Classification of Poisons

- **Based on their toxic effects in the body as:**
- ✓ Poisons which cause death by anoxia
  - Poisons which make hemoglobin incapable of transporting oxygen e.g. Carbon monoxide, nitrites
  - Poisons which inhibit cellular respiratory enzymes e.g. Cyanides
  - Poisons which destroy haemopoietic organs e.g. Radioactive substances
- ✓ Poisons, which on contact cause irritation or corrosiveness of the organs (skin) or damage the organ through which they are excreted (GI tract, respiratory tract, urinary tract) e.g. Irritant gases, alkaline corrosives, corrosive inorganic acids, corrosive organic acids and heavy metals
- ✓ Poisons, which damage protoplasm or parenchyma. These poisons produce local irritation and after absorption cause damage to the cells and capillaries e.g. Phosphorus and carbon tetrachloride
- ✓ Poisons, which affect the nerve cells and fibers e.g. Hypnotics, narcotics, anesthetics, alcohol, some alkaloids and glycosides
- **Based on their chemical and physical nature as;** organic poisons, inorganic poisons, gaseous poisons, nitrogenous and non-notrogenous organic poisons etc.
- **Based on their behavior during separation procedures as;** volatile poisons, non-volatile organic poisons isolated by solvent extraction, metallic poisons and miscellaneous poisons.
- **Based on their origin** as plant poisons, toxins, venoms etc.
- **Based on their use** as antimicrobials, anticoccidials, anthelmintic, anesthetics etc.
- **Based on the source** as naturally occurring and man-made

Guidelines for the classification of poisons based on the dose

Extremely toxic	<1mg/kg
Highly toxic	1-50 mg/kg
Moderately toxic	50-500 mg/kg
Slightly toxic	0.5-5 g/kg
Practically non-toxic	5-15 g/kg
Relatively harmless	> 15 g/kg

Acute Lethal Dose of Certain Compounds

- The acute lethal dose some compounds are furnished below.

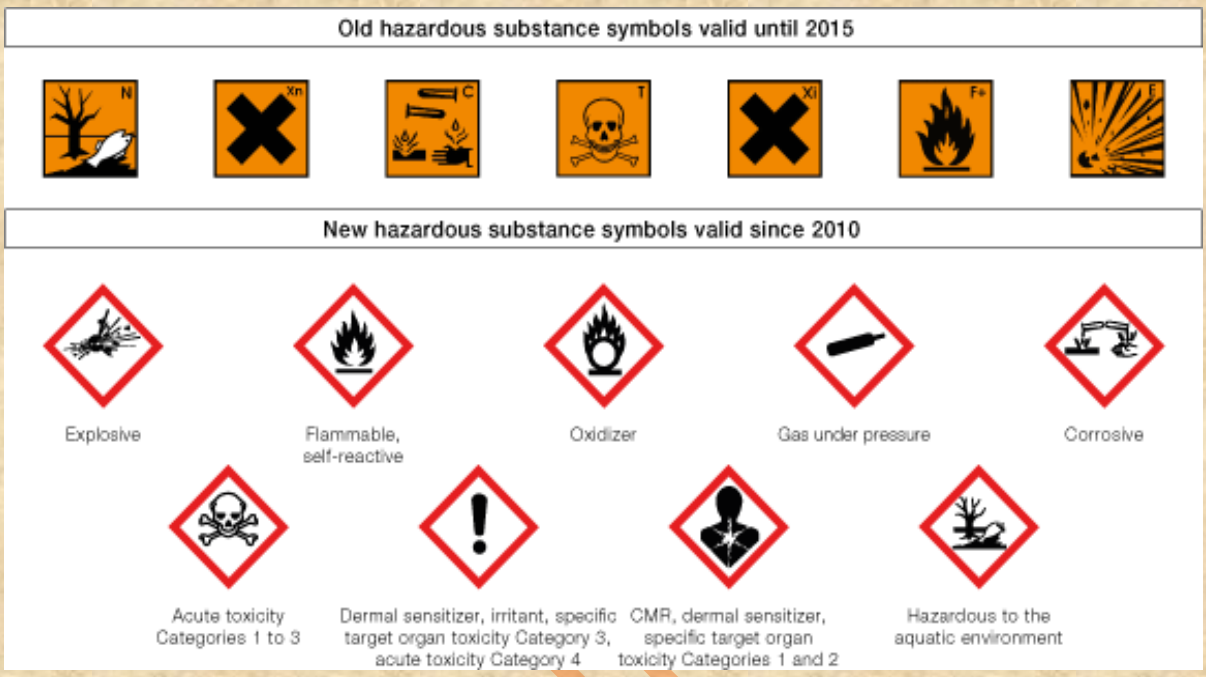
mg/kg	Toxins, venoms and poisons
1,000,000	Water
10,000	Ethanol, other alcohols, anesthetics
1,000	Iron salts, vitamins
100	Barbiturates, General anesthetics
10	Morphine, some snake venoms
1	Nicotine and many plant poisons
0.1	Curare, Sea snake venoms, Jellyfish toxins
0.01	Tetrodotoxin
0.001	Ciguatoxin, Palytoxin
< 0.0001	Botulinum toxins

