

# Toxicology

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### **A. What is Toxicology?**

Toxicology is the study of how natural or man-made poisons cause undesirable effects in living organisms.

🌐 **What are harmful or *adverse* effects?** Harmful or *adverse* effects are those that are damaging to either the survival or normal function of the individual.

🌐 **What is Toxicity?** The word “toxicity” describes the degree to which a substance is poisonous or can cause injury. The toxicity depends on a variety of factors: dose, duration and route of exposure, shape and structure of the chemical itself, and individual human factors.

🌐 **What is Toxic?** This term relates to poisonous or deadly effects on the body by inhalation (breathing), ingestion (eating), or absorption, or by direct contact with a chemical.

🌐 **What is a Toxicant?** A toxicant is any **chemical** that can injure or kill humans, animals, or plants; a poison. The term “**toxicant**” is used when talking about toxic substances that are produced by or are a by-product of human-made activities. For example, **dioxin** (2,3-7,8-tetrachlorodibenzo-*p*-dioxin {TCDD}), produced as a by-product of certain chlorinated chemicals, is a toxicant. On the other hand, **arsenic**, a toxic metal, may occur as a natural contaminant of groundwater or may contaminate groundwater as a by-product of industrial activities. If the second case is true, such toxic substances are referred to as toxicants, rather than toxins.

🌐 **What is a Toxin?** The term “**toxin**” usually is used when talking about toxic substances produced naturally. A toxin is any poisonous substance of microbial (bacteria or other tiny plants or animals), vegetable, or synthetic chemical origin that reacts with specific cellular components to kill cells, alter growth or development, or kill the organism.

🌐 **What is a Toxic Symptom?** This term includes any feeling or sign indicating the presence of a poison in the system.

🌐 **What are Toxic Effects?** This term refers to the health effects that occur due to exposure to a toxic substance; also known as a poisonous effect on the body.

🌐 **What is Selective Toxicity?** “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.

🌐 **How Does Toxicity Develop?** Before toxicity can develop, a substance must come into contact with a body surface such as skin, eye or mucosa of the digestive or respiratory tract. The dose of the chemical, or the amount one comes into contact with, is important when discussing how “toxic” a substance can be.

🌐 **What is a 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. An acute exposure occurs over a very short period of time, usually 24 hours. Chronic exposures occur over long periods of time such as weeks, months, or years. The amount of exposure and the type of toxin will determine the toxic effect.

🌐 **What is 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. This relationship is important in determining the toxicity of a particular substance. It relies on the concept that a dose, or a time of exposure (to a chemical, drug, or toxic substance), will cause an effect (response) on the exposed organism. Usually, the larger or more intense the dose, the greater the response, or the effect. This is the meaning behind the statement “the dose makes the poison.”


🌐 **What is the threshold dose?** Given the idea of a dose-response, there should be a dose or exposure level below which the harmful or adverse effects of a substance are not seen in a population. That dose is referred to as the ‘threshold dose’. This dose is also referred to as the **no observed adverse effect level (NOAEL)**, or the **no effect level (NEL)**. These terms are often used by toxicologists when discussing the relationship between exposure and dose. However, for substances causing cancer (**carcinogens**), no safe level of exposure exists, since any exposure could result in cancer.

🌐 **What is meant by ‘individual susceptibility?’** This term describes the differences in types of responses to hazardous substances, between people. Each person is unique (because our genes differ in approximately 0.1% of the three billion base pairs that comprise the human genome), and because of that, there may be great differences in the response to exposure. Exposure in one person may have no effect, while a second person may become seriously ill, and a third may develop cancer or toxicity symptoms.

🌐 **What is a “sensitive sub-population?”** A sensitive sub-population describes those persons who are more at risk from illness due to exposure to hazardous substances than the average, healthy person. These persons usually include the very young, the chronically ill, and the very old. It may also include pregnant women and women of child-bearing age. Depending on the type of contaminant, other factors (e.g., age, weight, lifestyle, sex) could be used to describe the population.

🌐 **What are “toxicokinetics” and “toxicodynamics?”** Toxicokinetics describes the fate of toxic compound in the body. The measurement of the time course of absorption, distribution, biotransformation, and excretion of toxic compounds (sometimes referred to as pharmacokinetics). Toxicodynamics describes the determination and quantification of the sequence of events at the cellular and molecular levels

leading to a toxic response to an environmental agent (sometimes referred to as pharmacodynamics).

 **What are “toxicogenetics and toxicogenomics?”** Toxicogenetics describes consideration of stable and heritable alterations in the genome that are able to influence the relative susceptibility of an individual (or group of individuals) to the adverse health effects that may result from exposure to an exogenous material. Toxicogenomics, on the other hand, describes analysis of gene-expression changes induced in a biological system by exposure to a xenobiotic. The two disciplines are linked; polymorphisms that alter biological function may change the spectrum of genes regulated in response to a toxicant. In this way, toxicogenetic differences can underpin variations in toxicogenomic response. In the future, toxicogenomic data from global gene-expression profiling and toxicogenetic data from genome-wide single nucleotide polymorphism (SNP) mapping will facilitate the identification of genes and pathways that determine relative susceptibility to potentially toxic substances.

