

# TOXICOLOGY

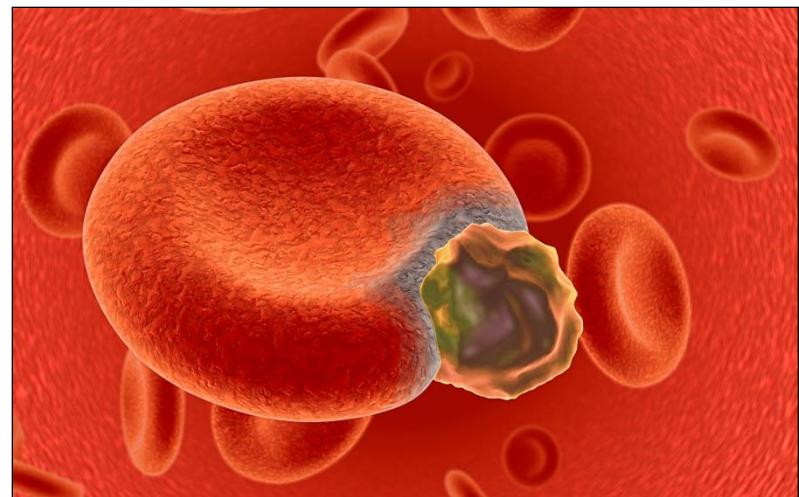
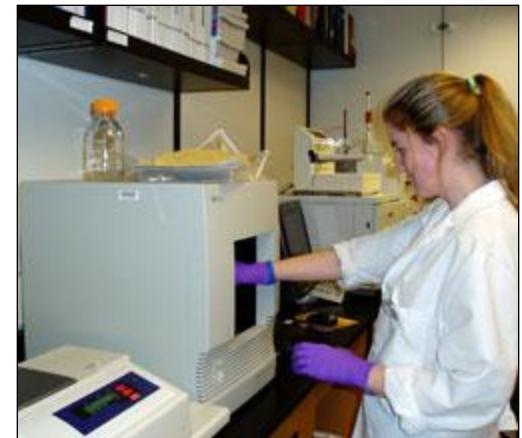


Paracelsus (1493-1541)  
**'Father of Toxicology'**

"All chemicals are poison and nothing is without poison, only the dose permits something not to be poisonous."

# What is Toxicology?

- Toxicology helps create a safer world
- Definition: The study of the negative effects of chemical and physical agents on living organisms
- Modern toxicology uses chemicals as tools to understand molecular/cellular biology



# INTRODUCTION

- Toxicology can be defined as, “the study of the adverse effects of chemicals or physical agents on living organisms”.
- **All substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy.**

# Environmental Health Paradigm

## *Exposure Assessment*

Emission Sources       $\leftrightarrow$       Environmental  
Concentrations

## *Effects Assessment*

Internal Dose       $\leftrightarrow$       Human Exposure

$\uparrow\downarrow$

Health Effects

# TOXICOLOGY TERMINOLOGY

- **Toxic:** This term majorly related to a chemical which is poisonous or have deadly effects on the body by inhalation (breathing), ingestion (eating), or absorption, or by direct contact with a chemical.
- **Toxicant:** A toxicant (toxic substance) is anything that can produce an adverse biological effect. It may be chemical, physical, or biological in form. For example cyanide (chemical), radiation (physical) and snake venom (biological) represent various forms of toxic substances

- **Toxin:** toxic substances produced naturally.
- A toxin is any poisonous substance of microbial, vegetable or synthetic chemical origin that reacts with specific cellular components to kill cells, alter growth or development or kill the organisms.
- **Toxicity:** The word “toxicity” describes the degree to which a substance is poisonous or can cause injury.

# **TYPES OF TOXIC EFFECTS**

- **Lethal effect**
- **Sub-lethal effect**
- **Acute effect**
- **Chronic effect**
- **Local effect**
- **Systemic effect**
- **Cumulative poisons**
- **Synergistic effect**

Toxic effects can be :

- **Lethal** : resulting in the death of individuals
- **Sub-lethal**: effects not directly resulting in death
- **Acute effect**: characterized by sudden and severe exposure and rapid absorption of the substance. An acute exposure occurs over a very short period of time, usually 24 hours.

**Examples:** carbon monoxide or cyanide poisoning.

- **Chronic effect** : characterized by prolonged or repeated exposures of a long duration. It occurs over long periods of time such as weeks, months or years.

**Examples:** lead or mercury poisoning.

- **Local effect:** an adverse health effect that takes place at the point or area of contact (skin, the respiratory tract, eyes etc.).

**Examples:** strong acids or alkalis.

- **Systemic effect** : an adverse health effect that takes place at a location distant from the body's initial point of contact.

**Examples:** arsenic affects the blood, nervous system, liver, kidneys and skin; benzene affects bone marrow.

- **Cumulative poisons**: characterized by those chemicals that tend to build up in the body as a result of numerous chronic exposures. The effects are not seen until adverse health effect takes place.

**Example:** heavy metals.

- **Synergistic effect:** When two or more hazardous materials are present at the same time, the resulting effect can be greater than the effect predicted based on the additive effect of the individual substances. This is also called a potentiating effect.

**Example:** (i) exposure to alcohol and chlorinated solvents (ii) simultaneous exposure to smoking and asbestos.

- **Dose:** The most important factor that influences the toxic effect of a specific chemical is the dose.
- The dose is the actual amount of a chemical that enters the body.
- The dose received may be due to either **acute** (short) or **chronic** (long-term) exposure.
- The amount of exposure and the type of toxin will determine the toxic effect.
- This is important because for each chemical, a certain dose produces certain biological effects in the individual organism.

**Response:** Any biological effect caused by the exposure is called the *response*. Typically, as the dose of a toxic substance goes up, increasing numbers of organisms die or show signs of impaired health.

**Xenobiotic:** Xenobiotic is the general term that is used for a *foreign* substance taken into the body. It is derived from the Greek term *xeno* which means “*foreigner*.” Hence, xenobiotic is a chemical which is found in an organism but which is not normally produced or expected to be present in it. Xenobiotics may produce beneficial effects (*such as a pharmaceuticals*) or they may be toxic (*such as lead*).

- **Target organ:** An organ that is damaged by the xenobiotic or its metabolism.
- **Selective toxicity:** refers to species differences in toxicity between two species simultaneously exposed. “Selective toxicity” means that a chemical will produce injury to one kind of living matter without harming another form of life, even though the two may exist close together.

## Examples are:

- an **insecticide** is lethal to insects but relatively nontoxic to animals
- **Antibiotics** are selectively toxic to microorganisms while virtually nontoxic to humans
- **Sensitivity:** People vary widely in their sensitivity to the effects of a chemical. Many things determine how an individual will react to a chemical. These include age, sex, inherited traits, diet, pregnancy, state of health and use of medication, drugs or alcohol.

