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British Occupational  
Hygiene Society

The Chartered  
Society for Worker  
Health Protection

# Student Manual: M507

## Health Effects of Hazardous Substances

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## Version History

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## Feedback

We welcome feedback on this manual. Comments should be sent to the BOHS Qualifications Team at [qualifications@bohs.org](mailto:qualifications@bohs.org).

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## ABBREVIATIONS

ACDP	Advisory Committee on Dangerous Pathogens
ACGIH	American Conference of Governmental and Industrial Hygienists
AIDS	Acquired Immunodeficiency syndrome
AIHA	American Industrial Hygiene Association
AIOH	Australian Institute of Occupational Hygienists
ASCC	Australian Safety and Compensation Council
ATSDR	Agency for Toxic Substances and Disease Registry (US)
BOHS	British Occupational Hygiene Society
CAS	Chemical Abstracts Service
CCOHS	Canadian Centre for Occupational Health and Safety
CHIP	Chemical Hazards, Information and Packaging (Regulations)
CMR	Carcinogenic, mutagenic or toxic to reproduction
CNS	Central nervous system
CNT	Carbon nano-tubes
CSA	Chemical Safety Assessment
CSR	Chemical Safety Report
COSHH	Control of Substances Hazardous to Health (Regulations)
CWP	Coal Workers Pneumoconiosis
dB(A)	A-weighted decibels
DNA	Deoxyribonucleic acid
ECHA	European Chemicals Agency
ELISA	Enzyme linked immunosorbent assay
EPA	Environmental Protection Agency (US)
ES	Exposure scenario
EU	European Union
FEV	Forced expiratory volume

**ABBREVIATIONS (Cont'd)**

FVC	Forced vital capacity
GHS	Globally harmonised system
GIT	Gastro-intestinal tract
GMAW	Gas metal arc welding
GMO	Genetically modified organism
GRP	Glass reinforced plastic
HAART	Highly active anti-retroviral treatment
HAVS	Hand-arm vibration syndrome
HDI	Hexa-methylene diamine isocyanate
HEPA	High efficiency particulate arrestor
HIV	Human immuno-deficiency virus
HSE	Health and Safety Executive (UK)
IARC	International Agency for Research on Cancer
IBC	Intermediate bulk container
IgE	Immunoglobulin
ILO	International Labour Organisation
IOHA	International Occupational Hygiene Association
ISO	International Standards Organisation
LC <sub>LO</sub>	Lethal concentration (lowest)
LC <sub>50</sub>	Lethal concentration (50%)
LD <sub>LO</sub>	Lethal dose (lowest)
LD <sub>50</sub>	Lethal dose (50%)
LEV	Local exhaust ventilation
LOAEL	Lowest observed adverse effect level
MDHS	Methods for the Determination of Hazardous Substances (UK)
MDI	Diphenyl methane di-isocyanate

**ABBREVIATIONS (Cont'd)**

MIG	Metal inert gas
MMA	Manual metal arc
MMMF	Machine Made Mineral Fibre (or Man Made Mineral Fibre)
MMVF	Man Made Vitreous Fibre
MRSA	Methicillin-resistant Staphylococcus aureas
MSDS	Materials Safety Data Sheet
NIOSH	National Institute for Occupational Safety and Health (US)
NOAEL	No observed adverse effect level
nm	nanometre
NRL	Natural rubber latex
OECD	Organisation for Economic Co-operation and Development
OSHA	Occupational Safety and Health Administration (US)
PAH	Poly aromatic hydrocarbons
PBPK	Physiologically based pharmacokinetic
PBT	Persistent, Bio-accumulative and Toxic
PEF	Peak expiratory flow
PNS	Peripheral nervous system
PTFE	Poly tetrafluoroethylene
RAST	Radioallergosorbent test
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RCF	Refractory ceramic fibre
RMM	Risk Management Measure
RNA	Ribonucleic acid
RTECS	Registry of Toxic Effects of Chemical Substances
SAICM	Strategic Approach to International Chemicals Management
SAR	Structure activity relationship

**ABBREVIATIONS (Cont'd)**

SAW	Submerged arc welding
SBR	Styrene butadiene rubber
SCBA	Self Contained Breathing Apparatus
SMR	Standardised mortality ratio
TC <sub>Lo</sub>	Toxic concentration (lowest)
TC <sub>50</sub>	Toxic concentration (50%)
TD <sub>Lo</sub>	Toxic dose (lowest)
TD <sub>50</sub>	Toxic dose (50%)
TDI	Toluene di-isocyanate
TIG	Tungsten inert gas
TLV®	Threshold Limit Value
TWA	Time Weighted Average
UK	United Kingdom
µm	Micrometre (micron)
USA	United States of America
UV	Ultra-violet
vPvB	Very persistent, very bio-accumulative
VOC	Volatile organic compound
WEL	Workplace Exposure Limits
WHO	World Health Organisation

## 1. COURSE OVERVIEW

### 1.1 INTRODUCTION

This Course has been based in the most part on the module syllabus M507 Health Effects of Hazardous Substances published by the British Occupational Hygiene Society (BOHS), Faculty of Occupational Hygiene. The BOHS administers a number of such modules; further information on which can be obtained by visiting the BOHS website at [www.bohs.org](http://www.bohs.org).

At the time of publication every care has been taken to ensure that the majority of topics covered in the BOHS syllabus for the subject (M507) have been included in this Student Manual. Providers of training courses should check the BOHS website for any changes in the course content.

### 1.2 AIM OF COURSE

The course introduces students to the health hazards of substances that are used at work. It describes where hazardous substances are commonly used in industry and what their harmful effects can be. It also explains the underpinning principles of physiology, toxicology and epidemiology.

### 1.3 LEARNING OUTCOMES

On successful completion of this module the student should be able to:

- Provide definitions of commonly used toxicological terms
- Describe the main routes by which hazardous substances can enter the body, and the factors which influence their absorption, distribution, storage and elimination
- Describe the main sources of information on hazardous substances and processes
- Recognise hazardous substances in the workplace



- Describe the main features of the principal target organs affected by hazardous substances at work, and the factors which influence the degree of harm
- Describe the main routes of exposure for hazardous substances commonly encountered in the workplace
- Describe the health effects of some common hazardous substances
- Undertake basic interpretation of the results from epidemiological studies

#### **1.4 FORMAT OF MANUAL**

It should be recognised that the format presented in this manual represents the views of the editors and does not imply any mandatory process or format that must be rigidly observed. Presenters using this manual may well choose to alter the teaching sequence or course material to suit their requirements.

The material provided in this manual has been aligned with the presentations for each topic so students can follow the discussion on each topic.

## 2. INTRODUCTION TO TOXICOLOGY

### 2.1 INTRODUCTION AND HISTORICAL PERSPECTIVE

Toxicology has sometimes been described as the 'science of poisons'. However, this is a somewhat simplistic description. A more suitable definition of toxicology is:

“Toxicology is the study of the potential of any substance to produce adverse health effects on a living organism and the likelihood that such adverse effects might occur under specified exposure conditions”.

The principles of toxicology have been applied by humans for thousands of years. Early civilisations used a variety of materials because of specific effects ranging from medicinal (herbs and plant extracts) to harmful (cyanide extracted from peach kernels, aconite used on arrow tips for hunting).

Paracelsus (1493-1541) is widely regarded as the father of modern toxicology and is one of the most important early pioneers of the subject. He recognised the relationship between dose and response and is credited with the statement,

“All substances are poisons; there is none which is not a poison. The right dose differentiates a poison and a remedy...”

This concept is fundamental to our understanding of the principles of toxicology and it is also important when trying to protect the health of workers who may be exposed to toxic substances.

However, despite increases in our knowledge and understanding of toxicology it is often very difficult (or even impossible) to link the cause and effect of a disease. There are a number of reasons for this including the following:

- The health effect of concern may not occur at the time of exposure. Indeed, in many cases the effect may not be produced for a period of time after exposure (e.g. days or even years). For example asbestos or chromium-induced cancer may not manifest itself for many years after exposure has ceased
- The person who develops the health effects may no longer work with the substance that caused the effects, and the link between the exposure and the health effect may not be noted
- There may be a wide variation in genetic susceptibility between individuals to the effects of a hazardous substance.
- The effects of exposure to hazardous substances may also vary widely depending on the persons age, gender and health status
- There is also the added complication of combined effects of different substances. Exposure is rarely to only a single substance as a number of different substances may be present in the workplace and interactions between these different substances may significantly alter the severity of the effect on the person
- The effects of the hazardous substance may be altered by alcohol, tobacco or any recreational or prescribed drugs that the person may be taking
- Perhaps more surprisingly, there is also a lack of detailed toxicological information available for many of the materials commonly used industrially.

## **2.2 SOME BASIC TOXICOLOGICAL TERMS AND CONCEPTS**

### **2.2.1 Acute and chronic effects**

When a substance affects the body the effect may occur immediately or it may not manifest itself for a period of time. In toxicology, the terms that are used to describe how rapidly adverse responses to hazardous substances occur are acute effects and chronic effects. Acute effects occur very rapidly during or immediately after exposure and generally tend to be of short duration. The effects are generally developed in response to a relatively high dose or high exposure concentration of the substance.

Symptoms of acute toxic effects vary from sudden death through to minor irritation of the skin, eyes, nose or throat. Examples of acute effects include the immediate eye and respiratory tract irritation to exposure to ammonia, burns to the skin caused by direct contact with strong acids or alkalis or narcosis from exposure to organic solvents.

Chronic effects tend to occur after long-term, repeated exposure to lower levels of a hazardous substance. Chronic or long-term effects are long lasting and develop gradually over long periods of exposure, usually months or years. Recovery once exposure stops is extremely slow and often incomplete; in fact the effects are often permanent.

Chronic effects include cancer, bronchitis, and dermatitis. Some examples of chronic toxicity are pneumoconiosis from (usually) long term exposure to coal dust and silicosis after exposures to quartz dusts.

### **2.2.2 Local and systemic effects**

Hazardous substances may induce a toxic response either locally or systemically.

- Local effects occur at the direct point of contact between the body and the substance, e.g. corrosive materials can cause burns; organic

solvents can cause de-fatting of the skin; irritant gases such as chlorine can cause pulmonary inflammation. These are examples of acute local effects. An example of a chronic local effect is nasal cancer caused by exposure to wood dust.

- Systemic effects occur when the material is absorbed into the body's systems and acts on organs remote from the point of contact of the body with the agent e.g. acute systemic effects from exposure to organic solvent vapours can include dizziness and unconsciousness. Examples of chronic systemic effects from exposure to lead (where the main route of entry is usually inhalation) include damage to the blood forming process in the long bones as well as harmful effects on the nervous system, kidneys and reproductive functions.

Some hazardous substances may produce both local and systemic effects (e.g. organic solvents).

### **2.2.3 Xenobiotic**

A xenobiotic is a chemical or substance which is not normally found or produced in a person or organism. They are also sometimes referred to as 'foreign' substances and include drugs, pesticides and many other synthetic chemicals.

### **2.2.4 Stochastic and non-stochastic**

Stochastic is a term to describe the likelihood of an event taking place. It is synonymous with random i.e. the event can occur purely by chance. An example is the possibility of developing malignant diseases such as cancer for which the probability of cancer occurring is a function of dose. Once a stochastic effect occurs, the consequence is independent of the initiating dose. Stochastic effects do not have a threshold dose below which they cannot occur.

In contrast, non-stochastic effects are characterized by a threshold dose below which they do not occur. Above the threshold dose, non-stochastic effects have a clear relationship between the exposure and the magnitude of the effect. Examples include inflammatory and degenerative diseases.

### 2.2.5 Types of combined effects

It is common that people are exposed to more than one hazardous substance at a time. The different substances may interact such that one substance may alter the toxicity of one or more of the chemicals present.

A number of possible interactions may occur:

- Additive effects
- Synergistic effects
- Potentiation
- Antagonism
- Independent

Additive effect – the combined effect of two substances is equal to the sum of the individual effects if each substance was encountered alone, examples include:

- Toluene and xylene – where both are irritant and narcotic, are similar chemicals and affect the same target organs.
- Organo-phosphorus insecticides – all organo-phosphorus pesticides inhibit cholinesterase activity

Synergistic effect – the combined effect of two substances is greater than the sum of the individual effects if each substance was encountered alone, examples include:

- Carbon tetrachloride and ethanol – both chemicals are hepatotoxic – but total liver damage caused by combined exposures is much greater than expected.
- Smoking and asbestos – this leads to a greatly increased lung cancer risk

Potentiation – a substance has no toxic effect, but when simultaneous exposure occurs with a second substance, the toxicity of the second chemical is enhanced. An example is:

- Carbon tetrachloride and iso-propanol – isopropanol alone is not hepatotoxic, but it increases the hepatotoxicity of carbon tetrachloride.

Antagonism – this is where the combined effect of two substances is less than the sum of the individual effects if each substance was encountered alone. An example is:

- Phenobarbitone and paradoxon (an organo-phosphorous pesticide) - phenobarbitone increases the rate of metabolism of paradoxon and reduces its toxicity.

Independent effect – where none of the above effects occur the toxic effects of each substance are unaffected by simultaneous exposure. An example is:

- Lead and xylene.

### **2.2.6 Limitations of toxicity testing data**

Much of our current knowledge of how substances affect human health has been gathered from toxicity testing. Toxicity testing is usually conducted on animals, raising questions regarding how relevant these studies are to man. For example the dose or concentration of a substance required to kill 50% of rats may be very different to that required to kill 50% of say guinea pigs, or indeed humans. It is therefore very difficult to extrapolate toxicity tests to humans. The answer requires knowledge of absorption, distribution, biotransformation and excretion from the body.

In predicting the adverse effects likely to be found in humans from the results of animal studies, reliance has to be placed on the many similarities

in anatomy, biochemistry, physiology and reactions to poisons of other animals and humans. There are numerous examples of similar qualitative and quantitative responses in humans and animals but differences are common and it must never be assumed that people will react in the same way as other animals. Equally, not every effect found in animals will necessarily occur in man.

### 2.3 PHYSICAL FORMS OF HAZARDOUS SUBSTANCES

Hazardous substances occur in many physical forms and knowledge of these is essential in understanding routes of entry, typical exposure scenarios as well as determining appropriate control methods. It is worthwhile, therefore, to define the different physical forms in which the hazardous substances may occur as follows:

- **Gas** - a formless fluid that completely occupies the space of any enclosure at 25°C and 760mm Hg. Examples include oxygen nitrogen and carbon dioxide.
- **Vapour** - the gaseous phase of a material normally liquid or solid at ordinary temperature and pressure. Examples include benzene and mercury vapour from evaporation of the liquid forms.
- **Aerosol** - a dispersion of particles of microscopic size in air; may be solid particles (dust, fume, fibre) or liquid particles (mist).
  - **Dust** - airborne solid particles that range in size from 0.1 - 100µm in diameter. Examples include wood dust from cutting and sanding operations and quartz dust from crushing of rocks.



- **Fume** - airborne solid particles generated by condensation from the gaseous state. The particles that make up fumes are very small, usually less than 1 micron in diameter. In most cases the volatilised solid reacts with oxygen in the air to form an oxide. Examples include fume from high temperature cutting or welding of metals.
  
- **Mist** – airborne liquid droplets generated by condensation from the gaseous state or by the break up of a liquid by splashing or atomising. Examples are oil mist produced during cutting and grinding operations, acid mists from electroplating, and paint spray mist from spraying procedures.
  
- **Fibre** – a thin and greatly elongated solid substance. Examples include asbestos and glass fibres.

### 3. TYPES OF HEALTH EFFECTS

#### 3.1 ASPHYXIATION

An asphyxiant is a substance that can reduce the level of oxygen in the body to dangerous levels. Asphyxiants can be divided into two general types.

- Simple asphyxiants (e.g. nitrogen, argon) - they are chemically inert but prevent normal respiration by reducing the oxygen level in the air. This may occur by the asphyxiant simply displacing oxygen in an enclosed environment.
  - Air normally contains about 21% oxygen. If this is reduced below about 16% it can result in unconsciousness and at lower levels can lead to death.
- Chemical asphyxiants prevent the body utilising oxygen for normal cellular metabolic processes. The amount of oxygen in the air being breathed in is normal but the body cannot use it.
  - Haemoglobin, found in red blood cells, transports oxygen around the body as a complex called oxyhaemoglobin. Carbon monoxide will displace the oxygen and bind more tightly to the haemoglobin to form the very stable carboxyhaemoglobin. This reduces the amount of haemoglobin available to transport oxygen, possibly to dangerous levels and the body effectively suffocates
  - Hydrogen cyanide is an extremely potent and fast-acting asphyxiant which acts by preventing the biochemical process that converts sugars to energy

Many other substances can cause asphyxiation either directly by chemical action, or indirectly by displacing oxygen from the air. People at particular risk are those who work in confined spaces e.g. fuel tanks, compartments on ships, sewers and pits.

### **3.2 IRRITATION**

An irritant is a substance that can cause reversible inflammation on contact with a body tissue such as the skin or mucous membranes.

The body's response to an irritant may manifest in a number of ways including the following:

- Skin – red or blotchy at point of contact
- Eyes – itchy, painful, red or watery
- Nose – itchy or runny
- Upper respiratory tract – coughing, sneezing – in severe cases the lungs may produce excess fluid causing breathing difficulties

Examples of irritants include gases such as ammonia, chlorine, and oxides of nitrogen. Vapours from liquids such as formaldehyde can also cause irritation. Dermal exposure to solvents may also play a role in irritation due to the de-fatting of skin.

In addition to the acute effects of irritants outlined above chronic exposure can lead to other health effects. Chronic exposure to a respiratory irritant can lead to bronchitis and chronic exposure to a skin irritant may lead to dermatitis.

The symptoms of dermatitis include dry, flaking skin as well as itching, redness and inflammation. It is important not to confuse irritant contact dermatitis with allergic contact dermatitis which is a type of skin hypersensitivity. The latter involves an autoimmune response typical of those agents that cause sensitisation.

An extreme form of irritation is from contact with corrosive substances that can cause tissue damage, similar to burns, from which the tissues do not generally recover. Examples of corrosive substances include concentrated hydrochloric acid, sodium hydroxide, and chromic acid. It should be noted that a corrosive substance at lower concentrations, may only cause irritation.

### **3.3 NARCOSIS**

A narcotic substance is one that depresses the normal function of the central nervous system (CNS). Initially exposure to narcotic substances may lead to symptoms of fatigue and headache as well as feelings of light headedness and euphoria. At higher exposures, effects may include dizziness, nausea, unconsciousness and death. A very common group of substances that can cause narcosis are organic solvents. Alcoholic drinks, which contain ethanol, can produce narcotic effects.

### **3.4 SYSTEMIC TOXICITY**

Toxicity is the degree to which a substance is able to damage an exposed organism. Systemic toxicity describes the adverse effects caused by a substance that affects the body at organs remote from the point of contact with the body. These effects may be caused by the substance itself or by a metabolite or breakdown product of the substance. Due to the metabolic processes within the body the liver and kidney are particularly susceptible to damage by toxic substances.

Examples include the damage caused by cadmium in the kidney and organic solvents such as carbon tetrachloride that cause liver damage because of the way they are broken down by this organ. Other examples

include the neurological deterioration caused by accumulation of lead in the central nervous system.

### **3.5 GENOTOXICITY AND CARCINOGENICITY**

#### **3.5.1 Genotoxicity**

Genotoxicity is a term used to describe the ability of a chemical to induce damage to the genetic material in a cell. Such substances are termed genotoxic or mutagenic.

These are important effects since damage to genetic material can disrupt the normal function of a cell and can lead to irreversible changes called mutations. A mutation is a permanent change to the genetic material that can lead to changes in the functioning of a cell or tissue because it alters the genetic message being carried.

If mutations occur in germ cells they can be passed on to the offspring where the effects may then be seen. In non-germ (somatic) cells, mutation may result in changes to the way that normal cell division is regulated so that it becomes uncontrolled and can lead to the development of cancer.

#### **3.5.2 Carcinogenicity**

Carcinogenicity is the ability of a substance to induce cancer. A substance that can cause cancer is termed a carcinogen. Cancer is a disorder of cells in the body which is characterised by abnormal cell division and growth. It begins when one or more cells fail to respond to the normal control mechanism and continue to divide in an uncontrolled manner.

As ultimately the induction of cancer is believed to be a consequence of mutations; then substances that are genotoxic are often considered to be likely to possess carcinogenic activity. However, not all carcinogens are

necessarily genotoxic themselves (or through metabolites). An example of this is asbestos. There must therefore be a non-genotoxic mechanism.

It is thought that repeated damage to tissues may stimulate an increased rate of cell division. As background agents such as radiation are continually causing background damage to genetic material (which is also being constantly repaired by cells) any increase in cell division may help to make this "background" damage become permanent as mutations rather than be repaired.

Thus stimulation of cell division may itself lead to induction of cancer although the substance inducing the stimulation may not itself possess genotoxic activity. A non-genotoxic mechanism such as repeated damage to tissues may explain why some substances appear to cause cancer at high doses in animal tests but do not appear to cause cancer in humans at lower exposure levels.

### **3.5.3 Benign and malignant tumours**

The new growths whether caused by mutagens or any other mechanism are called tumours or neoplasms and may be either "benign" or "malignant".

- Benign tumours include warts, polyps and fibroids. A benign tumour can grow large enough to cause pain and may damage nearby organs, however, these tumours do not invade surrounding tissues and do not spread to other sites in the body. They can usually be removed surgically without likelihood of recurrence. They are usually not life threatening (unless they are growing near a key internal organ).
- Malignant tumours can spread (or *metastasise*) throughout the body by invading neighbouring tissues, entering blood vessels, lymphatic vessels and other spaces with development of secondary tumours.

They tend to be aggressive, respond poorly to surgery and / or chemotherapy and radiotherapy, and are usually life threatening.

#### **3.5.4 Difficulties in identifying carcinogens**

There are many potential causes of cancer and it is often difficult to prove a causal link between exposure to a certain chemical and subsequent cancer. A particular problem in establishing causes of cancer is that in many cases there is a long latent period between exposure and development of cancer. This may be many years or even many decades.

However, there is significant evidence that tumours may develop after occupational exposure to a number of different chemicals. Cancer caused by industrial exposure may occur in many different organs, some examples are listed below:

<u>Site of cancer</u>	<u>Substance</u>
Lung	Asbestos, chromium, nickel carbonyl, rubber fume
Nasal sinuses	Wood dust
Liver	Vinyl chloride monomer
Kidney	Cadmium
Bone marrow	Benzene
Skin	Mineral oils, tar

#### **3.5.5 Classifications of carcinogens**

Several organisations and bodies provide lists of known or "suspect" carcinogens, classified into different categories. It is important to note that the classification is complicated and is not universally agreed upon. Some of these are given below.

Two non-regulatory schemes in common use are those of the International Agency for Research on Cancer (IARC) and the American Conference of Governmental and Industrial Hygienists (ACGIH).

The IARC Monographs on the Evaluation of Carcinogenic Risks to Humans have been evaluated for more than 900 environmental agents and exposures. Each exposure is classified into one of five groups according to the strength of the published evidence for carcinogenicity.

Group 1	Carcinogenic to humans
Group 2A	Probably carcinogenic to humans
Group 2B	Possibly carcinogenic to humans
Group 3	Not classifiable as to carcinogenicity to humans
Group 4	Probably not carcinogenic to humans

The complete list of the evaluations can be found at <http://monographs.iarc.fr> (accessed May 2009)

The ACGIH system uses the following notations:

- A1 Confirmed Human Carcinogen:
  - The agent is carcinogenic to humans based on the weight of evidence from epidemiologic studies.
  
- A2 Suspected Human Carcinogen:
  - Human data are accepted as adequate in quality but are conflicting or insufficient to classify the agent as a confirmed human carcinogen; OR, the agent is carcinogenic in experimental animals at dose(s), by route(s) of exposure, at site(s), of histologic type(s) or by mechanism(s) considered relevant to worker exposure.

The A2 is used primarily when there is limited evidence of carcinogenicity in humans and sufficient evidence of



carcinogenicity in experimental animals with relevance to humans.

- A3 Confirmed Animal Carcinogen with Unknown Relevance to Humans:
  - The agent is carcinogenic in experimental animals at relatively high dose, by route(s) of administration, at site(s), of histologic type(s) or by mechanism(s) that may not be relevant to worker exposure. Available epidemiologic studies do not confirm an increased risk of cancer in exposed humans. Available evidence does not suggest that the agent is likely to cause cancer in humans except under uncommon or unlikely routes or levels of exposure.
  
- A4 Not Classifiable as a Human Carcinogen:
  - Agents which cause concern that they could be carcinogenic for humans but which cannot be assessed conclusively because of a lack of data. In vitro or animal studies do not produce indications of carcinogenicity which are sufficient to classify the agent into one of the other categories.
  
- A5 Not Suspected as a Human Carcinogen:
  - The agent is not suspected to be a human carcinogen on the basis of properly conducted epidemiologic studies in humans. These studies have sufficiently long follow-up, reliable exposure histories, sufficiently high dose, and adequate statistical power to conclude that exposure to the agent does not convey a significant risk of cancer to humans, OR, the evidence suggesting a lack of carcinogenicity in experimental animals is supported by mechanistic data.

Under the Globally Harmonised System of Classification of Labelling of Chemicals (see Section 11) which is now beginning to be implemented in

many countries, there are regulatory requirements to identify carcinogens on labels.

### **3.6 SENSITISATION - (ALLERGIC REACTION)**

Sensitisation is a term used to denote a process by which the body's immune system, carrying out what are its normal functions, produces an adverse reaction that can in some cases be of a serious nature. In effect the body treats a substance as if it was an invading micro-organism, against which it is defending itself. Hay fever induced by exposure to pollen is a typical example of a sensitisation response (in this case of the respiratory tract).

There are a number of different white blood cells and associated antibodies within the body that play a part in the body's defence and immune systems. One particular type of antibody, Immunoglobulin E (IgE) plays an important role in many allergic responses, and is particularly associated with the most severe hypersensitivities.

The first time an allergy prone person comes into contact with an allergen they make large amounts of specific IgE antibodies. After the first exposure the specific IgE antibodies remain attached to other cells within the blood serum for many years, ready to respond rapidly to subsequent exposure to that particular substance.

In industrial hygiene, the two main categories of sensitisers are respiratory sensitisers and skin sensitisers. Sensitisation normally develops over a period of time following repeated exposure of an individual to a chemical substance. Once someone becomes "sensitised" then they are always likely to respond adversely if they subsequently come into contact with the substance.

As described earlier, the substance interacts with the individual's immune system cells with the result that the substance is eventually "seen" as an

invading foreign body that needs to be isolated through a typical immune reaction.

For the skin this results in the release of histamine locally which can cause an inflammation of the skin (allergic contact dermatitis). This usually manifests as a red, itchy, scaly rash, often localised to the area of contact. It is a delayed hypersensitivity reaction which usually occurs between 6 and 48 hours after exposure. Less critical reactions include urticaria – an itchy rash on the skin consisting of a number of raised pale bumpy wheals surrounded by red skin (similar to nettle rash).

For the respiratory tract the release of histamine causes a range of effects including narrowing and inflammation of the airways, difficult in breathing and rhinitis (inflammation of the nose – e.g. hay fever like symptoms). In many cases the respiratory symptoms collectively are characteristic of asthma (which is a condition that can be induced by a number of factors including chemicals, cold air, exercise) and in fact the term “occupational asthma” is often used as an alternative to respiratory sensitisation.

In extreme cases, if an individual is particularly sensitised then the reaction can be very severe leading to arrest of the heart (anaphylactic shock).

As stated earlier, the two main categories of sensitisers in the workplace are respiratory sensitisers and skin sensitisers. Examples of skin sensitisers include chromium, nickel, latex and epoxy resin adhesives that can cause contact dermatitis.

A number of substances are known to be respiratory sensitisers. Some of the more common examples are given below:

- Isocyanates
- Grain and flour dusts
- Rosin-cored solder fume (colophony)
- Animal proteins

- Dusts of some woods
- Detergent and bakery enzymes
- Antibiotics

There are a number of different assessment methods that are available for determining whether or not a person is allergic to a particular substance. These include lung function tests (or spirometry), challenge testing, skin prick testing and blood IgE testing. These are examined in more detail in Section 6.3

### **3.7 REPRODUCTIVE EFFECTS**

A substance may affect an individual by reducing their fertility, thereby making it more difficult, or impossible, to have offspring. These are reproductive toxicants and examples include some glycol ethers, lead, and some pesticides.

Another category is developmental toxicants (often referred to as teratogens) that can cause damage to a developing foetus. While these substances may not harm the mother they may result in physical abnormalities of the child, or affect its development after birth. Examples of these include lead, methyl mercury and thalidomide.

