Toxic substances - characteristics, classification and hazards

Toxicity is the capability of a poison, or toxin, to produce injury in an animal, a human being or the environment. Many poisons cause harm to living tissues at very small doses because they interfere with one or more of the large number of complex chemical processes that take place continuously in all living creatures. These processes are catalysed by enzymes and often a poison works by blocking the action of an enzyme or by changing the direction of a particular process.

To appreciate the hazards presented by poisonous substances it is helpful to know some general principles that apply to all living creatures.

All living things are composed of cells. One of the simplest creatures is the amoeba, which is in fact a single cell about the size of a full stop. It may be found in pond water and can carry out all the processes necessary to live in itself – breathing, eating, elimination of waste products and reproduction (where it divides into two identical cells). A human body is composed of about 250 different types of cell. All living cells have certain common features and a typical living animal cell is shown below. It is important to note that red blood cells do not have a nucleus as they are designed to transport oxygen, and lose their nuclei after they are fully grown, before being released from the bone marrow into the blood stream.

The two parts of a cell that are especially sensitive to poisons are:

- The mitochondrion (the power-house of the cell)
- The nucleus (the control centre of the cell)

**The mitochondrion**

In the mitochondrion a chemical called adenosine triphosphate (ATP) is generated by a complex series of reactions in what is referred to as the ‘respiratory chain’.

The overall reaction may be represented as: 4H+ + O_2 + 4e- = 2H2O

As a result of the energy liberated by this process, 34 molecules of ATP are generated. The oxygen comes from the air inhaled and every living cell must be adequately supplied with oxygen if it is to function properly. All cells require a continuous supply of ATP, which supplies the energy necessary to sustain life. All muscle cells are powered by ATP, so breathing and the beating of the heart depend on a continuous supply of ATP to the relevant cells. All nervous impulses depend on ATP, so to think or to use any senses requires a continuous supply of ATP. Each adult uses and synthesises many millions of ATP molecules every minute of the day. Many acute poisons act by reducing supplies of ATP to the cells or vital organs of the body, so that muscles or nerve cells cease to function normally.
The nucleus

This contains the chromosomes, which in turn are made up of genes. The basic material of all chromosomes and genes is deoxyribonucleic acid (DNA); all the functions of the cell are controlled through the DNA. If a cell is to divide into two healthy cells to replace cells that become worn out, the DNA must be copied perfectly. Anything that affects the DNA may injure the cell.

Three possible effects of a poison are to:

- Slow down the cell
- Kill the cell
- Cause the cell to go out of control and develop into a tumour, or a cancer (here the time-scale may be many years, because even a small tumour will contain about 1,000,000,000 cells)

Important characteristics of different types of cell

Some cells are replaced on a regular basis, such as those that line the intestine or red blood cells (made in the bone marrow). Skin cells are also continuously renewed; the outer layers of skins are dead cells that are shed continuously. However, nerve cells and brain cells do not change very much and are not replaced if they get damaged.

Absorption of poisons

Chemicals can cause poisoning if they reach sensitive parts of a person or living organism in sufficiently high concentrations and for a sufficient length of time. For a chemical to cause harm it must enter the body. Poisons may be absorbed into the body in four main ways:

Inhalation - Through the lungs

Gases and vapours, mists, smokes and dusts and fibres (depending on their size and shape) can all be absorbed in this way. The peak retention depends on aerodynamic shape with particles of 1-2 micrometres (\text{mm}) being retained most effectively. Larger diameter dusts do not penetrate the lungs but tend to be trapped further up the respiratory tract where cilia eventually return them to the oesophagus. From the oesophagus, dusts tend to be excreted through the gut and it is possible that the dusts may cause toxic effects as though they were ingested like food. Most inhaled dust will enter the gut directly and may chemically react with the gut or interfere with microorganisms living in the gut. Systemic action is also possible (effecting the whole body or many organs).

Irritation by dust particles is also possible, but tends to depend on the solids being dissolved. Asbestos fibres cause fibrosis and cancer even though they are insoluble; a similar effect can occur with man-made mineral fibres. Insoluble particles such as coal and silica dusts readily cause fibrosis of the lung.