# Routes of Exposure

- Toxins enter the body by several routes:

## Ingestion

- to exert a systemic effect, they must be absorbed into circulation
- most are absorbed by passive diffusion
- If not absorbed they may produce local effects, such as diarrhea, bleeding or mal-absorption of nutrients
- The gastrointestinal (GI) tract, which protects the inner body from contaminants (toxins) that have been ingested

## Inhalation

- The membranes within the lungs, which protect the inner body from contaminants that have been inhaled.

## Transdermal absorption

- The skin, which protects the body from contaminants outside the body

Before toxicity can develop, a substance must come into contact with a body surface such as skin, mucosa of the digestive or respiratory tract.

# DOSE-RESPONSE RELATIONSHIPS

- All chemicals, including essential substances such as oxygen and water, produce toxic effects when taken in large doses.
- **Dose is a very significant factor in toxicology.** The statement “the dose makes the poison” aptly describes the role of the dose .

For example,

- The caffeine in a normal human diet does not cause illness, but just 50 times this amount could kill you.
- Oxalic acid in spinach is harmless in amounts we normally eat, but could lead to kidney damage if 5 to 10 kg were consumed at single sitting.

# Dose-response

- Dose-response is a relationship between exposure and health effect, that can be established by measuring the response relative to an increasing dose.
- The dose-response relationship is based on observed data from experimental animal, human clinical, or cell studies.

## What is a dose?

- Dose is the amount of a substance administered at one time.
- Dosage is the amount per unit weight of the exposed individual.
- Exposure is characterized by
  - Number of doses
  - Frequency of dosing
  - The total period of time for the exposure .

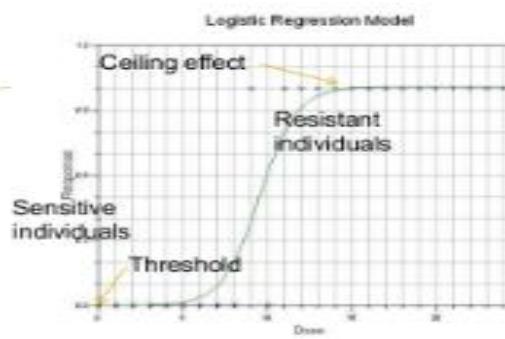
## Dose-response curve

The cumulative curve is used to show data

Y-axis: Response % (lethality, toxic response, effective drug dose)

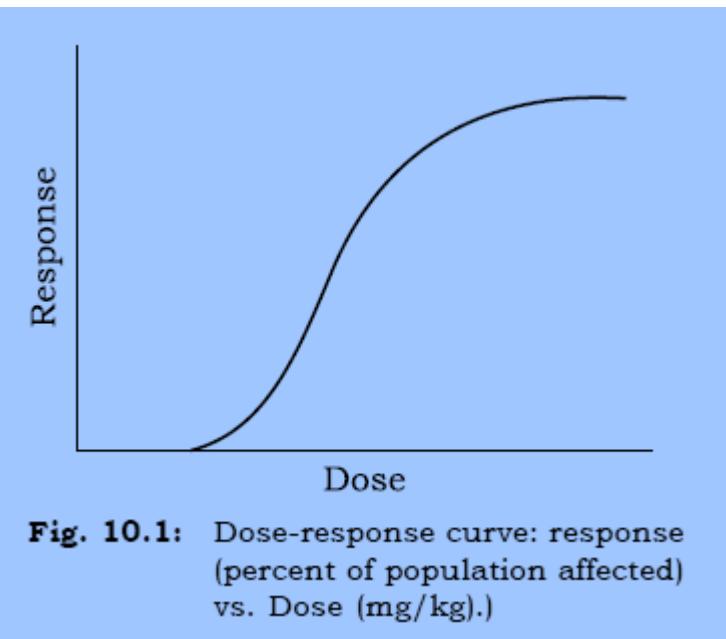
X-axis: Dose (mg) Dose may be on a linear or a log scale  
No response below threshold

Ceiling effect: no difference once all individuals are affected

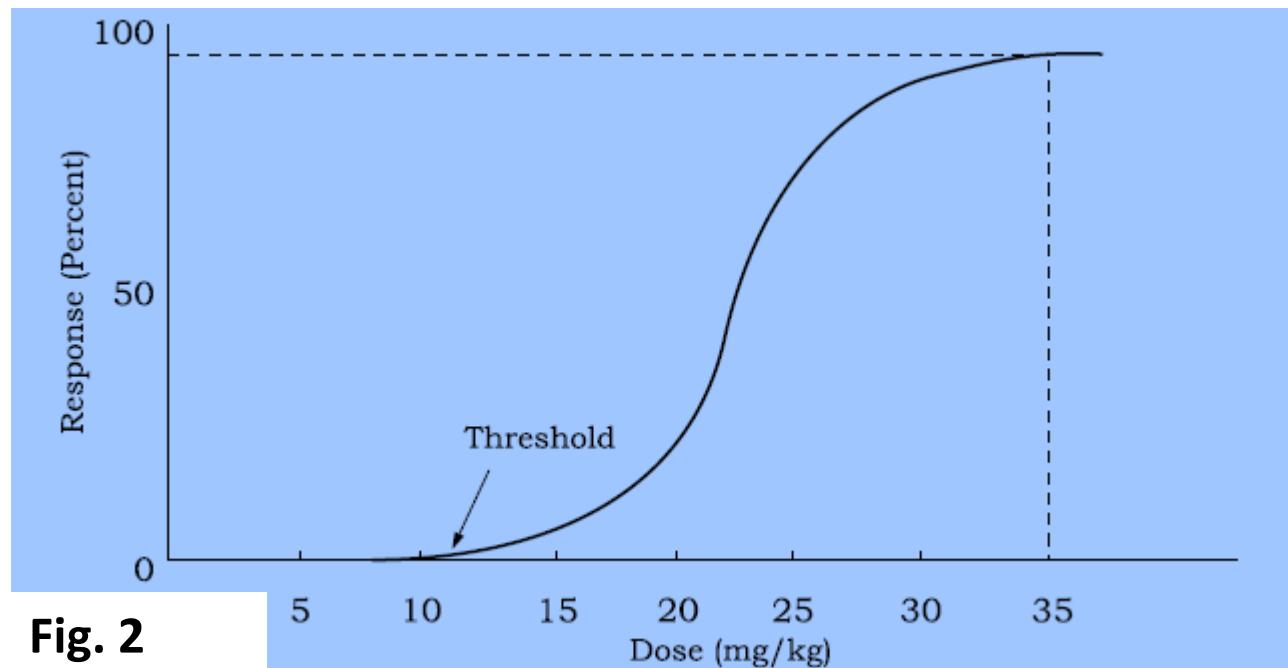


- The measured dose (usually in milligrams, micrograms, or grams per kilogram of body-weight) is generally plotted on the X axis and the response is plotted on the Y axis.
- It is the logarithm of the dose that is plotted on the X axis, and in such cases the curve is typically **graded** or **sigmoidal** with the steepest portion in the middle.
- For most types of toxic responses, there is a dose, called a **threshold**, below which there are no adverse effects from exposure to the substance.

In Fig 2, no toxicity occurs at 10 mg whereas at 35 mg 100% of the individuals experience toxic effects.



