Occupational Health & Safety Practitioner

Reading

INTRODUCTION TO TOXICOLOGY

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Contents

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PO Box 294, WEST PERTH WA 6872.
Tel: Toll Free 1300 307 877.
Email: institute@worksafe.wa.gov.au

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OVERVIEW

This reading introduces the subject of industrial toxicology which aims to protect the health of the workers who may be exposed to a toxic substance either directly or indirectly through their workplace activities. The reading describes the physical forms of toxic substances, routes of entry into the body, and the absorption, distribution and effects of toxic substances.

Objectives

After reading this information you should be able to:

- detail routes of entry into the body;
- recall how a toxic substance is absorbed; and
- outline classifications of the effects of toxic substances.

Author

Monica Lee
B. ApSc, Grad Dip OH&S

Section 1: INTRODUCTION

Glossary of terms

When they are first used, glossary terms are indicated with an asterisk (*). Make sure that you are familiar with the **Glossary of terms** before going any further.

MICROMETRE (μm)	Measure of the distance 10^{-6} metres, and is represented by the symbol μm.

1.1 What is toxicology

Toxicology is the study of adverse effects of an agent on living organisms.

The roots of toxicology date back to early humans where survival was dependent, to a certain extent, on the recognition of what food sources could safely be eaten. The word "toxic" derives from the early Greek use of poisoned arrows. There are many sub-sections of toxicology, which examine specific areas such as clinical, environmental, forensic and industrial toxicology.

Industrial or occupational toxicology specifically examines the adverse effects of toxic agents in relation to persons during the course of their work. The need for this sub-section of toxicology has arisen from the identification of adverse health effects resulting from exposure to toxic agents in the workplace. Therefore the aim of industrial toxicology is to protect the health of the workers who may be exposed to a toxic substance either directly or indirectly through their workplace activities.

It is this area of toxicology that this reading examines.

1.2 Hazard and risk

When discussing toxicology there is the need to understand the difference between toxicity, hazard and risk.

Toxicity can be defined as: the capacity of an agent to produce damage to organisms. This usually refers to functional (systemic) damage but may be developmental in respect of tissue and skeleton in the case of the embryo. The damage may be permanent or transient.

KEY POINT
It does not automatically follow that using a toxic substance in a workplace will result in an adverse health effect to those workers who are exposed.

Hazard can be defined as: an intrinsic capacity associated with an agent or process capable of causing harm.

Risk can be defined as: the likelihood that a substance will cause harm in the circumstances of its use.

Because the outcome of an adverse effect is dependent on the hazard being realised, it does not automatically follow that use of a toxic substance in a workplace will result in an adverse health effect to those exposed. Indeed, other factors such as the route of entry into the body, duration of exposure, dose, physical state of the substance, controls, age, sex and physical state of the worker can all affect the risk.

Section 2: WHAT PHYSICAL FORMS DO TOXIC SUBSTANCES TAKE?

Toxic substances can occur in many physical forms. Knowledge of the physical form is essential in determining appropriate control methods, particularly in the use of respiratory protection. Proctor describes the forms as:

Gas: A formless fluid that completely occupies the space of any enclosure at 25°C and 760 torr pressure.

Vapor: The gaseous phase of a material that is liquid or solid at 25°C and 760 torr pressure.

Aerosol: A dispersion of particles of microscopic size in a gaseous medium; may be solid particles (dust, fume, smoke) or liquid particles (mist, fog).

Dust: Airborne solid particles (an aerosol) that range in size from 0.1 to 50 μm* and larger in diameter.

Fume: An aerosol of solid particles generated by condensation from the gaseous state, generally after volatization from molten metals. The solid particles that make up a fume are extremely fine, usually less than 1.0 μm in diameter. In most cases, the volatized solid reacts with oxygen in the air to form an oxide. Common examples include cadmium oxide fume, welding and lead burning.

Smoke: An aerosol of carbon or soot particles less than 0.1 μm in diameter that results from the incomplete combustion of carbonaceous materials such as coal or oil. Smoke generally contains droplets as well as dry particles.

Mist: An aerosol of suspended liquid droplets generated by condensation from the gaseous to the liquid state or by the breaking up of a liquid into a dispersed state, such as by splashing, foaming, or atomizing. Mist is formed when a finely divided liquid is suspended in the atmosphere. Examples are the oil mist produced during cutting and grinding operations, acid mists from electroplating, acid or alkali mists from pickling operations, and paint spray mist from spraying procedures.

Fog: A visible aerosol of a liquid, formed by condensation.