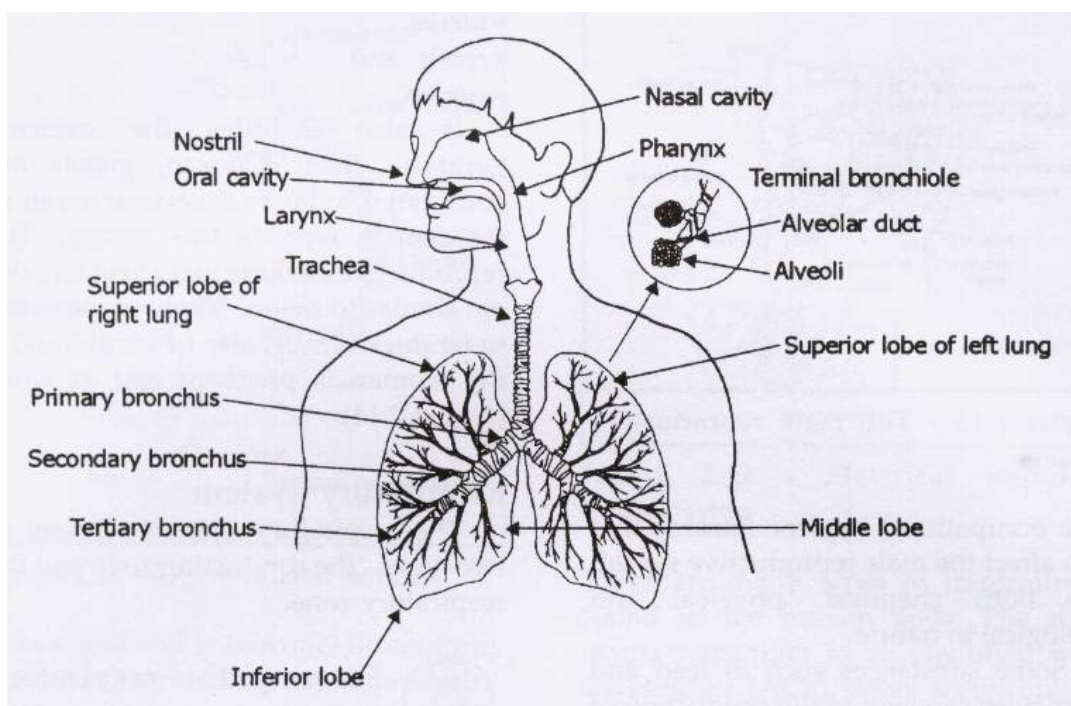
## 4. BASIC HUMAN BIOLOGY AND TARGET ORGANS

### 4.1 RESPIRATORY SYSTEM

#### 4.1.1 Structure of the respiratory system

The respiratory system consists of the airways, the lungs and the respiratory muscles that mediate the movement of air into and out of the body. Inhaled air passes from the nose and mouth through the trachea and into the branched structures of the lungs called bronchi.

Air then travels along the bronchioles to its ending (the terminal bronchiole) which is covered in tiny multi lobed sacs called alveoli where most of the gas exchange occurs.



(Source: Tranter 1999 – *Reproduced with permission*)

**Figure 4.1 – Respiratory System**

From an occupational perspective, inhalation is usually the main route of absorption of hazardous materials. The lungs have a very large surface

area and an excellent blood supply, both of which facilitate absorption. The barrier between inhaled air and the systemic circulation is very thin therefore absorption may be very rapid. In addition to substances being absorbed through the lungs, insoluble particles such as silica and asbestos can lead to lung damage.

The respiratory system can be broadly divided into three areas, and materials in different physical states will be absorbed in different regions;

- Naso-pharynx or head airways region
- Tracheo-bronchiolar region
- Alveolar region or deep lung

The term 'upper respiratory tract' is often used – this corresponds to the first two areas above.

**The naso-pharynx** region consists of the nose, mouth and pharynx (throat). Nasal hairs can filter out large particles and the nasal cavity is lined with a moist mucous membrane which can also trap foreign particles. Small surface hairs called cilia move the trapped particles towards the nose to be sneezed out.

In addition, the mucous membranes moisten and warm the air as it is inhaled. This process is enhanced by the nasal turbinates which divide the main pathways into a number of separate channels thus increasing the area of mucous membrane in contact with the air. It should be noted that breathing through the mouth by-passes the nasal filter and the nasal cavity. If irritant substances penetrate to the throat a coughing reflex is initiated.

**The tracheobronchiole** region consists of the trachea, which then branches into the two primary bronchi, which further divide into progressively finer bronchi and bronchioles. With each division the total cross sectional area of the air passages increases and the velocity of the air movement reduces. By the time the air has reached the terminal

bronchioles the flow rate has reduced to very low levels meaning that diffusion down concentration gradients becomes the main transport mechanism. This has consequences for particle deposition which will be examined later.

**Table 4.1 – showing the cross-sectional area of the airways, and rate of airflow (for a volume flow of 100 millilitre per second)**

	Area (cm <sup>2</sup> )	Flow rate (cm / sec)
Trachea	2.0	50
Terminal bronchioles	80	1.25
Respiratory bronchioles	280	0.36
Alveoli	10 – 20 x 10 <sup>5</sup>	Negligible

(Source: Harrington and Gardiner (1994) – Occupational Hygiene)

These upper airways are lined with mucous membranes which are also lined with cilia (hair-like extensions from cells lining the airways). These slowly sweep trapped particles upwards to the throat where they are swallowed or spat out. This clearing mechanism is known as the ‘mucociliary escalator’. While the particle may be cleared from the lung, if it is swallowed it may then be absorbed in the gastro-intestinal tract.

**Alveolar region** – the bronchioles terminate in millions of alveoli. In an adult there are approximately 300 – 600 million alveoli with a total surface area of about 100 – 200 square metres. Gas exchange between the air and the blood takes place across the thin walls (only one or two cells thick) of the alveoli. The alveoli are surrounded by blood capillaries so oxygen diffuses from the alveoli into the bloodstream and carbon dioxide diffuses from the blood into the alveoli for exhalation.

There are no cilia in the alveoli and particles may be retained for a long period (months or even years). Although there are no cilia in the alveoli there are phagocytes (a range of different white blood cells that engulf and digest the deposited particles) which travel throughout the alveoli. One important type of phagocytic cells in humans are macrophage cells. Having

taken up the particle the phagocyte or macrophage transports it from the alveoli either to the muco-ciliary escalator or via the lymphatic system.

#### 4.1.2 Particle deposition in the respiratory system

Airborne particulates found in the workplace vary greatly in size ranging from below 1 micron in diameter to up to about 100 micron in diameter. The size of the particle is important for two main reasons:

- The smaller the particle the longer it is likely to remain airborne and be carried by air movement. Larger particles settle out more quickly
- Secondly particle size is very important in determining where in the respiratory system the particle is likely to deposit

Particle sizes quoted in most literature and standards refer to the diameters of the particles. This is more correctly defined as the 'aerodynamic diameter' of the particle. Most particles are not perfect spheres and occur in many shapes and different densities. The concept of the aerodynamic diameter which combines the effect of size, density and shape was developed to understand how these particles would behave in air.

The aerodynamic diameter of a particle is the equivalent diameter of a perfect sphere of unit density that would behave in air in the same way as the particle in question. It is possible to calculate aerodynamic diameters for different types of particles, but this is outside the scope of this course.

**Deposition mechanisms** - there are four main mechanisms by which deposition of particles in the respiratory system may occur:

- Interception
- Impaction
- Sedimentation
- Diffusion



Interception occurs mainly in the nose and nasal cavity where large particles (about 10 to 100 micron diameter) are too large to penetrate the passages between the nasal hairs or the nasal turbinates.

Impaction occurs mainly in the head airways and at the bifurcations (divisions) of the larger bronchioles. Particles in the airstream fail to negotiate branches in airways and impact onto the airway wall. Particles typically in the range 5 to 30 micron deposit at these points by this mechanism.

Sedimentation of smaller particles (typically between 1 and 5 micron) typically occurs in the small bronchioles and alveoli. These particles settle out due to gravity in these areas where the air velocity is very low.

Diffusion of the smallest particles (typically less than 1 micron) onto the alveolar membrane can occur in the alveoli where the airflow is negligible. Particles move at random (Brownian motion) until they collide with the alveolar membrane. Many small particles may remain suspended for long enough for them to be exhaled directly.

The sizes of particles that deposit in different parts of the respiratory system and the deposition mechanism are not sharp dividing lines, but will overlap. Also the deposition will be affected by flow rate so will differ between when at rest and when breathing heavily on exertion.

As stated above, the site where toxic substances will be deposited in the lung largely depends on the size of the particle and its shape and density. Larger particles will be trapped in the upper respiratory tract, with only smaller particles entering the alveolar region.

### 4.1.3 Particle size fractions

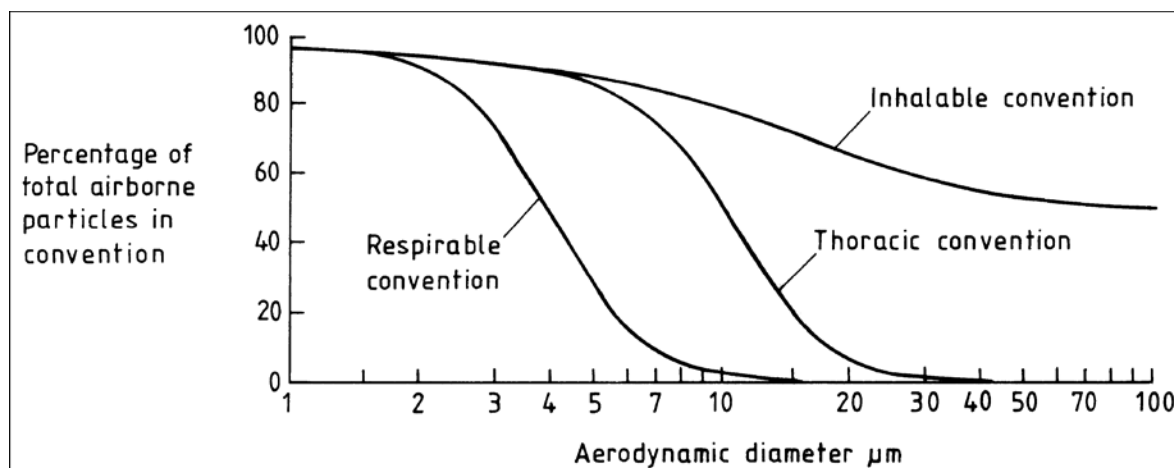
The behaviour and deposition of any particular particle after entry into the respiratory system and the body's response depends largely on the size of the particle. In general there are two size fractions of interest to industrial hygienists and these are termed *inhalable* (or *inspirable*) and *respirable*.

Inhalable dust is the fraction of airborne material which enters the nose and mouth during breathing and is therefore liable to deposition anywhere in the respiratory tract. The inhalable fraction depends on the prevailing air speed and direction around the person, as well as breathing rate and whether breathing is via the nose or mouth.

A standardised definition of the size fraction for inhalable dust is given in ISO 7708 – 'Air Quality – Particle Size Fraction Definitions for Health-Related Sampling', upon which many National Standards are based. In practical terms, for total inhalable dust the maximum particle size is about 100 microns.

Respirable dust is that fraction that penetrates to the deep lung (the alveolar region) where gas exchange takes place. The respirable fraction will vary between individuals and will also depend on the breathing rate of the person. As with inhalable dust there is a standardised definition of the respirable dust size fraction given in ISO 7708, upon which many National Standards are based. The particle sizes of respirable dust are generally up to 10 microns.

The curve is reproduced below in Figure 4.2. Note that in all cases as the size of the particle increases, a smaller percentage of particles reach the particular target area. For instance nearly 100% of particles of 1 micron are likely to reach the alveoli, 50% at 4.25 micron, dropping to a few percent at about 10 micron aerodynamic diameter.



(Source: BS EN 481:1993 Workplace atmospheres – Size fraction definitions for measurement of airborne particles – reproduced with permission)

**Figure 4.2 – Inhalable, thoracic and respirable conventions as percentages of total airborne particles**

Another size fraction that is sometimes quoted is the *thoracic* fraction, which is the size fraction that deposits anywhere within the lung (including the gas exchange) region.

#### 4.1.4 Absorption of gases and vapours

Gases and vapours mix and move freely with the air being breathed in. However, before gases and vapours reach the lower regions of the lung they must pass through the upper respiratory tract. This region of the lung is extremely moist, and highly water-soluble gases such as ammonia and formaldehyde will readily dissolve and be absorbed. In many cases highly water-soluble gases are also irritants.

Less water soluble gases and vapours such as phosgene and organic solvents will pass to the alveolar region but the amount absorbed will be influenced by their solubility in blood.

#### 4.1.5 The lung as a target organ

There are a number of health effects that may occur in the lungs ranging from irritation to cancer. The following illustrate the range of effects together with examples of substances that can cause the effects.

**Irritation** - acute irritation of the upper respiratory tract can be caused by highly water-soluble gases such as ammonia and hydrogen chloride. Symptoms include coughing, irritation of mucous membranes as well as pain in eyes mouth and throat. Higher concentrations can cause release of fluid into the surrounding tissues leading to swelling (oedema).

Irritant mists or aerosols such as soluble chromium (VI) salts, as well as many metal oxide fumes can also cause irritation of the upper respiratory tract. In addition, dusts such as machine made mineral fibre can cause irritation and coughing

Acute irritation of lower respiratory tract (deep lung) can be caused by less water-soluble gases such as phosgene and nitrogen dioxide. This causes irritation of mucous membranes and pulmonary oedema. This division between areas affected is a little arbitrary and it should be noted that irritant gases may affect both areas of the lung if exposure is high. Irritation can also be caused by severe exposure to many metal fumes e.g. cadmium oxide which can cause an acute chemical pneumonitis (inflammation of the lungs) which may be fatal.

In addition to acute effects chronic irritation of upper and lower respiratory tract can cause permanent lung damage with repeated exposure and may also cause bronchitis or emphysema (see below).

**Pneumoconiosis** – this can be defined as the accumulation of dust in the lungs. It can be divided into two broad categories depending on the reaction of the lungs to the presence of the dust. It may occur as a fibrotic or as a benign pneumoconiosis.

- **Fibrosis or fibrotic pneumoconiosis.** The macrophage system is a very efficient mechanism by which foreign particles may be removed from the alveoli. However, in some situations the macrophages are not able to engulf the particles and remove them. For example, asbestos fibres may be too long to fit inside a macrophage. Or with crystalline silica in the form of quartz, the macrophage cells engulf the particle but then die. In these situations chemicals released from the macrophage cells attract fibroblasts (cells that produce fibrous tissue) that can cause fibrotic changes in the lungs.

The fibrotic tissues replace or cover the thin cells that line the bronchioles and alveoli and restrict the passage of oxygen. Also, the elasticity of the lung tissue is significantly reduced. These effects can lead to breathlessness and reduced lung function. This fibrosis can cause progressive scarring over many years and may be fatal.

- **Benign pneumoconiosis.** Metal dusts, such as iron, tin and barium can cause so-called "benign" pneumoconiosis. They do not damage the alveoli or lead to fibrosis. Changes in the lung may show as rounded or nodular opacities on X-ray, but these are not associated with other symptoms or pulmonary function abnormalities.

**Emphysema** – in emphysema, the alveoli become enlarged and the individual alveoli walls break down and merge. This leads to the formation of fewer, larger alveoli resulting in a reduced surface area for gas exchange. Symptoms include breathlessness and cough. It is a chronic condition and can be caused by smoking and other pollutants such as cadmium oxide.

**Lung cancer** – this is a growth of abnormal cells in the lungs. It may be triggered by a number of substances including rubber fume, arsenic, hexavalent chromium, asbestos as well as by smoking. In most cases of lung cancer a tumour develops in the bronchi. Symptoms include coughing,

pain and breathing obstruction. Cells from the cancer may spread (or metastasise) from the lungs to other parts of the body and is often fatal.

#### 4.1.6 **Respiratory sensitisation**

There is a range of allergic conditions that can occur when a substance causes an immune response upon exposure or contact with the tissues of the respiratory system, leading to respiratory sensitisation.

**Rhinitis** – this is a rapid allergic reaction that affects the nose, throat and eyes. The nose can become ‘blocked’ or may produce excessive mucus and become ‘runny’. The eyes become swollen, red, itchy and watery. It can be caused by a wide range of substances such as pollen, organic dusts and some chemicals.

**Occupational asthma** – this is the term given to an inflammation and allergic constriction of the bronchi and bronchioles. This constriction, together with increased mucus production and inflamed tissue further narrow the airways. Symptoms include a tight chest, breathlessness and wheezing, with particular difficulties with breathing out. This allergic reaction often occurs after repeated exposure over a period of time, after which the person becomes sensitised to very low exposure levels.

Respiratory sensitisers that may induce asthma-like symptoms include isocyanates; solder fume, some metals (e.g. platinum and cobalt) as well as a wide range of organic materials. These include latex, vegetable dusts, animal proteins in fur and feathers, detergents and enzymes.

**Extrinsic allergic alveolitis** – this is an inflammation of the terminal bronchioles and alveoli. Acute symptoms include delayed flu-like symptoms, fever, headache, muscle pain and cough. Chronic effects may include fibrosis and breathlessness on exertion, which may be disabling.

It is often caused by inhalation of respirable fungal spores or dried animal proteins. Mould and fungal spores are likely to build up in situations where vegetable products are stored in damp conditions. Historically, a number of names specific to a particular process or industry have been used to describe the health effect. These include 'Farmer's lung' which is caused by inhalation of spores from mouldy grain or hay.

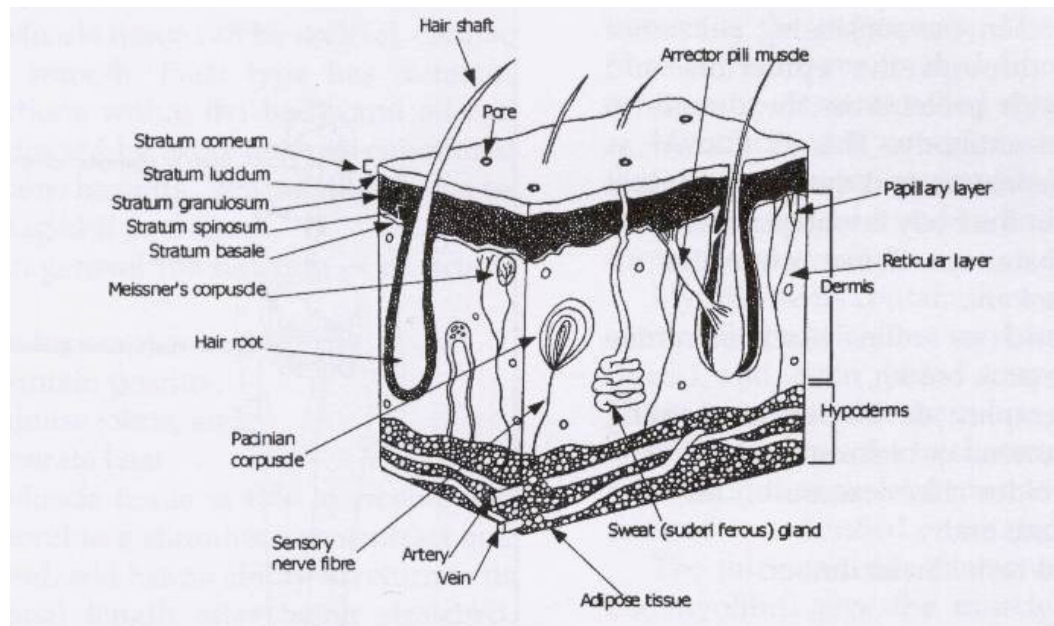
**Byssinosis** – this is caused by exposure to dust produced during machine spinning and weaving of cotton and some other vegetable fibres such as flax and hemp. Symptoms develop after many years of exposure and include tight chest, breathlessness and cough. In chronic cases breathing difficulty occurs due to irreversible airways obstruction which can be disabling.

## **4.2 SKIN**

### **4.2.1 Structure and function**

The skin is often known as the largest organ of the body and as the interface with the surroundings it provides protection against the physical hazards such as heat, radiation and abrasion, as well as against chemicals and bacteria. Its other important functions are insulation and temperature regulation, sensation and Vitamin D and B synthesis.

The skin can be divided into three layers – epidermis (outer layer), dermis and hypodermis (subcutaneous tissue). The thin outer layer or epidermis provides a tough barrier against injury. It also acts as a barrier to water and water-soluble substances. Below the epidermis is the dermis – a deeper layer of connective and elastic tissue that contains blood vessels, nerve fibres, hair follicles, sweat glands and sebaceous glands. Beneath the dermis is the hypodermis (the sub-cutaneous layer) which includes fat cells that provides some insulation and cushioning.



(Source: Tranter 1999 – *Reproduced with permission*)

**Figure 4.3 – Diagram of the Layers of the Human Skin**

The epidermis can be further divided into 3 layers;

- the outer stratum corneum (or cornified layer) which consists of flattened dead cells that provide protection and is covered by a surface film of sebum which is slightly acidic and also acts as an anti-bacterial agent.
- the stratum lucidum (or granular layer) which can make melanin (a brown pigment that protects against UV radiation).
- the stratum granulosum (or germinative layer) where new cells are made by division. These cells move outwards to the surface where they continuously replace the dead cells on the surface.

The dermis contains the capillaries that provide blood supply. In addition it contains sweat and sebaceous glands, and hair follicles that continue through to the surface of the epidermis. Nerve endings are also present in the dermis.



### 4.2.2 The skin as a route of entry

As stated earlier, the epidermis is impermeable to water-soluble materials; however, the underlying dermis is freely permeable to all substances. As a result damaged skin decreases the protection provided by the epidermis. Damaged skin should be protected by wearing plasters or gloves. In any case, it is always advisable to protect the skin from exposure to hazardous substances and good standards of personal hygiene should be maintained.

Other factors that increase the potential for permeation include warm, moist skin, pre-existing skin disease, degreased skin and when substances can be kept in contact with the skin such as when they are trapped (“occluded”) under gloves or clothing.

Lipid soluble substances are able to permeate through intact skin. Examples of substances with high skin permeability are organophosphate pesticides and phenol. These can be absorbed through the skin in quantities sufficient to cause death.

### 4.2.3 The skin as a target organ

There are a number of conditions that can be caused by exposure to a range of different substances. These include irritant contact dermatitis, allergic contact dermatitis, folliculitis, pigment disturbances, ulceration and cancer.

**Dermatitis** – this can be defined as any inflammatory disease of the skin. It manifests as reddening of the skin (erythema) together with scaling and cracking. The affected parts may also become swollen and itchy and sometimes blistered. Dermatitis is very common and is difficult to treat successfully. It can be divided into two categories – irritant contact dermatitis and allergic contact dermatitis.



(Source: HSE Hairdressing: What does dermatitis look like 2008 – Reproduced under the terms of the Click-Use licence)

***Figure 4.4 Typical appearance of dermatitis***

Irritant contact dermatitis is the most common occupational skin disease. All workers may be affected, particularly if the exposure is repeated and prolonged. Typical skin irritants include detergents, organic solvents, acids, alkalis (including cement), oxidising agents and some plants.

Allergic contact dermatitis affects those workers who are sensitised to that particular substance. Once sensitised, the symptoms will occur even on exposure to extremely low levels of the substance. Examples of substances that can cause allergic contact dermatitis include nickel, epoxy resin adhesives and latex (often gloves). The causative agent may be confirmed by patch testing to confirm a positive allergic response.

**Other skin conditions** - Folliculitis is caused by the sebaceous gland pores becoming blocked and causing acne like lesions. Substances that may cause folliculitis include oils, greases and waxes.

Some substances may cause pigment disturbances to the skin. This may result in de-pigmentation (some phenols) or more commonly it results in hyper-pigmentation. Tar and some insecticides can cause reddening and darkening of the skin, while silver salts can cause a blue-grey discolouration.

Ulceration of the skin is a well documented effect of exposure to chromic acid (hexavalent chromium) in the chromium plating industry. Exposure to cement which contains hexavalent chromium in cements can also cause ulceration. Other examples include antimony and mercury fulminate.

Skin cancer can be caused by a number of different substances including polyaromatic hydrocarbons (PAH's), coal tar, soot, asphalt and arsenic. However, the cause of the largest number of skin cancers is from exposure to ultra-violet light (sunlight or industrially produced UV light). Excessive exposure to ultra-violet light is particularly associated with production of melanomas (cancer of the melanin producing cells in the skin).

## **4.3 NERVOUS SYSTEM**

### **4.3.1 Structure and function**

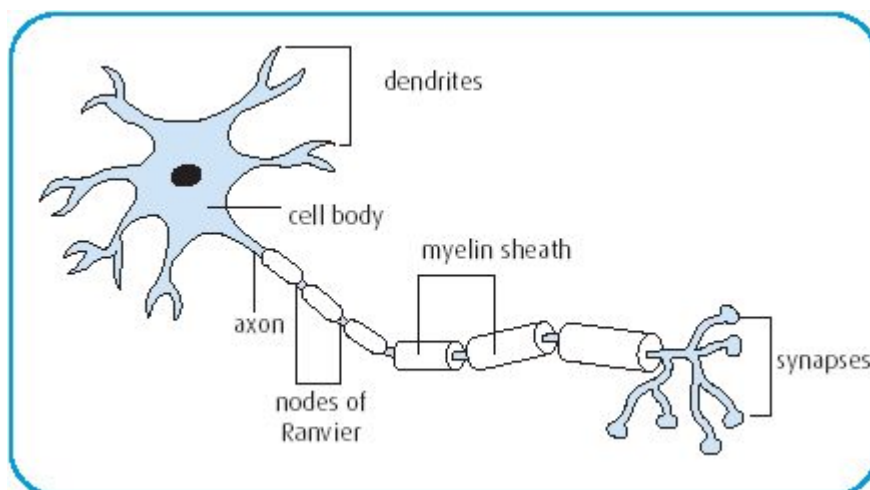
The nervous system controls and co-ordinates the activities and functioning of the body. It also responds to external stimuli in a precise rapid manner. It can be divided into two anatomical divisions; the central nervous system (CNS) and the peripheral nervous system (PNS).

The central nervous system consists of the brain and spinal cord and the peripheral nervous system comprises all the other nerves. The peripheral nerves constantly send information to the central nervous system which processes it and sends signals back to the peripheral nervous system.

The nervous system can also be divided into two functional divisions; the motor nerves and the sensory nerves. The motor nerves control movement (i.e. the muscles) and can be further split into the somatic system that control voluntary movement and the autonomic that control involuntary movement such as heart beating and breathing. The sensory nerves are involved in the sensation of touch, pain, temperature, sight, sound and balance.

The basic functional unit is the nerve cell or neuron. This has a cell body with a central nucleus. Originating from the cell body are long projections, called axons, along which nerve impulses travel rapidly. The axons are coated by the myelin sheath, (a fatty substance) that helps to insulate and protect the axon. The presence of the myelin sheath also increases the speed of the nerve impulse transmission.

Nerve impulses are transmitted along the axon as electrical signals caused by the rapid depolarisation and repolarisation of the axon which changes the balance of sodium and potassium ions between the axon and outside.



(Source: Multiple Sclerosis Trust – reproduced with permission)

**Figure 4.5 Diagram of nerve cell**

The axon terminates at the synaptic knob which is located close to the target cell. The gap between the end of the synaptic knob and the target

cell is called the synapse. The nerve impulse travels down the axon to the synaptic knob. When it reaches this point it triggers the release of chemicals (neurotransmitters) such as acetylcholine that travel across the synaptic gap to the target cell. This triggers a response in the target.

#### 4.3.2 Nervous system as a target organ

There are a number of ways that the correct functioning of the nervous system can be affected. This includes structural damage to the neuron or the myelin sheath, or functional damage including depolarisation of the axon or interference with the normal transmission of signals across the synapse.

**Structural damage to neuron** - lead can damage the myelin sheath slowing nerve impulse transmissions. Mild symptoms include tiredness and lassitude. In severe cases the peripheral nervous system may not be able to control muscles in the limbs producing muscular weakness often showing as foot and wrist drop.

N-hexane can cause swelling of the axon and degeneration of the axon and myelin sheath. As with lead this causes muscular weakness and sensory motor loss particularly to the hands and feet. Manganese is another example of a substance that damages the axon causing symptoms resembling Parkinson's disease such as tremor and difficulty in walking and speaking.

Mercury damages the sensory nerves, causing hearing, speech and vision problems as well as general sensory motor loss resulting in tremors or shaking. Another group of chemicals, (organo-metallics) that includes tetraethyl lead and methyl mercury can readily reach the brain. Over exposure can lead to severe central nervous system effects ranging from irritability to memory loss, convulsions and psychiatric disturbances.

**Functional damage to the nerves** – many volatile organic compounds (solvents) act as central nervous system depressants. They have a high affinity for lipid rich tissues (such as the myelin sheath). They absorb into the cell membranes, causing the membrane to increase in volume impairing nerve impulse conduction. They can cause narcotic and anaesthetic effects such as drowsiness, loss of feeling, unconsciousness and death. In addition chronic exposure to some solvents such as toluene and xylene is linked to long-term neurological damage.

Nerve impulses travel along the axon by changes in the sodium and potassium levels within the axon. These changes cause rapid depolarisation and repolarisation of the nerve. Some substances such as organo-chlorine pesticides cause this process to become prolonged. This causes the nerves to become hyper-excitabile causing tremors.

In addition, there are some substances such as organo-phosphorous pesticides that interfere with chemical transmission across the synapse. In this case the acetylcholine is not hydrolysed by the target cell enzymes. This causes excessive activation of the target with excessive muscle contraction and paralysis.

#### **4.4 CIRCULATORY SYSTEM**

##### **4.4.1 Components and function**

The main components of the cardiovascular or circulatory system are the heart, the blood and the blood vessels. The blood vessels consist of arteries, capillaries and veins. Arteries bring the oxygenated blood, pumped from the heart, to the tissues and the veins bring the deoxygenated blood back to the heart. Blood passes from arteries to veins through capillaries, which are the thinnest and most numerous of the blood vessels.

Blood is composed of a liquid matrix (plasma) in which a number of different types of cells are suspended. There are three types of cells, red cells, white cells and platelets. All three types of blood cell are produced mainly in the bone marrow of long bones.

Red blood cells (erythrocytes) - red blood cells are the most numerous and are responsible for the transport of oxygen. The main component of red blood cells is haemoglobin. Oxygen from the lungs combines with this to form oxyhaemoglobin. This is carried in the bloodstream throughout the body and in the capillaries it releases the oxygen which passes through the vessel walls to the cell. Carbon dioxide produced by the cells is transferred to, and binds with the haemoglobin. This is transported to the lungs where the carbon dioxide is released and exhaled.

In addition to the transport of oxygen and carbon dioxide, the blood also transports nutrients, waste, toxins and heat around the body.