## B. The Field of Toxicology

Toxicology addresses a variety of questions. For example, in agriculture, toxicology determines the possible health effects from exposure to pesticides or herbicides, or the effect of animal feed additives, such as growth factors, on people. Toxicology is also used in laboratory experiments on animals to establish dose-response relationships. Toxicology also deals with the way chemicals and waste products affect the health of an individual.

## C. Sub-disciplines of Toxicology

The field of toxicology can be further divided into the following sub-discipline:

☑ Environmental Toxicology is concerned with the study of chemicals that contaminate food, water, soil, or the atmosphere. It also deals with toxic substances that enter bodies of waters such as lakes, streams, rivers, and oceans. This sub-discipline addresses the question of how various plants, animals, and humans are affected by exposure to toxic substances.

☑ Occupational (Industrial) Toxicology is concerned with health effects from exposure to chemicals in the workplace. This field grew out of a need to protect workers from toxic substances and to make their work environment safe. Occupational diseases caused by industrial chemicals account for an estimated 50,000 to 70,000 deaths, and 350,000 new cases of illness each year in the United States.

☑ Regulatory Toxicology gathers and evaluates existing toxicological information to establish concentration-based standards of “safe” exposure. The standard is the level of a chemical that a person can be exposed to without any harmful health effects.

☑ Food Toxicology is involved in delivering a safe and edible supply of food to the consumer. During processing, a number of substances may be added to food to make it look, taste, or smell better. Fats, oils, sugars, starches and other substances may be added to change the texture and taste of food. All of these additives are studied to determine if and at what amount, they may produce adverse effects. A second area of interest includes food allergies. Almost 30% of the American people have some food allergy. For example, many people have trouble digesting milk, and are lactose intolerant. In addition, toxic substances such as pesticides may be applied to a food crop in the field, while lead, arsenic, and cadmium are naturally present in soil and water, and may be absorbed by plants. Toxicologists must determine the acceptable daily intake level for those substances.

✔ Clinical Toxicology is concerned with diseases and illnesses associated with short term or long term exposure to toxic chemicals. Clinical toxicologists include emergency room physicians who must be familiar with the symptoms associated with exposure to a wide variety of toxic substances in order to administer the appropriate treatment.

✔ Descriptive Toxicology is concerned with gathering toxicological information from animal experimentation. These types of experiments are used to establish how much of a chemical would cause illness or death.

The United States Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), and the Food and Drug Administration (FDA), use information from these studies to set regulatory exposure limits.

✔ Forensic Toxicology is used to help establish cause and effect relationships between exposure to a drug or chemical and the toxic or lethal effects that result from that exposure.

✔ Analytical toxicology identifies the toxicant through analysis of body fluids (e.g. urine, blood, bile, oral fluid, vitreous humor or cerebrospinal fluid) and tissues (brain cortex, liver, heart, kidney, fat tissues), stomach content, and/or drug paraphernalia. Hair is mostly used to detect long-term exposure to drugs of abuse. Assessment of drugs effects on behavior and performance, and evaluation of toxic effects, can be made only after determination of the concentrations of drugs and of their active metabolites in blood. Urine is the matrix of choice for drug detection and identification. Oral fluid will become the matrix of choice for roadside testing of drugs impairing driving capability.

✔ Mechanistic Toxicology makes observations on how toxic substances cause their effects. The effects of exposure can depend on a number of factors, including the size of the molecule, the specific tissue type or cellular components affected, whether the substance is eas-

ily dissolved in water or fatty tissues, all of which are important when trying to determine the way a toxic substance causes harm, and whether effects seen in animals can be expected in humans.

## II. Classification of Toxic Agents:

Toxic substances are classified into the following:

### A. Heavy Metals

Metals differ from other toxic substances in that they are neither created nor destroyed by humans. Their use by humans plays an important role in determining their potential for health effects. Their effect on health could occur through at least two mechanisms: first, by increasing the presence of heavy metals in air, water, soil, and food, and second, by changing the structure of the chemical. For example, chromium III can be converted to or from chromium VI, the more toxic form of the metal.

### B. Solvents and Vapors

Nearly everyone is exposed to solvents. Occupational exposures can range from the use of “white-out” by administrative personnel, to the use of chemicals by technicians in a nail salon. When a solvent evaporates, the vapors may also pose a threat to the exposed population.

### C. Radiation and Radioactive Materials

Radiation is the release and propagation of energy in space or through a material medium in the form of waves, the transfer of heat or light by waves of energy, or the stream of particles from a nuclear reactor.

### D. Dioxin/Furans

Dioxin, (or TCDD) was originally discovered as a contaminant in the herbicide Agent Orange. Dioxin is also a by-product of chlorine processing in paper producing industries.