Section 3: ROUTES OF ENTRY INTO THE BODY

Toxic substances can enter the body via a number of routes, depending on the physical and chemical properties of the specific substance. These routes of entry are:

- inhalation - through the lungs;
- absorption - via the skin through the epidermal cells, sweat and sebaceous (oil) glands and hair follicles, and eyes;
- ingestion; and
- injection.

KEY POINT
Toxic substances can enter the body via inhalation, absorption, ingestion or injection.

Of these, the main routes of concern in industrial exposures are via inhalation and skin.

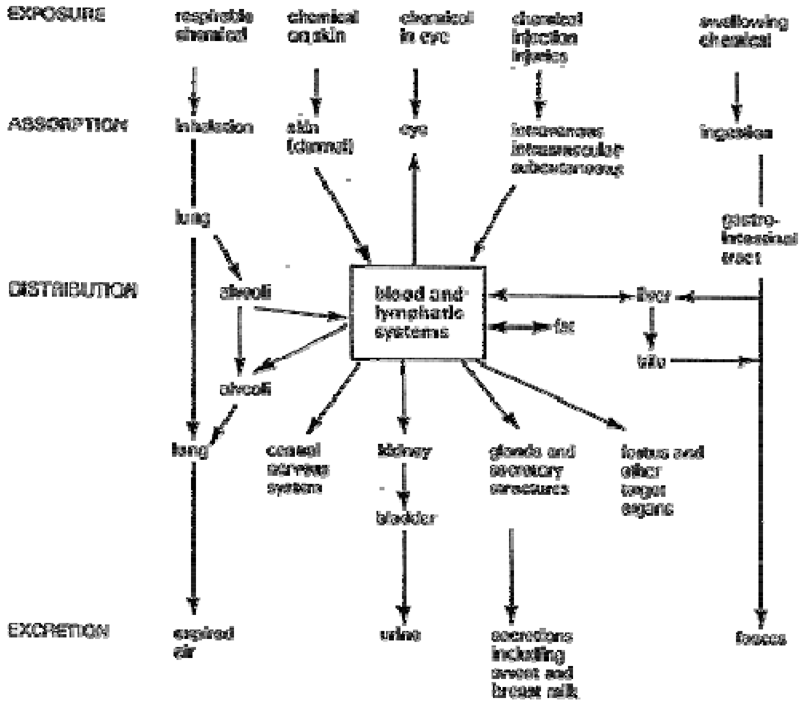
Inhalation is the most common route of entry as many industrial toxic substances are present in an airborne form. Entry via the skin and eyes are through direct contact with a substance.

Ingestion is not a common route and predominantly occurs through poor hygiene practices as a result of workers eating or smoking with contaminated hands. This route of entry may become significant in work process involved with toxic substances such as lead in assay laboratories and radiator repair workshops.

An interesting case where ingestion became a major route of entry was in the case of a 28-year-old electrician who presented himself to a hospital following a 4-month history of abdominal pain and constipation. Routine blood testing showed that his blood lead level was three times the maximum acceptable level in occupationally exposed adults. The source of the lead was discovered in the plastic insulation of electrical cable. The electrician had chewed his way through at least a metre a day of the cable for at least 10 years as a substitute for smoking (Ward et al).

Section 4: ABSORPTION, DISTRIBUTION, AND EXCRETION OF TOXIC SUBSTANCES

Absorption, distribution and elimination of toxic substances can be schematically represented as follows:



4.1 Absorption

For a toxic substance to cause harm, a person must be exposed and the substance absorbed into the body via the lungs, skin and gastrointestinal tract and into the blood and lymphatic systems. The toxic substance can then be transported throughout the body. An exception is that some toxic substances can cause harm without being absorbed, such as caustic and corrosive substances, which act at the point of contact.

4.2 Via the lungs

The respiratory system can be simplistically divided into:

- the upper respiratory tract comprising of the nose, throat, trachea and major bronchial tubes; and
- the lungs, including the bronchioles and alveoli.

Various factors influence the absorption of toxic substances in the respiratory system. These include the physical form such as gases and vapours; aerosol and particulate size; and lipid and water solubility. The lungs can absorb large amounts of a toxic substance due to the large surface area and high blood flow.

Gases and Vapours

Absorption of gases and vapours mainly takes place in the lungs. However, before they reach the lungs they pass through the upper respiratory tract. The upper respiratory tract contains moisture and highly water soluble gases such as ammonia and formaldehyde will be readily dissolved. Substances that are less soluble will pass on down to the alveolar region of the lungs. The amount absorbed into the lungs is also dependent on the toxic substance's solubility in blood.