White blood cells (leucocytes) - the main role of white blood cells is to protect the body against infection from invading organisms. They are of two main types; phagocytic cells and immunocytic cells. Phagocytic cells can be thought of as scavenger cells. They physically engulf and destroy foreign bodies and bacteria. The role of immunocytic cells is complex but antibodies are produced that directly attack specific organisms such as viruses.

Platelets (thrombocytes) help to seal damaged blood vessels by starting the clotting process to help to prevent blood loss.

#### **4.4.2 Blood as a target organ**

The correct functioning of the blood can be affected in a number of ways. Some substances damage the red blood cells, other interfere with the

normal uptake of oxygen by the red blood cells, while others affect the production of new blood cells.

**Haemolysis** – haemolysis (breakdown of the red blood cells) occurs when the red blood cell membrane is damaged and the cell destroyed. Breakdown products from this haemolysis reach the kidney and may damage or overload the kidney function. Haemolysis is characterised by the appearance of blood breakdown products in the urine which turns red. Substances that can cause rapid haemolysis include arsine (arsenic trihydride) and stibine (antimony trihydride).

**Carboxyhaemoglobin formation** - as described above, haemoglobin in the red blood carries oxygen to the cells in the form oxyhaemoglobin and removes carbon dioxide. However, other substances may also bind to the haemoglobin preventing normal uptake of oxygen.

Carbon monoxide is the most common example of this type of substance. It binds very strongly to the haemoglobin, replacing the oxygen to form carboxyhaemoglobin. As the amount of carboxyhaemoglobin in the blood increases it decreases the ability of the blood to transport the normal supply of oxygen to the cells.

Symptoms of carbon monoxide poisoning include headache, lethargy, dizziness, unconsciousness and death. Exposure to carbon monoxide often occurs directly from inhalation of products of incomplete combustion. Typical sources include combustion engine and boiler exhausts as well as metal smelting and processing.

Exposure to dichloromethane can also give rise to elevated levels of carboxyhaemoglobin as carbon monoxide is produced in the body as a breakdown product of the metabolism processes.

**Methaemoglobin formation** - methaemoglobin is an oxidation product of haemoglobin with no oxygen carrying capacity. Some substances such as



aromatic amines (e.g. aniline) can produce elevated levels of methaemoglobin. This reduces the oxygen carrying capacity of the blood.

**Anaemia** – this is a disorder when the amount of haemoglobin in the blood is reduced. It may be caused by substances that affect the normal production or synthesis of haemoglobin in the bone marrow. A common example of a substance that can cause anaemia is inorganic lead that accumulates in bones. Benzene also interferes with red blood cell production causing anaemia.

**Leukaemia** – this is the name given to a group of blood disorders in which abnormal white blood cells are produced in large numbers in the bone marrow. These replace or crowd out normal white blood cells. Benzene is a well documented example of a substance that can cause leukaemia.

## 4.5 LIVER

### 4.5.1 Structure and function

The liver is one of the largest organs in the body and is located in the abdominal cavity. It has many functions and can be thought of as a complex chemical processing site. Amongst its main functions are the following:

- Metabolism (biotransformation) of fats, carbohydrates and proteins
- Biotransformation of alcohol and organic chemicals to increase water solubility for excretion by the kidneys
- Production of bile to aid fat digestion in the small intestine
- Storage of iron and some vitamins
- Production of plasma proteins

By virtue of its position in the circulatory system, the liver receives a high blood flow from the hepatic artery and also from the hepatic portal vein which carries blood from the digestive tract to the liver. The liver is the first organ to receive blood from the digestive tract and is therefore liable to be exposed to high concentrations of substances absorbed from the intestinal wall.

The liver is the main site for biotransformation processes in the body and metabolic changes either detoxify or in some cases produce metabolites that are more toxic. In either case the liver may be at risk.

The functional unit of the liver is the liver lobule. These are groups of cells which lie between the hepatic artery and the portal vein and the central vein. Blood that may contain toxins passes over these cells which contain enzymes that are involved in the biotransformation processes. The detoxified blood passes into veins within the lobule prior to joining the central vein for return to the circulatory system.

#### **4.5.2 The liver as a target organ**

Damage to the liver may take a number of forms. Some substances may cause a build up of fatty material as a product of biotransformation. Another acute effect is necrosis (or death) of the liver lobule cells. Chronic health effects include cirrhosis – a build up of fibrous tissues within the liver and cancer.

Fat accumulation in the liver may occur with excessive exposure to alcohol and many chlorinated organic solvents. Cirrhosis can arise from chronic exposure to many organic solvents and is most commonly associated with excessive consumption of alcohol. Cirrhosis is often a pre-cursor to the development of liver cancer. Some metal compounds e.g. arsenic compounds are also linked to the development of liver cancer.

It should be noted that there are sometimes synergistic effects from exposure to alcohol and organic solvents such as carbon tetrachloride.

In addition to liver cancers linked to fibrotic changes such as cirrhosis of the liver, there are a few specific liver cancers. One such cancer associated with exposure to vinyl chloride monomer is angiosarcoma of the liver.

## **4.6 KIDNEY**

### **4.6.1 Structure and function of the kidney**

The kidneys perform a range of functions as follows:

- Excretory functions
  - Filtration of waste products from normal metabolic processes from the blood
  - Excretion of water-soluble toxins or their metabolites and excess salts in urine
- Regulatory functions - they have a principle role in the homeostasis (or regulation) of many body systems such as
  - Sodium, potassium and other salts in the blood
  - pH (acidity) of the blood
  - Body water and blood fluid levels
- Specialised functions
  - Production of some hormones and vitamin D

The kidneys are located within the abdominal cavity, near the spine, just below the ribcage. Each kidney consists of about 1 million filtering units termed nephrons, each consisting of a glomerulus, ball-shaped network of capillaries, and a network of tubules. Blood plasma is filtered by the glomerulus, and the resultant liquid passes through the tubular system where some water and nutrients are re-absorbed.

Humans produce about 1.5 litres of urine over 24 hours, although this amount may vary according to circumstances. Increased fluid intake generally increases urine production, while increased perspiration and respiration may decrease the amount of fluid excreted through the kidneys. A reduced intake of water will normally result in less urine production as well.

The kidney plays a crucial role in regulating electrolytes in the human blood (e.g. sodium, potassium, calcium). pH balance is regulated by the removal of excess hydrogen ions ( $H^+$ ) from blood. In addition, they remove urea, a nitrogenous waste product from the metabolism of proteins from amino acids. The metabolism process forms ammonia which is transported by blood to the liver and detoxified to a less harmful by-product called urea.

#### **4.6.2 Kidney as a target organ**

The kidneys are vulnerable to damage for a number of reasons. They receive a high blood flow so can be significantly exposed to any toxins within the blood stream. Also as part of their regulatory and excretory function for water soluble toxins and metabolites they re-absorb water from the tubules. This re-absorption concentrates toxins in the tubules.

Kidneys can be damaged by a range of substances, the most common examples can be broadly split into two categories – those that damage the glomeruli and those that block or damage the tubules or interfere with tubular re-absorption.

Acute renal failure may occur when urine production is reduced, allowing urine and other waste products to accumulate in the blood. An example of this is when red blood cells are damaged releasing haemoglobin into plasma. This can block the tubules causing renal failure; the appearance of haemoglobin in the urine causes the urine to turn red. Arsenic trihydride and stibine (antimony trihydride) can cause this effect.

Chronic kidney damage or renal failure can occur when a significant number of the nephrons are damaged or die. The remaining nephrons are then over-loaded resulting in reduced filtration efficiency. The presence of proteins and glucose in the urine is indicative of chronic failure.

Many heavy metals such as cadmium, mercury and lead can accumulate in the kidney and cause chronic kidney failure. These metals can remain for many years in the kidney e.g. cadmium has a biological half-life of greater than 10 years. A characteristic low molecular weight protein is found as a result of kidney damage by cadmium.

Mercury is a well documented cause of kidney failure; again the site of damage is the tubule, leading to the appearance of protein in the urine. Lead reduces the tubules ability to re-absorb glucose phosphate and amino acids leading to their appearance in the urine. The damage may be reversible in the short-term but may become irreversible if exposure is prolonged, leading to kidney failure.

Chronic kidney damage and renal failure can be caused by many halogenated hydrocarbons (e.g. carbon tetrachloride and chloroform). Biotransformation of these substances in the liver produces a metabolite that damages kidney tissue.

#### **4.7. REPRODUCTIVE SYSTEM**

The role of male and female reproductive systems is to produce offspring. Exposure to some hazardous substances may affect the ability to produce offspring or may affect the development of the unborn child.

In males effects include reduced sperm counts or reduced sperm motility. Substances that can cause these effects include some pesticides,

oestrogen (pharmaceutical manufacturing), some glycol ethers and lead. In females effects include menstrual disorders caused by carbon disulphide or inorganic mercury. In addition some substances may lead to an increased risk of miscarriage such as some glycol ethers, lead and some anaesthetic gases.

Developmental toxicants (teratogens) are substances that can affect the embryo or foetus. They are often relatively non-toxic to the mother. The development of the child is affected which can lead to abnormalities or functional defects.

Organic mercury can affect the development of brain cells leading to central nervous system defects. Thalidomide is a classic example of a teratogen which caused upper and lower limb defects. Lead can cross the placental barrier and can cause severe swelling of the brain and destruction of neurons. It may also cause spontaneous abortion or premature birth. Affected offspring who survive are likely to show mental retardation, epilepsy or blindness.

## 5 BASIC TOXICOKINETICS

The effect of a hazardous substance depends on the level or concentration of the substance that is present in the body's systems. The levels will depend on the rate (or "kinetics") of absorption, distribution (and storage), metabolism (or biotransformation) and elimination. Eventually, equilibrium is reached which depends on the action of the body on the substance, and the action of the substance on the body.

The study of these processes is called toxicokinetics (sometimes referred to as pharmacokinetics).

### 5.1 ABSORPTION

Within the workplace there are four possible routes of entry of hazardous substances into the body:

- Inhalation – via the lungs
- Direct contact – via the skin and eyes
- Ingestion – via the gastrointestinal tract (GIT) and
- Injection – via direct puncture of the skin

For a substance to exert a systemic toxic effect it must first enter the circulation by crossing the body's natural barriers. In all cases (except by direct injection), the toxic material has to cross a biological membrane to enter the body. The two main ways this can occur are via passive diffusion or active transport.

- Passive diffusion requires a positive concentration gradient i.e. the substance tends to diffuse across a membrane from a high

concentration to a lower concentration. Other factors that influence the ability to cross a biological membrane include lipid (or fat) solubility, molecular size and degree of ionisation. Generally, small, lipophilic, non-ionised molecules cross biological membranes more quickly than larger, water soluble ones.

- Active transport involves a specific “carrier” protein that transfers the xenobiotic across the plasma membrane. Active transport can move molecules against a concentration gradient. This mechanism is particularly important in the elimination of substances via the kidney and liver by enabling active movement of water-soluble substances across the largely lipid (fatty) nature of the plasma membrane.

### **5.1.1 Inhalation**

From an occupational perspective, inhalation is usually the main route of absorption of hazardous materials. The lungs have a very large surface area and an excellent blood supply, both of which facilitate absorption. The barrier between inhaled air and the systemic circulation is very thin therefore absorption may be very rapid. Once absorbed, distribution around the body is usually rapid since the substance is transported via the bloodstream.

In addition to substances being absorbed through the lungs, insoluble particles such as silica and asbestos can deposit in the lungs and may lead to lung damage.

### **5.1.2 Direct contact (skin or dermal absorption)**

The epidermis (outer layer) of the skin is impermeable to water soluble materials. However, some substances can enter the bloodstream by crossing the body's external membranes i.e. skin and eyes. Such substances tend to be highly fat-soluble such as organic solvents. Other substances with high skin permeability include organophosphate pesticides



and phenol which can be absorbed through the skin in quantities sufficient to cause death.

While the outer epidermis is impermeable to water-soluble materials, the underlying dermis is freely permeable to all substances. Consequently, damaged skin decreases the defence afforded by the epidermis.

Splashes or vapours of liquids can lead to entry of foreign materials into the bloodstream via the skin or eye. This is especially for those substances that are highly fat-soluble. Local effects such as irritation may also be apparent.

### **5.1.3 Ingestion**

Ingestion of hazardous substances via the oral route is less common in the workplace but can occur as a result of carelessness or poor personal hygiene e.g. eating and drinking at the work station or without adequate washing of hands. It may also occur by swallowing of airborne contaminants when exposure to excessive levels of coarse airborne particulates occurs.

Following oral absorption, substances will be carried in the blood to the liver via the hepatic portal vein and then to the heart. From the heart blood is circulated to all the organs in the body.

### **5.1.4 Injection**

A direct route of entry occurs when substances are absorbed through cut or broken skin, or by injury with contaminated sharp objects such as needles or broken glass. If it is clear that direct entry of substances into the bloodstream is of concern, the risk can be managed by protecting cuts and abrasions, correct disposal of broken glass, sharps etc., and safe working practices.

## 5.2 DISTRIBUTION AND STORAGE

Once absorbed into the body, substances are transported around the body predominantly via the blood and lymphatic systems.

The main components of the cardiovascular or circulatory system are the heart, the blood and the blood vessels. The blood vessels consist of arteries, capillaries and veins. Arteries bring the oxygenated blood, pumped from the heart, to the tissues and the veins bring the deoxygenated blood back to the heart. Blood passes from arteries to veins through capillaries, which are the thinnest and most numerous of the blood vessels.

Substances may attach to red blood cells or proteins in blood plasma and may target specific organs. Once in the blood stream it can be distributed around the body in a number of ways depending on its physicochemical properties. If a substance is lipid soluble, of small molecular size, and is non-ionised it is likely to cross cell membranes and enter body tissues. Water-soluble materials remain dissolved in the plasma, while highly fat-soluble agents will deposit and remain in the body's fat stores.

The lymphatic system is a complex network of lymphoid organs, lymph nodes, ducts and vessels that produce and transport lymph fluid from tissues to the circulatory system. It is a major component of the immune system.

The lymphatic systems has three interrelated functions

- Removal of excess fluids from body tissues
- Absorption of fatty acids and subsequent transport of fat to the circulatory system
- Production of immune cells (such as lymphocytes, monocytes and antibody producing cells called plasma cells).

Some substances may accumulate in specific tissues e.g. carbon monoxide displaces oxygen from the haemoglobin in the blood to form

carboxyhaemoglobin. Similarly, some substances may be stored in particular tissues, for example lead is accumulated in bones.

Two particular membranes require particular consideration, the 'blood-brain barrier' and the placental barrier.

The placental barrier is very thin and susceptible to permeation by many substances, particularly those that are lipid soluble. Therefore, developing offspring may be particularly at risk from hazardous substances e.g. lead and solvents.

Similarly if substances are able to penetrate the blood-brain barrier then the central nervous system may be affected. The barrier protects the brain against water soluble substances but is permeable to lipid soluble substances, such as organic solvents and organo-metal compounds, which can exert narcotic and toxic effects.

### **5.3 METABOLISM**

Strictly speaking, what we are concerned with in toxicokinetics is xenobiotic metabolism, rather than the more common concept of oxidative metabolism or metabolic rate. However, for simplicity we will use the term metabolism rather than xenobiotic metabolism throughout this text.

A major factor influencing absorption and retention of a substance in the body is its lipid solubility. For a substance to be eliminated from the body effectively it needs to be in a more water soluble form, thereby facilitating excretion via the kidneys in urine. This is achieved via a process of metabolism (or biotransformation) and is one of the most important areas in toxicokinetics. The main objectives of metabolism are;

- To detoxify the hazardous substance
- To increase the water solubility of the substance to facilitate excretion by the kidney

Although all tissues are involved in metabolism the main site where biotransformation takes place is the liver. Although metabolism is a necessary process in our bodies and can convert toxic substances into non-toxic ones ready for excretion through the kidneys, it sometimes can cause the opposite effect i.e. the metabolite produced may be more toxic. An example of this is n-hexane which is metabolised to 2,5-hexanedione which can cause peripheral neuropathy.

A knowledge of the breakdown products of a substance is also useful in biological monitoring since the presence of a particular metabolite may be the only indication that exposure to a hazardous substance has taken place. An example of this is the elevated level of carbon monoxide in exhaled breath seen following dichloromethane exposure.

The majority of biotransformation pathways are controlled by complex enzyme systems which catalyse specific biochemical processes. Biotransformation can be broadly differentiated into phase 1 and phase 2 reactions.

- There are a range of different phase 1 reactions including oxidation, reduction and hydrolysis. The most common of these is oxidation which is catalysed by an enzyme system called the Cytochrome p450 system largely located in the liver and kidneys but also found in other tissues. Phase 1 reactions tend to produce a molecule that is more water soluble and more chemically reactive.
- Phase 2 reactions involve the reaction or conjugation of the phase 1 product with another endogenous (produced or originating from within the body) compound to produce a highly water soluble complex.

The following examples illustrate the principles of biotransformation.

### 5.3.1 Biotransformation of benzene

The major route of biotransformation involves phase 1 oxidation, catalysed by the Cytochrome p450 enzyme to phenol, followed by conjugation with a sulphate donor compound to form phenyl sulphate - a highly water soluble compound.

The metabolism of benzene also results in formation of many different intermediates and end products. A number of these intermediates are believed to be responsible for the carcinogenic activity of benzene and this represents one example where the toxicity is due to the intermediate or metabolite rather than the parent substance itself.

### 5.3.2 Biotransformation of dichloromethane

This is another example of a substance that undergoes multiple metabolic pathways and produces products which are more toxic than the parent substance. Two pathways exist:

- Phase 1 oxidation catalysed by the cytochrome p450 enzyme followed by phase 2 conjugation resulting in the formation of carbon monoxide and carbon dioxide
- Direct phase 2 conjugation with glutathione resulting in the formation of formaldehyde (a suspected carcinogen)

### 5.3.3 Biotransformation of methanol

The main pathway of methanol biotransformation is regulated by the enzyme *alcohol dehydrogenase* which converts methanol to formaldehyde. This is subsequently converted to methanoic acid and then carbon

dioxide. Methanoic acid can accumulate in the retina, which can result in blurred vision and blindness.

#### **5.4 EXCRETION**

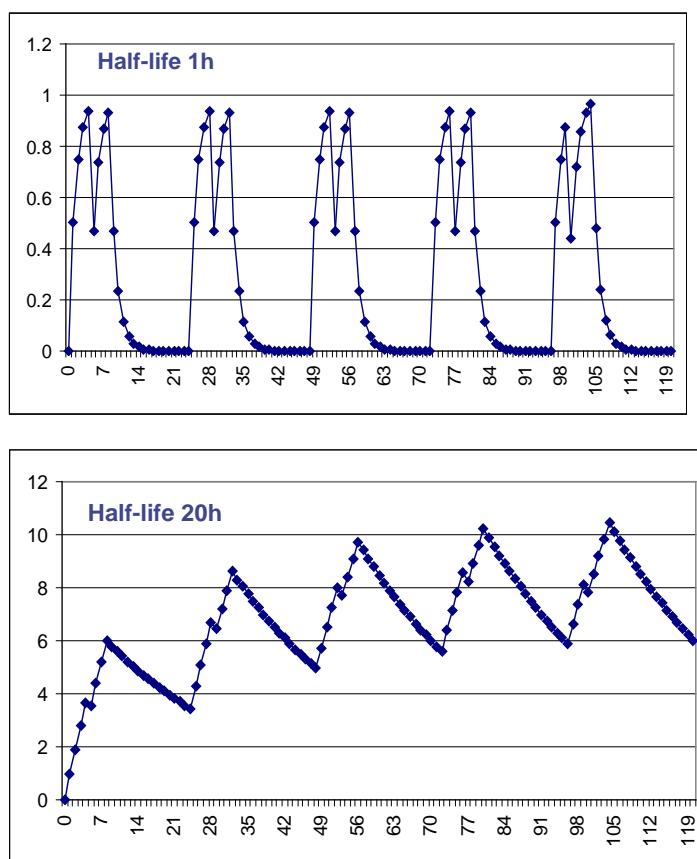
Following absorption, the substance or metabolite will ultimately be eliminated from the body by the processes of excretion. If a substance is removed rapidly, the potential for adverse effects is reduced. Conversely, if retention is prolonged, the potential for adverse effects is greater.

Excretion rates can be described in terms of its half-life which refers to the time taken for the concentration of a substance, for example in plasma, to decrease by half from a given point. Half-lives can vary greatly for different substances and can have a significant influence on their potential toxicity.

For instance cadmium has a half life in the body of between 10 and 20 years, so exposure to cadmium over a period of time is likely to gradually increase the total amount stored, or accumulated, in the body. Conversely, for a substance with a short half life (e.g. carbon monoxide with a half life in the body of a few hours) the amount of the substance in a body fluid such as blood will fall rapidly on cessation of exposure.

This concept can be illustrated by the example where a person may be exposed to a substance at a dose below the levels at which adverse effects occur during an eight hour shift. In the intervening 16 hours before they restart work, there is no exposure and the levels of the substance in the blood will start to reduce. If the half life is only a few hours, the level of the substance in the blood will return to zero and repeat exposure on the following day will again not lead to health effects.

However, if the work pattern is changed to say, 12 hour shifts with 12 hour recovery periods, the levels of the substance in the blood may not return to zero and exposure on subsequent days may increase the level in the blood, perhaps to significant levels.



**Figure 5.1** Effect of different half-life on accumulation of substance in the body

The main routes of excretion of hazardous substances are:

- Renal (via the kidneys) -The kidney is the main route of excretion for small, water-soluble molecules; large molecules such as proteins cannot cross the kidney's filtration membranes, whilst lipid-soluble substances are reabsorbed from the kidney tubules.
- Biliary (via the liver and GIT) - Excretion via bile – a secretion produced by the liver – is the second most important route of elimination of substances from the body, and for some materials (such as lipid soluble) may be the most important. Bile passes from the liver to the gall bladder and then onto the gastrointestinal tract.
- Pulmonary (exhalation via the lungs) – The lungs may be an important route of excretion for volatile substances.
- Secretory (in fluids such as sweat, semen, tears – a minor route)

## 6 DOSE - RESPONSE CURVES AND TOXICITY TESTING

### 6.1 INTRODUCTION TO DOSE-RESPONSE CURVES

'Dose-response' and 'dose-response relationship' describe the effect on an organism caused by differing levels of exposure (or dose) to a stressor (usually a chemical). The dose-response curve is a crucial tool to understand the levels at which chemicals, drugs or pollutants begin to exert harmful effects and the degree of harm to be expected at various levels.

Data relating to the amount of drug or pollutant can be plotted on a graph against the response of the organism. The resulting curve can then be used to show a number of points including:

- the 'no-effect level', where no effect occurs or no effect is detectable
- the threshold-dose of the 'stressor', the level at which the effect starts to occur and
- the levels at which the effect occurs in a set percentage or all of the organisms

The dose response of a population is that proportion of the population which experiences a specific effect following exposure of the total population to specified harmful contaminant. The correlation of the response with estimates of the dose provides a dose-response relation, which is normally expressed as a graph, with percentage of population affected on the y axis and estimated dose on the x axis (see Figure 6.1).

There are a number of terms that are used to describe particular points on the dose-response curve including:

- LD<sub>50</sub> – Lethal Dose, 50% - the dose that kills 50% of the test animals. The units used are in milligrams of substance per kilogram body weight of the test animal.



- LC<sub>50</sub> – Lethal Concentration, 50% - the concentration of a gas or vapour that kills 50% of the test animals.
- TD<sub>50</sub> - Toxic dose, 50% – the dose at which 50% of the test animals show a particular effect
- TC<sub>50</sub> - Toxic concentration, 50% – the concentration of a gas or vapour at which 50% of the test animals show a particular effect

### 6.1.1 No Observed Adverse Effect Level

The “no observed adverse effect level” (NOAEL) is an experimentally derived value and reflects the dose at which no adverse effects were observed in the studies available. The robustness of the NOAEL depends on many factors including the type(s) of study and its design (number of animals, experimental protocols etc). Effects, particularly adverse effects, are generally manifestations of the change in an organ and particularly the cells of the organ.

In toxicology, the NOAEL is specifically the highest tested dose or concentration of a substance at which no adverse effect is observed in the exposed test species (usually animals or cells). The NOAEL plays an important role in the risk assessment of the substance.

Another important toxicological concept is “lowest observed adverse effect level” (LOAEL) or the lowest dose or concentration that causes any observed adverse effect. Thus by definition the NOAEL is less than the LOAEL.

Other terms sometimes encountered include in toxicity testing include LD<sub>LO</sub> and LC<sub>LO</sub> which are the lowest doses or concentrations at which death occurs and TD<sub>LO</sub> and TC<sub>LO</sub> which are the lowest doses or concentrations at which a test animal shows a particular effect. These terms are effectively the same as the lowest observed adverse effect level (LOAEL).

As these determinations of exposure and effect have generally been established in species other than humans, various safety or uncertainty factors are applied before this data is used in the establishment of workplace exposure standards.

In many instances factors of 10 times have been used to take into account inter-species variation and a further factor of 10 times to take into account variability within humans. However, care must be taken with this type of approach as there is limited scientific basis for these factors and specialist toxicological advice should always be sought.

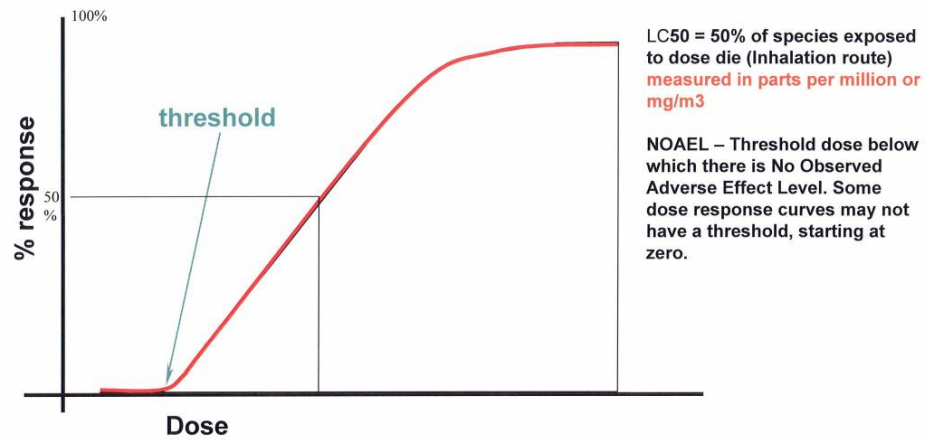
### **6.1.2 Threshold**

The term "threshold" is used in toxicology to describe the dividing line between no-effect and effect levels of exposure. It may be considered as the maximum quantity of a chemical that produces no effect or the minimum quantity that does produce an effect. Every effect produced by a chemical, whether it is beneficial, indifferent, or harmful, has a threshold.

For a given population, as illustrated by the dose response relationship (Figure 6.1), it is clear that thresholds exist because it can be determined experimentally that certain low levels of exposure will produce no detectable effect, and that as the dosage is increased the effect appears.

The precise threshold for a given effect can, and usually does, vary within certain limits with different species, as well as between individuals within a species. Indeed, within a population there will be variability – not everybody will have the same response. It can be shown that each point on a dose-response curve represents a normal distribution of responses within the sample populations.

## The dose-response curve



(Source: BP International – reproduced with permission)

**Figure 6.1 Typical dose-response curve**

Since the dose-response relationship is a continuum, somewhere between the experimental no-effect and effect levels is the turning point known as the threshold.

Dose-response curves typical of those plotted from data obtained in chronic toxicity experiments exist for a number of contaminants. It is very important to recognise that such a curve is drawn from only several points, one for each exposure group in the experiment. The greater the number of exposure groups, the greater the number of points, and hence, the greater the accuracy of the curve that is drawn. But without an infinite number of points, the precise shape of the dose-response curve cannot be known.

The curve is interpreted as follows: with chronic exposure of increasing doses up to the threshold, no effect is detectable because some biochemical or physiological mechanism handles the chemical in a manner that prevents an effect from occurring. At the threshold, the defence mechanism is saturated, or in some manner overwhelmed, for the more susceptible individuals and the effect begins to appear. With increasing

doses, increasing numbers of individuals show the effect until finally a dose is reached where all of the members of the population show the effect (ceiling level).

The threshold concept is of great importance to toxicologists because it permits them to make judgements about the potential risk, or lack thereof, to humans from exposure to chemicals.

Another question relates to the shape of dose-response curves for carcinogens as they approach zero doses. The inability of toxicology to answer this question by experiment has given rise to a scientific controversy concerning whether or not there is a threshold (no-effect level) for carcinogenic effects. If there is no threshold, extension of the experimentally derived dose-response curve to zero effect would yield a line that would go through the origin (zero dose). If there is a threshold, the extended line would meet the abscissa at some point greater than zero dose.

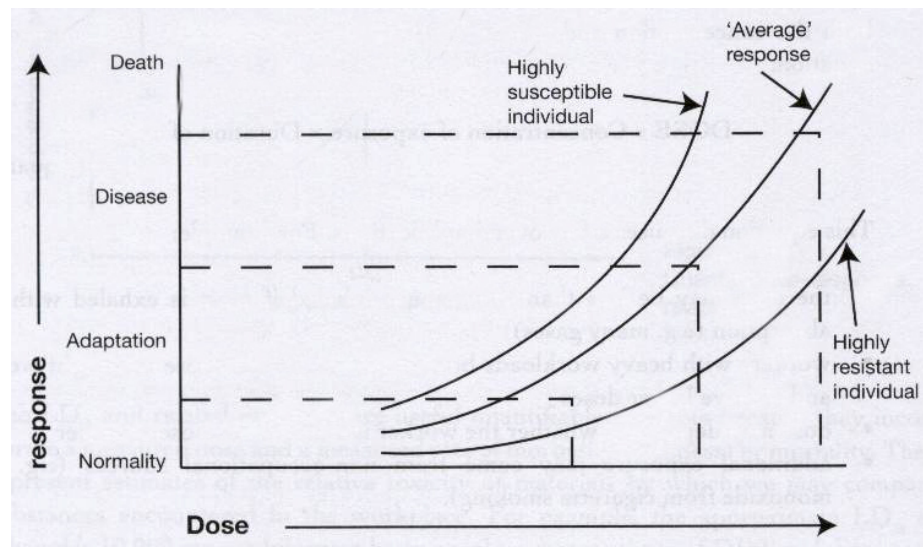
In regard to carcinogens, it is important to note that it is rare to have any data except for high doses, so the estimate of the shape of the dose response curve below the lowest actual data point must typically cover many orders of magnitude. If a threshold cannot be identified, then approaches to this problem vary around the world depending on national policies. For example, in the US a quantitative risk assessment approach using mathematical modelling is used, whereas in the UK a limit is established using a risk management approach (control to as low a level as is reasonably practicable).

