agents</u> responsible for:***

- ➢ adverse effects,
- ➢ the mechanisms involved,
- ➢ the damage that may ensue,
- ➢ testing methodologies to determine the extent of damage, and
- ➢ ways to avoid or repair it.

❑***Toxicology is traditionally associated with chemical exposures, such as:***

- *the effects of drugs,*
- *industrial chemicals,*
- *pesticides,*
- *food additives,*
- *household products, and*
- *personal care items.*

❑*In addition toxicology is concerned with **physical hazards**, such as radiation and noise.*

What is the toxic substance?

❑Toxic substances include:-

- ***Toxins*** it formally should be used to refer to toxic substances produced biologically.
- ***Xenobiotics*** is a term referring to substances, whether **toxic** or **not**, foreign to a given organism.

❖NOTE:-

- There are any number of other terms which could be used to delineate the broader category of substances which are toxic, regardless of origin.
- **Examples are** *toxicant*, *toxic agent*, and *toxic substance*.

❖Toxins are poisons that originate from:

- ➢plants and
- ➢microbial organisms
- ➢and also include venoms released by animals in order to injure predators.

❖Example

- **Aflatoxin** is a toxin produced and released from the fungus ***Aspergillus*** that grows on ***foods*** such as **corn** and **nuts**.
- Exposure to aflatoxin is associated with an increased risk of **liver cancer**.

❖Toxicant (Poison)

- any **agent** capable of producing a **deleterious response** in a **biological system.**

❖Adverse effects

- any change from an organism’s normal state.

Goal of The study toxicology

❖ ***The study of toxicology serves society in many ways:***

not only to **protect** **humans** and the **environment** from the **deleterious effects**

of toxicants, **BUT** also to facilitate the **development** of **more selective**

toxicants **such as** **anticancer** and **other** **clinical drugs**, **pesticides**, **and** **so forth**.

What is a Poison?

All substances are poisons;

there is none that is not a poison.

The right dose

differentiates a poison and a remedy.

Paracelsus (1493-1541)

“the dose makes the poison.”

Solely the **dose** determines that a thing is **not** a **poison**

So Toxicology is the study of:

- How toxicants **enter** the organism
- How toxicants **effect** the organism
- How toxicants are **eliminated** from (leave) the organism

❖ *All substances are* ***toxic*** *if taken in the* ***wrong quantities***

❖ How toxicants enter organism?

- **Inhalation** (*mouth* or *nose* to *lungs*) then into **blood.**
- **Ingestion** (*mouth* to *stomach*) then into **blood.**
- **Injection** (*cuts, punctures* in *skin*) into **blood.**
- **Dermal absorption** (*through skin*) into **blood.**

❑Typical Effectiveness of Route of Exposure:

iv > inhale > ip > im > ingest > topical

❖ How toxicants effect the organism?

A. **Irreversible Effects**

B. **May or may not be reversible**

A- Irreversible Effects

- Carcinogen - *causes cancer*
- Mutagen - *causes chromosome damage*
- Reproductive hazard - *damage to reproductive system*
- Teratogen - *causes birth defects*

B- May or may not be reversible

- Dermatotoxic – affects skin
- Hemotoxic – affects blood
- Hepatotoxic – affects liver
- Nephrotoxic – affects kidneys
- Neurotoxic – affects nervous system
- Pulmonotoxic – affects lungs

❖ Elimination of toxins

- **Excretion** through kidneys, liver and lungs.

- **Detoxification** is the biotransformation of chemicals into something less harmful.

- **Storage** in fatty tissue.

