

Basic Toxicology Reference

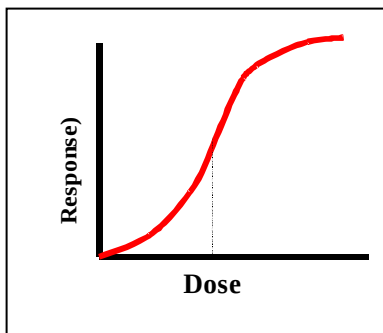
Many chemicals commonly used in laboratories are toxic. Laboratory employees must be thoroughly familiar with toxic properties of the chemicals they work with in order to minimize their risk. The risk of developing a toxic effect is related to both the extent of exposure as well as the inherent toxicity of a chemical. Since we can not change the inherent toxicity of a chemical (except by substitution), we must minimize exposure to reduce the risk. Fortunately the modern laboratory incorporates many features which assist in minimizing exposures.

Reviewing the following toxicology concepts will assist you in understanding the toxic properties of chemicals, how to recognize toxic responses, and how to minimize your risk:

- Dose response
- Routes of entry into the body
- Acute and Chronic Health Effects
- Local vs Systemic Health Effects
- Measures of Toxicity
- Physiological classification of toxic responses

Dose Response

A substance can only produce the harmful effect associated with its toxic properties if it reaches a susceptible biological system in sufficient concentration (a high enough dose). The toxic effect of a substance increases as the exposure (or dose) to the susceptible biological systems increases. For all chemicals there is a



range of doses that result in a graded effect between the extremes of no effect and 100% response (toxic effect). All chemical substances will exhibit a toxic effect given a large enough dose. If the dose is low enough even a highly toxic substance will cease to cause a harmful effect. The toxic potency of a chemical is thus ultimately defined by the dose (the amount) of the chemical that will produce a specific response in a specific biological system.

“All substances are poisons; there is none which is not a poison. The right dose differentiates a poison....” Paracelsus (1493-1541)

“Routes of entry into the body

Route of exposure describes the way the chemical gets into or onto the body. Chemicals may have serious effects by one route, and minimal effects by another. Hazardous chemicals may enter the body by:

- Absorption through the **respiratory tract** via inhalation.
- Absorption through the **skin** via dermal contact.
- Absorption through the **digestive tract** via ingestion. (Ingestion can occur through eating or smoking with contaminated hands or in contaminated work areas.)

- **Injection:** Introducing the material directly into the bloodstream. (Injection may occur through mechanical injury from “sharps”.)

In the laboratory the primary routes of chemical exposure is through inhalation and dermal contact. Having a laboratory with good general ventilation and using a chemical fume hood can prevent inhalation exposures. Wearing appropriate chemical protective clothing prevents dermal contact. Good hygiene habits, such as regular washing your hands, and using tongs or other tools to pick up sharp objects, will prevent exposure through ingestion or injection.

Acute and Chronic Health Effects

Acute health effects are characterized by sudden and severe exposure and rapid absorption of the substance. Normally, a single large exposure is involved. Adverse health effects are often reversible. Examples: carbon monoxide or cyanide poisoning.

Chronic health effects are characterized by prolonged or repeated exposures over many days, months or years. Symptoms may not be immediately apparent. Health effects are often irreversible. Examples: lead or mercury poisoning, cancer.

Local vs Systemic Health Effects

A Local effect refers to an adverse health effect that takes place at the point or area of contact. The site may be skin, mucous membranes, the respiratory tract, gastrointestinal system, eyes, etc. Absorption does not necessarily occur. Examples: strong acids or alkalis.

Systemic effect refers to an adverse health effect that takes place at a location distant from the body's initial point of contact and presupposes absorption has taken place. Examples: arsenic effects to the blood, nervous system, liver, kidneys and skin; benzene effects to the bone marrow.

Substances with systemic effects often have “target organs” in which they accumulate and exert their toxic effect.

Some substances that cause systemic effects are cumulative poisons. These substances tend to build up in the body as a result of numerous chronic exposures. The effects are not seen until a critical body burden is reached. Example: heavy metals.

When exposure occurs to several substances simultaneously the resultant systemic toxic effect may be significantly greater in combination than the additive toxic effect of each substance alone. This is called a synergistic or potentiating effect. Example: exposure to alcohol and chlorinated solvents; or smoking and asbestos.

Measures of Toxicity

The inherent toxicity of a substance is one of the factors that determines how a material should be handled in the laboratory. Substances may be acutely toxic, chronically toxic, or both.