For respiratory sensitisers, the same problems of lack of information on NOAEL and dose-response relationships can exist and so a similar approach may be required as to that for non-threshold carcinogens.

It is very important, as background to all considerations of the threshold, to recognise that detectable biological effects are not universally adverse.

What should be recognised is that in any group of test subjects there are some susceptible individuals (hypersensitive) who are affected at low concentrations of the test contaminant and there are also some highly resistant individuals (hyposensitive) who are not affected at high concentrations but there are the vast majority of “average” individuals in the middle (Figure 6.2).

It is important to recognise that some hypersensitive individuals may be in a work group and that they may suffer adverse health effects at exposures below the recognised exposure standard.



(Source: AIOH 2007 – Reproduced with permission)

**Figure 6.2 – Variability of Human Exposure to Dose**

For each substance, no matter how toxic, there exists a dose level called the threshold of intoxication, which the human body is capable of accepting and detoxifying without injury to itself. It is this principle that the major exposure standards used within the western world are based upon.

### 6.1.3 Slope of curve

Another characteristic of the shape of the dose-response curve that may be examined is the slope of the curve. Knowledge of the shape and slope of

the dose-response curve is extremely important in predicting the toxicity of a substance at specific dose levels. Major differences among toxicants may exist not only in the point at which the threshold is reached but also in the percent of population responding per unit change in dose

Dose-response curves for some substances show a steep curve (rise rapidly from the threshold point to the ceiling level). This indicates that particular care may need to be taken to prevent excessive exposure as the undesired consequences of that exposure will occur at levels only slightly above threshold levels.

On the other hand, a relatively flat slope suggests that the effect of an increase in dose is generally minimal and that there is much greater variation in the likelihood of the effect occurring in the whole exposed population.

## **6.2 TOXICITY TESTING**

### **6.2.1 Types of toxicity testing**

In order to make judgements on likely risks and the appropriate measures required to mitigate against them, it is necessary to gather information on the hazardous toxicological properties of chemical substances.

Clearly we are interested in the effects of substances on human health and so of course toxicological data from human exposure in principle provides the most useful information. Data are available from studies looking at populations of humans exposed, for example, in the course of their work (this is covered further in section 7). In general, though, these do not provide the broad range of information required to understand all the potential toxicological hazards of a substance.

Consequently, a range of approaches have been developed to investigate the various areas of toxicological hazard; these are covered briefly below. A toxicologist will use all the information available to develop a picture of the toxicity profile of a substance. A starting point will often be the physico-chemical properties such as the pH of the substance (if this is very high or low then in general it will be assumed that the substance is corrosive) and a consideration of its structure. If a substance has a structure very similar to another substance or substances (e.g. is part of a chemical group or family) then it may be possible and reasonable to compare the toxicity of the two (or across the group) where data already exist (this is called structure activity relationship, SAR, or group approaches).

Usually, however, having considered these possibilities, it is likely that more information will be required and some experimental testing will be needed. The use of animals in these experiments, though in some parts of the world a controversial issue, remains the main approach for gathering information. In some areas of toxicity testing, though, there have been some significant advances in recent years to replace animal tests, reduce the numbers used or refine experiments to reduce suffering. Approaches replacing animals generally use cells or tissues in “culture” (e.g. test tubes and Petri dishes) and are known as *in vitro* (Latin for “within the glass”) methods.

Where animal testing is carried out (often for regulatory purposes) they are usually conducted to established international guidelines (e.g. OECD Guidelines). This is to ensure that they meet certain agreed standards and that the results are acceptable to different regulatory authorities around the world. It is by no means the case that such studies are the only source of toxicity information and toxicological research not conducted to these protocols but published in established scientific journals can contribute significantly to the database for any substance.

In general, most toxicity studies are carried out in rodents, particularly special bred laboratory rats, mice, guinea pigs and rabbits. Some studies

may use dogs and non-human primates, though this is generally not common for workplace chemicals.

The following sections give a brief overview of testing for the different types of toxicity in the following broad categories: toxicokinetics, acute toxicity, including skin and eye irritation, sensitisation, genotoxicity, repeated dose (sub-acute, sub-chronic and chronic) toxicity, reproductive and developmental toxicity and carcinogenicity.

### **6.2.2 Toxicokinetic studies**

Although not testing for a toxic effect, the study of how a substance is absorbed, distributed, metabolised and excreted from the body often provides important information to help understand its potential to induce toxicity. These studies are known as toxicokinetic studies though the term pharmacokinetic is also sometimes used (this is more often in relation to pharmaceutical compounds).

In general toxicokinetic studies involve administering a substance (which is often labelled in some way e.g. with a radioactive atom as part of the molecular structure) to animals, via one of the main routes of uptake. The presence of the substance (or its metabolites or the radiolabel) in various tissues and excreta is then measured for a period (up to a few weeks sometimes) of time to determine the fate of the chemical. Specialised studies may be carried out *in vitro* (e.g. using extracts of cells, often liver cells) to look at how the substance is metabolised by cell enzymes. The aim is to build up a picture of how much chemical is taken up by different routes, where it gets to in the body, how the body metabolises it and what metabolites are formed (as some of these may be toxic whereas the chemical itself is not) and how much, and by what routes, is excreted from the body over the observation period.



Some methods have been developed whereby uptake across the skin can be measured in the laboratory using pieces of animal or human skin (the latter where national ethical considerations allow).

There have also been considerable developments in computer aided modelling of toxicokinetics (called physiologically-based pharmacokinetic, PBPK-modelling) to try to help predict how a substance will behave in the body. These models, based on biological principles, describe the body and its organs and tissues mathematically and use these principles to describe and predict the fate of chemicals in the body. They can be used as a means of extrapolating from one species or route of exposure to another and/or across a range of doses and exposure patterns.

### 6.2.3 Acute toxicity studies

The term acute toxicity in the testing context usually refers to experiments to determine the effects seen rapidly following a single dose of a chemical.

**Acute systemic toxicity** - the aim of these types of studies is to provide information on what general toxicity might be seen if someone was exposed to a single, relatively high dose of a chemical (e.g. an accidental poisoning). In these studies a substance is administered to groups of animals as single doses. For solids and liquids this is often via the oral route and for gases, vapours and dusts by inhalation over a fixed period of time (usually 4 hours).

A dermal test can also be conducted whereby the substance is applied to the skin usually under a dressing to keep it in place. Following administration the animals are observed, usually for at least two weeks afterwards in order to look for signs of toxicity. At the end of the observation period the animals will have a general examination of their body organs to look for signs of organ and tissue damage as markers of toxic effects.

Historically, these studies were designed to identify a statistically derived value known as the LD<sub>50</sub> or LC<sub>50</sub>– the dose or concentration that would on average result in the death of 50% of the test population of animals over a specified time period. This crude measure was and is useful as a way of making relative comparisons of the acute toxicity of substances in order to rank them in terms of their severity in inducing acute toxicity.

However, such studies often overlooked more critical information such as toxic signs which may be useful indicators as to how a chemical exerts its effect. Other methods (such as the “Fixed Dose Procedure” and “Acute Toxic Class Method”) have been developed which use fewer animals and depend more on signs of toxicity rather than just mortality. In general one will still find LD<sub>50</sub> or LC<sub>50</sub> values cited (e.g. in Safety Data Sheets) but the results from the other methods are becoming more readily available and are now part of regulatory schemes having established international guidelines.

**Irritation studies** - some substances can cause localised inflammation on contact with the skin, eye and respiratory tract – in the worst cases this damage can be extremely severe leading to corrosive destruction of the tissue. Clearly if it can be predicted that a substance is likely to be corrosive (e.g. strong acids or alkalis) in an undiluted form then it would not be reasonable or ethical to undertake any animal testing.

Traditionally, skin and eye irritation tests use animals, usually specially bred laboratory rabbits. For skin irritation, the test substance is applied to the rabbit skin under a dressing for a few hours, with moistening if required for solid substances, and then the dressing is removed. The skin is then assessed by looking for redness (erythema) and swelling (oedema) and a scoring system based on the severity of the reaction seen is used to provide a semi-objective method for judging the degree of the response.

Observations will be made for up to 14 days after the treatment to look for reversibility of response. Regulatory schemes use the severity and duration

of the scores to formally classify substances as irritants. For eye irritation, the substance is instilled into the lower eyelid of the eye sack and the severity of the response judged by scoring the redness and swelling of the conjunctiva and eyelids, the opacity of the cornea and effects on the iris over a period of up to 21 days.

Significant efforts have been made to find alternative non-animal test methods for assessing the skin and eye irritation potential of substances. These efforts have resulted in internationally validated methods becoming available which use *in vitro* systems for skin irritation and corrosion.

Although not routinely investigated, the ability of substances to cause irritation of the respiratory tract can be tested both in animals and humans. Studies in humans are usually designed to measure sensory irritation – that is subjective feelings of irritation (itching, soreness) in the eyes and upper airways. Such studies are often used as the basis for establishing, for example, occupational exposure limits, but care needs to be taken when interpreting such experiments. Usually, this type of study involves exposing volunteers to a test atmosphere and requiring them to record what they experience.

Animal experiments can also be undertaken to investigate sensory irritation using changes in breathing rates as objective measures of response. These breathing changes are related to the way sensory nerves in the respiratory tract respond to stimulation by the substance involved. In some repeated exposure experiments (see section below) signs of irritation of the respiratory tract may also be observed.

#### **6.2.4 Sensitisation studies**

Testing whether a substance is able to induce a sensitisation response is normally carried out in animals. For skin sensitisation, traditionally guinea pigs have been used. There are a number of different experimental

protocols that have been developed but all basically depend upon giving the guinea pigs a series of exposures via the skin. After a break from this “induction” phase (inducing the immune system to respond) another part of the animal’s skin is then exposed to a lower (non-irritant) dose of the chemical. If the substance has sensitising properties then this is manifest through a skin reaction which can be scored for severity (similar to the approach used for skin irritation). A substance will be considered as a skin sensitiser depending upon the proportion of test animals responding at a specified level of response.

The above approach can sometimes be unpleasant for the guinea pigs, particularly where a second substance is used to stimulate the immune system. Consequently, another approach has been developed in mice which uses fewer animals and results in less severe responses. This test depends on measuring the proliferation (rate of cell division) in cells of the immune system involved in the induction of the sensitised state, rather than testing to see if the animals respond to a subsequent challenge to show that they are sensitised as in the guinea pig test. In this type of experiment the skin on the mouse ear is treated with the substance of interest and then the animals are given radioactively-labelled precursors of DNA molecules to help detect increased cell division. After the induction period, lymph nodes are collected and the radioactivity measured to judge the increase in cell division and if it meets a specified level (usually at least a three-fold increase) then the substance is judged to have the potential to be a skin sensitiser.

For humans who exhibit signs of skin sensitisation (e.g. rashes typically induced by these kinds of substance) then “challenge” tests can be performed under medically supervised conditions by injecting substance under the skin or placing it on the skin surface to see if a response is induced. This is clearly useful for helping to diagnose the condition and identifying the causative agent.

Attempts have been made over many years to develop tests for predicting if a substance has respiratory sensitisation potential but it has been difficult to obtain consistency in appropriate animal models. The guinea pig has been used most often and the approach has been to expose them repeatedly to attempt to develop the immune sensitised state and then subsequently with a challenge dose with measurement of, for example, breathing rates and blood antibodies being made. However, no single method has emerged as the basis for establishing a recognised, validated guideline.

As for skin sensitisation, humans with occupational asthma can undertake medically supervised challenge tests for diagnostic purposes in order to determine causative agents and severity of response.

### **6.2.5 Repeated dose toxicity studies**

In most workplace situations exposure to a chemical usually will occur repeatedly at relatively low levels over relatively long periods of time. Testing for the effects of repeated exposure to a chemical is carried out in animals, most often rats, over varying periods of time. The most often used exposure periods are 28 days (sub-acute testing), 90 days (sub-chronic) and for one or two years (chronic), the latter often being part of testing for the potential of a chemical to cause cancer (carcinogenicity).

Exposure is most commonly undertaken by the oral route, either by a tube (gavage) directly into the stomach but alternatively, particularly for chronic exposure periods, with the chemical incorporated into the animals' diet or drinking water. Less commonly, animals may be exposed via inhalation to vapours, gases or dusts if this is appropriate (e.g. that is the most likely and/or important route of exposure). Inhalation testing is technically very demanding and expensive which is why it is less commonly used. The least often method of repeated exposure is by application to the skin.

Three dose levels are usually used with an unexposed (i.e. receiving the same treatment procedure but without the chemical present) group acting as controls. Normally the top dose is designed to induce clear toxic effects and the other two doses less effect and no effects. The shorter term experiments can act as a guide for dose selection for the longer term experiments for the same chemical.

Where experiments have only been performed via one route of exposure then when assessing systemic toxicity it may be necessary to make judgements about relative uptake (dose) by different routes and allow for the fact that local effects may occur.

At the end of the overall exposure period a range of measurements will be made on the animals, ranging from body and organ weights, assessment of blood levels of tissue parameters (e.g. liver and kidney associated enzymes, red and white blood cells) and macro- and microscopic examination of samples of tissues from the main organs of the body (the range of organs and tissues examined increases with increasing length of exposure period). In the longer term studies, extra groups of animals may be exposed and examined during the exposure period so that development of effects and their underlying mechanisms can be more thoroughly studied. Some studies may be designed to investigate specific effects, for example toxicity to the nervous system.

In general, the shorter term studies use fewer animals in smaller group sizes with groups of both male and females being used. The longer term experiments use larger group sizes (to allow for some losses during the time of the experiment) and, particularly for the two year studies, to increase the statistical power of the studies to detect substance-related effects.

The main outcome of these types of experiments is to produce information on the type of toxicity the substance possesses, potential target organs and tissues (both locally and systemically), the dose-response relationship (i.e. the variation in the magnitude of the effect with increasing dose) and if

possible the No Observed Adverse Effect Level (NOAEL) – the dose producing no observed adverse effects.

Note that some changes may occur at the NOAEL but these may not be considered as adverse by the toxicologist and so are not thought of as contributing to the toxicity of the substance. It is also worth noting that in some cases the effects seen may or may not be induced in humans. Sometimes the mechanism leading to the effect may not be possible in humans because of species differences and in other cases may be less severe. However, adverse effects seen are considered as markers that a substance possesses the ability to induce toxicity on repeated exposure and without any further detailed information this is taken as being of concern for human health.

The above describes briefly the way standardised toxicity testing studies conducted to internationally validated and accepted guidelines are carried out, usually in relation to regulatory requirements. However, one may often find that, for a particular chemical, experiments have been published in scientific journals that are not necessarily conducted to these protocols but have investigated specific issues of interest relating the toxicity of the substance. These will have been through standard peer review procedures and can add usefully to the knowledge base of the toxicity profile of the substance and the understanding of its relevance to humans.

#### **6.2.6 Genotoxicity studies**

There is a relatively wide range of tests available to look at the potential of a substance to induce genetic damage. Some look at the ability of a chemical to generally damage the genetic material or attempts by the cell to repair it, whereas others look at a substance's ability to cause specific mutations that can be measured by changes in cell function (e.g. the ability of the cell to make or use certain enzymes).

The availability of this wide range of tests has led to the development of strategic approaches where experiments on cells *in vitro* are used to screen initially for a chemical to be genotoxic. The *in vitro* studies usually include tests in bacterial cells (called the Ames test after the person who first developed them) which detect mutations and cells derived from mammals that are used to detect damage, its repair or mutations.

The Ames test is based on the assumption that a substance that is genotoxic (mutagenic) to the strain of Salmonella bacteria used in the test may also be a carcinogen i.e. cause cancer. While some carcinogens do not give a positive Ames test (and vice-versa) the ease and low cost of the test make it valuable as a screening test. Some experiments use yeast cells or fruit flies (*Drosophila melanogaster*).

The *in vitro* experiments include exposing the cells to the just the chemical itself and also to it in the presence of a liver extract intended to investigate the possibility that its metabolism may generate genotoxic metabolites. If this battery of tests is negative then usually the substance is considered as not possessing genotoxic potential and no further testing is required.

If these experiments in cells demonstrate a substance to have genotoxic potential, then studies can be performed to determine whether this activity would be expressed in animals. Generally these studies are performed in mice (other rodent species can be used) which receive one or two doses of the chemical and then measurements made in bone marrow derived cells to look for signs of genetic damage. Positive results in these animal studies would be taken to mean that the substance has the ability to induce genetic damage and in somatic cells this might mean that it is potentially a cancer causing agent.

If genetic damage is detected in the normal (somatic) cells of animals then further tests can be carried out to see if mutations could be formed in germ cells by the chemical and these passed on to offspring. This is usually carried out by dosing parental animals and then looking for damage to the



genetic material of germ cells (in sperm, as this is easier to detect) or for specific changes in the offspring which are known to be due to mutations being passed on from the parents. If positive responses are observed then this is taken as evidence that the substance has the potential to induce heritable genetic damage.

The type of strategic approach outlined above has been developed over many years. However, this step-wise approach is used mainly in regulatory settings and it is possible to find studies published in scientific journals that use these techniques (and others) but not necessarily in a step-wise fashion. As for other toxic properties, these published studies provide useful information to add to the overall picture about genotoxic potential.

#### **6.2.7 Reproductive and developmental toxicity studies**

Some chemicals may have the potential to cause toxicity to the male and/or female reproductive systems and functions and/or to the developing offspring. Useful information on toxicity to reproduction may be obtained by examination of the reproductive organs in repeated dose studies.

Testing for a chemical's ability to cause toxicity to reproduction is normally carried out in rats or mice. The approach used is relatively straightforward in that groups of male and female animals of reproductive age are dosed with a range (usually up to three) of doses of the substance of interest and then allowed to breed in pairs: a control group that does not receive the chemical but otherwise undergoes the same procedures is also included. Dosing is repeated over a number of weeks.

Effects on reproduction can be observed, by alterations in mating behaviour or by reductions in the numbers of offspring produced compared to control groups. In some cases, some of the offspring can be used to continue dosing and these then mated in pairs to look at the effects through more than one generation of animals (these are called multi-generation studies).

More complex studies can be undertaken to investigate specific aspects and mechanisms by which the chemical may be acting on reproductive organs. For example, only male or female animals might be dosed or special measurements made of how the offspring develop in their learning ability. As for repeat dose studies, such experiments will provide information on dose-response relationships and no effect levels.

Although effects on the developing offspring can be observed in the above types of experiments some tests can be carried out that are specifically designed to investigate these aspects. These experiments usually use rats or rabbits as the test species where groups of pregnant female animals are dosed for a fixed number of days over the period from implantation of the developing offspring to just before birth to cover development and growth in the uterus. The highest dose is designed to induce some level of general toxic effects in the pregnant females. At the end of the experiment (usually just before the animals would normally give birth) the offspring and females are examined.

If the treatments are toxic to the developing offspring then a range of effects may be observed. For example, normal development may have ceased. In some cases the chemical may have affected the normal development of for example the limbs of the animals resulting in malformations, an effect called teratogenesis (thalidomide is a typical example of a substance that has this property).

Sometimes the effects may be very subtle and can just be small changes in growth rate or in sexual or intellectual development. In situations where effects are only seen in the presence of toxicity to the mother careful and specialist interpretation may be needed in order to determine whether the effects were secondary to this or directly by the substance on the developing offspring.

### 6.2.8 Carcinogenicity studies

Testing for carcinogenic properties is basically an extension of the chronic two-year repeated dose studies. Larger groups (50 male and female) of animals (usually rats and/or mice) receive two years (in some cases it may be lifetime) exposure to doses of chemical; a control group will received the same treatment but without the chemical present. The highest dose is usually designed to cause a small toxic effect but not enough to cause excessive numbers of deaths. Extra groups may be used to look at different times to studies any possible mechanisms of cancer induction, such as increased cell proliferation in expected target tissues.

The animals are observed for the duration of the experiment and any that die are examined for the presence of tumours. At the end of the exposure period, all remaining animals are examined for the development of any tumours and its type (e.g. benign, malignant) is determined. A wide range of body organs and tissues are also examined macro- and microscopically. If there is a significant increase in the number of tumours appearing in treated animals compared to an unexposed control group then this may be indicative of the substance having carcinogenic properties in humans.

However, this interpretation is dependent upon a number of factors. For example, although the increase may be statistically significant at one dose, no dose-response relationship may be seen and so the biological significance may be questionable. Knowledge of the pattern of tumour formation in the species being used is also important since some strains of laboratory rodents may be prone to develop certain types of tumours when stressed and the substance used may not be critical. Also tumours may occur in rodents in organs not possessed by humans or through mechanisms that would not be expected to occur in man. Overall, therefore, the interpretation of such studies is complex and requires specialised knowledge and experience.

### **6.3 ALLERGY ASSESSMENT METHODS IN HUMANS**

There are a number of different assessment methods that are available for determining whether or not a person is allergic to a particular substance. These include lung function tests (or spirometry), challenge testing, skin prick testing and blood IgE testing.

#### **6.3.1 Lung function tests**

Lung function tests (sometimes called pulmonary function tests) are undertaken to evaluate how well the lungs are working. They are used to assess and differentiate conditions such as asthma, pulmonary fibrosis and chronic obstructive pulmonary diseases including emphysema and chronic bronchitis.

The most common test uses a spirometer which measures the amount (volume) and the speed (flow rate) of air that can be inhaled and exhaled. They are undertaken breathing into a mouthpiece attached to the spirometer. Typically, in the most common test, the person is required to take the deepest breath they can and exhale as hard as possible for as long as possible.

One limitation of lung function testing is that it is highly dependent on patient co-operation and effort. The test is also normally repeated at least three times to ensure reproducibility.

The results of the lung function tests are usually given in terms of the basic data i.e. litres of air and litres per second, and also as a percentage of the typical or “predicted values” for people of similar characteristics (age, gender, height etc). Interpretation of the results must be undertaken by suitably qualified medical professionals, however, results within about 20% of the predicted values are usually considered “normal”.

Some common terms used in lung function tests are defined below:

- FVC – Forced vital capacity – the total amount of air in litres that can be blown out after maximum inhalation
- FEV1 – Forced expiratory volume in 1 second – the amount of air in litres that can be blown out in one second
- FEV1/FVC – FEV1% - the ratio of FEV1 to FVC. In healthy adults this should be approximately 75 – 80%
- PEF – Peak expiratory flow – the maximum flow of air in litres per second at the start of the exhalation

### **6.3.2 Challenge tests**

Spirometry can also be part of a bronchial challenge test. This may be undertaken to determine whether sudden contraction of the bronchioles (or bronchospasm) is as a result of exposure to a particular substance or environmental condition. It is useful to confirm the specific substance that is causing the sensitisation, but it should only be undertaken if other ways of diagnosing the sensitivity are ineffective.

Starting with a small amount, the challenge involves exposure to increasing doses of the substances in question. Challenge tests are only undertaken under full medical supervision as it is possible that a severe reaction may occur.

### **6.3.3 Skin prick allergy tests**

Skin prick testing is usually the first test recommended when an allergy is suspected. The main advantages are that it is a simple, quick (providing results within about 20 – 30 minutes) and inexpensive form of testing.

It can give useful information in all forms of allergy including allergies to substances that are inhaled or ingested. The test is undertaken by suitably qualified medical personnel.

Substances that are suspected cause of the allergy are mixed with liquid to make a solution. The arm is marked with a marker pen to identify the point of application of each drop. Up to 20 different allergen solutions may be tested at a time by applying a drop of each solution to the marked position on the forearm.

The skin beneath the drop is then pricked with a needle. This is usually not painful as only the top surface of the skin is pricked. However, this is sufficient to introduce a very small amount of the substance into the skin.

The skin is then observed for a reaction, this will occur within a short period of time. A positive reaction is when the skin at the point of test becomes red and itchy within a few minutes. The area then becomes red and swollen with a “weal” in the centre, much like the reaction to a nettle sting. This normally reaches a maximum size after about 15 – 20 minutes and usually clears within about an hour.

#### **6.3.4 Patch testing**

Skin prick testing is a way that suspected allergens are introduced into the body. It is therefore used to tests for allergies that do not necessarily occur on the skin. Patch testing is different in that it places substances on the surface of the skin and aims to identify skin allergens.

The test involves the application of various test substances to the skin under adhesive tape that are left in place for 48 hours. The sites are examined after this period and again a further 48 hours later. The patches are usually applied to the upper back. Any reaction to the substance is classified to established criteria (see Section 2.5.3).

The distinction between allergic and irritant reactions is of major importance. An irritant reaction is most prominent immediately after the patch is removed and fades over the next day. An allergic reaction takes a few days to develop, so is more prominent on day five than when the patch is first removed.

### **6.3.5 Serological tests**

Serological tests involve analysis of the blood serum for the presence and quantification of specific IgE antibodies in circulating blood serum. There are a range of different techniques such as RAST (radioallergosorbent test), UniCAP system and ELISA.

The details of the various techniques are beyond the scope of the course. However, it is important to ensure that any laboratories used to undertake these tests take part in suitable external proficiency testing programmes.

Serological tests are useful:

- As a quantitative measure of specific IgE antibody in a particular individual
- For individuals who are taking antihistamine drugs which suppress skin prick test reactions
- For individuals with such extensive skin disease that skin prick tests are difficult to undertake

However, serological tests are invasive requiring blood sampling, is relatively costly and the results are not available immediately. The skin prick test is less invasive, provides immediate results and is generally less expensive.

## **7. EPIDEMIOLOGY**

### **7.1 INTRODUCTION**

Epidemiology may be defined as “the study of the distribution and determinants of health-related events in specified populations, and the application of this study to the control of health problems”.

(Occupational Hygiene – Harrington and Gardiner)

In an industrial hygiene context it can be described as a scientific process that attempts to link the effects of factors such as exposure to toxic chemicals to disease, or if relevant, mortality. Statistical correlations are developed to indicate the degree of risk that someone with a particular exposure pattern has of contracting a specific disease.

Epidemiological studies tend to be complex and are generally beyond the remit of most industrial hygienists. However, it is important that the hygienist is able to understand the principles of epidemiology. This should enable them to more confidently appraise information from epidemiological studies and to collect information in a form that will be of use for an epidemiological study.

### **7.2 REASONS FOR UNDERTAKING EPIDEMIOLOGICAL STUDIES**

Much information on the likely health effects of exposure to substances can be derived from animal tests, in-vitro tests and comparison with similar chemicals. However, often the only valid technique to establish the actual health risks in the population is by means of an epidemiological study.

The purpose of epidemiological studies is to establish a link between exposure to a substance and development of a disease or ill-health. Examples where a clear association between exposure and ill-health was established by epidemiological studies include:



- Angiosarcoma of the liver and exposure to vinyl chloride monomer
- Mesothelioma of the pleura and exposure to asbestos

However, in most cases clear evidence is not available and many studies suffer from limitations and deficiencies. Historical data such as workplace conditions and exposure levels may be unclear or not valid. In addition they may be problems of bias or other confounding factors in the selection and monitoring of the groups under study.

### **7.3 EPIDEMIOLOGICAL TERMS**

#### **7.3.1 Incidence and prevalence rates**

The incidence is the number of new cases of ill-health or disease that occur in a population in a period of time. Commonly it is expressed in terms of a number of new cases per 1000 people in the group under study per year.

The prevalence is the total number of cases of ill-health or disease that exist in the population at a particular point in time. Prevalence is not only affected by the incidence of new cases but also the severity and duration of the effects.

Studies may express findings in terms of morbidity (e.g. number of cases of a particular illness) in the group, or of mortality (death) rates.

#### **7.3.2 Measures of frequency**

The incidence or prevalence rates give information on the number of people in a group or population that show the effect in question. What is required is a measure of whether these rates are higher, lower or the same as 'normal'.

To establish this we need another group or population as a comparison. This group is termed the reference group or reference population. (Some texts use the terms control group or control population). One of the biggest potential difficulties in epidemiological studies can be identifying a suitable reference population. The reference population should differ from the group under study only in the fact that they have not experienced the exposure under question.

The incidence rate of say “number of deaths from mesothelioma from exposure to asbestos in shipyard workers” can now be compared with the reference population to give a ratio or ‘Standardised Mortality Ratio (SMR)’. The standardised mortality ratio can be defined as:

“The ratio of the number of events observed in a population to the number that would be expected if the population had the same distribution as a reference population”.

As the name indicates it is a ratio, therefore if there is no difference between the group under study and the reference population it would have a standardised mortality ratio of 1. Similarly, if there was a greater than expected number of deaths or events noted the standardised mortality ratio would be greater than 1.

However, an area of possible confusion is that a number of texts and organisations quote standardised mortality ratios as a percentage of the expected number of deaths or events. In this case, if there is no difference between the group under study and the reference population it would have a standardised mortality ratio of 100. Similarly, if there was a greater than expected number of deaths or events noted the standardised mortality ratio would be greater than 100.

As stated earlier, in order to give valid conclusions, the comparison population must be matched to the group under study. One of the main

areas of difficulty is matching the groups in terms of age distribution. Also care needs to be taken when comparing death rates against the death rates for the general population.