- The acute lethal dose of strychnine (a monoterpenoid indole alkaloid) is 2 mg/kg.

Symbolic Representation of Hazard / Toxic Xenobiotics

- Hazard symbols have come a long way from the rudimentary drawings used to designate poison in the early 1800s.
- As a result of updated OSHA (Occupational Safety and Health Administration) chemical labeling requirements, 2016 marks the first full year of adoption of the Globally Harmonized System of Classification and Labeling of Chemicals (GHS) in the U.S.
- The GHS system, part of OSHA's Hazard Communication Standard (HCS), consists of nine symbols, or pictograms, providing recognition of the hazards associated with certain substances. Use of eight of the nine are mandatory in the U.S., the exception being the environmental pictogram (see below).
- Each pictogram covers a specific type of hazard and is designed to be immediately recognizable to anyone handling hazardous material.

❖ In addition to pictograms, labels are required to include a signal word ("danger" or "warning"), a brief hazard statement and a precautionary statement outlining ways to prevent exposure.



- **Health Hazard:** A cancer-causing agent (**carcinogen**) or substance with respiratory, reproductive or organ toxicity that causes damage over time (a chronic, or long-term, health hazard)

- **Flame**: Flammable materials or substances liable to self-ignite when exposed to water or air (pyrophoric), or which emit flammable gas.

- **Exclamation Mark:** An immediate skin, eye or respiratory tract irritant, dermal sensitizer or narcotic.

- **Gas Cylinder**: Gases stored under pressure, such as ammonia or liquid nitrogen.

- **Corrosion:** Materials causing skin **corrosion/burns** or eye damage on contact, or that are corrosive to metals.

- **Exploding Bomb:** Explosives, including organic peroxides and highly unstable material at risk of exploding even without exposure to air (self-reactives).

- **Flame Over Circle:** Identifies oxidizers. Oxidizers are chemicals that facilitate burning or make fires burn hotter and longer.

- **Skull and Crossbones:** Substances, such as poisons and highly concentrated acids, which have an immediate and severe toxic effect (acute toxicity).

- **Environmental Hazard:** Chemicals toxic to aquatic wildlife. (Non-Mandatory)

- **Biohazard:** Biological substances that pose a threat to human health

- **Radiation:** Damaging to living tissue, possibly causing DNA damage and mutations

❖ In addition to the symbols, colour codes and numbers are used to categorize poisons. Blue colour is used to indicate the toxic effects on health, red on the flammability, yellow on the irritability and white as a special code.