Aerosols and Particulates

The site where toxic substances will be deposited largely depends on the size of the particle. Large particles are trapped in the upper respiratory tract; with only smaller particles of less than 1 μm, able enter the alveolar regions of the lungs. The large particles deposited in the nose are predominantly cleared through sneezing or being blown out. Particles deposited further down the respiratory tract may be cleared through the mucociliary action by being moved back up into the nasal area where it may be swallowed and absorbed in the gastro-intestinal tract.

4.3 Via the skin

The skin consists of three layers:

- the epidermis which is the outer layer;
- the dermis which is the middle layer; and
- the hypodermis which is the inner layer.

The epidermis and dermis contain the sweat and sebaceous (oil) glands and hair follicles. Toxic substances are predominantly absorbed through the epidermis. Absorption of a toxic substance through the epidermis is dependent upon the condition of the skin, thickness of the skin and blood flow at the point of contact. Damaged skin, through abrasion or removal of skin lipids from exposure to alkali or acid substances, decreases the defence afforded by the epidermis. The water content of the epidermis can also play a role, depending on the water solubility of the toxic substances.

Thickness of the skin at the point of contact also plays a role in the amount of a toxic substance absorbed, with skin on the palms and soles being thicker than skin on the abdomen, back, arms, and legs which are thicker than the skin in the genital area. Those regions with thicker skin can offer greater resistance to toxic substances than those regions with thinner skin.

Some highly toxic substances, such as organophosphate pesticides used in controlling of insects, can be absorbed through the skin in sufficient quantities to cause death.

4.4 Via the gastrointestinal tract

Absorption of a toxic substance can take place anywhere along the length of the gastro-intestinal tract. Factors which influence absorption include the chemical and physical properties of the substance, and site characteristics such as acidic or alkaline state.

4.5 Distribution

Once absorption of a toxic substance has taken place, the toxic substance is distributed throughout the body via blood, lymph or other body fluids. Of these blood is the most important vehicle. Simplistically, the substance can then be:

- stored in the body in areas such as liver, bones, and fat;
- eliminated directly through faeces, urine, or exhaled air; or
- bio transformed/metabolised where the final form is more readily excreted.

4.6 Excretion

Excretion of toxic substances can occur via exhaled air and from secretions including sweat, breast milk, faeces and urine.

Section 5: EFFECTS OF TOXIC SUBSTANCES

Toxic substances can cause a variety of effects on the body and can therefore be classified in a variety of ways. The toxicity of substances is dependent on the route of entry, duration of exposure, and the reaction of the body to that substance. Increasing the dose or amount of a toxic substance increases the effect. Such effects can be classified by:

KEY POINT
Toxic substances can enter the body via inhalation, absorption, ingestion or injection.

- duration of the effect;
- site of Action;
- organ they effect; and
- response produced.

5.1 Duration of the effect - acute or chronic

Acute effects are when exposure to a toxic substance, generally after a single dose, results in an adverse effect either immediately or shortly after the exposure. The exposures tend to be of a high concentration and may result in an irritation, illness or in an extreme case death where the toxic substance is absorbed rapidly. An example of this is a fatality in Western Australia involving a laboratory worker who spilt approximately 100ml of 70% hydrofluoric acid onto his upper leg.

Chronic effects are when exposure to a toxic substance, generally multiple doses over a long period of time, result in an adverse reaction some time after the exposures have ceased. The doses tend to be of low concentration and the signs and symptoms of exposure are slow to develop. Often exposure is not apparent to the worker, as there are no obvious signs and symptoms. Some chronic effects such as cancer can occur some 20-30 years after the exposures.

Both acute and chronic effects can either be reversible or irreversible in nature. The target site or body organ and its response to the toxic substance largely determines whether or not the effect is reversible. The same toxic substance can produce different effects in acute exposure when compared to chronic exposures. The signs and symptoms may therefore vary widely.

5.2 Site of action – local or systemic effects

Local effects are where the toxic effect has occurred at the point of contact with the body. This commonly occurs with corrosive or irritant substances.

Systemic effects are where the toxic substance has been absorbed into the body and distributed via the bloodstream to a susceptible organ(s). The resultant toxic effect may be seen in an area quite distant from the initial point of contact.

5.3 By the organ they effect

This includes:

Hepatotoxins. Toxic substances that cause effects to the liver are called hepatotoxic. The liver is a major organ in the metabolism, detoxification and elimination of many toxic substances once absorption has taken place. It is therefore not surprising that many substances are hepatotoxic. Some examples are chloroform, ethylene dibromide and vinyl chloride.

Nephrotoxins. These substances cause effects to the kidney and include such substances as cadmium, mercury, toluene and paraquat.

Neurotoxins. These cause effects to either the central or peripheral nervous system and include such substances as lead and pesticides.