The volume of air inhaled and exhaled with each normal breath increases with physical exertion; the rate of physical work will directly affect the amount of toxic material a person inhales from a contaminated atmosphere.

Ingestion: Through the gastro-intestinal tract
Such a process could occur through bad housekeeping, such as eating food in laboratories, but generally results from accidental exposure.

The physical state of a toxic substance can have an important bearing on the ease with which it may be absorbed by the body. Fine sub-division, and in some cases, the fact of solubility or insolubility in water, may aid absorption. Barium chloride, which is soluble in water and is a component of ternary eutectic chloride (a well known fire-extinguishing medium), is very poisonous, whereas the insoluble barium sulphate is not poisonous, and is used in the barium meal administered to patients for X-ray photographs of their gastro-intestinal tract.

**Dermal absorption: Through the skin**

There is far lower awareness of this mode of absorption. Certain liquids, including methanol (methyl alcohol), organic mercury compounds, organophosphate pesticides and benzene can be absorbed in this way.

Toxic materials may also enter the body through cuts and grazes, although this is not a common entry route.

**Injection: Through an opening in the skin**

Normal skin provides an excellent barrier to most chemicals. When the skin is punctured in some way (e.g. by a syringe needle, from handling animals or broken glassware, from cuts and grazes, etc.) this protection is bypassed. Any poison or toxic contamination on the skin or on the device causing the puncture wound is capable of directly passing into the bloodstream and eventually finding its way to internal organs where it may exert its toxic effect.

When decontaminating skin, care should be exercised to not rub so hard that it becomes damaged. Reddening of the skin is a sign that it is being damaged and further decontamination effort may be counter-productive as it may require injection.

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**Descriptive terms used in poisoning**

Terms used to describe cases of poisoning:

- **Acute:** adverse health effects occur within a short time (typically up to a few days) after exposure to a single dose (or given concentration) of poison.
- **Chronic:** delayed health effects that occur many years after exposure to a poison and that persist over a long period of time. In industry the effects generally occur by repeated exposures over a period of days, months or years.
- **Local:** the site of action of an agent and means that action takes place only at the particular
area of contact between the organism and a toxic material. Absorption does not necessarily occur. Local effects occur usually to the skin, eyes and respiratory tract.

- **Systemic:** the site (target organ) or region of toxic action is other than at the point of contact between the organism and the poison and presupposes that absorption and distribution of the toxin has already taken place in the body. With systemic effects the whole body or many organs can be affected. Methylene chloride is an example of a substance causing systemic toxicity; once inhaled this material can be metabolised to carbon monoxide that initially may cause feelings of euphoria (similar to alcohol). At higher concentrations unconsciousness can result and repeated exposures to the material can lead to permanent brain damage.

- **Teratogen:** substance that causes mental or physical harm to an unborn foetus. The harm cannot be passed on to future generations. The drugs lysergic acid diethylamide (LSD), methyl mercury, rubella virus (German measles) and herpes virus are teratogens (X-rays and gamma rays also can act as teratogens).

- **Mutagen:** can cause physical or mental harm to an unborn foetus. The harm can be passed on to future generations.

- **Carcinogen:** material that can cause cancer.

- **Irritant:** chemical that is not corrosive but that causes a reversible inflammatory effect on living tissue by chemical action on the local site of contact. This effect is often referred to as irritation and typical sites of contact on the body are skin, eyes and the respiratory system.

**Allergens and hypersensitivity** - an allergy is the tendency of the body to react adversely to certain substances; hay fever, hives and some types of asthma are typical examples of allergies. Allergens are different from irritants as they require interaction with the body's immune system to generate their effect (see below). The allergic effect depends on the individual's sensitivity to the allergen; whereas an irritant acts on an individual in a non-specific manner (i.e. the effect of an irritant on an individual is largely not dependent on that individual's sensitivity to the irritant).

An allergic reaction is really composed of two contacts with a foreign substance. In the first contact the defence mechanisms of the body detect the foreign substance, an antigen, and manufacture antibodies against it. This change in the body is sometimes referred to as sensitisation and any subsequent exposure to the same antigen provokes a massive response from the body; the condition known as an allergy. In some allergic reactions, cells affected by the antigen–antibody reaction may liberate toxic chemicals such as histamine, which is responsible for some of the symptoms that accompany certain allergies, including a runny nose, itching eyes and hives. Thus, anti-histamine drugs are sometimes prescribed.