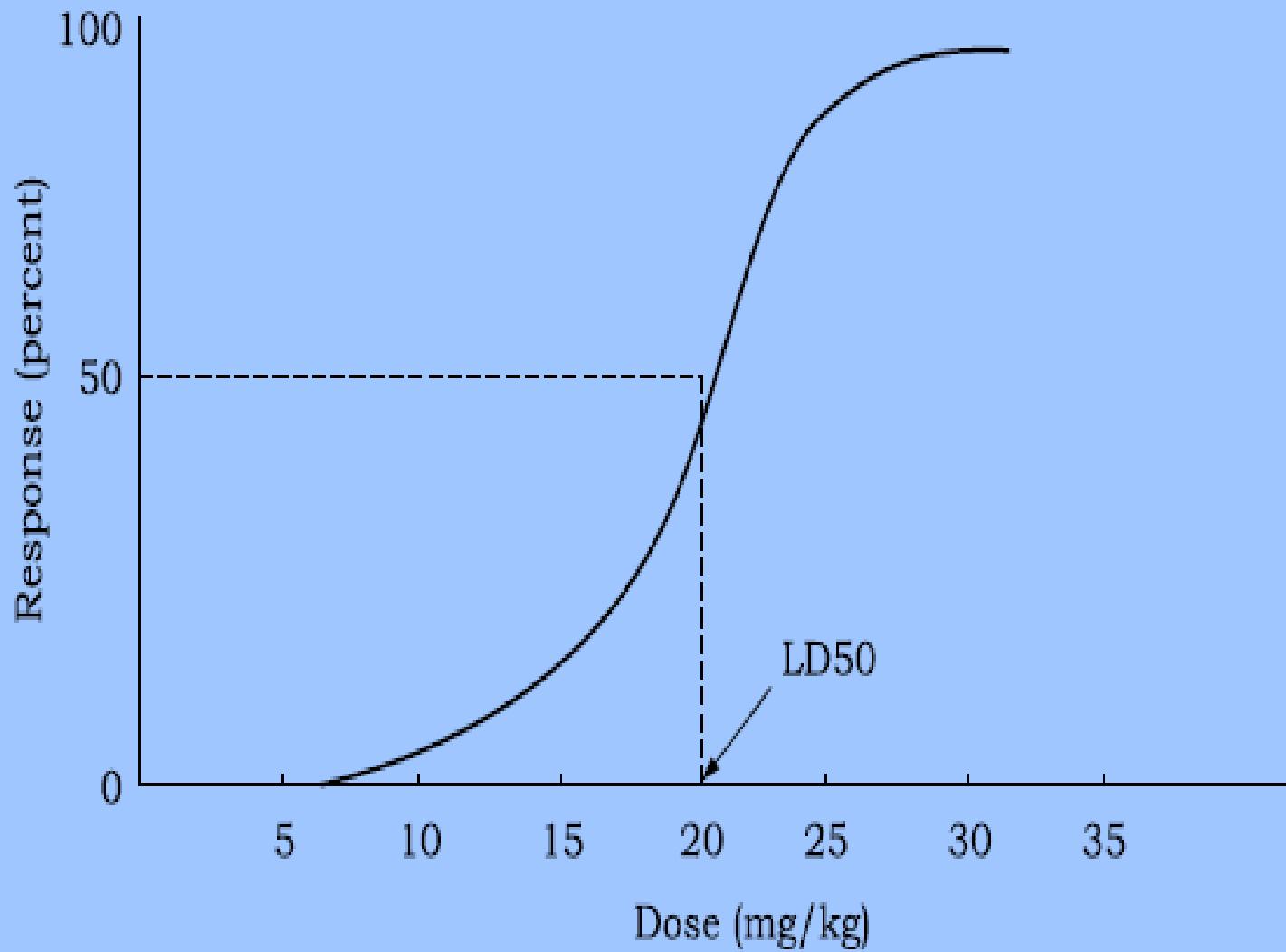
**Fig. 10.1:** Dose-response curve: response (percent of population affected) vs. Dose (mg/kg.).



**Fig. 2**

# Dose-response curve and Toxic Effects

- Dose-response curves are used to derive dose estimates of chemical substances.
- A common dose estimated for acute toxicity is the LD50 (Lethal Dose 50%). This is a statistically derived dose at which 50% of the individuals will be expected to die.
- LD0 represents the dose at which no individuals are expected to die. This is just below the threshold for lethality. LD10 refers to the dose at which 10% of the individuals will die.



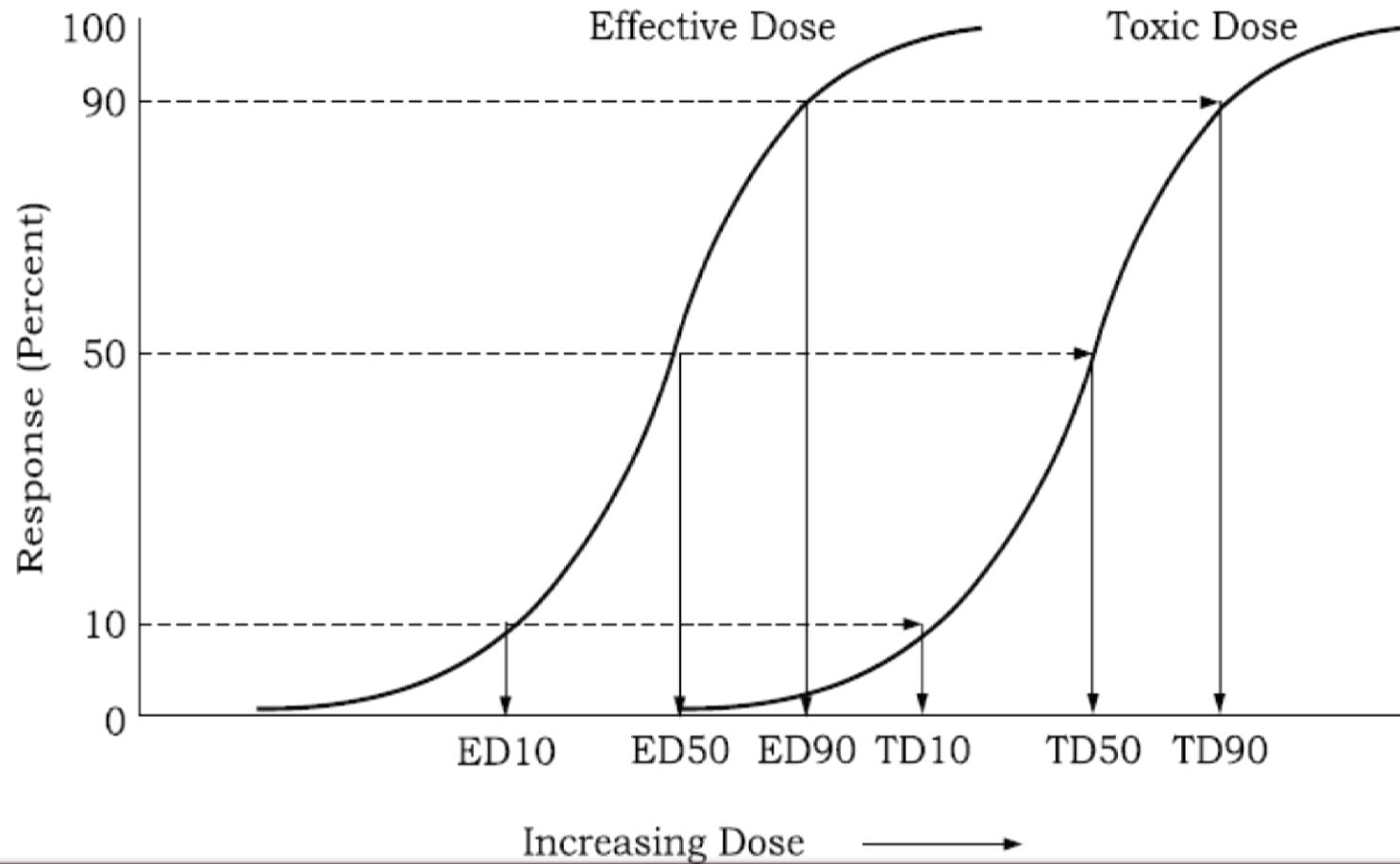
**Fig.3:** showing amount of dose (20mg/kg) of LD50 at response 50%