The general population is by definition less healthy than the working population as it includes people who are unable to work due to ill-health. In addition, workers who suffer ill-health tend to leave work. As a result working populations tend to have a lower standardised mortality ratio, i.e. less than 1 (or less than 100) when compared to the general population. This is known as the 'healthy worker effect'

### 7.3.3 Causation or association

The main objective of epidemiology for industrial hygiene is to identify the causes of ill-health or death by studying the distribution of cases in a group being studied (who have been exposed to different levels of a substance such as a chemical) when compared to another reference population.

It is important to differentiate between epidemiological association and causation. A study may show a link (or association) between a factor such as exposure to a particular chemical and a health effect. However, this by itself does not necessarily mean that there is a direct causal link. The association may be spurious or it may be indirect through other known or unknown variables.

There are a number of criteria that can be examined to provide support for a causal link. A series of time tested criteria for determining whether an association is causal were developed by Sir Austin Bradford-Hill in 1965. These include the following:

**Strength of association:** There is more confidence in the causality of strong associations than in weak ones.

**Temporality:** Does the cause precede the effect, and is the time interval reasonable?

**Dose response:** Do the responses occur more frequently at higher exposure levels?

**Biological plausibility:** Does the association seem reasonable or consistent with current scientific understanding?

**Consistency:** Has the association been observed by different investigators, in different places and at different times?

Other criteria include specificity, coherence, experimental evidence and analogy. None of the nine criteria can bring indisputable evidence for or against a cause and effect hypothesis, nor do they necessarily carry equal weight. Rarely, will all nine points be present in the proof of the hypothesis, however the more there are, the stronger the association. What they can do, to a greater or lesser extent, is support or refute the hypothesis.

The quality of the study should also be assessed. Those with appropriate statistical analysis and those that are published in peer reviewed journals carry more weight. Claims of causation should not be made lightly as poorly justified claims can be very misleading.

An example of how the criteria can be used is given below, examining the well documented link between smoking and lung cancer:

**Strength of association:** Lung cancer incidence rates are far higher for smokers than non-smokers

**Temporality:** Smoking in the vast majority of cases preceded the onset of lung cancer

**Consistency:** Different types of study (e.g. prospective and retrospective studies) and also studies of males and females produced the same result.

**Biological plausibility:** The theory that smoking causes tissue damage which over time could result in cancer in the cells was highly plausible

**Coherence:** The theory that smoking causes lung disease “made sense” given current knowledge

**Specificity:** Lung cancer is best predicted from the incidence of smoking

**Dose response relationship:** Data showed a linear relationship between amount smoked and incidence of lung cancer

**Experimental evidence:** Tobacco tar applied to rabbit’s ears produced cancer in the ear tissue over time

**Analogy:** Induced smoking in laboratory rats showed increased lung cancer.

#### 7.3.4 Bias

All epidemiological studies are subject to bias, which may be from a number of different sources. Selection bias can occur in the assembly of the group under study and / or the control group. Information bias relates to the quality and accuracy of the data gathered as well as errors by the interviewer or interviewee.

Confounding is a factor which independently influences both the exposure and the outcome and thereby suggests a spurious direct relationship between the two. Many of these factors can be controlled at the planning stage of the study.

For example, a study may have been undertaken to investigate occurrence of lung cancer in a group of workers exposed to a chemical. It may show an increased incidence of lung cancer in the exposed group, compared to the unexposed control group. However, it is possible that the exposed group contains a higher proportion of smokers, which can also cause lung cancer, than the control group. Another possible factor would be that the age profile of the two groups was not matched.

### 7.3.5 Statistical significance

An important aspect of epidemiological studies is to determine statistically whether or not an apparent causal association between exposure and outcome is likely to be down to chance or not. The aim is to show that the causal association between exposure and the outcome is statistically significant – that is, it is unlikely to have occurred by chance. There are a number of statistical tests that can be used to attempt to establish the degree of confidence to the findings.

In most studies the definition of statistically significant is that there is a 95% or better confidence that the results were not due to chance i.e. there is less than a 5% or 1 in 20 chance that the association was a random association. This is sometimes written as a probability of ' $p < 0.05$ '. The lower the probability or significance level the stronger the evidence.

Establishing that the findings are statistically significant is an important part of the process, however, that in itself is not enough to confirm causality. It simply shows that the connection is unlikely to be purely by chance. At this stage the other criteria developed by Bradford-Hill need to be examined.

## 7.4 TYPES OF EPIDEMIOLOGICAL STUDIES

### 7.4.1 Longitudinal studies

Longitudinal studies follow a group of people over a period of time with repeated observations of risk factors or health factors or both. They vary widely in size and duration (perhaps even over many decades). Two common types of longitudinal study are cohort and case-control studies.

**Case-control studies** - these are used to identify factors that may have caused a particular effect or illness. They tend to be retrospective i.e. they

study a group of people who have the effect or illness (the 'cases') and compare with another group who do not have the effect or illness (the 'controls') together with information of past exposure to a particular factor or substance.

One of the biggest problems with retrospective occupational epidemiological studies is gathering accurate data on past exposures. In addition it is often difficult to avoid possible confounding factors when choosing the control group. As a result case-control studies are not generally the most robust studies but they are often used to identify exposure / disease relationships which can then be investigated more fully.

**Cohort studies** – a cohort study follows a group of people who are exposed to particular substance or agent. The crucial difference between a case-control study and a cohort study is that the cohort group is identified before the appearance of the illness or effect manifests itself. A comparison group is also identified either from the general population or from another similar group or cohort who have had little or no exposure to the substance or agent in question.

The nature of the study tend to be prospective i.e. it gathers data over a period of time to gather data on the incidence of the effect in question. Cohort studies are generally considered to be potentially the most robust type of study. However, by their nature they tend to take a long time to complete and as such can be complex and expensive.

#### **7.4.2 Cross-sectional studies**

A cross-sectional study involves observation of a group at a particular moment in time and can be thought of as a 'snap-shot' of the prevalence of the effect or illness. The group under study can be compared with a similar matched comparison group.

They generally represent a relatively quick and inexpensive way to investigate the issue of concern. However, as the study only deals with a particular moment in time it cannot give any information on exposure and outcome as a time-dependant relationship. Also it is not suited to study of an effect that is uncommon.



## 8 OVERVIEW OF HEALTH EFFECTS

### 8.1 INTRODUCTION

The following section gives an overview highlighting some of the hazardous properties and health effects of a selection of the main substances that may be encountered in industry. It does not attempt to give information on dose-response relationships which are important in real-life exposure situations. When dealing with any particular substance it is important to seek out more detailed and authoritative information so that appropriate and proportionate measures can be taken to reduce risks.

### 8.2 GASES

#### 8.2.1 Introduction

In general, gases may be grouped as

- Simple asphyxiants e.g. nitrogen, methane, inert gases such as helium and argon
- Chemical asphyxiants e.g. carbon dioxide, carbon monoxide, hydrogen sulphide, hydrogen cyanide
- Upper respiratory tract irritants e.g. ammonia, sulphur dioxide
- Lower respiratory tract irritants e.g. oxides of nitrogen, phosgene

#### 8.2.2 Simple asphyxiants

These gases are only likely to be a danger when their concentration in inhaled air is sufficient to cause a significant reduction in oxygen levels. Normal levels of oxygen in air are about 20.9%. If the level of oxygen in the air is reduced below about 14% it will lead to rapid breathing and tissue damage followed by loss of consciousness and death as oxygen levels reduce further.

**Nitrogen (N<sub>2</sub>)** - nitrogen is the main constituent of air. In addition, nitrogen has industrial uses in ammonia production, as an inert atmosphere and as a freezing agent. In hyperbaric work, such as diving, nitrogen becomes toxic, causing narcosis.

**Helium and Argon (He and Ar)** - Helium and argon are two common examples of inert gases. They do not react chemically and do not as such cause any health effect. However, they are simple asphyxiants and at higher concentrations they can cause asphyxia by reducing the oxygen content of the air. They are commonly used as inert gas shields in welding processes as well as purging gases for chemical plant that has contained flammable vapours.

**Methane (CH<sub>4</sub>)** - methane is the product of the anaerobic decay of organic matter. Hence, it is found in sewers and wherever biodegradable organic matter can decompose. It is also a natural constituent of fossil fuel reserves. Natural gas, contains a large percentage of methane. It is also explosive at high concentrations.

### 8.2.3 Chemical asphyxiants

**Carbon dioxide (CO<sub>2</sub>)** - carbon dioxide occurs naturally as a product of combustion and of gradual oxidation, and hence can occur wherever combustible or organic materials are to be found. Industrially, it is found as a by-product of brewing, coke ovens, blast furnaces and silage dumps. It has a wide use as an industrial gas, e.g. in the carbonisation of drinks, brewing and refrigeration. It is heavier than air and, in concentrated form, can produce 'pools' of inert atmosphere in low, unventilated places such as sumps and sewers.

Carbon dioxide is sometimes classified as a simple asphyxiant as at lower levels (less than about 3% it acts as a simple asphyxiant). However, at

higher levels, carbon dioxide, unlike methane and nitrogen, is capable of affecting the medullary respiratory centre, so is generally considered as a chemical asphyxiant. Effects begin to occur at a concentration of 3%, initially headaches and lethargy, followed by rapid breathing, whilst, at 10% or more, loss of consciousness is rapid.

**Carbon monoxide (CO)** - carbon monoxide is a colourless, odourless gas that is produced by the incomplete combustion of carbonaceous compounds. It is produced as a by-product of mining, smelting, foundry work, petrochemical processes and many processes involving combustion.

Carbon monoxide binds very strongly to haemoglobin, leading to elevated carboxyhaemoglobin levels and consequently a diminished oxygen-carrying capacity of the blood. Acute health effects include giddiness, headache and drowsiness. Rapid loss of consciousness may occur at concentrations in excess of 3500 ppm. Brain damage and death can occur at higher concentrations.

**Hydrogen cyanide (HCN)** - Hydrogen cyanide is a colourless gas with a bitter almond-like odour. It can be produced by contact of cyanide salts with acid. It is used in precious metal extraction and the plating industry and is also used as a fumigant. It inhibits the action of cytochrome oxidase, thus disrupting cellular respiration. Acute health effects include rapid onset of headache, convulsions and death.

**Hydrogen sulphide (H<sub>2</sub>S)** - Hydrogen sulphide is a colourless gas with the smell of rotten eggs. It has no major industrial uses but it can occur wherever sulphur and its compounds are being used or are decomposing. It inhibits the cytochrome oxidase (similar to hydrogen cyanide). Acute health effects include watering eyes and mucous membrane irritation in low concentrations. In high concentrations, paralysis of the respiratory centre can cause sudden unconsciousness.

#### 8.2.4 Respiratory tract irritants

The somewhat arbitrary division into upper and lower respiratory tract irritants is largely on the basis of solubility. Highly water soluble gases, such as ammonia, chlorine and sulphur dioxide, exert their main irritant effect on the upper respiratory tract. This, unless the exposure is prolonged and severe, saves the lungs. Conversely, gases of low solubility, such as oxides of nitrogen and phosgene, have little effect on the upper respiratory tract; their effect is delayed and the main damage is borne by the lungs.

**Ammonia (NH<sub>3</sub>)** - ammonia is a colourless gas with a pungent odour. It is very soluble in water producing a caustic alkaline solution. It is used in the manufacture of fertilisers, refrigerants and as a catalyst and chemical reagent.

Acute health effects include irritation to the eyes, mucous membrane and upper respiratory tract. At higher concentrations severe, and often fatal, respiratory tract damage occurs, with pulmonary oedema.

**Chlorine (Cl<sub>2</sub>)** - chlorine is a greenish-yellow gas of pungent odour, over twice as dense as air. It forms hydrochloric acid with water, which can cause severe damage in high concentrations. It is used in chemical and pharmaceutical production, water disinfection in swimming pools and plastics manufacture.

Acute health effects include severe upper respiratory tract irritation leading to pulmonary oedema and death in those unable to escape its effects. Recovery from an acute exposure may be prolonged. Chronic effects include bronchitis.

**Hydrogen chloride (HCl)** - hydrogen chloride is a colourless gas with a strong irritating odour. On exposure to air it forms dense white corrosive aerosols. On contact with water it forms hydrochloric acid. It has many

industrial applications including, metal cleaning and pickling, electroplating, leather tanning, refining and manufacture of fertilisers and dyes.

Acute health effects include irritation to the eyes, mucous membrane and upper respiratory tract. At higher concentrations severe and often fatal, respiratory tract damage occurs, with pulmonary oedema. Long term exposure to low levels can cause chronic health effects including respiratory problems and eye and skin irritation.

**Hydrogen fluoride (HF)** - hydrogen fluoride is a colourless gas which rapidly dissolves in water to form hydrofluoric acid. A major use of hydrofluoric acid is as a raw material in the plastics industry for production of fluorinated polymers such as polytetrafluoroethylene (PTFE) and refrigerants. In addition it is used as a pickling agent in stainless steel production, in the semi-conductor industry and for etching glass.

Hydrofluoric acid is extremely corrosive. A particular problem is that exposure to hydrofluoric acid may not be immediately apparent. It interferes with nerve function and burns may not initially be painful. Exposures can go un-noticed leading to more serious injury. It is also able to penetrate intact skin and attack underlying bone structures.

**Oxides of nitrogen (NO, NO<sub>2</sub>)** - nitrogen dioxide (NO<sub>2</sub>) is a reddish-brown gas with a pungent odour and is of greater industrial hygiene importance. It is used in the manufacture of nitric acid, explosives and jet fuel. It is also generated during some types of welding and diesel engine operation.

Acute health effects of nitrogen dioxide exposure are insidious, due to slow progression of pulmonary irritation some 8 - 24 hours after exposure. Severe exposure can result in death from pulmonary oedema within 48 hours.

Nitric oxide (NO) is a colourless gas, with little known effect in humans.

**Ozone (O<sub>3</sub>)** - ozone is an oxidising agent and is used as a water fumigant steriliser and as a bleaching agent. It is also generated during arc welding (especially when the weld creates very little fume i.e. metal inert gas welding and aluminium welding).

Acute health effects include respiratory tract and mucous membrane irritation. Exposure to high concentrations can lead to pulmonary oedema.

**Phosgene (carbonyl chloride) (COCl<sub>2</sub>)** - phosgene is a sweet-smelling, highly toxic gas. It can be produced as a breakdown product of burning chlorinated hydrocarbons, including many plastics. Acute health effects include mild early symptoms followed by insidious onset of severe pulmonary oedema within 24 - 48 hours.

**Sulphur dioxide (SO<sub>2</sub>)** - sulphur dioxide is a colourless gas with a pungent odour and a density twice that of air. It produces sulphuric acid on dissolving in water. It is used in the chemical and paper industries, as a fumigant and as a preservative. It can also be produced as a common by-product of smelting sulphide ores.

Acute health effects include severe irritation of mucous membranes. The respiratory tract irritation is so severe that exposure to moderate levels can rapidly lead to severe pulmonary oedema and death. Chronic effects include bronchitis.

### 8.2.5 Other gases

**Arsine (AsH<sub>3</sub>)** - arsine (arsenic trihydride) is an example of a metal hydride. It is used in the semi-conductor industry and is a powerful haemolytic agent (breaks down red blood cells). This can cause severe anaemia from the destruction of red blood cells and cause the urine to become dark red. Death may occur from severe kidney damage or consequent kidney failure.

Arsine can also be produced inadvertently from interaction of arsenic impurities in metals with acid.

**Nickel carbonyl (Ni(CO)<sub>4</sub>)** - nickel carbonyl is a colourless, odourless gas. It is generated during nickel refining where nickel carbonyl enables nickel to be extracted from the ore and subsequently released from the carbonyl gas in nearly 100% pure form.

Acute health effects include headache, nausea and vomiting. These symptoms may subside and be followed later by pulmonary irritation and oedema. Chronic effects include cancer of nasal sinuses and lungs.

## **8.3 ORGANIC SOLVENTS AND VAPOURS**

### **8.3.1 Introduction**

In chemistry the term 'organic' refers to substances whose molecular structure is based on a number of carbon atoms. Organic materials cover a huge range of substances and may be solids, liquids or gases. They are extensively used as raw materials and reagents in a wide range of industries including plastics, pharmaceuticals and pesticides as well as their use as solvents, degreasing agents and fuels.

The term 'solvent' strictly applies to any substance (including water) that can dissolve or dilute another substance. However, the term 'solvent' is often used to refer to volatile organic liquids and it is in this context that we will use the term. Organic solvents are also widely used as raw materials in chemical manufacturing and processing as well as in many industrial processes.

Most organic solvents are liquids at normal ambient temperatures with boiling points ranging from about 35°C to over 200°C. However, solvent

vapours are produced from the liquid at temperatures below the boiling points.

Organic solvents are generally absorbed by two main routes of entry – inhalation of the solvent vapour and skin absorption. Solvent vapours are rapidly absorbed through the lungs and enter the bloodstream from where they can affect other parts of the body (causing systemic effects on target organs). Solvents in contact with the skin can cause local effects as well as being absorbed through the skin into the bloodstream.

Organic solvents cover a wide range of substances including:

- Aliphatic hydrocarbons e.g. pentane, hexane, heptane
  - These are used in fuels and also as solvents. They are used widely in inks, surface coating and adhesives. Hexane is used as a chemical feedstock and also for the extraction of oils and fats from natural products.
- Aromatic hydrocarbons e.g. benzene, xylene, toluene
  - Benzene is found in petrol, typically at levels at or below 1%. It is an excellent solvent but its use in many products has reduced because of its toxicity (known carcinogen). Its major role is as a chemical feedstock in the production of many other chemicals such as cyclohexane, styrene and phenol.
  - Toluene is a constituent of petrol due to its high octane properties and it is also widely used as a chemical feedstock, e.g. to produce benzene and toluene di-isocyanate. It is also widely used as a process solvent, and as a component in adhesives, surface coatings and inks.
  - Xylene is widely used as a solvent for paints, adhesives, rubber solutions, and pesticides and is widely encountered in industry. It is readily absorbed through the skin and also rapidly penetrates many materials used for protective clothing.
- Halogenated hydrocarbons e.g. dichloromethane, carbon tetrachloride



- Alcohols, glycols, ethers, esters and ketones

Solvents may be encountered as single substances, mixtures or as formulated products. Many industrial solvents, particularly hydrocarbons, are mixtures of many compounds and known by generic or trade names.

The risk to health from exposure to a solvent will depend on a number of factors including toxicity, exposure level and volatility. The rate of evaporation of different solvents varies widely. An indication of volatility is given by the vapour pressure – the higher the vapour pressure the greater the potential for significant generation of vapour.

Solvent vapours are heavier than air and in a still environment a saturated vapour cloud will tend to sink towards the floor. However, for lower solvent vapour concentrations the density is not significantly different to that of air and normal air movement is usually sufficient to disperse and dilute these vapours.

However, high concentrations can build up within storage tanks or sumps where air movement is restricted or when large quantities of solvent vapour are released. Strict precautions are necessary at operations that involve the entry of workers to tanks, enclosed vessels, pits or other confined spaces where solvents may be present or have leaked.

### 8.3.2 Exposure to organic solvents

**Closed plant** - production of solvents and their use in chemical processing is usually undertaken in an enclosed plant. However, exposure to solvent liquids and vapours can occur in a number of situations

- Maintenance work – unless the plant is thoroughly drained and purged, potential exposure can occur as pipework is

opened and pumps and valves are removed for repair or servicing

- Fugitive emissions – there are likely to be emissions during normal plant operation, and as a result of leaks from valves and joints
- Contact with liquid and vapour as a result of spillages

**Transfer of solvents** - exposure to solvent vapours can occur during transfer of solvents or solvent-based products between vessels, tanks or drums. Solvent vapours can be generated from the delivery nozzle and particularly by displacement of the air from the vessel being filled. Filling of a vessel, particularly if it previously contained solvents, may displace air that may be nearly saturated with solvent vapours from the vent, unless it is connected back to the vessel being emptied or to a solvent trap. For smaller scale operations control may be achieved by local exhaust ventilation around the filling point or by operating within a ventilated enclosure.

**Use of solvent based products** - solvent vapours are produced by evaporation from the work area during processes such as screen printing, painting and surface coating. The amount entering the general workplace will depend on the quantities used and the efficiency of any local exhaust ventilation.

Individual exposure varies greatly depending on how close the worker is to the vapour source and the amount of time that they are in the vicinity. Apart from exposure during normal work, potentially higher exposures can occur during non-routine tasks such as maintenance and cleaning of equipment. Used cleaning cloths can generate additional solvent vapours unless stored and disposed of safely.

There are many different organic solvents, with differing properties and health effects. However, many possible health effects are common to most organic solvents and are listed below.

### **8.3.3 General Health effects**

These health effects may occur on exposure to any organic solvent and can be divided into acute and chronic effects.

#### **Acute (short-term) health effects**

- Narcotic health effects including
  - Headaches
  - Drowsiness
  - Nausea
  - Dizziness
  - Unconsciousness
  - Death
- De-fatting of skin, leading to possible cracking and irritation of skin

#### **Chronic (long-term) health effects**

- Dermatitis
- Liver damage
- Kidney damage
- Brain and nervous system effects - irritability, sleep disorders, dementia, peripheral neuropathy
- Possible effects on foetus and reproductive systems

### **8.3.4 Specific information for selected organic solvents**

In addition to the generic health effects outlined above, many solvents can cause specific health effects. These are summarised in table 8.1.

**Table 8.1 – Specific health effects of some organic solvents**

<b>Solvent</b>	<b>Industrial uses</b>	<b>Health effects (in addition to generic effects)</b>
Benzene	Styrene, phenol and cyclohexane production. Also plastics, paints, pharmaceuticals, dyes	Known human carcinogen. Affects bone marrow, anaemia, can cause leukaemia
Carbon tetrachloride	Degreaser, solvent, manufacture of refrigerants	Liver and kidney damage. Synergistic effects with alcohol
Chloroform (trichloromethane)	Solvent, manufacture of fluorocarbons and plastics	Liver and kidney damage. Synergistic effects with alcohol
Dichloromethane	Paint and varnish remover. Solvent, fumigant	Metabolic breakdown forms carboxyhaemoglobin in blood resulting in reduced oxygen carrying capacity
Glycol ethers (some)	Solvents for paints and inks	Possible reproductive effects
Ketones (e.g. acetone and methyl ethyl ketone (MEK))	Solvents	No specific health effects
n-Hexane	Solvent, also in fuels, glues	Can cause nerve damage. May lead to weakness and possible paralysis of hands and lower limbs (peripheral neuropathy)
Tetrachloroethane	Solvent, chemical processing	Irritant, central nervous system depressant. Liver and kidney damage.
Tetrachloroethylene	Solvent, dry cleaning agent, fumigant	Powerful narcotic, irritant. Liver and kidney damage.
Toluene	Benzene manufacture, paint solvent	Irritant, cardiac arrhythmias. Liver and kidney damage.
Trichloroethane	Degreasing, solvent	Irritant
Trichloroethylene	Degreasing	Powerful narcotic, synergistic with alcohol. Irritant
Xylene	Solvent, chemical manufacture	Mucous membrane irritant

## **8.4 OTHER SELECTED ORGANIC LIQUIDS**

There are a number of other organic liquids that are widely used in industrial processes and manufacturing. While many of these have solvent properties, their primary uses are as a result of their reactive nature. Table 8.2 gives a number of examples and two of them (styrene and isocyanates) are examined in more detail below.

### **8.4.1 Styrene**

Styrene is readily absorbed by inhalation and is also absorbed through the skin. Major health effects are acute and narcotic (e.g. upper respiratory tract irritation, drowsiness, dizziness and collapse).

The major use of styrene is for production of styrene-butadiene rubber (SBR). It is also used as a carrier for resin in glass reinforced plastics (GRP) and other polystyrene based products such as fillers, coatings, paints and carpet backing.

Glass reinforced plastics manufacture exposes large numbers of workers to styrene (e.g. boat and aircraft manufacturing, container manufacturing and vehicle repairs). In addition to the hazards from styrene other hazards arise from the reinforcing glass fibre and other chemicals such as catalysts and accelerators.

In glass reinforced plastics manufacturing, the degree of exposure to styrene varies with the size of the application, the duration of exposure and the level of ventilation. The solvent evaporates over a period of time and if the area of application is large, it is sometimes difficult to apply local exhaust ventilation effectively.

There are particular problems when working on large structures where the operator needs to work within a relatively confined area, such as

inside a hull of a ship. In situations such as this the supply of fresh air within the hull may be appropriate.

#### 8.4.2 Isocyanates

Isocyanates are a group of reactive organic compounds that contain the isocyanate group (-NCO). The most commonly used isocyanates include diphenyl methane di-isocyanate (MDI), toluene di-isocyanate (TDI) and hexamethylene di-isocyanate (HDI). The vast majority of the total isocyanates used are MDI and TDI.

Isocyanate formulations are supplied as two-part 'polyurethane systems' comprising a di-isocyanate component and a polyol resin. The two components are mixed together by the user and once mixed quickly cures or sets to form the finished product.

Isocyanates are used in the manufacture of flexible and rigid foams, such as polyurethanes and coatings such as paints and varnishes. Flexible foams are usually based on TDI and have widespread use in furniture, mattresses and packing materials. With flexible foams, a foaming or blowing agent is also added to cause the foam to rapidly expand to fill the required space.

Rigid foams used for insulation products and solid packing materials are usually MDI based. MDI is also used as a binder in the manufacture of other products such as particle boards, and sand-based foundry moulds.

Isocyanates are also used widely to produce two part polyurethane paints. Often the paint is applied by spraying with a consequent high potential for exposure. After spraying the paint may be cured by heat.

**Health effects of isocyanates** - isocyanates are irritating to the skin and eyes, mucous membranes and respiratory tract. Very high exposure can

cause death by acute pulmonary oedema. However, it is the allergic reaction that is usually of most concern. Respiratory sensitisation may occur after a single peak exposure to isocyanates. After sensitisation, asthmatic attacks may occur at very low exposure levels, which may be much less than the relevant occupational exposure limit.

Once someone is sensitised, the only option to prevent reoccurrence of the symptoms is usually the complete prevention of isocyanate exposure. This may be possible by removing the worker from direct contact with the source of isocyanate exposure, but this may not always be a practical option and the person may need to find alternative employment.

In normal use common controls are substitution with isocyanates or isocyanate pre-polymers with lower volatility eg MDI for TDI (TDI is the most volatile isocyanate), use of local exhaust ventilation, breathing apparatus, powered respirators and health surveillance.

**Table 8.2 – Specific health effects of selected organic liquids**

<b>Substance</b>	<b>Industrial uses</b>	<b>Main health effects</b>
Aniline	Dyes, pharmaceuticals, rubber processing	Converts haemoglobin to methaemoglobin – reduces oxygen carrying capacity of blood. Moderate exposure may cause cyanosis, severe poisoning may cause anoxia and death.
Formaldehyde	Plastics and resin manufacture, disinfectant, preservative, chemical production	Severe irritant, possible respiratory sensitiser, possible carcinogen
Isocyanates	Production of polyurethane foams, 2-pack epoxy paints	Potent respiratory sensitiser. Permanent pulmonary disability
Phenol*	Insecticides, disinfectants, pharmaceuticals	Corrosive, readily absorbed through skin, burns. Potential mutagen.
Styrene	Rubber production, plastics, glass reinforced plastics	Irritant, central nervous system depressant.
Vinyl chloride	Plastics manufacture, rubber manufacture	Raynaud's phenomenon, angiosarcoma (cancer) of the liver

\*Note: Phenol is actually a solid, but is usually encountered as a concentrated liquid

## 8.5 METALS AND METAL COMPOUNDS

### 8.5.1 Aluminium (Al)

Aluminium is used extensively because of its corrosion resistance, strength and its light weight. It is used for structural components in the aerospace industry as well as other areas of transportation and building structures.

Exposure may occur during aluminium production, as well as to dust from grinding of aluminium products and as oxide fumes from welding.

**Health effects** - Inhalation of finely divided aluminium or aluminium oxide may cause pulmonary fibrosis.

Aluminium may also be implicated in the development of Alzheimers disease. Typical symptoms include damage to the central nervous system, loss of memory, trembling.

Other soluble aluminium compounds such as aluminium chloride present a potentially greater hazard as they can be hydrolysed by moisture on mucous membranes / lung linings to release hydrogen chloride (a severe irritant)

### 8.5.2 Arsenic and its inorganic salts (As)

Arsenic is produced primarily as a by-product in the smelting of lead and copper ores where arsenic is present as an impurity. Major uses for arsenic are as wood preservatives, pesticides and herbicides, in alloys to improve their hardness as well as in the semi-conductor industry.

Chronic exposure to arsenic may occur by exposure to dust in smelting processes.



**Health effects**

- **Acute** - severe gastroenteritis, nausea, vomiting, stomach pains. This may lead to severe fluid loss, coma and death.
- **Chronic** - dermatitis, skin pigment abnormalities and possible skin cancer. Also gastrointestinal disturbances, irritation of respiratory tract and cancer of the lung and liver.

A compound of arsenic that is used in the semi-conductor industry is arsine (Arsenic trihydride –  $\text{AsH}_3$ ). Arsine is a powerful haemolytic agent (breaks down red blood cells). This can cause severe anaemia from the destruction of red blood cells and cause the urine to become dark red. Death may occur from severe kidney damage or consequent kidney failure.

Arsine can also be produced inadvertently from interaction of arsenic impurities in metals with acid.

**8.5.3 Beryllium (Be)**

Beryllium is used in alloys where corrosion resistance and hardness is required. A common alloy with copper (containing 2 – 4% Be) is used for electrical connectors and relays for the electrical industry, in nuclear reactors and aerospace industries. Beryllium is also used in high heat resistance ceramics.

Inhalation of dust and fume of metal and oxide can occur during machining, grinding and welding of Beryllium containing alloys.