The chemical most widely known as an individual cause of allergy is toluene di-isocyanate (TDI). One exposure can sensitise a person, so that subsequent exposures can cause severe asthmatic attacks.

Some people maintain that certain food additives, such as the yellow dye tartrazine (E102), can cause allergies in certain cases.

Convulsant: a material that results in violent, abnormal, uncontrollable contraction or series of contractions of muscles in the body. The convulsions produced are often referred to as seizures. Convulsions may have an organic origin or may be induced using drugs. Some typical causes of
seizures are:

- High fever (e.g. in heatstroke, infections)
- Brain infections (e.g. meningitis, malaria, tetanus)
- Metabolic disorders (e.g. high/low levels of sugars or sodium)
- Inadequate oxygen supply to the brain
- Structural damage to the brain (e.g. through accident, stroke)
- Exposure to toxic drugs/substances (e.g. amphetamines, lead, strychnine)
- Withdrawal after heavy use of alcohol or sedatives including sleeping pills
- Prescription drugs.

It is believed that seizures are caused by disorganised and sudden electrical activity in the brain.

**Dose**

A major factor in cases of poisoning is the dose received. Substances not normally regarded as poisonous may become so if the dose is sufficiently massive (usually resulting in acute effects). It is therefore not always easy to make a clear-cut distinction between poisonous and non-poisonous substances. The concentration of poisonous material is not the only factor to be considered when assessing the degree of poisoning experienced, and other factors can also have an important influence:

- Duration of exposure
- Sizes of particles or physical state
- Affinity for human tissue materials
- Solubility in human tissue fluid
- Sensitivity of human tissues and organs
- Age of a person
- Health of an individual

**Occupational exposure limits (OEL)**

In an attempt to limit long-term damage to industrial workers by chronic exposures to poisons, the Health and Safety Executive (HSE) has, via the COSHH Regulations, established limits to the airborne concentrations of poisons to which workers can be exposed.

The ideal underlying the original occupational exposure limits (OELs) was that it was possible to define average levels of substances in air that could be inhaled continuously by an industrial worker during a working shift (normally taken as eight hours/day), every week (normally taken as five working days) for their working life (normally taken as 40 years), without any ill effects.
occurring. That is still the ideal, but it is not always possible to achieve it; this was recognised in the COSHH Regulations.

OELs are intended to be used to control the exposure of workers to airborne hazardous substances in the workplace and are not designed to deal with serious accidents or emergencies such as a major gas release arising from plant failure.

Airborne control levels for hazardous substances that are recommended in the COSHH Regulations are reproduced in the current Health and Safety Executive (HSE) Workplace exposure limits, which is reviewed periodically. The document contains information on a single type of OEL known as the workplace exposure limit (WEL).

These control levels for gases and vapours in air are usually expressed in parts per million (ppm) by volume or parts of gas per million parts of air. Concentrations of dusts, smokes and fumes are often quoted as milligrams per cubic metre (mg m⁻³) of air at a standard temperature and pressure.

Workplace exposure limits (WELs) are OELs set under the COSHH Regulations to protect the health of workers. WELs are defined as the maximum concentrations of hazardous substances in air averaged over a reference period (i.e. a time-weighted average or TWA) to which employees maybe exposed by inhalation.

An eight-hour reference period is used to control exposures to a hazardous substance during a typical work shift. WELs quoted for this period of time are known as long-term exposure limits.

A 15-minute reference period is used to prevent acute effects such as eye irritation, coughing, etc. that may arise following exposure for a few minutes. WELs for this period of time are known as short-term exposure limits. For substances where a long-term limit is quoted but no short-term limit is specified, it is recommended that a figure of three times the long-term limit is used as a guideline for controlling short-term peaks.

When making an assessment on the chronic risk of a substance, it would be prudent to identify any hazard statements associated with the material to ascertain the long-term health effects on affected humans. Under the CLP Regulations these statements must appear on packaging labels when the materials are transported, unless they are exempted.