- For inhalation toxicity, air concentrations are used for exposure values. Thus, the LC50 is utilized which stands for **Lethal Concentration** 50%, the calculated concentration of a gas lethal to 50% of a group.
- Occasionally LC0 and LC10 are also used.
- **Effective Doses** (EDs) are used to indicate the effectiveness of a substance. Normally, effective dose refers to a beneficial effect (relief of pain). It might also stand for a harmful effect (paralysis). Thus the specific endpoint must be indicated.

ED0	effective for 0% of the population
ED10	effective for 10% of the population
ED50	effective for 50% of the population
ED90	effective for 90% of the population

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

TD0	toxic to 0% of the population
TD10	toxic to 10% of the population
TD50	toxic to 50% of the population
TD90	toxic to 90% of the population



**Relation between Effective dose (ED) and Toxic dose (TD)**

- **TD50 (toxic dose)**: The dose required to elicit a defined toxic effect (e.g. fatty liver, fever, etc.) in 50% of the sample population .
- TD50 is used to indicate responses such as reduced enzyme activity, loss of hearing, nausea etc, whereas
- **ED50 (Effective Dose )**: Generally used for drugs - the dose required to have a therapeutic or other effect in 50% of sample population.
- ED50 of Paracetamol would be the dose that relieves high temperature of the body in 50% of the people.
- **LD50 (lethal dose)**: The dose required for lethality in 50% of the sample population.
- LD95 is used for insecticides and pesticides so that 95% of the insect population dies. For human health, chemicals having LD0 are used so that no one dies.

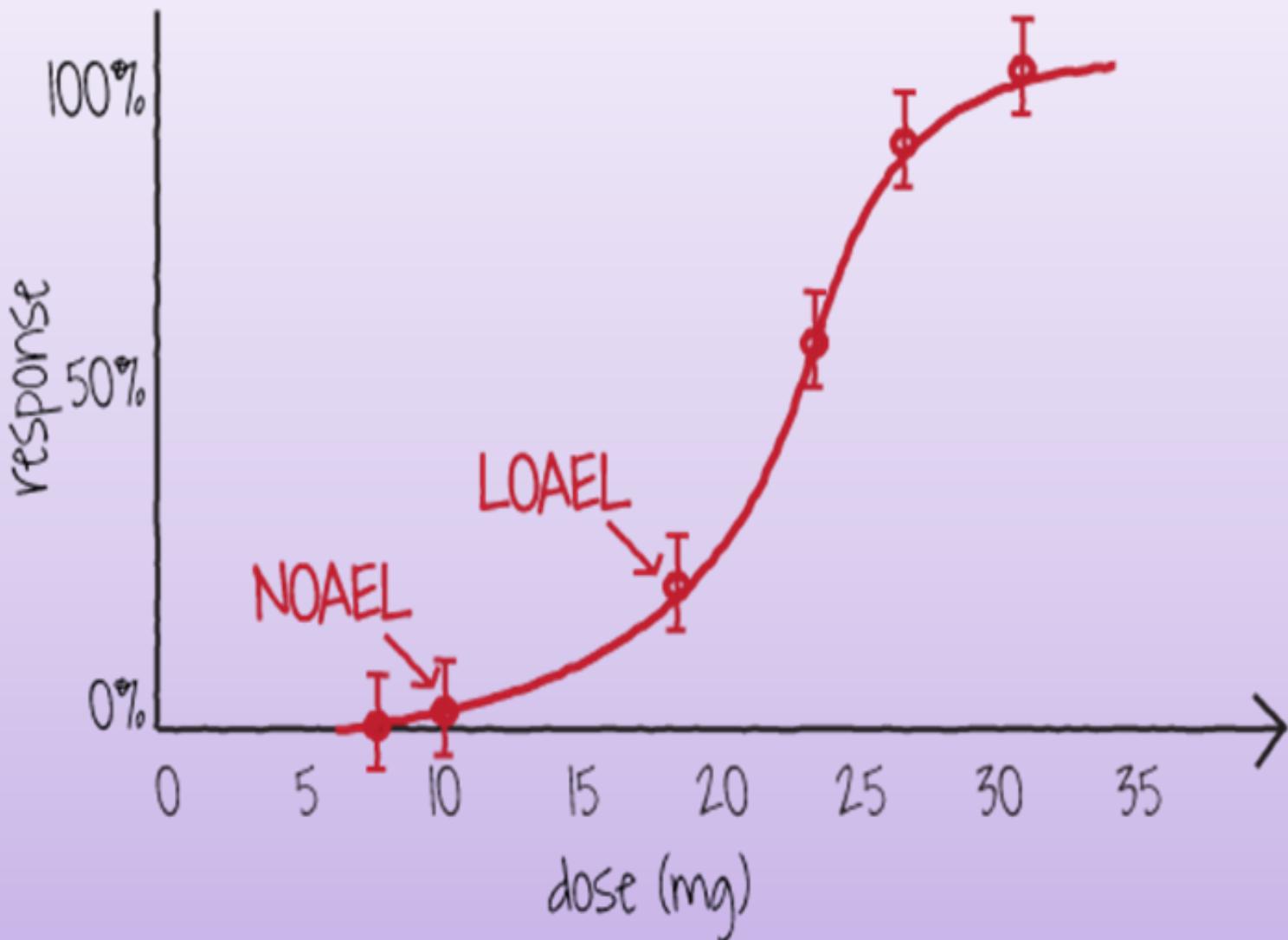
# Some examples at different doses

<i>Substance</i>	<i>Non-Toxic or Beneficial Dose</i>	<i>Toxic Dose</i>	<i>Lethal Dose</i>
<b>Alcohol</b> <i>Ethanol Blood Levels</i>	0.05%	0.1%	0.5%
<b>Carbon Monoxide</b> <i>%Hemoglobin Bound</i>	<10%	20–30%	>60%
<b>Secobarbital</b> ( <i>sleep aid</i> ) <i>Blood Levels</i>	0.1 mg/dL	0.7 mg/dL	> 1 mg/dL
<b>Aspirin</b>	0.65 gm (2 tablets)	9.75 gm (30 tablets)	34 gm (105 tablets)
<b>Ibuprofin</b> <i>E.G., Advil &amp; Motrin</i>	400 mg (2 tablets)	1,400 mg (7 tablets)	12,000 mg (60 tablets)

# NOAEL and LOAEL

- No Observed Adverse Effect Level (NOAEL)
- Low Observed Adverse Effect Level (LOAEL)
- They are the actual data points from human clinical or experimental animal studies.