**Health effects**

- **Acute** - inflammation of the lungs and respiratory tract, pneumonitis
- **Chronic** - lung disorders including cough, shortness of breath and marked changes (non-cancerous growths in the lung) noted on X-ray. Beryllium is also considered to be carcinogenic.

#### 8.5.4 Cadmium (Cd)

It occurs naturally as cadmium sulphide with zinc blende. Cadmium metal is produced as by-product in zinc, lead and copper production. It is used for plating of steel to impart corrosion resistance properties, in a number of steel alloys, in nickel / cadmium batteries, and as a stabiliser and colourant in plastics.

Cadmium exposure may occur from inhalation of dust from general machining and processing of cadmium and cadmium compounds. Once absorbed by the body cadmium has a long biological half-life (10 – 30 years) so it may be detected a long time after exposure has occurred.

Inhalation of cadmium oxide fume (often seen as a brown fume) can also occur from zinc smelting, welding and cutting of cadmium coated steel and smelting of scrap metal.

##### Health effects

- **Acute** – can cause irritation of respiratory system. High exposure to cadmium oxide fume can cause severe chemical pneumonitis and oedema in the lungs, which can be fatal.
- **Chronic** - emphysema and scarring of the lungs can be caused by all forms of cadmium. However, potentially the most significant chronic effect is damage to the kidney. This is as a result of accumulation of cadmium in the kidney and resultant loss of kidney filtration function. This is indicated by the presence of low molecular weight proteins in the urine. Cadmium may also cause cancer in the kidney.

#### 8.5.5 Chromium (Cr)

Chromium can exist in several different forms (valencies) – the metal, chromium(III) compounds and chromium(VI) compounds. Chromium(III) exists naturally, the other two types are produced by industrial processes. Chromium(III) and chromium (VI) are also known as trivalent chromium and hexavalent chromium respectively.

Chromium is widely used in alloys for corrosion resistant materials and in stainless steels. It is also widely used in chromium plating processes. It is also used as a pigment, in leather treatment, fungicides and wood preservatives and in some cements.

Exposure to chromium dust and fume can occur in the production, machining and welding of chromium metals and alloys. In particular it should be noted that welding can produce hexavalent chromium. Chromic acid mist (also chromium(VI)) can be produced during electroplating processes. Skin contact with chromium compounds can also occur when using pigments or cement.

### **Health effects**

- **Acute** – these are caused mainly by irritant and corrosive effects of chromic acid and its salts. The main effects are skin irritation and ulceration, also ulceration and possible perforation of the nasal septum.
- **Chronic** – the main area of concern is lung cancer (from hexavalent chromium). Also chronic exposure can result in persistent irritant dermatitis and sensitisation.

### **8.5.6 Cobalt (Co)**

Cobalt is used in high performance steel alloys where it hardens the alloy so that the strength of the alloy is maintained at high temperatures. Also alloys are cutting and wear resistant. Exposure can occur by inhalation of dust and fume from metal processing, grinding and welding.

**Health effects** – Cobalt can affect the lung, including respiratory irritation, asthma like symptoms, fibrosis and sensitisation. IARC has listed cobalt as possibly carcinogenic (category 2B).

### 8.5.7 Copper (Cu)

Copper is widely used due to its excellent thermal and electrical conductivity. It is also corrosion resistant and malleable (easily shaped). It is used in electrical and electronic products in most industries and buildings. It is also used in pipework, alloys, in electroplating processes and in the manufacture of wood preservatives, pesticides, fungicides and herbicides. Exposure to copper dust and fume by inhalation can occur during metal processing, grinding and welding.

**Health effects** – exposure to copper can cause irritation of nasal mucous membranes and the eyes. Fumes from hot processes such as welding can produce metal fume fever. Symptoms include flu-like symptoms that often occur at the start of a week or particularly after exposure occurs after a period away such as a holiday. The effects usually last about 48 hours.

### 8.5.8 Iron (Fe)

Iron forms the basis of many iron and steel alloys. Exposure by inhalation of dust and fume can occur during metal processing, grinding and welding.

**Health effects** – the main effects are from chronic inhalation of high concentrations of iron which can result in the development of a benign pneumoconiosis, called siderosis which is observable as an X-ray change.

### 8.5.9 Lead (Pb)

Lead is a very soft, highly malleable metal that is very resistant to corrosion. In terms of industrial hygiene two categories of lead compounds are considered – firstly, lead and inorganic lead compounds and secondly, organic lead compounds.

Lead is widely used in metal products, sheet metal, solders and pigments. It was also widely used as an additive (tetra ethyl lead) in petrol. Other uses of lead include in batteries, pottery glazes and in lead crystal glass.

Exposure to lead and inorganic lead compounds usually occurs through inhalation of dust and fume from metal processing, grinding and welding. Significant levels of lead fumes can be produced at temperatures above about 450 °C. Lead is readily absorbed through the lungs. Ingestion is also a possible route of entry where poor hygiene standards occur.

Once in the body the lead is transported by the red blood cells and stored mainly in the bone marrow where it interferes with haemoglobin production.

Organic lead compounds (mainly tetra ethyl lead) are absorbed as a vapour by inhalation and are also readily absorbed through the skin.

**Health effects** – lead and inorganic lead compounds – a range of effects can occur including anaemia, fatigue, loss of appetite, abdominal pains, muscular weakness and possible brain damage.

Lead can enter a foetus through the placenta of the mother and cause serious damage to the nervous system and brain. This necessitates stringent control of exposure to lead for females of reproductive capacity. Lead can also impair male fertility.

For organic lead compounds health effects are more associated with psychiatric disturbances such as insomnia, hyperactivity and mania.

### 8.5.10 Manganese (Mn)

Most manganese is used in the production of a range of steel alloys such as stainless steels, tool steels and high temperature steels. Manganese is used as it hardens and strengthens the steel. It is also used in dry cell batteries, glass and ceramics.

Exposure to manganese is usually by inhalation of dust and fume from mining, metal processing, grinding and welding.

Manganese oxide can cause respiratory and mucous membrane irritation. Chronic absorption of manganese can cause insomnia, mental confusion, fatigue and symptoms similar to Parkinson's disease.

### 8.5.11 Mercury (Hg)

Mercury is the only metal that is a liquid at room temperature. As such mercury vapour is produced even at room temperature and at higher temperatures significant levels of vapour can be produced. It is used as the pure metal in thermometers and barometers. Mercury is also used in batteries, mercury vapour fluorescent lighting, amalgams, pharmaceuticals and as a seed dressing (organic mercury compounds only).

Exposure to mercury vapour is by inhalation (metallic mercury is poorly absorbed by ingestion). Exposure to mercury salts usually occur by inhalation of dusts.

**Health effects** – organic mercury compounds such as methyl mercuric chloride are generally more toxic than inorganic forms such as mercuric chloride. Chronic exposure to all forms of mercury can cause damage to brain, disruption of the central nervous system, neuro-psychiatric disorders with symptoms including neurosis and paranoia.

Motor neurone disturbances and visual field constriction more commonly associated with organic mercury compounds.

### 8.5.12 Nickel (Ni)

Nickel is extracted from its sulphide ore by the Mond process. As part of this process nickel reacts with carbon monoxide to produce nickel carbonyl (a known carcinogen) as an intermediary in the production of nickel metal.

Nickel is used in a range of steel alloys, including stainless steels. It is also used in nickel cadmium batteries, as a coating in electroplating and in ceramics. Exposure to nickel is usually by inhalation of dust and fume from metal processing, grinding and welding.

#### Health effects

- **Acute** - allergic contact dermatitis and sensitisation ('nickel itch'), nickel oxide fume can cause pneumonitis.
- **Chronic** - cancer of the nasal sinuses and lung cancer.

### 8.5.13 Vanadium (V)

Vanadium is used in high performance steel alloys. Vanadium hardens the alloy and increases the malleability of the products. It is also used in catalysts and insecticides. Vanadium may be present in high concentrations in some crude oils, this may lead to build up of vanadium in oil fired boiler residues

Exposure to vanadium is usually by inhalation of dust and fume from metal processing, grinding and welding.

#### Health effects

- **Acute** – can cause irritation of lungs, mucous membranes and gastro-intestinal disturbances.
- **Chronic** – bronchitis, skin lesions, severe trembling and green discolouration of the tongue!

#### 8.5.14 Zinc (Zn)

Zinc is used in electroplating (galvanised steel) and as a major constituent of brass (5 – 40%). Zinc chloride is used as a flux material. Exposure to zinc is usually by inhalation of dust and fume from metal processing, grinding and welding.

**Health effects** – fumes from hot processes such as welding can produce metal fume fever. Symptoms include flu-like symptoms that often occur at the start of a week or particularly when exposure occurs after a period away such as a holiday. The effects usually last about 48 hours.

Zinc chloride is corrosive to skin and lungs.

### 8.6 DUSTS AND PARTICULATE MATERIALS

As with the previous sections, the following examples are used to illustrate some of the hazardous properties and health effects of a selection of dusts and other particulate materials. It is not intended to be a comprehensive listing of the range of substances that may be present as a significant dust hazard in industry.

#### 8.6.1 Crystalline silica



Crystalline silica (silicon dioxide) is the most abundant compound in the earth's crust and is a common airborne contaminant in many industrial situations and processes.

The most common form of crystalline silica is quartz although it can also appear as tridymite or cristobalite. These are less common than quartz but are considered to have a greater potential to cause fibrosis. Cristobalite can be formed from quartz at high temperature.

With sufficient exposure, crystalline silica can cause silicosis, a typical pneumoconiosis that develops after years of exposure. This is a chronic disease where a reduction in lung function occurs due to the production of scar tissue. Exceptionally high exposure can cause acute or accelerated silicosis within months with significant impairment or death occurring within a few years. In addition, there is an increased risk of lung cancer in silicosis sufferers.

The size fraction of concern is the respirable fraction (less than 10 micron) as silicosis is caused by the particles depositing in the alveolar region of the lungs. Respirable particles are formed whenever silica-bearing rock is drilled, blasted, cut or crushed into finer particles.

Different types of rock contain different amounts of silica. Typical values are:

- Sand and sandstone > 90%
- Granite and slate up to 40%
- Ball clays 25%
- Limestone < 1%

In addition to mining and quarrying of silica-bearing rock exposure to quartz can also occur in a wide range of industries. Sand is widely used as a mould material in metal casting and foundry processes. Significant concentrations of airborne crystalline silica dust can be produced during the

removal of the sand mould as well as during cleaning of sand residues from the finished casting.

The pottery industry uses a range of raw materials where crystalline silica may be present in significant quantities such as ball clay, kaolin, stone and quartz. Indeed, silicosis has historically been a major problem in the pottery industry. Improved methods of production and better controls have reduced the incidence of this disease.



(Source: HSE LEV Trainer Adviser Briefing Days – reproduced with permission)

**Figure 8.1 – Disc cutting of stone block**

Ovens, kilns and furnaces are lined with refractory material. A large amount of refractory materials are used in the manufacture of metals such as in blast furnaces and other furnaces. Other industries as examples where refractory materials are used include gas, coke plants, cement and lime, ceramics and glass.

These refractory materials are produced from a range of materials some of which may contain high levels of quartz. This is a particular concern as after being subjected to high temperatures this may be converted to cristobalite. Replacement of furnace linings presents particular problems of high levels of respirable dust generation.

## 8.6.2 Nanoparticles

'Nanotechnology is a broad interdisciplinary area of research, development and industrial activity which has been growing rapidly world wide for the past decade. It is a multidisciplinary grouping of physical, chemical, biological, engineering, and electronic, processes, materials, applications and concepts in which the defining characteristic is one of size.

Nanoparticles are the end products of a wide variety of physical, chemical and biological processes some of which are novel and radically different, others of which are quite commonplace'.

(Source: HSE RR274 Nanoparticles: An occupational hygiene review – Reproduced under the terms of the Click-Use licence)

Nanomaterials are usually defined as particulate materials with at least one dimension of less than 100 nanometres (nm). One nanometre is  $10^{-9}$ m. By comparison a human hair is approximately 70,000 nm (70 micron) in width and a blood cell is approximately 5,000 nm wide.

The small size of nanomaterials gives them specific or enhanced physico-chemical properties compared with the same materials at the macro scale. This has led to great interest in their potential development for different uses and products.

As the size of the particles reduces the proportion of atoms on the surface compared to atoms in the bulk of the material increases dramatically (i.e. they have a very high surface area to volume ratio). It is thought that this is one of the major factors that cause the difference between properties of nanomaterials compared to the bulk materials.

In addition, the small sizes of the particles mean that the lung macrophages may not be able to detect and deal with them. They are able to penetrate cell membranes and may deposit in cells and be transported around the body and deposit in vulnerable organs.

Examples of nanomaterials include:

- Nanosilver – used for its anti-bacterial properties
- metal oxide nanoparticles – titanium dioxide nanoparticles in coatings impart self-cleaning properties, zinc oxide nanoparticles have superior UV blocking properties in sunscreens than its bulk equivalent
- carbon nanotubes (CNT) – uses based on the fact that they are light and exceptionally strong fibres (tensile strength about 50 times greater than steel)
- fullerenes (of which carbon-60 products are perhaps the best known) – these have potential uses as lubricants and electrical conductors

Nanoparticles present possible dangers, both as potential health effects to individuals and also to the environment. However, it is recognised that at present, the extent of knowledge about the potential health and environmental impacts of nanoparticles lags significantly behind the rate of innovation.

Apart from the lack of toxicological data (particularly on chronic effects) available for many of the nanomaterials, there are also further difficulties in assessing exposure risks. It is thought that the most appropriate metric for assessment of inhalation exposure risk is particle surface area. However, there are no effective methods currently available by which surface area can be assessed in the workplace.

Initial approaches have taken existing exposure limits and reduced them by a factor of about 10 to take into account potential increased risks and the considerable uncertainties that exist.

Control approaches to nanomaterials also have to be examined as controls based on normal particle filtration and even HEPA filters may not be adequate or appropriate.

### **8.6.3 Diesel engine exhaust**

Diesel engine exhaust is a complex mixture of gases, vapours and particulate matter. It contains the products of combustion including elemental carbon, carbon monoxide, aldehydes, nitrogen dioxide, sulphur dioxide and a large range of different organic breakdown products including polycyclic aromatic hydrocarbons. Most of the contaminants are absorbed onto the elemental carbon particles which are generally less than 1 micron in size which can reach the alveoli.

The International Agency for Research on Cancer (IARC) considers diesel particulate matter to be probably carcinogenic to humans. In addition, recent research has indicated that a range of non-malignant adverse health effects may be induced following excessive exposure to diesel particulate.

Acute effects of diesel engine exhaust include irritation of the nose, eyes and respiratory tract as well as headache and fatigue. Chronic effects may include bronchitis and decrease in respiratory tract functions. It can also exacerbate the symptoms of asthma.

### **8.6.4 Latex**

Natural rubber latex (NRL) is a milky fluid obtained from the rubber tree. As with many natural products it contains proteins to which some people may develop an allergy. There are two types of allergy associated with latex; Type I – caused by the natural proteins and Type IV – caused by some of the chemicals (mostly accelerators) used in converting the natural rubber latex to a usable item.

The main categories of workers most at risk from latex allergy include the following:

- Healthcare workers (e.g. surgeons, nurses, dentists, laboratory workers etc) – the widespread use of latex based gloves presents particular problems in this industry sector
- Other workers exposed to latex based gloves on a regular basis (e.g. car mechanics, catering and electronics trades)
- Industrial rubber manufacturing workers who may be exposed to high amounts of latex over an extended period of time

Gloves are the single most widely used device containing natural rubber latex. The UK Health and Safety Executive have stated that:

“Single use disposable natural rubber latex gloves may be used where a risk assessment has identified them as necessary. When they are used they must be low-protein and powder-free”

(Source: HSE About latex allergies: – Reproduced under the terms of the Click-Use licence)

In many situations risk assessment will show where there is a risk of contact with blood or body fluid contact (e.g. surgery and health care etc) latex gloves provide the best protection against blood borne pathogens. They are the best choice provided the worker and patient are not sensitised to latex. If either is sensitised then natural rubber latex gloves and equipment should not be used.

Latex gloves are often used in for example; catering, domestic services, motor industries, hairdressing and other industries and if there is no contact with blood or body fluids they should be substituted by an alternative non-latex product.

### 8.6.5 Enzymes

Enzymes are specific types of proteins that occur in all living cells. There are two main types of enzymes, metabolic enzymes and digestive enzymes:

- Metabolic enzymes – catalyse and regulate biochemical reactions that occur within the cell. These are produced in the body, particularly by the liver and pancreas
- Digestive enzymes – these are fundamental to the process of digestion where they catalyse the breakdown of proteins, fats and carbohydrates in food. These are produced in the body and secreted into the digestive tract and are also introduced into the digestive system in the foods themselves.

Human digestive enzymes include pepsin, lipase, protease and amylase. These and many other enzymes can be manufactured and are widely used industrially, in the detergent, food and brewing industries as well as produced for food supplements.

Examples of enzyme use include pectinase used to produce and clarify fruit juices, amylase to break down flour into soluble sugars and protease in cheese production and meat tenderising. Protease is also used in 'biological' detergents to speed up the breakdown of proteins in stains such as from blood or egg.

All enzymes, being proteins, are potential allergens and can have particularly severe effects if inhaled as a dust. Once an individual has developed an immune response, further exposure may bring about a severe and possibly fatal response in a hypersensitive person. Workers in these industries who may be exposed to enzymes should be screened for allergies and respiratory problems.

To minimise the potential for inhalation of enzyme dust, dry enzyme preparations have largely been replaced by liquid preparations. Where dry preparations must be used as in the formulation of enzyme based detergents potential problems have been reduced by encapsulating or granulating the enzyme. If dry enzyme powder has to be handled and used, this should be undertaken in closed systems.

In addition to the potential problems of exposure to enzymes in the manufacturing environment, end users of products containing enzymes such as detergents, need to be aware of the potential problems and allergic responses.

#### **8.6.6 Flour and other food components**

Many foods and food components can cause allergic responses in individuals. Examples include:

- Flour
- Grain dust
- Bakery dust
- Egg protein
- Fish protein

Flour is extensively used in the food industry and has a number of health hazards associated with it. It is a fine dusty material and can generate an airborne dust that can be inhaled. Health effects include rhinitis, as well as occupational asthma and dermatitis. The allergic response is either from the flour itself, from amylase enzyme or from other ingredients such as egg powder.

Apart from the health hazards described above, fine combustible dusts such as flour dust can present an explosion risk if present at high concentrations.



## 8.7 MINERAL FIBRES

### 8.7.1 Asbestos

Asbestos is the term for a group of naturally occurring hydrated silicate minerals that have proved commercially useful. The term asbestos is applied to six such minerals that can be grouped into two main categories:

- Serpentine group
  - Chrysotile (white asbestos)
  
- Amphibole group
  - Amosite (brown asbestos)
  - Crocidolite (blue asbestos)
  - Anthophyllite, Tremolite and Actinolite

The first three are the forms that have been widely used. Asbestos was readily available, cheap to extract and ideal for many manufacturing purposes. Its main properties are its strength, chemical resistance, flexibility, non-combustibility and good thermal and electrical insulation.

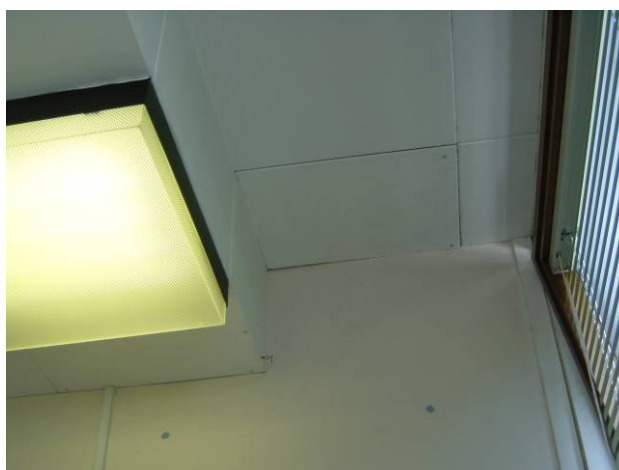
These useful properties led to a vast range of applications and asbestos products are now widely distributed in buildings, vehicles and domestic and industrial items. These products include

- Pipe and boiler lagging
- Sprayed coatings – thermal and acoustic insulation and as fire protection to ceilings and structural steel.
- Insulation boards - fire protection as wall and ceiling panels and as lining panels to ducts and lift shafts.
- Asbestos cement - corrugated or flat sheeting, rainwater pipes, gutters, tiles, cladding, flues etc.



(Source: Gully Howard Technical Ltd)

**Figure 8.2 Insulation (lagging) to pipework and calorifiers**



(Source: Gully Howard Technical Ltd)

**Figure 8.3 Asbestos insulating board ceiling tiles**

Other uses include friction materials, protective clothing, rope insulation, gaskets, floor tiles and 'artex'.

**Health Hazards** – in the UK, a country which has used asbestos extensively as fire protection, thermal insulation and building materials around 4000 people die each year from asbestos related diseases and it is expected that this could rise to 6 - 8,000 a year by the year 2015.

Asbestos is only a health risk in situations where it can enter the lungs. This can occur if fibres become airborne and are inhaled. Asbestos can split lengthways into finer fibres. The three main diseases associated with exposure to asbestos are asbestosis, mesothelioma and lung cancer.

- **Asbestosis** - a fibrotic pneumoconiosis that causes a progressive loss of elasticity and lung function. It only occurs in people exposed to large amounts of asbestos, normally over many years. The fine fibres are not readily removed and damage the scavenging cells that arrive to remove them leading to formation of scar tissue or fibrosis.
- **Lung Cancer** - the risk of developing lung cancer is increased for people who smoke and for people who are exposed to asbestos. For those who are exposed to asbestos and who smoke the risks are greatly increased – i.e. synergistic. There is no known safe level – blue and brown are particularly implicated – white to a much less extent.
- **Mesothelioma** - a malignant growth in the pleura (the lining of the lung) or more rarely the peritoneum (lining of the abdominal cavity). Mesothelioma may develop any time from 15 to 50 years after the first exposure to asbestos. There is no known safe level – blue and brown are particularly implicated – white to a much less extent.

In the past those considered to be most at risk were involved in the importation of asbestos, or manufacture of asbestos products. The workers considered most at risk now are those who may disturb asbestos during repair, maintenance and refurbishment work on buildings.

Due to the health hazards associated with asbestos other materials are slowly replacing it. However, it continues to be inadvertently discovered on

a regular basis. This can put workers and sometimes building occupants at risk. To control risks from asbestos procedures must be in place to identify, assess and manage asbestos.

### 8.7.2 Machine made mineral fibres (MMMMF)

It is known that asbestos fibres can cause a variety of health effects including fibrosis and cancers of the lung and pleura. As replacements for asbestos have been developed, concerns have been raised regarding possible health effects from these synthetic fibrous materials.

Synthetic vitreous fibres; often called 'Machine-Made Mineral Fibres' or 'Man-Made Mineral fibres' (MMMMF) include continuous glass fibres, insulation wools made of glass, rock or slag fibres, and refractory ceramic fibres, which are generally aluminium silicates.

Usually the continuous glass fibres are used to reinforce other materials such as plastics. Insulation wools are used mainly as thermal and acoustic insulation. Refractory ceramic fibres are used mainly in high temperature insulation products.

**Synthetic vitreous fibre manufacturing** - continuous glass fibres are fine filaments of nearly uniform diameter produced by extruding molten glass through small diameter holes. Their diameters are relatively large (usually 5 to 15 micron or greater) compared to those in the insulation wools. These large diameters, together with the narrow range of diameters produced during manufacture, eliminate many potential chronic respiratory effects, as the fibres are too large to be inhaled into the lower respiratory tract.

Insulation wools and refractory ceramic fibres are made in processes in which molten material is dropped onto either a series of spinning discs or wheels, or molten material drawn off by blowing with steam or hot gases. These methods result in the production of fibres with a range of diameters

much wider than that of continuous filaments. All of the insulation wools and ceramic fibres will contain some fibres with diameters of less than 3 micron which could become respirable.

**Health effects of synthetic vitreous fibres** - it is a particular concern that the synthetic fibrous materials, which have been used as a replacement for asbestos, may produce similar effects to asbestos if of a comparable size.

The International Agency for Research on Cancer (IARC) in 1988 had originally placed glass wool, rock wool, and slag wool into IARC Group 2B (possibly carcinogenic to humans) based on inadequate evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals. It also placed continuous filament glass into Group 3 (not classifiable as to carcinogenicity to humans based on inadequate carcinogenicity in human studies and experimental animals).

A review was conducted in 2001 as a result of new research and evidence. This placed rock wool, insulation glass wool, slag wool and continuous filament glass into Group 3 "because of inadequate evidence of carcinogenicity in humans" along with their relatively low biopersistence, whereas refractory ceramic fibres and some special purpose glass wools (not used in insulation materials) have been placed in Group 2B due to their seemingly high biopersistence.

Occupational exposure to synthetic vitreous fibres can cause acute irritation of the skin, eyes and upper respiratory tract causing congestion of nasal passages, sore throat and coughing. The symptoms usually disappear soon after ceasing exposure.

Exposure to airborne fibres is usually well controlled during the manufacture of synthetic vitreous fibre products. However, other tasks such as insulation, construction and removal activities can generate high fibre levels. Fibre concentrations generated depend on how confined the work area is, as well as the duration and type of work.



(Source: Steve Bailey – reproduced with permission)

**Figure 8.4 Re-lining a furnace with refractory ceramic fibre blocks**



(Source: Steve Bailey – reproduced with permission)

**Figure 8.5 Re-lining a furnace with refractory ceramic fibre blocks**

Furnace wrecking and demolition work involving vitreous synthetic fibres may present particular problems with some refractory ceramic fibre products where these products have been heated to temperatures in excess of about 1000°C. At these temperatures these materials can undergo partial conversion to cristobalite (a crystalline form of silica that is hazardous by inhalation).

## 9 COMMON INDUSTRIAL PROCESSES

### 9.1 INTRODUCTION

There is a wide range of industrial processes that use and produce hazardous substances. In the following sections a number of common processes are briefly described. The purpose of this is to illustrate typical exposure scenarios and ways in which exposure to hazardous substances commonly occurs.

It is not intended to be a comprehensive listing of industrial processes, nor is it intended to identify all the potential hazards likely to be present in the particular processes. The range of processes selected has been chosen to cover a wide range of industry sectors and should provide the student with an overview of many of the workplace hazards commonly encountered.

### 9.2 MATERIALS HANDLING

The following section looks briefly at a range of handling operations for both solids and liquids. These handling operations are found in many industries (e.g. paints, inks, pesticides, pharmaceuticals, polymers, chemicals, mining, agriculture etc) and are often the source of exposure to hazardous substances.

In accordance with good industrial hygiene practice consideration should always be given to prevention of exposure. This may be by elimination or substitution of the substance with a less hazardous material. Where this is not practicable a combination of engineering, process and operational controls, together with instruction and training may be required to achieve adequate control. In many operations, local exhaust ventilation may be necessary and as a last resort all the above may need to be supplemented by the use of personal protective equipment.

### 9.2.1 Handling of solids and powders

Dust generation under normal working conditions depends essentially on movement of some sort. This may occur at all stages of the process from delivery of the material to the factory through various transfers, weighing, sieving, filling and mixing operations.

**Selection of materials** - In some situations, dust generation can be reduced or eliminated by using dust reduced forms of the substance which contain small quantities of a binder. In addition the material may be supplied in the form of pellets, granules or flakes which are less liable to generate airborne dust. Completely dust free forms such as pastes or powders dispersed in liquids may also be available. All of these options are dependant on whether the reduced dust form of the substance is compatible with the process requirements.

**Bulk powder delivery and transfer** - Large quantities of bulk material may be supplied in bulk road or rail tankers or in tote bins, which are then discharged into silos. Delivery from tankers by pneumatic conveying is efficient and clean. However, it is reliant on the quality of the seals between the tanker and the discharge point, and between the tote bin and the silo. These seals and the flexible ducting need to be maintained in good condition to prevent leaks as the ducting may be at positive pressure.

Direct feed of bulk materials from storage silos to mixing may avoid the need to handle the powder. While these systems are generally totally enclosed, there may be a need to incorporate vents to account for air displaced during silo filling and powder transfer. This displaced air which will contain high levels of airborne dust must be cleaned prior to discharge.

Bulk powder transfer is often undertaken by moving belt conveying systems. These usually involve a number of transfer points at which dust can become airborne. The amount of dust generated can be minimised by



reducing the height of the drop from the conveyor to a minimum and by reducing any cross draughts. Conveyor transfer points may need to be partially enclosed with local exhaust ventilation incorporated.

Bulk materials may also be delivered in paper or plastic bags; intermediate bulk containers (IBC's) such as aluminium totes or octabins or woven polyurethane sacks. Whenever dusty materials are transferred, handled or used, spillages may occur. It is important that there are good standards of housekeeping and cleanliness to minimise exposures and contamination. Wet wiping methods and use of industrial vacuum cleaners are preferred to the use of brushes which will render airborne settled dust deposits.



(Source: Steve Bailey – Reproduced with permission)

**Figure 9.1 – Split bag containing sodium carbonate**

**Dust generation at powder handling processes** - Dust generation can occur at a number of different processes including weighing, sieving, charging (filling) of vessels and mixing (formulation). Whenever containers are charged or filled with powders air, which may be dust-laden, is displaced from the container. Depending on the amounts and toxicity of the powders being handled full or partial enclosure may be required incorporating local exhaust ventilation.



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**Figure 9.2 – Manual loading of open mixer from drum**

A common potential problem is opening and emptying of bags containing powders. The use of enclosed and automated bag and powder handling plant can significantly reduce dust exposures. Systems are available that automatically open, empty, evacuate and bale empty bags.