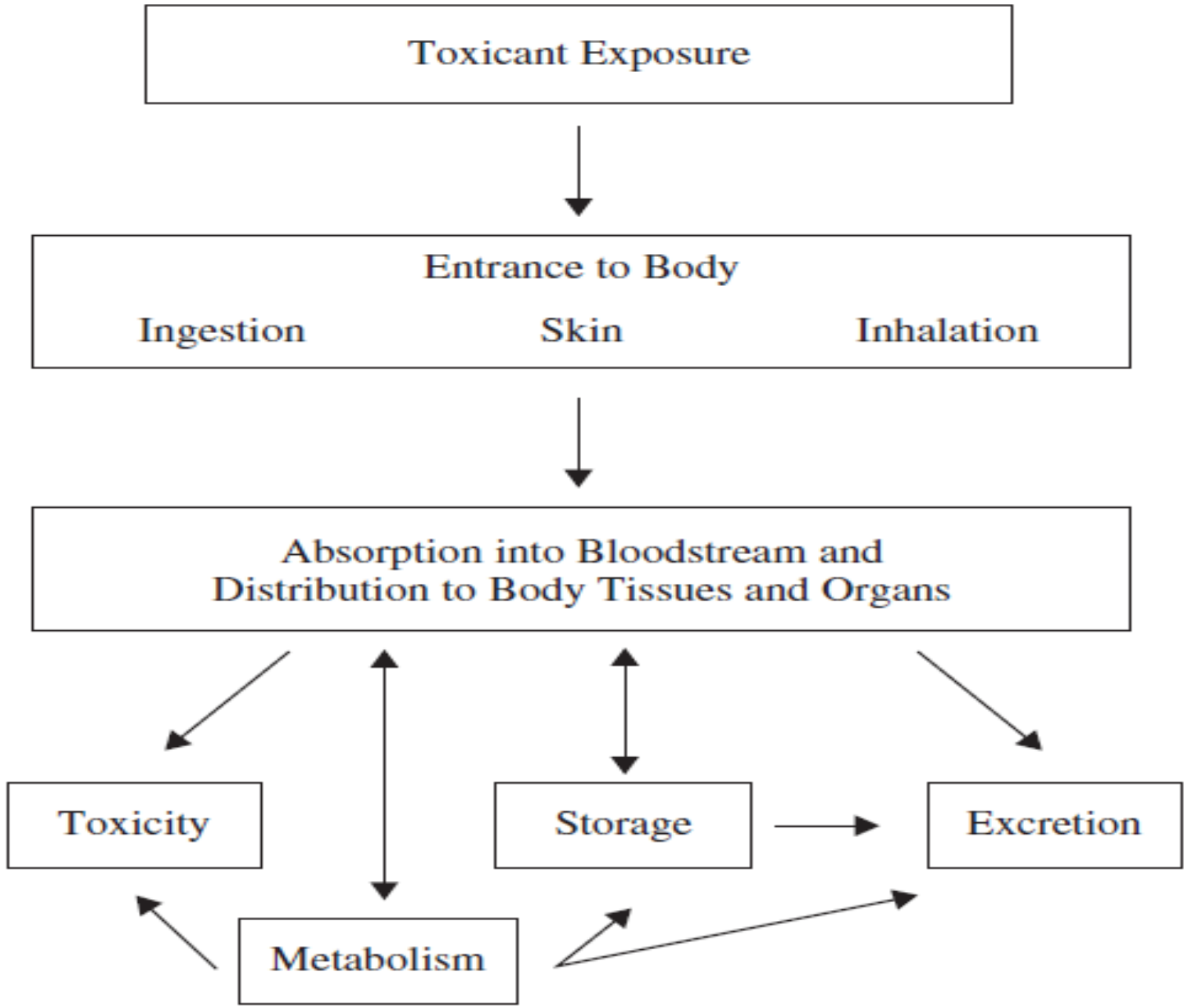

Figure 1.1 Fate and effect of toxicants in the body.

Difficulties in Toxicological Studies

- Major Problem:

  - **No** ethical way to get human volunteers, hence need to use

    "model" systems of rats, cats, dogs, rabbits, etc.

EXPOSURE

❖CHARACTERISTICS OF EXPOSURE:

- **Toxicity** to a biological system **requires** that **sufficient concentrations** of the "active" form of a chemical accumulate at the site of action for a **requisite period of time**.
- Many **chemicals** possess relatively **low toxicity** in their "native" form **but**, when acted on by **enzymes in the body**, are converted to intermediate forms that **interfere** with normal cellular biochemistry and physiology.

❖**Major factors that influence toxicity as it relates to the exposure situation for a specific chemical are:-**

1) Route and Site of Exposure

2) Duration and Frequency of Exposure

1) Route and Site of Exposure

❖The major routes for entry of toxic chemicals into the body are:

I. the **gastrointestinal** tract (ingestion)

II. the **lungs** (inhalation),

III. and the **skin** (topical, percutaneous, or dermal).

- **Chemicals** generally produce the *greatest effect* and the *most rapid response* when given directly into the bloodstream (the intravenous route).
- Typical Effectiveness of Route of Exposure:

  iv > inhale > ip > im > ingest > topical

➢ **The route** of administration can **influence the toxicity** of chemicals.