Types of Poisoning

Acute

- Acute poisoning is associated with exposure to a relatively large, often single, dose of a toxic agent, this being followed by rapid manifestation of more severe clinical signs of intoxication.
- It is also defined as sudden violent syndrome caused by a single large dose of poison.

Sub-Acute

- In sub-acute poisoning the exposure level is lower and the survival time longer, than in acute poisoning, but the period between exposure and manifestation of signs of poisoning and possible death is again relatively short.
- Symptoms of toxicity develop gradually.
- In sub-acute toxicity studies, low doses of poisons are administered for a period of 90 days.
- These tests are performed to study, the No Observed Effect Level or No Observed Adverse Effect Level and to identify the specific organ(s) affected by the test compound after repeated administration.

Chronic

- Chronic poisoning is usually caused by multiple exposures to the poison, while individual quantities are not sufficiently large to produce clinical intoxication.
- It is also defined as persistent lingering condition brought about by small repeated doses.
- A relatively long delay is observed between the first exposure to the toxic agent and the eventual development of signs of poisoning.
- Agents that causes chronic poisoning exhibit a cumulative effect. They either accumulate within the body or produce additive tissue damage. Once this level becomes critical, symptoms of poisoning develop.
- In some cases, the development of symptoms of poisoning may be noticed many months after the exposure, even if there is no contact with the poison during the intervening period.
- In the chronic toxicity studies, the exposure time is six months to two years for rodents and one year for non-rodents.

Toxicity Testing

- Different types of testing methods are undertaken to test the toxicity of drugs and chemicals.
- This includes acute toxicity, sub-chronic toxicity, chronic toxicity, developmental toxicity, reproductive toxicity, phototoxicity, behavioral toxicity, hypersensitivity, ocular and skin irritation tests, mutagenicity, teratogenicity and carcinogenicity.
- In addition, toxicokinetic studies are conducted to estimate the toxicity. In many of these studies rodents are used as experimental animals

Chronicity Factor

- The ratio of acute to chronic LD 50 doses is known as chronicity factor.
- Compounds with cumulative effects have a high chronicity factor.
- A chronicity factor greater than 2.0 indicates a relatively cumulative toxicant.
- Chronicity factor may be influenced by the tendency to accumulate vs. being rapidly eliminated or detoxified.
- It may also be influenced by cumulative and progressive damage that occurs from repeated toxic insults to a target tissue.
- A compound may have low acute toxicity, but if it has the tendency to accumulate in body tissues it can cause sub-acute or chronic toxicity. Such toxicants are termed as cumulative poisons.
- The chronicity factor gives an indication of cumulative effects of poisons.
- However, chronicity factor may be influenced by the tendency to produce tolerance.
- The biological system may tolerate higher dose after prolonged exposure. Potassium cyanide is an example. Its acute LD50 is 10 mg/kg, but pre-exposed animals tolerate 250 mg/kg. Therefore, the chronicity factor is 0.04 for potassium cyanide.