Weighing of mix ingredients may also be undertaken automatically in an enclosed system; however, if manual weighing is required the use of ventilated booths or laminar flow cabinets may be appropriate for hazardous substances.

Sieving of some products may be required to break up agglomerates or ensure that only products of a certain size range are included. If the process is not fully enclosed, local exhaust ventilation is usually needed. Vibratory action is often used and planned maintenance of sieves, joints and connections is important.

## 9.2.2 Handling of liquids

As with solids, exposures to liquids and their vapours can occur at a range of common operations. Bulk liquids may be supplied in bulk road or rail tankers or in drums which may be transferred to storage tanks. Transfer from tankers by enclosed transfer is efficient and clean. However, it is reliant on the quality of the seals between the tanker and the discharge point. These seals and the pipework and hoses need to be maintained in good condition to prevent leaks. Seals and joints on pipes, valves and pumps also need to be maintained in good condition to prevent leaks and fugitive emissions.



(Source: Steve Bailey – Reproduced with permission)

**Figure 9.3 – Delivery of methanol from tanker**

Direct feed of liquids from storage tanks to point of use may avoid the need to come into contact with the liquid. While these systems are generally totally enclosed, there may be a need to incorporate vents to account for air displaced during tank or container filling. This displaced air may contain high levels of solvent vapour which should be recovered or captured using local exhaust ventilation.

Exposure to liquids may also occur when pipework and vessels need cleaning or maintenance. Systems need to be in place to ensure they are effectively purged of hazardous materials prior to work.

Whenever containers are charged or filled with liquids such as solvents; air which may contain high levels of solvent vapour is displaced from the container. Depending on the amounts and toxicity of the liquids being handled full or partial enclosure may be required incorporating local exhaust ventilation.

Precautions need to be in place whenever liquids are transferred to minimise the potential for spills and splashes. Other simple precautions such as use of lidded containers and closing containers can reduce exposure to vapours from evaporation of liquids.



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***Figure 9.4 – Paint bench – open tins and rags soaked in thinners can be a source of exposure***

### **9.3 WORKING WITH METALS**

There is a range of different techniques that may be used to process and fabricate metal products. This includes grinding, machining and welding of metals and metal alloys.

#### **9.3.1 Grinding**

Grinding involves the use of a bonded abrasive to wear away parts of a work piece to correct its dimensions, remove imperfections or increase the

smoothness of a surface. Natural abrasives (e.g. diamond and sandstone) have been largely replaced by artificial abrasives. These include aluminium oxide, silicon carbide (carborundum) and synthetic diamonds.



(Source: HSE: Working with us on Noise and Hand-Arm Vibration 2008 – Reproduced under the terms of the Click-Use licence)

**Figure 9.5 – Grinding**

A variety of tools may be used to undertake grinding including grinding wheels as well as grinding discs and belts.

Historically, a high incidence of silicosis occurred with the use of sandstone grinding wheels. Modern grinding wheels are usually made of corundum (an oxide of aluminium) and do not contain significant amounts of crystalline silica. However, silica dust may still be produced from materials being ground – e.g. sand residues on sand castings. Local exhaust ventilation is required for most grinding, belt sanding and finishing operations.





(Source: Steve Bailey – Reproduced with permission)

### **Figure 9.6 – Grinding**

In addition to the risks from inhalation of airborne dusts, grinding operations may also generate high noise levels and possibly significant levels of vibration leading to a risk of hand-arm vibration syndrome (HAVS), also known as “white finger”.

### **9.3.2 Machining of metals**

Machining of metal products is undertaken using a variety of machines including lathes, drills and saws. These processes generally produce relatively large metal particles and so airborne dust generation is low. Grinding processes produce much finer dust and are therefore of more concern in this respect. The main health hazard from machining is related to cutting fluids which lubricate and cool the process.

There are three main types of cutting fluids used;

- Mineral oils – mineral oils of various viscosities are used together with additives to provide specific characteristics
- Soluble oils – soluble water-in-oil cutting fluids are mineral oils that contain emulsifiers and additives including rust inhibitors and

bactericides. They are diluted with water in varying ratios before being used

- Synthetic fluids – synthetic cutting fluids are solutions of non-petroleum based fluids, additives and water

Exposure to cutting fluids during work or maintenance may cause contact dermatitis. Water-based cutting fluids may contain bacteria and cause infections, and the emulsifiers may dissolve fats from the skin. Oil folliculitis can occur with prolonged exposure to oil-based cutting fluids. Dermatitis is best controlled by good hygiene practices and minimising exposure.

Occupational exposure to oil mists and aerosols may cause a variety of respiratory effects, including asthma, chronic bronchitis and impaired pulmonary function.

### 9.3.3 Welding and thermal cutting

Welding is a generic term referring to a process by which metals are joined together. This is often achieved by melting the metal in the area to be welded and adding a filler material to form a pool of molten metal which solidifies on cooling to form a strong joint. Common sources of heat are:

- A gas flame produced by the combustion of fuel gas such as acetylene or propane with air or oxygen
- An electric arc, struck between an electrode and a workpiece or between two electrodes
- Resistance to passage of electric current

**Gas welding** – this generally uses a combination of oxygen and acetylene. The gases are fed to a hand held welding torch to produce a flame. The heat melts the metal faces of the parts to be joined, causing them to flow together. A filler metal or alloy with a lower melting point than the parts to be

joined is usually added. Chemical fluxes are used to prevent oxidation and facilitate the welding process.

**Arc welding** – an electric current is used to strike an arc between an electrode connected to an electric supply and the materials to be welded. The arc can generate temperatures up to about 4,000°C when the pieces to be welded fuse together.

As with gas welding a filler metal or alloy is added to the joint. This may be achieved by melting the electrode (consumable electrode process) or by melting a separate filler rod which is not carrying the electric current (non-consumable electrode process).

To ensure a strong weld is achieved it is vital that the welding area is shielded from the atmosphere to prevent oxidation and minimise contamination. The two main ways that this protection can be achieved are by use of a flux or by use of an inert gas shield.



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**Figure 9.7 – Arc welding**



In flux-shielded arc welding the consumable electrode consists of a metal core surrounded by the flux as a coating. The metal electrode core acts as the filler material for the weld. The flux coating also melts covering the molten metal with slag and by generating carbon dioxide envelopes the welding area with a protective atmosphere.

In gas-shielded arc welding, a blanket of inert gas (e.g. argon, helium, nitrogen or carbon dioxide) seals off the atmosphere and prevents oxidation and contamination during the welding process. The two most common types of gas-shielded arc welding are metal inert gas (MIG) welding sometimes known as gas metal arc welding (GMAW) and tungsten inert gas (TIG) welding.

**Resistance welding** – this uses the heat generated by the resistance to the passage of a high electric current through components to be welded. Heat generated at the interface between the components brings them to welding temperatures and small pools of molten metal are formed at these points.

A common type of resistance welding is spot welding of thin metal sheets. Two electrodes simultaneously clamp the sheets together and electric current passes through the sheets. Weld strength is lower for this type of welding but it is very easily automated and is energy efficient. It is widely applied by industrial robots as in car manufacturing.

**Health hazards of welding** – airborne contaminants (including fumes and gases) from welding and flame cutting arise from a variety of sources:

- the metal being welded, the metal in the filler rod or constituents of various types of steel (e.g. nickel or chromium)
- any metallic coating on the article being welded (e.g. zinc and cadmium on plated metals)

- any paint, grease or dirt on the article being welded (e.g. carbon monoxide, carbon dioxide and other irritant breakdown products)
- flux coating on the filler rod (e.g. inorganic fluoride)
- action of heat or ultraviolet light on the surrounding air (e.g. nitrogen dioxide, ozone) or on chlorinated hydrocarbons (e.g. phosgene)
- inert gas used as a shield (e.g. carbon dioxide, helium, argon)

Fumes and gases should be removed at the source by provision of local exhaust ventilation. Where there is still a risk to health from toxic fumes and where local exhaust ventilation is not practicable a good standard of respiratory protective equipment is necessary.

Additional hazards can occur when welding is undertaken in confined spaces such as tanks and vessels and ventilation of the confined space is important. This is required to remove contaminants produced by welding and also to maintain sufficient oxygen levels. Gas welding uses up oxygen as part of the process and gas shielded arc welding introduces inert gases that can displace the oxygen in the space. Entry should only be permitted after the area has been certified as safe as part of a permit to work system.

Metal fume fever is associated with exposure to zinc oxide or copper oxide fumes which can occur in areas such as brass founding and welding of galvanized (zinc coated) steel. It is an acute effect that can occur within a few hours of exposure. Flu-like symptoms include cough, nausea and chills and fever. Recovery is usually complete within a day or two. It particularly affects people new workers and people returning to work after a break.

In addition to the chemical hazards other physical hazards are likely to be present. High noise levels may be generated in several welding processes. Intense levels of ultraviolet light are emitted by electric arc welding. Even

momentary exposure to ultraviolet radiation may produce a painful conjunctivitis (photokeratitis) known as “arc eye”. Exposure to the welder is prevented by use of visors or goggles that prevent passage of ultraviolet light and by use of screens to prevent exposure of others in the area. High levels of infra-red radiation may be produced from the hot surfaces leading to potential thermal stress issues.



(Source: Steve Bailey – reproduced with permission)

***Figure 9.8 – Arc gouging or cutting***

The following table summarises the main types of welding and any specific health hazards.

**Table 9.1 Main types of welding and specific health hazards**

Type of welding	Description	Specific health hazards
<b>Gas welding and cutting</b>		
Gas welding	The flame melts the metal surface and filler rod to form a joint	Metal fumes, nitrogen dioxide, carbon monoxide
Gas cutting	The metal is heated by a flame and is directed onto the point of cutting and moved along the line to be cut	Metal fumes, nitrogen dioxide, carbon monoxide
<b>Flux-shielded arc welding</b>		
Manual metal arc welding (MMA)	Uses a consumable electrode consisting of a metal core surrounded by a flux coating	Metal fumes, fluorides, ultraviolet radiation; ozone, nitrogen dioxide
Submerged arc welding (SAW)	Uses a consumable bare metal wire electrode. Granulated flux is deposited on the workpiece, which melts to produce a protective shield in the welding zone.	Metal fumes, fluorides, ultraviolet radiation, ozone, nitrogen dioxide
<b>Gas-shielded arc welding</b>		
Metal inert gas (MIG); gas metal arc welding (GMAW)	Uses a consumable metal wire electrode of similar composition to the weld metal. It is fed continuously to the arc.	Metal fumes, ultraviolet radiation, ozone, nitrogen dioxide, potential build up of inert gas
Tungsten inert gas (TIG); gas tungsten arc welding (GTAW)	The tungsten electrode is non-consumable, and filler metal is introduced as a consumable into the arc manually.	Metal fumes, ultraviolet radiation, ozone, nitrogen dioxide, potential build up of inert gas
<b>Electric resistance welding</b>		
Resistance welding (spot, seam, projection or butt welding)	High electric current at low voltage flows through the components from electrodes generating heat at the interface. Heat and pressure by the electrodes produces a weld. No flux or filler metal is used.	Metal fumes, ozone

## 9.4 SURFACE COATING AND TREATMENT OF METALS

There is a wide variety of techniques for finishing the surfaces of metal products so that they resist corrosion, fit better or look better including electrolytic polishing, electroplating, anodizing and galvanizing. In this text only electroplating and galvanizing will be examined.

Before electroplating can be undertaken the product must be thoroughly cleaned. A number of cleaning methods can be used including mechanical grinding, vapour degreasing, washing with organic solvents, “pickling” in concentrated acid or alkaline solutions and electrolytic degreasing.

### 9.4.1 Electroplating and galvanizing

Electroplating is an electrochemical process used to apply a metallic layer to a product e.g. nickel to protect against corrosion, chromium to improve the surface properties. The product, wired as the cathode, and an anode of the metal to be deposited are immersed in an electrolyte solution (which can be acidic, alkaline or alkaline with cyanide salts) and connected to a direct current.



(Source: Steve Bailey – reproduced with permission)

**Figure 9.9 – Electroplating bath with detergent foam**

Positively charged metal ions migrate from the metal anode to the cathode, where they are reduced to the metal and deposited as a thin layer. This continues until the new coating reaches the desired thickness, and the product is then washed, dried and polished.



(Source: Steve Bailey – reproduced with permission)

**Figure 9.10 – Electroplating bath fitted with local exhaust ventilation**

Galvanizing applies a zinc coating to a variety of steel products to protect against corrosion. Again, the product must be clean and oxide-free before processing in order that the coating adheres properly. This usually involves a number of cleaning or annealing processes before the product enters the galvanizing bath.

**Chemical hazards of electroplating and galvanizing** – the heated alkaline and acid solutions used in cleaning and treatments of metals are corrosive. They can cause burns and irritation to the skin and to mucous membranes and the eyes.

Nitric and hydrofluoric acid are a particular problem if inhaled, as it may be many hours before the effects on the lungs become apparent. Pneumonitis and potentially fatal pulmonary oedema may appear later in a worker who suffered little initial effect from the exposure. Skin contact with hydrofluoric acid can cause severe burns without pain being noticed for several hours.

Baths containing cyanide solutions are frequently used in electrolytic degreasing and electroplating. If cyanides react with an acid hydrogen cyanide can be generated. Fatal exposures may also result from skin absorption or ingestion of cyanides.

Chromic and nickel compounds are used in electroplating. Chromium compounds are usually present in the form of chromic acid, where the chromium is in its hexavalent state. This can cause burns and ulcers to the skin as well as perforation of the nasal septum. Nickel salts can cause allergic dermatitis and irritation. There is evidence that both chromium and nickel compounds are carcinogenic.

## **9.5 SOLDERING and BRAZING**

Soldering and brazing are similar processes where metal items are joined together by heating and melting a filler metal or alloy with a flux that flows into the joint. They differ from welding in that the metals being joined do not melt during the process as the filler metal has a much lower melting point.

Soldering and brazing are distinguished from each other in that soldering is undertaken at temperatures below 450 °C, whereas brazing is undertaken at temperatures above 450 °C.

Health hazards depend on the metal or alloys being melted and the type of flux used. Soft soldering using lead / tin alloy based solders is widely used in the electrical and electronics industries to make electrical connections.



(Source: Steve Bailey – reproduced with permission)

**Figure 9.11 – Soldering**

As soldering is undertaken at lower temperatures metal fumes are generally of little concern. The main health risk from soldering is from the breakdown products of the flux. The flux is commonly rosin based and the breakdown products from this are potent respiratory sensitizers.



(Source: HSE Rosin-cored solder fume assessment: Health and Safety Laboratory – reproduced under the terms of the Click-Use licence)

**Figure 9.12 – Fumes from soldering**

Rosin is a naturally occurring, solid, resinous material obtained from pine trees. The flux helps the soldering by cleaning the surfaces to be joined, increasing the flow of the solder and preventing oxidation.



The main health effects occur from the breakdown at high temperatures (or pyrolysis) of the rosin.

- When heated, particularly to temperatures above 200°C, rosin-based solder fluxes form fumes containing a range of resin acid particulates and other components as gases. Lower temperatures can significantly reduce the amount of fume produced. Between 250°C and 400°C particulate fume levels can triple.
- When inhaled, rosin-based solder flux fume can lead to occupational asthma. Rosin-based solder flux fume is regarded as one of the most important causes of occupational asthma. The effects are permanent and irreversible. Continued exposure, even to very small amounts of fume, may cause asthma attacks and the person affected may not be able to continue work with rosin-based fluxes
- The fume can also cause irritation to the eyes and upper respiratory tract. It has not been possible to identify a safe level of exposure below which occupational asthma will not occur. Exposure to all rosin-based solder flux fumes should, therefore, be avoided or kept as low as is reasonably practicable
- Without effective control, solder fume rises vertically and for manual operations is likely to enter the breathing zone of the worker. If not captured at source other people may be affected by build up of background levels. Adequate control often requires the use of local exhaust ventilation; this may be conventional LEV or a low volume high velocity system directly applied near the soldering iron tip. Health surveillance may also be required
- Soldering is also used to form joints in plumbing and pipe fitting. Use of a gas torch can raise temperatures high enough to produce lead fume. The use of lead free solders is sometimes required, but in either case, the risks from breakdown of the flux are still present

In general brazing uses borax or fluoride based fluxes. In 'silver soldering' – a type of brazing – the metal alloy or flux may contain significant quantities of cadmium. Cadmium free replacements are available with alloys containing silver, copper and tin.

## **9.6 DEGREASING**

Many industrial products need to be cleaned at one or more stages of their manufacture to remove unwanted dirt and grease that would interfere with subsequent processes such as painting, plating or soldering where cleanliness of the article is essential.

Solvents are used for degreasing a wide range of items from large metal panels to electronic components. Degreasing processes can be divided into two broad categories – cold degreasing and vapour degreasing.

Cold degreasing uses a solvent at ambient temperature. It includes hand cleaning by wiping and brushing as well as larger operations that use spraying of the solvent. In some cases immersion and use of ultrasonic cleaning is undertaken. Vapour degreasing involves immersing the article in solvent vapour that condenses on the article and runs off taking the grease and dirt with it.

### **9.6.1 Cold degreasing**

Dip cleaning is the simplest operation where the articles to be cleaned are immersed in the solvent. The cleaned articles are then removed by lifting out of the solvent (preferably in wire baskets so that they can freely drain excess solvent). Removal should be carried out slowly to allow sufficient drain time. Covers should be kept on dip tanks as far as possible to reduce

emission of solvent vapours into the workplace.

Wiping is more applicable for cleaning large items of equipment but solvent use should be kept to a minimum. Used cloths containing solvent residues should be stored in lidded containers and disposed safely.

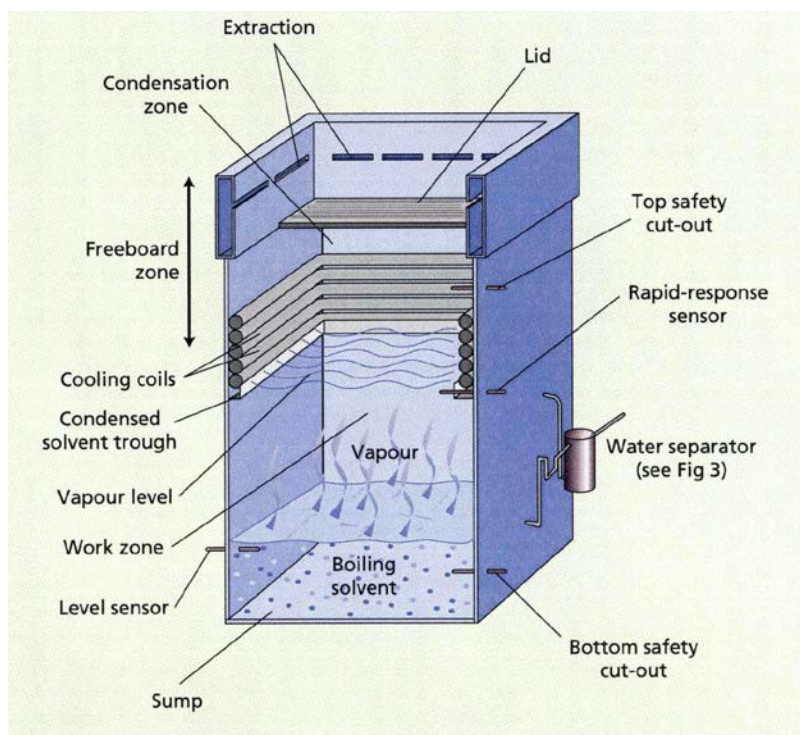
Brush cleaning can be used to dislodge particles which are not effectively removed by dipping or wiping. The item to be cleaned is usually placed in a tray to collect the solvent. Care needs to be taken to minimise splashing of the solvent.

Spraying is useful to clean areas that are inaccessible to wiping and brushing - it may avoid the need to dismantle components for cleaning. However, spraying can lead to high solvent vapour concentrations.

### **9.6.2 Vapour degreasing**

Vapour degreasing is an effective and widely used technique for cleaning of components. The vapour degreasing plant consists of a steel tank partly filled with solvent with a heater at the base. The solvent vapour rises to fill the tank to a height determined by a series of cooling coils in the upper part of the tank that act as a condenser.

There is usually a slotted duct (lip extraction) around the rim of the tank connected to an exhaust ventilation system to prevent escape of vapour from the tank.



(Source: Envirowise GG354 – Surface cleaning and preparation: choosing the best option – reproduced with permission)

**Figure 9.13 – Conventional top loading vapour degreaser**

When a 'dirty' component is lowered into the vapour layer formed above the heated solvent, the vapour condenses on the cold surface of the component and dissolves any soluble contaminants. As the vapour condenses, the liquid drains back into the boiling solvent, carrying some of the 'dirt' with it. This process continues as more vapour condenses on the component.

When the temperature of the component reaches that of the vapour, condensation on the component effectively ceases and the cleaning process stops. The cleaned components are then lifted slowly to drain fully while still within the tank. Various degrees of automation can be applied and plant can be integrated into conveyor production lines.

It is then removed and allowed to cool to normal temperature. The soluble and insoluble dirt removed collects in the sump at the bottom of the plant. When the concentration of oil and dirt in the sump reaches a certain level, the solvent is recovered by distillation and may be used again. After cooling the oily residue can be removed and discarded.



(Source: Steve Bailey – reproduced with permission)

***Figure 9.14 – Large vapour degreasing tank fitted with cooling coils and slot extraction at the rim***

Degreasing solvents that are commonly used in industry include trichloroethylene and tetrachloroethylene. For specific applications, various products containing individual solvents, mixtures of solvents or emulsions are available.

Poor operating methods and inadequate maintenance can lead to increased solvent emission in the working area. Common operating faults include:

- poor stacking of hollow bodies – e.g. tubes / cups should be stacked at an angle or rotated within the vapour zone to empty any solvents trapped in the article
- insufficient drying time – the components must be held in the

freeboard above the vapour layer for sufficient time to allow evaporation of solvent residues

- lifting the components at too high a speed
- excessive movement of components in the bath causing disturbance of the solvent vapour layer

Procedures need to be in place during maintenance and removal of sludge from the base of the tank. The tank may be considered a confined space and high concentrations of solvent vapour may be present. Safe work procedures including a permit to work may be required to prevent potentially fatal exposure.

It should be noted that chlorinated solvents are readily decomposed by hot surfaces and open flames. The toxic decomposition products include phosgene, hydrogen chloride and carbon monoxide. Smoking and hot processes such as welding should be prohibited in the vicinity of the degreasing operations.

## **9.7 PAINTING**

Paints and related products such as varnishes and lacquers are widely used in industry to provide a surface coating for corrosion protection, for appearance or other special purposes.

Health risks can arise from solvents, additives or in particular respiratory sensitisation from isocyanates in polyurethane paints. The risks vary considerably in because of the variety of products and constituents, the range of situations in which they are used and the different methods of application.

Solvent exposure is usually the most significant health risk during painting. The solvents used vary considerably between products and include aliphatic and aromatic hydrocarbons, ketones, alcohols, glycols

and glycol ethers and esters. The use of low solvent content or water based paints is becoming more widespread. (Water based paints still contain some solvents but these are at much lower concentrations).

The amounts of solvent in paints used vary considerably (e.g. 5 - 50%). However, the paint may be thinned at the point of use, and the thinner may be of different composition to the primary solvent.

Paint application methods fall into three main groups:

- paint is applied to the surface by brush or roller
- paint is applied by spray techniques
- the surface is immersed in paint and allowed to drain, as in dipping and flow coating.

In general, paint for spray application will contain more solvent than those for application by brush or roller.

### **9.7.1 Exposure to solvents in painting**

Painting with brush or roller involves relatively slow application of paints. The operator continually moves away from the most recently treated area and exposure largely depends on the general ventilation of the area.

Spray painting generally involves higher rates of application, larger areas and higher solvent content. Also spraying of liquids containing solvents can produce high levels of solvent vapour as the fine spray produced allows rapid evaporation of the solvent.

The use of respiratory protective equipment may be required if the area is enclosed or because of other constituents, e.g. applying anti-fouling paint

containing pesticide to the hull of a ship in dry dock or spraying an isocyanate paint to vehicles in a closed booth or to an aircraft in a hangar.

Spray painting of smaller items on a production line may be done with an automatic spray gun or by an operator from outside a ventilated open-fronted booth. Conventional air spraying is the most commonly used method of painting in industry. A potential problem with air spraying is that large quantities of solvent vapour may be generated and overspray of the paint is common.



(Source: HSE LEV Trainer Adviser Briefing Days – reproduced with permission)

**Figure 9.15 – Spraying isocyanate based paint in paint spray booth**

Electrostatic spraying; which has become more widespread places a charge on the paint mist particle so it is attracted to the part to be painted. This reduces rebound and overspray and consequently reduces mist and solvent exposure to the operator.

In powder coating, the paint powder is conveyed from a powder reservoir to the spray gun. In the gun, an electrical charge is imparted to the paint particles. The powder is sprayed onto the electrically grounded item to be coated and the parts baked to fuse the powder into a continuous coating.



Most industrial flow and spray painting operations require exhaust ventilation for control of solvent vapors at the point of application and also during drying and baking operations. The use of automated spray painting allows for greater use of ventilated enclosures and minimises worker exposure.

As stated earlier, particular care must be taken in the application of two-component urethane and epoxy paint systems that contain isocyanates which are potent respiratory sensitisers. This includes effective ventilation control and protective clothing. In addition where exposure cannot be effectively controlled by ventilation the operators should wear air-supplied respirators.

Dermatitis due to primary irritation and de-fatting from solvents or thinners is common. Skin contact must be minimised, adequate washing facilities should be available, and suitable protective equipment used by the operator.



(Source: Steve Bailey – reproduced with permission)

**Figure 9.16 – Paint mixing – skin and airborne exposure can occur to solvents and pigments**

In addition to the hazards from the solvents, there may also be hazards from pigments such as lead, cadmium and chromium compounds. Also some paints contain additives such as fungicides and pesticides.

## 10 SPECIFIC INDUSTRY PROFILES

### 10.1 INTRODUCTION

This section briefly describes some industries identifying the typical hazards associated with each industry. It is not intended to be a comprehensive listing of all the potential hazards likely to be present in the particular industries.

### 10.2 SMELTING AND REFINING OF IRON AND STEEL

The metal smelting (melting and reduction of metal ores to base metals) and refining industry processes metal ores and scrap metal to obtain pure metals or alloys (mixtures of different metals). The metals and alloys are then processed further to manufacture structural components, machinery, instruments and tools etc. Iron is widely found in the earth's crust in the form of various minerals or ores (usually as iron oxide). To produce iron, the iron ore is melted in a blast furnace. Iron ore, coke and limestone is continuously added to the furnace from the top while hot air (sometimes enriched with oxygen), is blown in from the bottom.



(Photograph reproduced with the permission of Wolverhampton Archives & Local Studies)

**Figure 10.1 – Blast furnace**

The hot air reacts with the coke to produce carbon monoxide and heat. The carbon monoxide then reacts with the iron oxide to produce molten iron and carbon dioxide. The limestone acts as a flux preventing oxidation of the molten iron and reacts with various impurities (particularly silicates) to form slag which forms a layer on top of the molten metal.

The furnace operates at high temperature (typically between 1,200°C and 1,600°C) and molten iron collects at the bottom of the furnace. The furnace is tapped (i.e. molten iron removed) periodically. At this stage the iron still contains relatively high levels of carbon and other impurities e.g. sulphur which need to be reduced or removed in subsequent refining to produce steels. Some of the iron is used to make cast iron but the majority is poured into large ladles where it is transferred, still molten, to the steel-making plant.

The main types of steel making furnaces are the basic-oxygen process converter and the electric arc furnace. The basic-oxygen converters produce steel by blowing air or oxygen into the molten iron and electric arc furnaces produce steel from scrap iron and sponge-iron pellets.

There are a range of alloys that incorporate other metals added to the furnace charge or to the molten metal to produce steels with special qualities (e.g. chromium and nickel to produce stainless steel, tungsten and cobalt to give hardness and toughness at high temperatures).

### **10.2.1 Chemical hazards of smelting and refining**

Exposure to a range of hazardous dusts, fumes and gases can occur during smelting and refining operations. Specific chemical health hazards include:

- Exposure to metal fumes during smelting, (particular metal depends on metals being worked)

- Exposure to silica and metal dusts during crushing and grinding of ores
- Exposure to silica dust during furnace maintenance operations

Many smelting operations can produce large amounts of sulphur dioxide from sulphide ores and carbon monoxide is commonly produced from combustion processes.

Specific hazards related to smelting and refining of some metals include nickel carbonyl in nickel refining, arsenic in copper and lead smelting and refining, and mercury and cyanide exposures during gold refining.



(Source: Brian Davies – used with permission)

***Figure 10.2 – Pouring molten gold***

### **10.2.2 Other industrial hygiene hazards of smelting and refining**

Thermal stress issues are common in the metal smelting and refining industry from the high levels of radiant heat that can be emitted from furnaces and molten metal. Infrared radiation from furnaces and molten metal can also cause eye damage including cataracts. High noise levels are also likely to be present in many areas of the smelting and refining processes.

### 10.3 FOUNDRIES

The foundry industry can be divided into two broad categories:

- ferrous foundries (iron and steel)
- non-ferrous foundries (e.g. aluminium, brass, bronze, magnesium)

Founding, or metal casting, involves pouring molten metal into a prepared heat-resistant mould (usually via a ladle). The mould may contain an internal core to form the dimensions of any internal cavity in the final casting. After pouring the mould and metal are allowed to cool. The mould and core material are then removed and the casting finished and cleaned.

There are a range of different types of mould that are used, but the most common iron foundry processes use sand moulds.

There are a number of types of furnace used to melt the metals including cupola (similar to blast furnaces), electric arc, electric induction and crucible furnaces (heated with gas or oil burners). In addition to the hazards of heat and metal fumes common to all types of furnace, evolution of carbon monoxide is a potential problem with cupola and crucible furnaces.