Haematoxins. These cause effects to the cells in circulation and bone marrow and include substances such as benzene and arsine.

Immunotoxins. These cause effects to the immune system.

Pulmonotoxins. These cause effects to the lungs and include substances such as silica dust and asbestos fibres.

5.4 Responses they produce

Including:

Cancer. A malignant tumour may spread to other organs of the body. Toxic substances which cause this effect are called carcinogenic and include substances such as asbestos and coal tar pitch volatiles.

Birth Defects. Substances that cause abnormalities in a developing foetus are called teratogens and include substances such as thalidomide.

Mutation. A change in the genetic material of cells.

Irritation. Irritation is the aggravation of whatever tissue a substance comes into contact with and is normally reversible.

Asphyxiants. Asphyxiants are substances that interfere with the oxygenation of the tissues and may be either simple or chemical.

Simple asphyxiants are substances, which are inert gases that dilute or displace the atmospheric oxygen to below the level needed to sustain tissue respiration. If the level becomes too low then death can occur. Examples of substances that are simple asphyxiants include carbon dioxide and nitrogen.

Chemical asphyxiants prevent the uptake of oxygen by the blood; or interfere with the transporting of oxygen from the lungs to the tissues; or prevent normal oxygenation of tissues. Examples of chemical asphyxiants include carbon monoxide and hydrogen cyanide.

Section 6: TOXICITY TESTING

Knowledge of the toxicity of a substance can be gained from epidemiology studies.

Epidemiology may be defined as the study of the distribution and determinants of disease frequency. These studies can include:

- retrospective studies;
- prospective studies; or
- cross sectional studies.

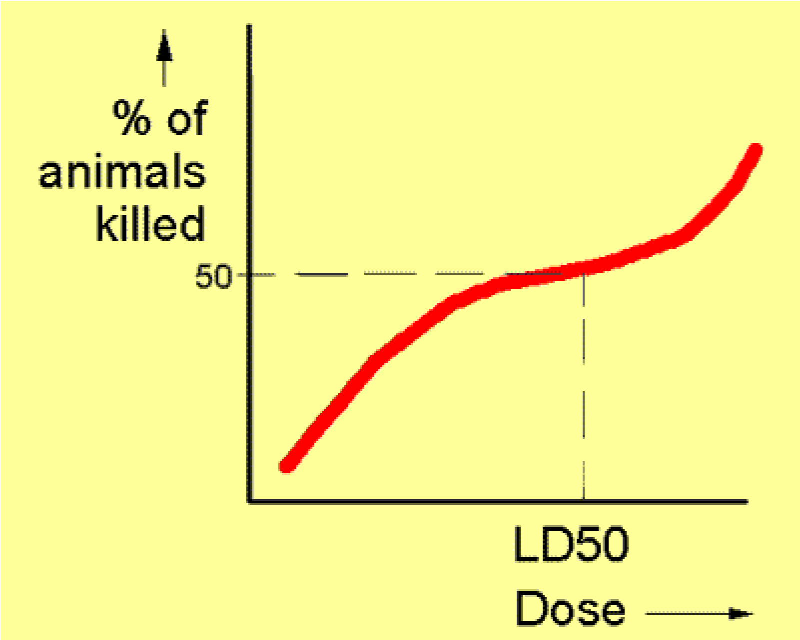
Retrospective studies involve identifying exposed populations at a point in the past and determining who in the populations have developed a disease. Prospective studies involve identifying a group in the present exposed to a substance and following them into the future to see if any develop a disease. Cross-sectional studies involve observing exposure and disease simultaneously.

Animal testing involves the use of test animals, such as mice, rats, dogs and fish, in controlled circumstances, being exposed to concentrations of a substance over certain time periods to determine any toxicological effects. Effects are generally observed from acute exposures administered to the test animals via inhalation, ingestion and dermal routes; and also chronic exposures where the agent is administered over a long time period.

The advantage of animal testing is that new chemicals can be tested to determine toxic effects prior to introduction into the workplace. A major limitation in animal studies is applying the results to humans, as animal responses to an agent may differ greatly to the response in humans and the response from one animal group may differ to another animal group.

Some information obtained during animal testing includes the determination of LD50 and LC50 levels. This information is used in the process of determining exposure standards for humans in the occupational environment.

LD_{50} is a dose of a substance that produces death in 50% of a population of experimental animals. It is usually expressed as milligrams per kilogram (mg/kg) of body weight, and is expressed figuratively as follows:



LC_{50} is a concentration of a substance in air that is estimated to produce death in 50% of experimental animals.

There are other defined dose levels which are used, but these are not defined and discussed in this reading.

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