Untoward Effects Due to Poisonous Substances

- There are other untoward effects caused by poisonous substances irrespective of the poisoning being acute, sub-acute or chronic. These may be produced by certain drugs even at therapeutic dose levels.
- Allergy –The individual becomes sensitized to a previous dose of the same material.
- Teratogenicity (Greek word meaning monster) – The exposure to certain naturally occurring or man-made agents during certain stages of gestation results in malformations of the offspring. Teratogen is defined as an agent which, when administered during gestation, produces nonlethal structural or functional changes in the embryo or fetus. Some plants and drugs have been identified to cause teratogenicity. For example: plants like *Veratrum* and *Lupinus* and drugs like thalidomide and colchicine.
- **Carcinogenicity** – The agent after a considerable delay may induce neoplasia. The compound has the ability to transform normal cell into progressively and uncontrollably proliferating ones.
- **Mutagenicity** – The agent induces mutation or changes through a change in the genotype or genetic material of a cell by covalent modification of bases in DNA particularly generation of DNA, which passes on when the cell divides.
- Certain common terms used in toxicology studies include
- **Parts Per Million (ppm)** is the term commonly used to express the quantity of toxicant mixed within another substance (e.g., feed) 1 ppm = 0.0001% = 1 mg toxicant/kg feed.
- **Lethal concentration (LC)** is the lowest concentration of compound in feed water or even in air that causes death. It is expressed as milligrams of compound per kilogram of feed (**parts per** million or **billion** as ppm or **ppb**)
- **Toxic concentration (TC)** relates to the first recognition of toxic effects. The specific (threshold) toxic effects should be identified when a toxic concentration is given.
- **Highest nontoxic dose (HNTD)** is the largest dose that does not result in clinical or pathologic drug-induced alterations.
- **Toxic-dose-low (TDL)** is the lowest dose that will produce alterations; administration of twice this dose is not lethal.
- **Toxic-dose-high (TDH)** is the dose that will produce drug-induced alterations and administration of twice this dose is lethal.

- **Lethal dose (LD)** is the lowest dose that causes death in any animal during the period of observation. LD_{50} is a commonly used measure of toxicity.
- **Median Lethal Dose (LD_{50})** is the dose at which a toxicant causes lethality in 50% of the population or animals exposed to that particular agent/compound.
- **No observed adverse effect level (NOEL or NOAEL)** is the largest dose that will produce no deleterious effects when administered over a given period of time. This study is generally conducted in two species (rats and dogs) at three doses by the route of choice.
- **Reference dose (RfD)** is the highest dose expected to have no effect on the species of interest (often human beings) despite a lifetime of exposure. The RfD may be set at 1/10 of the HNTD or 1/10 of the NOAEL.
- **Maximum tolerated dose (MTD)** is sometimes used to indicate maximum tolerated dose (highest dose not causing death). Other times it is used to indicate minimum toxic dose (lowest dose causing any abnormality). Thus, it is best to ask what is meant by MTD.
- **Safety factor (SF)** reflects the quality of the toxicological investigation and the degree of certainty with which the results can be extrapolated to human beings.

Common Causes of Poisoning

- The materials causing intoxication in animals may be naturally occurring or man-made.
- **Naturally-occurring** - These are either inorganic materials or minerals, plants and the products of moulds, venomous snakes, toads and insects. The inorganic materials include fluoride, nitrates, copper, molybdenum, selenium and lead.
- **Man-made hazards** – Man made hazards may cause accidental, malicious or intentional and occupational poisoning. The agents of interest include industrial products or by-products, domestic materials, pharmaceutical preparations and feed additives.
- **Industrial materials** - Proximity of industrial and agricultural operations in association with inadequate control of emissions. The harmful agents, which may be involved, include inorganic materials arsenic, lead, molybdenum, fluoride, cadmium, mercury, copper and chromium and the organic substances ethanol, cyanide and fluoroacetamide. Discharge of sulphur dioxide and acid rain, accidental discharge of radioactive material and the disposal of radioactive material and industrial waste chemicals.
- **Domestic materials -** Lead in roofing felt, linoleum, piping, paint, accumulators, used engine oil, golf balls, fishing weights and shot, phenolic materials in bituminous floor coverings, discarded clay pigeons, creosote and disinfectants, toxic plants incorporated into or used as bedding, house plants, gases such as ammonia, carbon monoxide or hydrogen sulfide, fuel oils, herbicides and human medicaments.
- **Pesticides -** This includes herbicides, fungicides, molluscicides, insecticides and rodenticides.
- **Medicaments -** Misuse or over dosage of pharmaceutical material can produce intoxication.
- **Dietary constituents -** Inadequate cooking or poor storage of diets or their constituents, addition of excessive quantities or inadequate mixing of the recommended quantities of preservatives or growth-promoter feed additives, and either the incorporation of toxic materials into the diet or their use in feedstuffs