Acute toxic effects (those that occur after a single exposure) of substances are typically measured in animals (rats and mice) and defined in terms of the lethal dose 50 (LD₅₀) or lethal concentration 50

(LC_{50}). The LD_{50} is defined as the amount of chemical that when ingested, injected, or applied to the skin of a test animal, will be lethal to fifty percent of the test population. The LD_{50} is typically expressed in milligrams of test substance per kilogram of body weight. The lethal dose of highly volatile chemicals is typically expressed as the airborne concentration that will be lethal to fifty percent of the test population (LC_{50}). The LC_{50} is typically reported as an airborne concentration (parts per million, mg per cubic meter, etc.) over a specified time period (example: 10 ppm; 4 hours).

Toxicity Classes: Hodge and Sterner Scale				
Commonly Used Term	Routes of Administration			
	Oral LD_{50} (single dose to rats) mg/kg	Inhalation LC_{50} (exposure of rats for 4 hours) ppm	Dermal LD_{50} (single application to skin of rabbits) mg/kg	Probable Lethal Dose for Man
Extremely Toxic	1 or less	10 or less	5 or less	1 grain (a taste, a drop)
Highly Toxic	1-50	10-100	5-43	4 ml (1 tsp)
Moderately Toxic	50-500	100-1000	44-340	30 ml (1 fl. oz.)
Slightly Toxic	500-5000	1000-10,000	350-2810	600 ml (1 pint)
Practically Non-toxic	5000-15,000	10,000-100,000	2820-22,590	1 litre (or 1 quart)
Relatively Harmless	15,000 or more	100,000	22,600 or more	1 litre (or 1 quart)

The lower the value of the LD_{50} and LC_{50} the more toxic the substance. Although the lethal dose varies between test animal species and animals and humans, the relative toxicity of substances is usually constant. Therefore a highly toxic substance in an animal model is likely to be highly toxic to humans.

The potential for a substance to cause **chronic health effects** (such as target organ, cancer or reproductive effects) can be studied in human populations (epidemiology studies), animal test populations, or in some cases specific cell lines. Studies report the dose rate (milligrams of test substance per kilogram of body weight per day) that caused adverse health effects and/or the “no observed effect level” (NOEL) which is that dose at which no adverse health effect was observed. Materials that have been identified as causing chronic health effects should be handled in a manner that minimizes exposure.

Several organizations such as National Toxicology Program, International Agency for Research on Cancer, regularly report lists of chemicals known or reasonably anticipated to have severe chronic health effects.

Physiological classification of toxic responses

Toxic substances can be classified according to the physiological effects they have on the human body. This classification scheme separates toxic substances in the following categories:

- Irritant: Causes inflammation of the skin and mucous membranes (skin, eyes, nose, or respiratory system). Examples: ammonia, HCL, halogens, alkaline dusts and mists
- Corrosive: A material that can destroy human tissue. Includes both acids and bases and may be solids liquids or gases. Most common toxic material encountered in the laboratory.
- Asphyxiant: A material that deprives tissue of oxygen and causes suffocation.
 - Simple displace oxygen from atmosphere Example: nitrogen, helium, CO₂
 - Chemical interfere chemically with oxygen absorption, transport or utilization Example: CO, cyanide
- Anesthetic: Depresses the central nervous system Example: alcohols, halogenated hydrocarbons
- Chemicals that effect a specific target organ
 - Hepatotoxin: causes liver damage. Example: carbon tetrachloride (halogenated hydrocarbons)
 - Nephrotoxin: causes kidney damage. Example: chloroform, mercury, dimethyl sulfate
 - Neurotoxin: affects the nervous system. Example: mercury, lead, carbon disulfide
 - Hematopoietic toxin: affects the cellular components of blood or its ability to function Example: benzene, xylene, CO, cyanides
 - Pulmonary toxin: irritates or damages the lungs. Example: asbestos, silica ozone. chromium
 - Reproductive toxins: causes impotence or sterility in men and women. Example: lead, dibromodichloropropane
- Skin hazards: affect the dermal layer of the skin (defatten, rashes, irritation) Example: ketones, chlorinated compounds
- Eye hazards: affect the eye or vision (conjunctivitis, corneal damage) Example: organic solvents, acids, bases, alcohols
- Carcinogen: A material which can cause cancer. Example: asbestos, Bis-chloromethyl ether, benzene, acrylonitrile
- Mutagen: Anything which causes a change in the genetic material of a living cell. Many mutagens are also carcinogens.
- Teratogen: A material which interferes with the developing embryo when a pregnant female is exposed to that substance. Example: lead, thalidomide