- **For example**:

- a chemical that acts on the **CNS**, but is efficiently detoxified in the liver, would be **expected to be less toxic** when *given orally* than when given *via inhalation*, **because** the oral route requires that nearly all of the dose pass through the liver before reaching the systemic circulation and then the CNS.

2) Duration and Frequency of Exposure

- The duration and frequency for exposure of experimental animals to chemicals is classified according to four categories:

I. **acute**,

II. **subacute,**

III. **subchronic**,

IV. **and chronic**

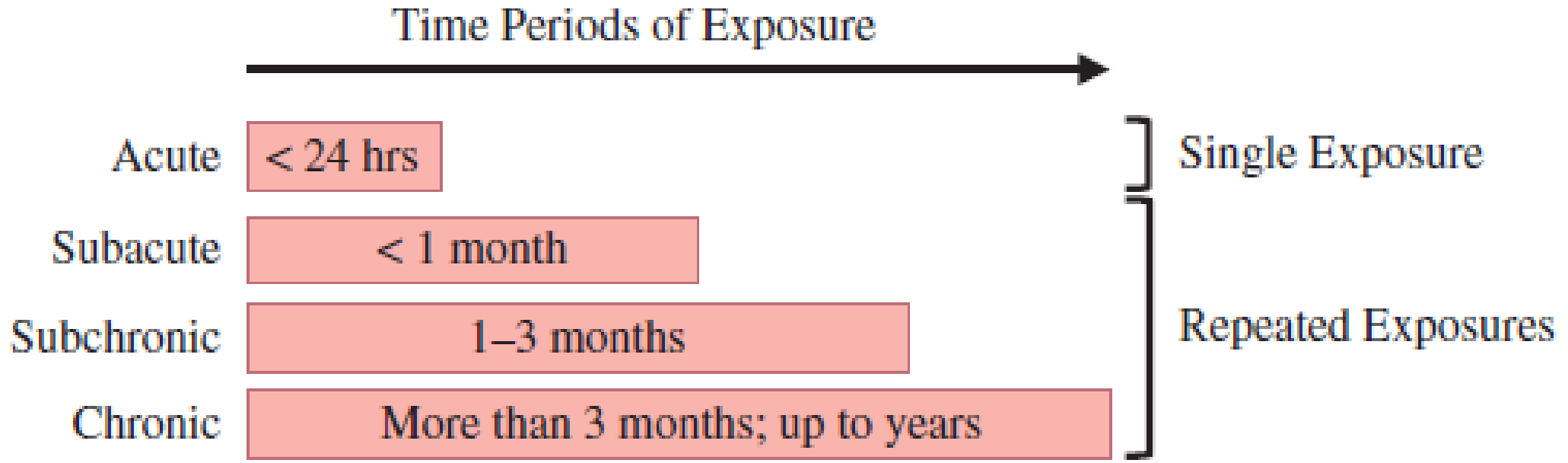

Figure 2-3. *Time periods of chemical exposure.* Single exposures to chemical are observed in acute studies of short duration. Repeated exposures to chemicals can occur over a range of time periods spanning short (subacute), intermediary (subchronic), and long periods (chronic).

❖ For many chemicals, the toxic effects that follow a single exposure are quite different from those produced by repeated exposure.

➢ **For example:**

- The primary, **acute toxic** manifestation of **benzene** is **CNS depression**, **but** **repeated exposures** can result in **bone marrow** toxicity and an increased risk for **leukemia.**

SPECTRUM OF UNDESIRED EFFECTS

- The spectrum of **undesired effects** elicited by chemicals can be broad.
- Some effects are harmful, whereas others are not.
- Prescription drugs produce a **number** of effects.
- but **typically** only **one** of these **actions** is intended to be **therapeutic**.
- And **all** of the other **responses** are referred to **as side effects**.
- **However**, **some** of these side effects may be **preferred** for **another therapeutic indication.**

❖For example:

- the drug ***sildenafil*** was originally developed to **reduce blood pressure** in patients.
- During the **clinical studies** of *sildenafil in hypertensive patients*, **male subjects** reported ***sustained erections*** as a **side effect**.
- **So**, the company subsequently **gained approval** of ***sildenafil*** for the **treatment** of **erectile dysfunction** under the brand name **Viagra®**

❖Some **side effects** of drugs are **never desirable** and are always **harmful** to the well-being of **animals** and **humans**.

❖These are referred to as the ***adverse***, ***deleterious***, or ***toxic*** effects of the **drug**.

Reference

Casarett and Doull's

TOXICOLOGY

The Basic Science of Poisons

Ninth Edition


Thank You