Every employer, including the fire and rescue service, has a responsibility to identify the materials in the workplace that may put employees' health at risk, to assess that risk and introduce the necessary controls to ensure exposures are below WELs and as low as reasonably practical (ALARP).
Employers have a legal responsibility to inform their staff about those materials in the workplace that may damage their health and to identify the effects of those materials. When managing an incident at which hazardous materials will be encountered, this responsibility falls to the incident commander.

Many poisonous substances have a characteristic smell (carbon monoxide is a well-known exception). In some cases the threshold of smell, or odour, is above the OEL value. That means a person can suffer from toxic effects without realising that a poisonous gas or vapour is present. Two common examples are benzene (WEL = 1 ppm, threshold odour concentration is about 100 ppm) and methyl alcohol (WEL = 200 ppm, threshold odour concentration is about 2000 ppm).

If information on the OEL is not available then it may be possible to use the threshold limit value (TLV) which is a roughly equivalent limit imposed on employers in the USA. Other limits associated with these basic TLVs are:

- Short-term exposure limits (STELs) for a 15-minute reference period
- Ceiling exposure limits (TLV-Cs) are for concentrations of materials that must never be exceeded, even instantaneously

Lethal dose 50 per cent (LD₅₀)

This is the concept used to assess the acute toxicity of a material.

It has long been recognised that if similar quantities of poison are given to different people (or animals) in a population, it will produce differing health effects. To have a quantifiable response to a poison, death is chosen as the discriminator as it is easily measurable. For this reason, lethality studies are normally carried out on animals. To obtain a representative value for lethality for an animal species, it is necessary to carry out tests on a group (or population) of animals so a statistical determination can be made on the amount of poison necessary to kill a certain percentage of the group in a certain time.
The lethal dose 50 per cent is thus defined as:

‘the quantity of poison that will kill one half of a batch of ten or more animals within 14 days’.

The LD<sub>50</sub> is expressed as milligrams per unit body weight (mg/kg).

When quoting values for the LD<sub>50</sub> it is necessary to quote the animal species being tested and the route the poison was given to the animal. For example the LD<sub>50</sub> may be quoted as:

LD<sub>50</sub> (oral, rat) = 414 mg/kg indicating that poison introduced to a group of 10 or more animals by ingestion (oral) at the level of 414mg/kg caused the death of half (50%) of the group within 14 days.

Owing to the above-mentioned dosage values being obtained mainly from studies of rats, mice and guinea-pigs, they should be regarded with caution, and if evidence concerning human beings is available it should be used in preference to that obtained from animal experiments. Individuals vary greatly in their susceptibility to poisons for reasons that are not well understood, and conditions that may be safe for some are not safe for all.

**Other terms**

Lethal concentration 50 Per Cent (LC<sub>50</sub>) is used to denote the concentration of a gas present in the atmosphere for a given period of time that eventually kills half of a batch of ten or more animals within 14 days.

LD<sub>LO</sub> and LC<sub>LO</sub> denote the lowest published lethal dose and concentration respectively. These figures, unlike LD<sub>50</sub> and LC<sub>50</sub>, are not statistically derived and are often obtained from post mortem examinations on accidental death victims.

When managing a release of toxic material, particularly when monitoring equipment is available, other limits or levels where symptoms may start to appear are more appropriate to use. This is particularly relevant to action taken to protect the public.

Internationally, levels such as Acute Emergency Guideline levels (AEGLs) and Immediately Dangerous to Life and Health (IDLH) are widely available from data sources and can be used to predict likely consequences of people exposure to a certain concentration for a predicted period of time. Figures are usually given in PPM.
The acute exposure guideline levels (AEGLs) describe the human health effects from once-in-a-lifetime, or rare, exposure to airborne chemicals. Used by emergency responders when dealing with chemical spills or other catastrophic exposures, AEGLs are set through a collaborative effort of the public and private sectors worldwide. AEGL values represent threshold levels for the general public. As mentioned, that includes susceptible sub-populations, such as infants, children, the elderly, people with asthma and those with other illnesses.

Immediately dangerous to life and health hazards

These levels are established by the American National Institute for Occupational Safety and Health (NIOSH). As exposure to airborne substances that are likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from such an environment. They are used by respirator manufactures and provide an upper limit for this type of respiratory protective equipment.