NOAEL	<b>Highest data point</b> at which there <i>was not</i> an observed toxic or adverse effect
LOAEL	<b>Lowest data point</b> at which there <i>was</i> an observed toxic or adverse effect



# CHEMICAL INTERACTIONS

- The effect that one chemical has on the toxic effect of another chemical is known as an **interaction**.
- Humans are normally exposed to several chemicals at one time rather than to an individual chemical.

**Some common examples are:**

- drinking water may contain small amounts of pesticides, heavy metals, solvents, and other organic chemicals
- air often contains mixtures of hundreds of chemicals such as automobile exhaust and cigarette smoke
- home influenza treatment consists of aspirin, antihistamines, and cough syrup taken simultaneously
- gasoline vapour at service stations is a mixture of 40-50 chemicals

# Types of Interactions

- The four basic types of interactions are:

<b>additivity</b>	a combination of two or more chemicals is the sum of the expected individual responses
<b>antagonism</b>	exposure to one chemical results in a reduction in the effect of the other chemical
<b>potentiation</b>	exposure to one chemical results in the other chemical producing an effect greater than if given alone
<b>synergism</b>	exposure to one chemical causes a dramatic increase in the effect of another chemical

- **Additivity** : Two central nervous system (CNS) depressants taken at the same time, a tranquilizer and alcohol, often cause depression equal to the sum of that caused by each drug.
- **Antagonism** is often a desirable effect in toxicology and is the basis for most antidotes.
- Examples : (i) swallowed poison is absorbed by introducing charcoal in the stomach
- (ii)Vitamin A and E reduce the effect of carcinogens in body
- **Potentiation** occurs when a chemical that does not have a specific toxic effect makes another chemical more toxic.
- Examples: (i) The hepatotoxicity of carbon tetrachloride is greatly enhanced by the presence of isopropanol. Such exposure may occur in the workplace.
- Rise in pH from 7 to 8 in aquatic ecosystem can increase toxicity of ammonia by 200% in fish.
- **Synergism** can have serious health effects. With synergism, exposure to a chemical may drastically increase the effect of another chemical.
- Example: Exposure to both cigarette smoke and asbestos results in a significantly greater risk for lung cancer than the sum of the risks of each.

# DAMAGES CAUSED BY THE TOXIC MATERIALS

- Toxicity is complex with many influencing factors; **dosage is the most important**. Xenobiotics cause many types of toxicity by a variety of mechanisms. Others must be metabolized (***chemically changed within the body***) before they cause toxicity.
- Many xenobiotics distribute in the body and often affect only specific **target organs**. Others, however, can **damage any cell or tissue that they contact**. The target organs that are affected may vary depending on dosage and route of exposure.
- For example, the target for a chemical after acute exposure may be the nervous system, but after the chronic exposure to the liver.

Toxicity can result from adverse cellular, biochemical, or macromolecular changes. Examples are:

- cell replacement, such as fibrosis
- damage to an enzyme system
- disruption of protein synthesis
- production of reactive chemicals in cells
- DNA damage

*Based on the above factors ,there are four basic types of damage caused by toxic materials:*

- **Physiological damage:** reversible/irreversible damage to the health of the organism.
- **Carcinogenesis:** induction of cancer
- **Mutagenesis:** induction of genetic damage / mutation(s)
- **Teratogenesis:** induction of birth defects

# TOXIC CHEMICALS IN THE ENVIRONMENT

- 1. *Outdoor Air Pollutants***
- 2. *Heavy Metals***
- 3. *Radiation and Radioactive Materials***
- 4. *Polychlorinated Biphenyls (PCBs),  
Polyaromatic Hydrocarbons (PAHs) and  
Volatile Organic Compounds (VOCs)***
- 5. *Pesticides***

# ***Heavy Metals***

- The **essential minerals**, such as Zn, Fe, Cu, Mn and Mg are required for normal growth and survival, while other metals such as Cd, Pb and Hg are only harmful to living systems.
- Heavy metals are everywhere in nature as components of the earth's crust. Plants can absorb and accumulate metals, which may be toxic. Industrial development has resulted in exposure to heavy metals in people because of increased production of by-products such as Cd, Hg, Cr and Zn.

# **IMPACT OF TOXIC METALS ON ENZYMES**

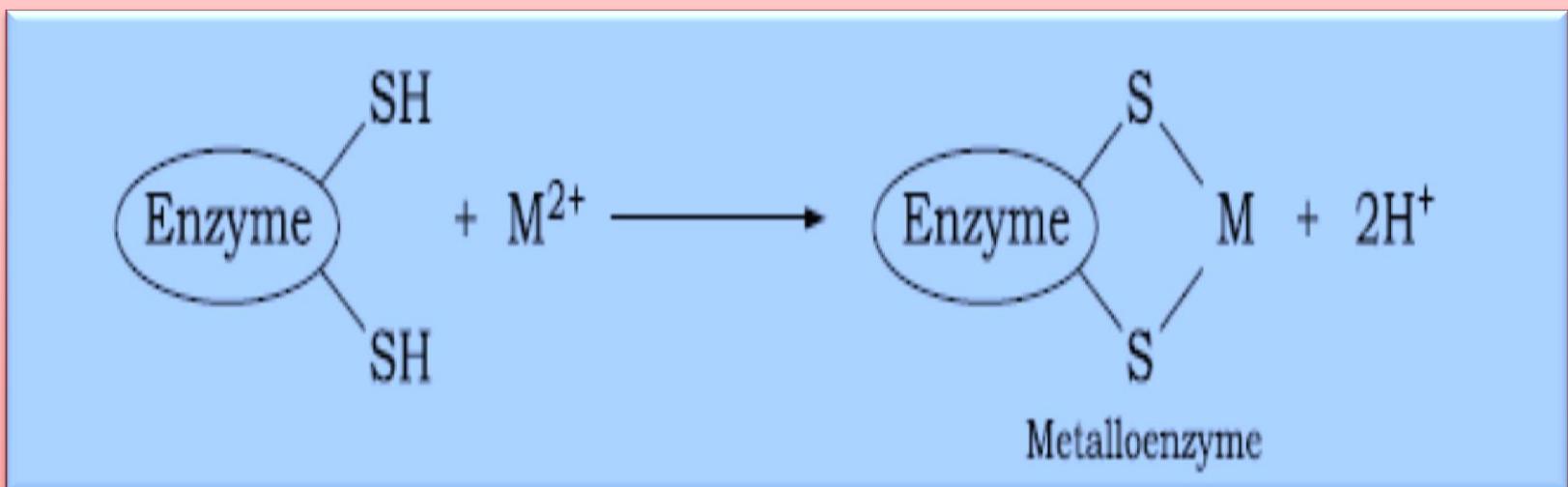
An enzyme is a large protein molecule that contains one or more active sites where interaction with the substrate takes place.