#### E. Pesticides

The EPA defines pesticide as any substance or mixture of substances intended to prevent, destroy, repel, or mitigate any pest. Pesticides may also be described as any physical, chemical, or biological agent that will kill an undesirable plant or animal pest.

#### F. Microbial toxins

Bacteria, fungi and algae are the microorganisms typically associated with microbial toxin production. Cholera toxin produced by *Vibrio cholerae* is the virulence factor responsible for the massive secretory diarrhea seen in Asiatic cholera (5 million cases each year).

#### G. Mushroom toxins

Several mushroom species (e.g. *Amanita phalloides*, *A. virosa*), produce a family of cyclic octapeptides called amanitins. Symptoms of intoxication appear at the end of a latent period of 6-48 hours during which the patient shows no symptoms. Death in 50-90% of the cases from progressive and irreversible liver, kidney, cardiac damage may happen 6-8 days after ingestion.

#### H. Plant Toxins

Different portions of a plant may contain different concentrations of chemicals. Some chemicals made by plants can be lethal. For example, taxol, used in chemotherapy to kill cancer cells, is produced by a species of the yew plant. One of the main toxic proteins is "**ricin**" from the seeds of castor bean plant. Perhaps, ingestion of just one milligram of ricin can kill an adult. The main alkaloid of *Aconitum* plants

is aconitine, a highly toxic diterpenoid alkaloid. Ingestion of a few grams of roots may result in death occurring from ventricular arrhythmias, which are most likely to occur within the first 24 hours.

## I. Animal Toxins

These toxins can result from venomous or poisonous animal releases. Venomous animals are usually defined as those that are capable of producing a poison in a highly developed gland or group of cells, and can deliver that toxin through biting or stinging. Poisonous animals are generally regarded as those whose tissues, either in part or in their whole, are toxic. Batrachotoxins are extremely potent cardiotoxic and neurotoxic steroidal alkaloids found in skin secretions from certain species of frogs (poison dart frogs). The most toxic frog is very likely the golden poison frog, *Phyllobates terribilis*.

## J. Subcategories of Toxic Substance Classifications

All of these substances may also be further classified according to their:

- ☞ Effect on target organs (liver, kidney, hematopoietic system),
- ☞ Use (pesticide, solvent, food additive),
- ☞ Source of the agent (animal and plant toxins),
- ☞ Effects (cancer mutation, liver injury),
- ☞ Physical state (gas, dust, liquid),
- ☞ Labeling requirements (explosive, flammable, oxidizer),
- ☞ Chemistry (aromatic amine, halogenated hydrocarbon), or
- ☞ Poisoning potential (extremely toxic, very toxic, slightly toxic)

## K. General Classifications of Interest to Communities

🌐 Air pollutants

## ● Occupation-related

## ● Acute and chronic poisons

All chemicals (or any chemical) may be poisonous at a given dose and through a particular route. For example, breathing too much pure oxygen, drinking excessive amounts of water, or eating too much salt can cause poisoning or death.

### III. Toxicological Information Sources

#### A. Electronic Databases

Information on toxic chemicals is available at the following sites:

(i) Compendium suisse des médicaments:

<http://www.kompendium.ch/Search.aspx?lang=fr>

(ii) Swissmedic: <http://www.swissmedic.ch/?lang=3>

(iii) Toxzentrum: <http://www.toxi.ch/fre/welcome.html>

(iv) OFSP: <http://www.bag.admin.ch/index.html?lang=fr>

(v) ILO Thesaurus 2005:

<http://www.ilo.org/public/libdoc/ILO-Thesaurus/french/tr1630.htm>

(vi) La liste des toxiques IGS: <http://igs.naz.ch/tox/fr/index.html>

(vii) ch.ch produits chimiques et toxiques:

<http://www.ch.ch/private/00070/00076/00618/00620/index.html?lang=fr>

(viii) Baies dangereuses:

<http://www.prevention.ch/baiesdangereuses.htm>

(ix) Les produits toxiques, la cigarette:

<http://www2.unine.ch/unisansfumees/page5333.html>

(x) EIG - EET - laboratoire de chimie générale, la classification des toxiques:

<http://wwwedu.ge.ch/po/eet/infoped/disciplines/Chimie/www/Toxique.htm>

(xi) ISPA: <http://www.sfa-isp.ch/index.php?langue=F>

(xii) Drogues illégales, la DEA:

[http://www.usdoj.gov/dea/programs/forensicsci/microgram/bulletins\\_index.html](http://www.usdoj.gov/dea/programs/forensicsci/microgram/bulletins_index.html)

(xiii) Swissmedic, les produits stupéfiants:

[http://www.swissmedic.ch/fr/industrie/overall.asp?theme=0.00105.0009.00001&theme\\_id=885](http://www.swissmedic.ch/fr/industrie/overall.asp?theme=0.00105.0009.00001&theme_id=885)