Toxic chemicals generally produce their toxicity by:

- **By forming complexes with the active sites on the enzymes.** The modified enzymes loose their ability to function properly, which leads to the malfunction or death of the affected cells. **Metals commonly bind to biological compounds containing oxygen, sulphur and nitrogen, which may inactivate certain enzyme systems or affect protein structure .**
- Sometimes, **light toxic metals may compete with or replace similar metals**, eg., Li competes with similar metal Na.
- In acute poisoning, **large excesses of metal ions can cause disruption of membrane and mitochondrial function in the cells and the generation of free radicals**

These steps can be illustrated by taking the example of heavy metals as toxic substance:

- Heavy metals are electrophilic and react with nucleophilic groups on proteins (enzymes) in the body. These nucleophilic groups are: – SH, – NH<sub>2</sub>, – CONH, –PO<sub>4</sub>



- As a result of binding to these groups on proteins, the heavy metal may compete with endogenous metals, e.g.  $\text{Ca}^{2+}$  or  $\text{Zn}^{2+}$  which also rely on binding to these proteins via the same groups.
- Heavy metal binding may lead to **disruption of enzyme function** e.g. **Pb interferes with haem biosynthesis** by inhibition of 8 aminolevulinic acid dehydratase (ALAD). This results in a reduction in plasma ALAD activity and an increase in plasma aminolevulinic acid.

# Arsenic

- It exists as As (0), As (III) and As (V)
- As (III) or arsenites are more toxic as compared to As (V) such as arsenates, due to greater cellular uptake.
- As (0) is considered non poisonous due to its insolubility in water and body fluids.
- Moreover inorganic As is generally more toxic than organic As.
- Decreasing toxicity (most to least): arsines, inorganic arsenites, organic arsenoxides, inorganic arsenates, arsenorganics with As valency +5 and metallic As.

## SOURCES:

1. *Natural* : ores- as arsenopyrite
2. *Commercial products*: Wood preservatives, insecticides, fungicides, paints and pigments.
3. *Industrial processes*: by-product of smelting process for metal ores-Pb, Au, Zn, Co, Ni. Burning fossil fuels.
4. *Electronic industry*: AsH<sub>3</sub> (Arsine gas) is used in microelectronics industry.
5. Gallium arsenide is used in microwave devices, lasers and light emitting diodes, semiconductor devices.
6. Volcanoes release 3000 tonnes per year and microorganisms release methylarsines ~ 20,000 tonnes per year.

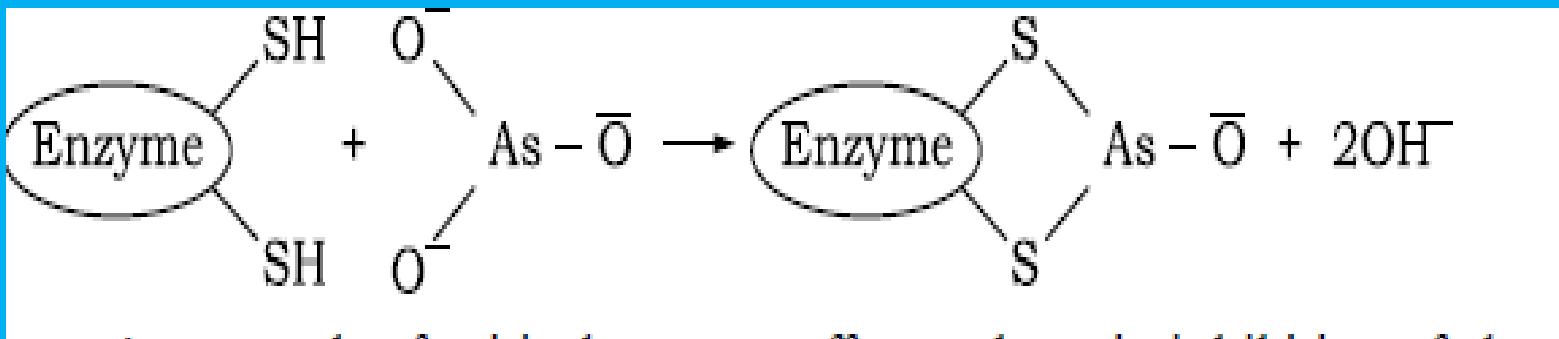
Although it is deadly poison but essential trace element with necessary intake as low as 0.01 mg/day.

## HEALTH EFFECTS:

1. ***Neurologic effects***: chronic effects lead to poisoning of nervous system, liver damage and results in gangrene of lower limbs. This condition is known as **black foot disease**.
2. ***Skin and lung cancer*** results from chronic exposure.
3. ***Renal effects***: leading to acute renal failure.
4. ***Cardiovascular effects***: May cause both diffusive capillary leak and cardiomyopathy resulting in shock.
5. ***Respiratory effects***: produces irritation of respiratory mucosa.
6. ***Reproductive effects***: Infertility and miscarriages.
7. ***Gastrointestinal***: irritation of stomach and intestines

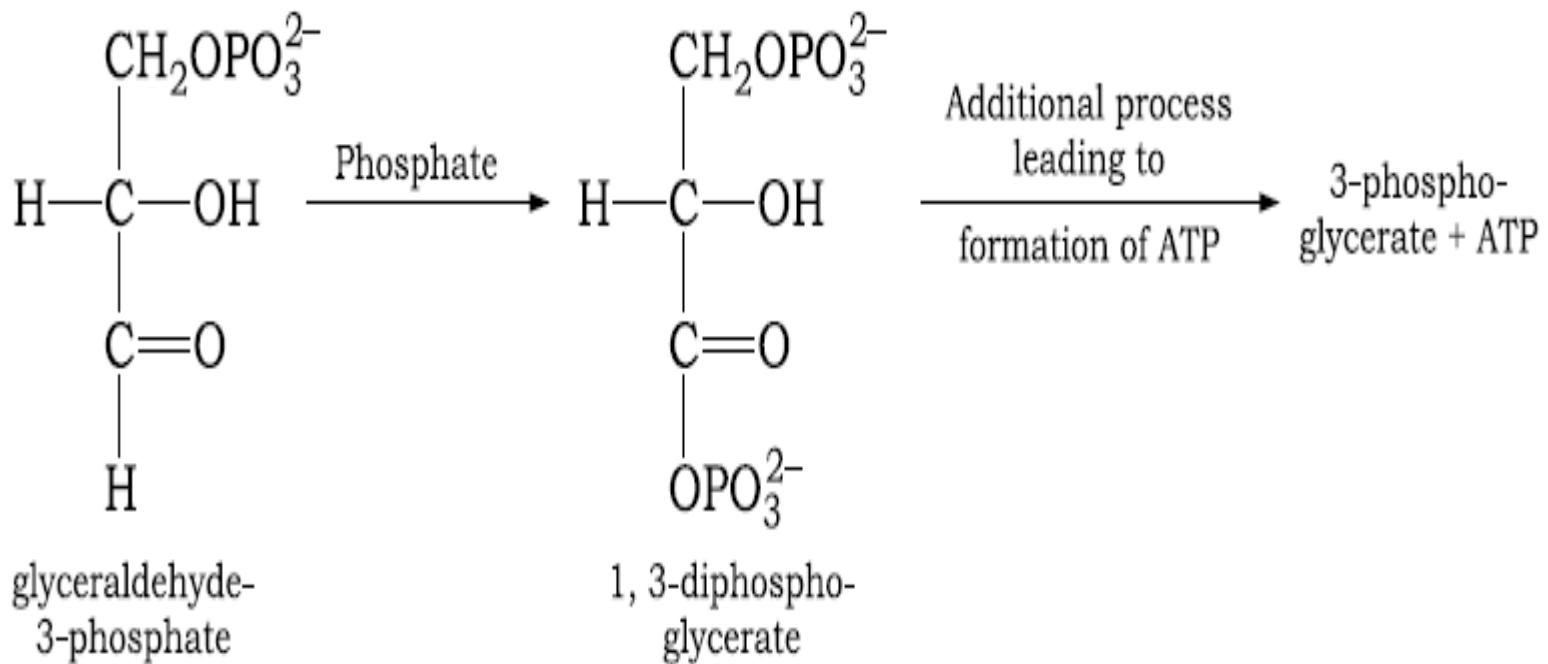
## BIOCHEMICAL EFFECTS:

- **Complexation with co-enzyme-** As (III) readily combines with –SH groups.

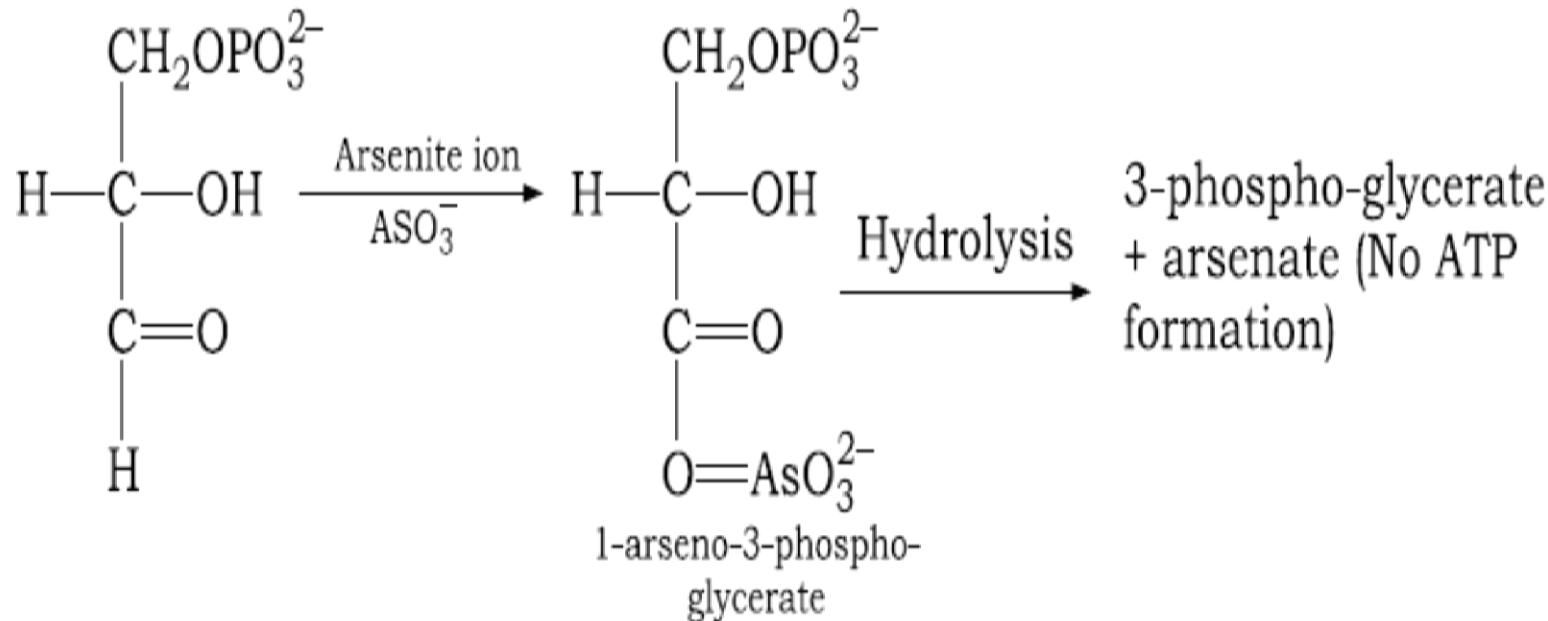


There is inhibition of pyruvate and succinate oxidative cycles leading to inhibition of ATP which is an important energy source. These are essential metabolic activities of cell respiration.

- **Uncoupling of phosphorylation:** As (V) replaces phosphorous in many biochemical reactions because of its chemical similarity. This leads to loss of high energy phosphate bonds and affects ATP formation. This is known as **arsenolysis**.



## Formation of ATP (Phosphorylation)



- As (V) substitutes phosphorus in biochemical reactions by virtue of its chemical similarity, leading to loss of high-energy phosphate bonds and effectively “uncouples” oxidative phosphorylation
- Arsenolysis takes place

- **Coagulation of proteins:** As (III) coagulates proteins by attacking sulphur bonds.
- **Arsine gas poisoning:** It rapidly fixes to RBCs producing irreversible cell membrane damage. It causes anaemia due to haemolysis.

# Mercury

- It is the third most toxic substance in the environment. It occurs naturally in the environment and exists in several forms: metallic mercury (elemental Hg), inorganic and organic mercury.

## SOURCES:

1. **Forms of mercury:** metallic Hg, mercuric sulphide (cinnabar ore), mercuric chloride and methyl mercury.
2. **Electronics and electrical industry:** Hg is used to produce vapour lamps, thermometers, fluorescent tubes and electrical products. Spills from these damaged articles may result in exposure to Hg vapours in indoor air.
3. **In medicine:** used in dental amalgams and various antiseptics agents.
4. **Chemical industry:** determination of nitrogen by kjeldahl method, cathode in electrolysis.

5. Hg may be released into air from biomass, fossil fuel burning.  
Air borne Hg is highly toxic when inhaled. Metallic Hg slowly evaporates when exposed to air.
6. Inorganic salts of Hg are used in skin lightening creams.
7. Hg on entering bodies of water, transforms to methyl mercury due to biological processes. Methyl mercury is highly toxic and bio-accumulative in nature.
8. Exposure: Mercury poisoning results from vapour inhalation, ingestion, injection or absorption through skin.

## **HEALTH EFFECTS:**

1. Organic Hg primarily affects the brain. Methyl Hg accumulates in central nervous system and may result in neurotoxic effects in adults.
2. Metallic Hg is slowly absorbed by the gastrointestinal system and is not as toxic as methyl mercury.
3. Inorganic Hg salts affect kidneys.

## BIOCHEMICAL EFFECTS:

- Hg has strong affinity for S. It interferes with enzymes function and protein synthesis by binding to sulfohydryl or thiol groups.
- The biochemical toxicology of Hg depends on the chemical form and entrance route into the body.

### Elemental Hg:

- Found in liquid form, easily vaporises at room temperature and is well absorbed through inhalation. From lungs it dissolves in blood plasma and from there it has access to diffuse into any cell in body.
- Once inside any cell in the body, Hg vapour itself unreactive, is oxidised to highly toxic  $\text{Hg}^{+2}$  ion. This oxidation process is mediated by **enzyme catalase**. This keeps most inhaled Hg vapour from reaching the brain.
- However, some elemental Hg vapour does reach the brain and there it is oxidised to  $\text{Hg}^{2+}$ . This divalent Hg leads to strange systems including **erethism (mad hatters disease)**, **tremors**, **gingivitis and excitability**.
- Elemental Hg is not well absorbed by the GI tract and therefore when ingested is only mildly toxic.

## Inorganic Hg:

- Found mostly in salt form is highly toxic and corrosive. It gains access in the body orally or dermally and accumulates mostly in kidney causing renal damage.
- In GI tract, acute poisoning produces a sloughing away of the mucosa to an extent that pieces of intestinal mucosa can be found in stools, producing loss of fluids and electrolytes.

## Organic Hg:

- Highly lipophilic (fat loving-high affinity for fat tissues), thus absorbed more completely in the GI tract. Alkyl organic Hg is distributed uniformly in the body accumulating in brain, kidney, liver, hair and skin.
- Mono methyl mercury is 100-1000 times more toxic than elemental Hg to humans. It affects the nervous system causing tremors, violent muscle spasms and death in extreme cases.

## Case study on Minamata Bay Episode

# Chromium

- Chromium is present in environment as: Cr (0), Cr (III) and Cr (VI).
- **Cr (III) occurs naturally in the environment and is an essential nutrient required by the human body to promote action of insulin in body tissues so that sugar, protein and fat can be used by the body.**
- **Cr (VI) is very toxic.** Cr (VI) and Cr (0) are generally produced by industrial processes.

## SOURCES:

- Naturally occurs in rocks, animals, plants, soil etc. Also in fruits, vegetables, meat and grains.
- Metallic Cr (0) is used mainly for making steel and other alloys.
- The naturally occurring mineral chromite in the Cr(III) form is used as brick-lining for high temperature industrial furnaces, for making metals and alloys and chemical compounds.
- Waste from electroplating can discharge Cr (VI).
- In air, Cr compounds are present as fine dust particles.

## **ROUTES OF EXPOSURE:**

- Cr (III) occurs mainly in fresh vegetables, fruit, meat, yeast and grain.
- Acidic foods in contact with stainless steel cans or cooking utensils might contain higher levels of Cr because of leaching.

## **HEALTH EFFECTS:**

- Cr (III) is an essential nutrient that helps the body to use sugar, protein and fat. An intake of 50-200 µg/day is recommended for adults.
- Without Cr (III) in diet, the body loses its ability to use sugars, proteins and fat properly, which might result in weight loss or decreased growth, improper function of nervous and diabetic like condition. Thus Cr (III) compounds are used as dieting supplements.
- Cr (VI) in general is toxic and breathing high levels ( $>2 \mu\text{g}/\text{m}^3$ ) such as in chromic acid or Cr (VI) trioxide, can cause irritation of nose, such as runny nose, sneezing, itching, nosebleeds, ulcers and holes in the nasal septum.

## BIOCHEMICAL EFFECTS:

- Cr is an essential trace element known to enhance the action of insulin, a hormone critical to the metabolism and storage of carbohydrates, fat and protein in the body.
- Cr (VI) is absorbed more easily by the body than Cr (III), but once inside the body Cr (VI) changes to Cr (III). It is distributed to various tissues of body, but most concentrates in kidney, muscle and liver.
- The **principal carrier protein for Cr is transferrin**, which also plays a critical role in movement of Cr from blood to low-molecular weight Cr (LMWCr) binding substance which is composed of glycine, cysteine, glutamic acid and aspartic acid. LMWCr then participates in insulin metabolism.
- Cr then passes through the kidneys and is eliminated in the urine in few days.

# Lead

- Found naturally in the Earth's crust.
- It is never found naturally as metal and is usually combined with two or more elements to form compounds.

## SOURCES:

- Found in Earth's crust and thus enters food and water supply.
- Used in manufacture of batteries, plastics, china and ceramic glass and paint products.
- Petrol- as tetraethyl lead.
- Used in plumbing. Lead pipes are used in water distribution system
- Paints- it is used as pigment and drying agent in primers, paints and enamels, inks, oils, resins and other surface coatings.

## **ROUTES OF EXPOSURE:**

- Through ingestion and inhalation. Total intake is about 225 µg/day out of which 200 µg/day excreted through urine while the rest is stored in bones.

## **HEALTH EFFECTS:**

- Pb poisoning includes lowered IQ, behaviour problem, mental retardation, kidney disease, heart disease, stroke and death.
- Symptoms of Pb poisoning include pain, numbness, muscular weakness, headache, abdominal pain, memory loss, weight loss, vomiting, irritability and anaemia.
- Lead at high concentration can cause convulsions, coma and death.

## BIOCHEMICAL EFFECTS:

Lead interacts with biological electron donor groups, such as sulphydryl groups and interferes with the multitude of enzymatic processes.

### Effects on Haematological system-

The major biochemical effect of Pb is on heme synthesis (the oxygen carrying component of haemoglobin).

- Pb is absorbed into blood plasma and finally accumulates in soft and hard tissues.
- In blood 95-99% Pb is sequestered in red cells, where it binds to haemoglobin and other components. This causes anaemia.

### Effects on Neurological system-

- It affects Central Nervous System (CNS) and alters the function of cellular calcium and inactivates the blood-brain barrier.
- This causes brain edema, which affects all parts of CNS and causes headaches, clumsiness, vertigo, coma, mortality etc.

## **Effects on Renal system-**

- Lead nephropathy (kidney damage) develops because of inhibitory effect of Pb on cellular respiration. Long-term heavy exposure may result in irreversible nephropathy.
- It affects reproductive system causing infertility in men and miscarriages and still births in women.
- In children, Pb impairs release of human growth hormone and insulin growth factor and interferes with skeletal calcium and cyclic AMP (adenosine monophosphate) functions, leading to abnormalities in bone growth.