(Source: HSE Foundries: Free leaflet 2008 – Reproduced under the terms of the Click-Use licence)

**Figure 10.3 – Foundry furnace**

### 10.3.1 Iron Foundries

Iron foundry processing can be divided into a number of different stages:

- preparation of mould
- metal melting and pouring
- removal of casting from mould (shakeout / knockout)
- cleaning of casting (fettling)

**Preparation of mould** – a mould is prepared to form the desired external shape of the casting. If there are to be hollow internal areas in the casting, suitable cores are required to form the internal configuration of the product.

The iron founding industry usually uses the traditional “green sand” moulds made from silica sand, clay, water and other organic binders. Cores are composed mainly of sand also contain binder materials to provide the correct amount of strength to the core. Depending on the particular process these binders may be isocyanate based or include phenol-formaldehyde or urea-formaldehyde resins.

The sand used to make the moulds is usually either damp or mixed with liquid resin, and is less likely to be a significant source of respirable dust at this stage.

**Melting and pouring** – melting and pouring of molten metal can produce significant quantities of metal oxide fumes. In addition, pouring the hot metal into the mould causes some of the binder materials in the mould or core to pyrolyse (break down at high temperature). A range of hazardous substances may be emitted including formaldehyde, carbon monoxide, polynuclear aromatic hydrocarbons (PAH's), isocyanates and amines.

In larger foundries, the assembled mould moves along a production line to a pouring station. A ventilated hood is usually provided at the pouring station,

together with a direct air supply to the operator position. Pouring may be automated or undertaken manually using a ladle. The poured mould continues along the production line through a cooling tunnel equipped with ventilation until mechanical shakeout. In smaller foundries, moulds may be poured individually on the foundry floor and allowed to burn off there.



(Source: HSE Health and Safety in the molten metals industry 2008 – Reproduced under the terms of the Click-Use licence)

**Figure 10.4 – Foundry worker**

A common type of furnace used in the iron founding industry is the cupola furnace. These need to be periodically withdrawn from use for repair and maintenance including the renewal of the refractory linings. Cupola repair involves employees working inside the cupola (a confined space) itself to mend or renew refractory linings.

Problems associated with renewal of refractory linings include thermal stress issues as the furnace cannot be allowed to cool completely. Also refractory ceramic fibre linings can be converted by prolonged heating to form cristobalite – a hazardous form of crystalline silica.

**Shakeout, casting extraction and core knockout** - after the molten metal has cooled, the rough casting is removed from the mould. The majority of the mould is separated from the casting by impact; the mould and casting are dropped onto a vibrating grid to dislodge the sand (shakeout). The sand



drops through the grid for cleaning and recycling. High airborne dust levels can occur as the sand has been in contact with hot metal and is very dry.

**Fettling (cleaning)** - after shakeout and core knockout initial cleaning of the castings includes removal of mould and core sand and other easily removable material with hand tools. After initial cleaning, fettling of the casting includes removal of burnt-on moulding sand, rough edges, surplus metal or other unwanted blemishes. A variety of grinding tools are used to smooth the rough casting including abrasive wheels and grinders.



(Source: HSE Vibration at work 2008 – Reproduced under the terms of the Click-Use licence)

**Figure 10.5 – Casting before and after fettling**

Shot blasting may be used to remove sand still adhering to the casting. Shot blasting should always be carried out in an enclosed area which is equipped with an efficient dust extraction and collection system.

Silica dust is a potential problem wherever sand is handled. Higher exposure levels are likely when housekeeping standards are poor and where castings are dusty or shakeout or blasting cabinets leak.

Silicosis and other mixed pneumoconiosis are the most common health effects in iron and steel foundries. In the foundry, the prevalence increases with length of exposure and higher dust levels.

### 10.3.2 Other foundries

**Steel founding** – the production processes in the steel foundry are very similar to those in the iron foundry. The main difference is that the molten metal temperatures are much higher. As a result, the silica in the mould may be converted by heat from quartz to cristobalite. In addition sand often becomes burnt on to the casting and this has to be removed by mechanical means, which gives rise to high dust levels.

**Light-alloy founding** - the light-alloy foundry uses mainly aluminium and magnesium alloys. In addition to any hazards from the aluminium and magnesium, these often contain small amounts of metals which may give off toxic fumes under certain circumstances.

Fluorspar is commonly used as a flux in aluminium melting, and significant quantities of fluoride dust may be released. Casting in permanent metal moulds, as in die-casting, has been an important development in the founding industry. Aluminium is a common metal in die casting as is zinc.

**Brass and bronze foundries** – In brass and bronze foundries the particular health hazards relate to the metals in the alloys being produced. Exposures to lead, copper and zinc are common in melting, pouring and finishing operations; particularly where alloys have a high lead composition. Zinc and copper fumes may cause metal fume fever. In addition, some high-duty alloys contain cadmium, which can cause chemical pneumonitis from acute exposure and kidney damage and lung cancer from chronic exposure.

**Precision founding** - precision foundries use the investment or lost-wax casting process where wax patterns are coated with fine refractory powder prior to building up the rest of the mould material. The wax is then melted out prior to casting or by introduction of the casting metals. Decomposition of the wax produces acrolein and other hazardous decomposition products.

## **10.4 MINING AND QUARRYING**

There are a range of industrial hygiene issues that may occur in the mining and quarrying industries. Common chemical hazards include exposure to airborne particulates, particularly crystalline silica (quartz), naturally occurring gases as well as combustion products from diesel powered machinery. In addition, noise, vibration, thermal stress and ionizing radiation are also likely to be of concern.

The extent of these hazards will depend on the type of mine or quarry, its depth, the composition of the ore and surrounding rock, and the method of mining. Individual exposure varies with the type of work, their proximity to the source of hazards and the effectiveness of control.

### **10.4.1 Airborne Particulate Hazards**

Crystalline silica is the most abundant compound in the earth's crust and is the most common airborne dust to which workers in mining and quarrying are exposed. The most common form of crystalline silica is quartz. Exposure to respirable quartz can cause silicosis (a fibrotic pneumoconiosis).

Drilling, blasting and cutting of rocks can produce very high levels of both inhalable and respirable dust. If the rocks contain silica potential exposures to respirable crystalline silica can be very high. Holes may be drilled by large percussion drills mounted on a tractor crawler or on a smaller scale by hand-held jack-hammers or drills.

The air that powers the drill is also used to blow dust and chips out of the hole. This produces high levels of dust which may need to be controlled by localised extraction systems or application of water to the drill hole. In addition to the dust hazards, noise and vibration may also be of concern.



(Source: HSE Dust and silica – reproduced under the terms of the Click-Use licence)

**Figure 10.6 – Crawler mounted drill with no dust control**

Other controls that provide protection are cabs with filtered air supply for drill operators and vehicle drivers. Appropriate respiratory protection may be required for worker protection as a temporary solution or if other controls are ineffective.



(Source: HSE Dust and silica – reproduced under the terms of the Click-Use licence)

**Figure 10.7 – Loading lorry using mechanical arm**



(Source: HSE Safe operation and use of mobile jaw crushers – reproduced under the terms of the Click-Use licence)

**Figure 10.8 – Mobile jaw crusher and conveyors**

Crystalline silica exposure can also occur at stone quarries where the rock is cut or crushed down to specified sizes. These processes together with subsequent grading (sieving), conveyor transfer, loading and transportation are all potential sources of airborne dust.

In both underground as well as surface coal mines, respirable coal mine dust is a hazard. It is a mixed dust, consisting mostly of coal, but can also include crystalline silica and other mineral dusts. The composition of coal dust varies with the coal seam, the surrounding rock strata and mining methods. As with mining and quarrying in general, dust is generated by blasting, drilling, cutting, conveying and transporting coal. Exposure also occurs in coal processing facilities.

Coal mine dust causes coal workers' pneumoconiosis (CWP) and contributes to the occurrence of chronic airways disease such as chronic bronchitis and emphysema.

The generation of coal mine dust can be reduced by changes in coal cutting techniques and its dispersion can be controlled by use of adequate mechanical ventilation and water sprays.



(Source: NIOSH – used with permission)

**Figure 10.9 – Longwall coal mining with water sprays**

#### 10.4.2 Other hazards

Many machines and vehicles used in mining and quarrying are diesel powered. Diesel engine exhaust is a complex mixture of gases, vapours and particulate matter. The most hazardous gases are carbon monoxide, nitrogen dioxide and sulphur dioxide. Carbon monoxide is a chemical asphyxiant and nitrogen dioxide and sulphur dioxide are acute respiratory irritants.

There are also many volatile organic compounds (VOCs) such as unburned hydrocarbons, aldehydes and polycyclic aromatic hydrocarbons (PAHs). Polycyclic aromatic hydrocarbons compounds can be adsorbed onto diesel particulate matter. Many polycyclic aromatic hydrocarbons compounds are carcinogenic and the International Agency for Research on Cancer (IARC) considers diesel particulate matter to be a probable carcinogen.

Exposure may also occur to naturally occurring gases such as methane (a simple asphyxiant) and hydrogen sulphide (a chemical asphyxiant) in coal

mines. Methane is also combustible and many coal mine explosions occur as a result of ignition of methane and the subsequent more violent explosions of coal dust that has been suspended by the shock of the original explosion.

Oxygen deficiency is possible in many mining operations. It can occur in many ways, oxygen can be displaced by another gas, such as methane, or it may be consumed either by combustion or by microbes in an air space with no ventilation.

There is a range of other airborne hazards to which specific groups of miners are exposed. Examples include exposure to mercury vapour in gold and mercury mining, exposure to arsenic, and risk of lung cancer, in gold and lead mining and radon gas may be a concern in uranium and other mines.

In addition to the chemical hazards, physical hazards such as noise and heat are major concerns. Noise is a particular problem in underground mines where high noise levels are generated by the mining machinery and the limited space means that the noise will reverberate, so noise exposure is greater than if the same sources were in a more open environment.

Heat is a hazard for both underground and surface miners. In underground mines, the principal source of heat is from the rock itself (the temperature of the rock increases by about 1 ° C for every 100 m in depth). Deep mines (deeper than 1,000 m) can pose significant heat problems with temperatures in excess of 40 ° C.

Apart from high air temperatures, other factors include high metabolic work rates, high humidity and heat generated by the mining equipment. For surface workers, high metabolic work rates, proximity to hot engines, air temperature, humidity and sunlight are the principal heat sources.

## 10.5 OIL AND PETROLEUM INDUSTRY

Petroleum, or crude oil, is a naturally occurring, flammable liquid that is found in rock formations and consists of a complex mixture of hydrocarbons and other organic compounds. Crude oil varies greatly from one oil field to another in both its composition and appearance. It can vary from a pale yellow free flowing liquid to a very viscous black liquid.

Crude oil is of little use in its raw state, it needs to be processed to produce products of commercial value by a series of physical and chemical changes. Three main types of hydrocarbons are found in crude oil – paraffins, naphthenes and aromatics.

Paraffins (or alkanes) – straight or branched chain hydrocarbons with varying numbers of carbon atoms per molecule such as

- 1 to 4 carbon atoms – methane, ethane, propane, butane and iso-butane (gases at normal temperatures and pressures)
- 5 to 8 carbon atoms – pentane to octane – generally refined into gasoline (petrol)
- 9 to 16 carbon atoms – nonane to hexadecane – generally refined into diesel fuel, kerosene and jet fuel
- 16 and upward carbon atoms – generally refined into fuel oil and lubricating oils

Naphthenes (or cycloalkanes) – these are saturated hydrocarbons containing one or more carbon ring. They have similar properties to alkanes but have higher boiling points. Examples include cyclohexane and dimethyl cyclopentane.

Aromatics – these are unsaturated hydrocarbons containing one or more 'benzene' ring. Examples include benzene, toluene and xylene.



### 10.5.1 Petroleum refining

As crude oil is a mixture of hydrocarbons with different boiling temperatures it can be separated by distillation into different groups (or fractions) of hydrocarbons that boil between two specified boiling points. Each of these fractions can be drawn off from the distillation column. The light gases pass out the top of the column, the gasoline fraction is drawn off from the top part of the column, with the naphtha, kerosene, gas oil and fuel oil fractions being drawn off from progressively lower parts of the distillation column.

Higher boiling residues remain at the bottom of the column and may be processed into lubricating oils, waxes or bitumen or used as feedstock for further processing or cracking. Alternatively it may be subject to a second distillation under vacuum to recover additional heavy distillates.

In order to produce the correct quantities of different products, each of the fractions may be processed by various methods such as

- Cracking (thermal and catalytic cracking) – breaking down larger hydrocarbons (high boiling point oils) into lighter products such as gasoline and diesel.
- Reforming – using heat, pressure and catalysts (often platinum) to convert paraffins and naphthenes to isoparaffins and aromatics which are used in high octane gasoline and petrochemical feedstock.
- Alkylation – conversion of alkenes such as propylene and butylene to isoparaffins

A number of contaminants are found in crude oil, such as nitrogen compounds, sulphur compounds and metals which need to be removed as they can damage the plant, the catalysts and the quality of the products. In addition there are limits on the amount of some impurities, such as sulphur, in products.

Sulphur is removed by mixing the entering feedstock with hydrogen at high temperature in the presence of a catalyst to form hydrogen sulphide. This

toxic gas is then removed from the hydrocarbon stream and converted to elemental sulphur which is a useful chemical.

Many of the substances used and produced in the refinery produce hydrocarbon vapours. The escapes of vapours are prevented by various means such as floating roofs on tanks to prevent evaporation as there is no room above the liquid for vapour to gather. Alternatively, if floating roofs are not practicable, vapours from tanks are collected in a vapour recovery system and returned to the product stream. In addition pumps and valves are regularly checked for vapour emissions and repaired if leakage is found.

## **10.6 PHARMACEUTICAL INDUSTRY**

There is a wide range of hazards that may be encountered within the pharmaceutical manufacturing industry. Many of the usual hazards found in any industry are present such as working with chemicals and solvents in the production areas, generation of airborne particulates and ergonomic issues.

However, a particular issue in pharmaceutical manufacturing is that the products are designed to be physiologically active. That is, they are designed to impact on human health at very low doses. While this may be desirable if you require the medication, it is undesirable for the worker to be exposed to the medication or active ingredient in the workplace.

Production of pharmaceuticals can be divided into two main stages – primary manufacture and secondary manufacture or formulation:

- Primary manufacture – production by the chemical reaction of a number of chemicals to form the active ingredient. The production of the active ingredient is usually undertaken in closed systems.

- Secondary manufacture or formulation – this is the process of mixing the active ingredient with other materials to form a product that is suitable for use by the final recipient.
  - The formulation materials are mixed with the active ingredient as a bulking material or used as a solvent to dissolve the materials
  - Pharmaceuticals are mixed with excipients (often inert bulking materials such as maize starch or magnesium stearate) to allow very low doses of active ingredient to be administered in manageable quantities, e.g. there is often only a few milligram of active ingredient in a tablet.



(Source: Steve Bailey – Reproduced with permission)

**Figure 10.10 – Addition of sack of powder to reactor**

Exposure limits for the active ingredients are usually assigned in the microgram (or even nanogram) per cubic metre range. This means that there needs to be an order of magnitude leap in control integrity with total containment being commonplace. Other controls commonly in place include segregated work area, local exhaust ventilation with HEPA filtration, disposable coveralls and where required high standards of respiratory protection.



(Source: Steve Bailey – Reproduced with permission)

***Figure 10.11 – Fully enclosed tablet press with extraction***

In addition to the problems of the active ingredient being physiologically active, many active ingredients may have other health effects such as respiratory sensitisation or may be teratogenic. Examples of active ingredients where ill-health effects have been observed in pharmaceutical production workers include hormones, antibiotics, tranquilisers and drugs that affect the heart.

## 11 REGULATORY CONSIDERATIONS

### 11.1 Risk and Safety Phrases

Where can information be obtained on hazardous substances? In general the primary source of information about any substance will be the supplier's Material Safety Data Sheet (MSDS) and the label fixed to the product. Care must however be exercised when using suppliers MSDS as an information source as the hazard information in the data sheet is sometimes incomplete or inaccurate.

Most countries require suppliers to provide users with a MSDS and under a United Nations sponsored scheme such documentation is moving towards a uniform format.

Many countries are participating in the development of a Globally Harmonised System of Classification and Labelling of Chemicals (GHS) through the United Nations. The GHS provides a uniform way of classifying chemicals, as well as informing chemical users about chemical hazards they may be exposed to.

The GHS builds on the attributes of existing national regulatory systems to form a single international system that has application across a wide range of chemicals and hazard types. The GHS when implemented will:

- enhance the protection of human health and the environment by providing an internationally comprehensible system for hazard communication
- provide a recognised framework for those countries without an existing system
- reduce the need for testing and evaluation of chemicals, and
- facilitate international trade in chemicals whose hazards have been properly assessed and identified on an international basis.

Pictograms are a key hazard communication tool within the GHS. They are designed to appear on chemical labels. The pictograms give an immediate indication of the type of hazard that the chemical may pose.

They are intended to be used in combination with other harmonised GHS elements which together convey information about the type, severity and management of chemical hazards. An example of the pictograms to use is provided in Figure 11.1.

Under the GHS these pictograms will be supported by hazard statements and precautionary statements which will replace the risk and safety phrases (eg R26 – very toxic by inhalation or S3 – keep in a cool place), which are currently used in many countries.

In addition, the pictograms will be supplemented by one of two signal words – ‘Danger’ or ‘Warning’ depending on the category of hazard class.

A significant number of countries have indicated they will implement the GHS as a key part of their national chemical regulation systems. Indeed, this has already started in the European Union where GHS forms the basis of the new classification, labelling and packaging requirements which will be progressively implemented.



(Source: ASCC Information Sheet)

**Figure 11.1 – GHS Pictograms**

## 11.2 SOURCES OF INFORMATION

### 11.2.1 Material safety data sheets (MSDS)

Information on the hazards that a substance or preparation may pose should be provided by the manufacturer or supplier. This information should be used as a starting point for the risk assessment undertaken by the user of the substance or preparation.

Material safety data sheets should conform to a standardised structure, with different sections for specific information types. The standard format is as shown below:

- Section 1 – Identification of substance / company
  - Chemical name including trade names
  - Name, address and contact numbers (including e-mail contact) of company
- Section 2 – Hazards identification
  - Hazard description, including risk and safety phrases and codes
- Section 3 – Composition / information on components of mixtures
  - Chemical identification numbers (CAS, EU etc)
  - Information on each component of mixtures
- Section 4 – First aid measures
- Section 5 – Fire fighting measures
- Section 6 – Accidental release measures
- Section 7 – Handling and storage
- Section 8 – Exposure controls / personal protection
  - Any regulatory exposure standards
  - Information on suitable types of personal protective equipment
- Section 9 – Physical and chemical properties
- Section 10 – Stability and reactivity
- Section 11 – Toxicological information
  - Results of toxicological tests
  - Health effects associated with the substance
  - Any evidence of carcinogenicity
- Section 12 – Ecological information
- Section 13 – Disposal considerations
- Section 14 – Transport information
- Section 15 – Regulatory information
  - Lists the hazard codes, risk phrases and safety phrases
- Section 16 – Other information



The quality and quantity of information on a material safety data sheet varies widely between different suppliers. In any case they cannot possibly anticipate all possible uses and applications of the product. Therefore, a specific risk assessment will need to be undertaken taking into account the particular situation and conditions of use. Indeed, in many countries it is a legal requirement to conduct a risk assessment before a substance is introduced into a workplace.

### 11.2.2 Literature

It is important that an industrial hygienist can access accurate and unbiased information on health hazards on substances to which people may be exposed. Risk assessment, risk management and hazard communication all require objective information.

Much information is now available on the internet and as electronic resources. This presents both opportunities and challenges for the hygienist. It has never been easier to obtain information from a number of different sources but care needs to be taken to ensure that the information is valid.

Similarly, most workers and the public now have access to the wide range of information available. It is an important part of the hygienist's role to interpret and communicate hazard and risk information in the context of the particular workplace.

**Peer-reviewed scientific literature** - this is potentially the most credible source of information, where the findings have been reviewed by other experts. These articles are usually published in professional journals such as the *Annals of Occupational Hygiene* (BOHS) and the *Journal of Occupational and Environmental Hygiene*. The articles or reports tend to be very technical and often it is sufficient to use the article summary.

**Governmental and other recognised organisations** - credible sources of information include government publications, including approved codes of practice and guidance. Examples include:

- United Kingdom Health and Safety Executive (HSE)
- Australian Safety and Compensation Council (ASCC)
- United States Occupational Safety and Health Administration (OSHA)
- United States National Institute for Occupational Safety and Health (NIOSH)
- United States Environmental Protection Agency (EPA)
- Canadian Centre for Occupational Health and Safety (CCOHS)

In addition there are a number of non-government organisations that are widely recognised and respected such as:

- World Health Organisation (WHO)
- International Labour Organisation (ILO)
- International Agency for Research on Cancer (IARC)
- European Agency for Safety and Health at Work

Documents include codes of practice, guidance documents and toxicological summaries.

**Occupational Health and Safety Databases** - there is a wide range of Occupational Health and Safety databases that can be accessed via the internet. Some databases are available free of charge but many (particularly full text databases) usually require a subscription. Examples include the following:

- ILO Encyclopaedia
- Agency for Toxic substances and Disease Registry (ATSDR) (US)
- International Program on Chemical Safety – Inchem
- Registry of Toxic Effects of Chemical Substances (RTECS)

**Other sources** - there are many other potential sources of information published on the internet. However, care needs to be exercised when using some sources, particularly those that are self-published as they may represent personal or organisational viewpoints that may or may not be supported by scientific evidence. Similarly, articles may be published in newspapers and popular magazines that have not been peer reviewed.

Another potentially valuable source of information is through discussion groups or web forums between specialists. Valuable information may also be obtained through relevant industrial hygiene professional associations such as:

- British Occupational Hygiene Society (BOHS)
- Australian Institute of Occupational Hygienists (AIOH)
- American Industrial Hygiene Association (AIHA)
- International Occupational Hygiene Association (IOHA)

### **11.2.3 REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals Regulations)**

For many years there have been a number of National databases detailing the hazards of chemicals that are used in industry. However, there has been concern that the system (particularly within the European Union) has been fragmented and slow to respond. In addition, as chemicals are traded internationally, chemical safety is a global concern and this has led to a number of international initiatives.

In 2006, the Strategic Approach to International Chemicals Management (SAICM) was launched involving more than 140 countries. SAICM aims to ensure that chemicals management throughout the world is such that it will help to reach the target set at the 2002 World Summit on Sustainable Development. This target is that “by 2020, chemicals are used and

produced in ways that lead to a minimisation of significant adverse effects on human health and the environment.”

REACH (The Registration, Evaluation, Authorisation and Restriction of Chemicals Regulations) is intended to help the European Union to achieve the objectives of SAICM and to streamline the previous legislative framework. REACH is currently the most ambitious chemicals legislation in the world and applies to all European Union countries. However, many other countries are also considering adopting the same approach.

REACH makes industry (producers and importers) responsible for assessing and managing the risks posed by chemicals and providing appropriate safety information to their users.

Registration of chemicals by manufacturers and importers is required for the vast majority of substances produced or imported in quantities greater than 1 ton per year. They are required to gather comprehensive information on the properties of the chemical and submit a technical dossier containing information on the chemical and how to effectively manage the risk entailed in its use.

In addition, specific authorisation may be required for substances of very high concern (carcinogens, mutagens, substances toxic to the reproductive system (CMR), and substances which are persistent, bio-accumulative and toxic (PBT) or are very persistent and very bio-accumulative (vPvB).

A comparison between the present system within the European Union and REACH is given in Table 11.1:

**Table 11.1 – Comparison between the present system and REACH**

Present system	REACH
There are gaps in our knowledge about many of the chemicals on the European market.	REACH will close the knowledge gaps by providing information on hazards and risks of chemicals produced or imported in volumes higher than 1 tonne/year per manufacturer / importer.
The 'burden of proof' is on the authorities: they need to prove that the risk from the use of a chemical substance is unsafe before they may impose restrictions.	The 'burden of proof' will be on industry. It needs to demonstrate that the risk from the use of a chemical can be adequately controlled, and recommend appropriate measures. All actors in the supply chain will be obliged to ensure the safety of the chemical substances they handle.
Notification requirements for 'new substances' start at a production level of 10 kg. Already at this level, one animal test is needed. At 1 tonne, a series of tests including other animal tests have to be undertaken.	Registration will be required for both old and new substances when the production or import reaches 1 tonne. As far as possible, animal testing will be minimised.
It is relatively costly to introduce a new substance on the market. This encourages the continued use of "existing", untested chemicals and inhibits innovation.	Innovation of safer substances will be encouraged under REACH through: more exemptions for research and development; lower registration costs for new substances; and the need to consider substitute substances when applying for authorisations.
Public authorities are obliged to perform comprehensive risk assessments that are slow and cumbersome.	Industry will be responsible for assessing the safety of identified uses, prior to production and marketing. Authorities will be able to focus on issues of serious concern.

Source: Memo/06/488 Q and A on the new Chemicals policy, REACH – EU Brussels 13<sup>th</sup> December 2006

For certain substances that are carcinogenic, mutagenic or toxic to the reproductive system (CMR substances), an authorisation will be granted if the producer or importer can show that risks from the use in question can be adequately controlled. This means that scientists can agree on a "safe threshold" below which a substance does not create negative effects to the human body or the environment.

For other CMR substances and substances with persistent, bio-accumulative or toxic properties (PBT, vPvB substances), where adequate control is not possible, an authorisation will only be granted if no safer alternative exists and if the socioeconomic benefits of the use of the substance outweigh the risks.

For all substances that are produced in quantities of 10 tons or greater per year, manufacturers and importers are required to prepare a Chemical Safety Assessment (CSA) and a Chemical Safety Report (CSR).

If the chemical safety assessment shows that the substance is classified as dangerous or is of very high concern (CMR, PBT or vPvB) then the manufacturers and importers are also required to generate Exposure Scenarios (ES) or risk assessments for the identified uses of the substance.

The assessment should:

- Address all the identified uses of the substance
- Consider all stages of the life cycle of the substance
- Consider the potential adverse effects of the substance
- Take into account the recommended risk management measures

Downstream users have a duty to use the substances safely according to the risk management information. They also have a duty to inform the manufacturers and importers how they use the substance if they use it differently to the documented exposure scenarios with the aim to make it an identified use.

It should be noted that for all substances (or preparations) that are classified as dangerous or are of very high concern (CMR, PBT or vPvB), manufacturers and importers must prepare and supply Safety Data Sheets (SDS) to downstream users and distributors recommending appropriate risk management measures.

To ease the introduction of REACH there is a phased implementation with substances of very high concern and substances produced in very large

quantities coming within the scope of REACH by the end of 2010. Smaller quantities of substances not of very high concern will come under the scope of REACH by 2013 or 2018 depending on quantities.

Day to day management of the technical, scientific and administrative aspects of REACH is the responsibility of the European Chemicals Agency (ECHA) in Helsinki.

## 12 BIOLOGICAL HAZARDS

### 12.1 INTRODUCTION TO BIOLOGICAL HAZARDS

The course and this manual concentrate on chemicals, their hazards and their occurrence in common industrial processes. This final section covers some of the issues associated with biological hazards. It is not intended as a comprehensive review of all biological hazards but as an overview of some common issues.

A fundamental difference between chemical and biological hazards is that biological agents, whether bacteria, viruses or moulds have the ability in the right conditions to rapidly replicate themselves. This means that the focus on control is not only avoidance of contact with the agent but also on ensuring that conditions favourable for growth of the organism are prevented.

The three main categories of biological agents that we will be covering examples of, are bacteria, viruses and fungi.

- Bacteria - single celled micro organisms that live in soil, water and air. There are many thousands of different types of bacteria – many are harmless, or even beneficial, but some bacteria are pathogenic - that is they cause disease. Examples of diseases caused by bacteria include Legionnaires disease, various types of food poisoning (e.g. salmonella) and anthrax. Antibiotics are used to treat bacterial infections.
- Viruses – tiny parasitic organisms that can only reproduce within living cells. They consist of nucleic acids (RNA or DNA) with a protein coat. Largest known virus approx 1000 x smaller than the average bacteria. Viruses cause many diseases including the common cold, influenza, measles, rabies, hepatitis and AIDS.



Antibiotics are ineffective against viruses but many viral diseases are controlled by vaccines.

- Fungi – simple plants lacking chlorophyll and normal plant structures (eg leaves, stems etc). Fungi include yeasts, moulds, mildews and mushrooms.

The response of each individual to exposure to micro-organisms depends on his or her state of immunity, i.e. the power of the individual to resist disease. There are many factors involved in immunity including:

- whether the individual has already experienced a particular illness
- immunisation levels
- individual resistance
- fatigue
- age

To simplify how risks from different organisms should be managed they are categorised into different risk groups. Control measures required should be matched to the risk group:

- **Risk Group 1** - (low individual and community risk). An organism that is unlikely to cause human or animal disease.
- **Risk Group 2** - (moderate individual risk, limited community risk). A pathogen that may cause human or animal disease and which might be a hazard to laboratory workers, but is unlikely to spread to the community, livestock or the environment. Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread is limited.
- **Risk Group 3** - (high individual risk, low community risk). A pathogen that can cause serious human disease but does not ordinarily spread from one individual to another.

- **Risk Group 4** - (high individual and community risk). A pathogen that usually produces serious human or animal disease and may be readily transmitted from one individual to another, directly or indirectly.

## 12.2 LEGIONELLA AND HUMIDIFIER FEVER

### 12.2.1 Legionella

Legionnaire's disease was first recognised in 1976, when an outbreak occurred among delegates attending an American Legion convention in Philadelphia. The causative agent was identified later as *Legionella pneumophila*.

The bacterium causes two patterns of disease in humans; Pontiac Fever (a mild flu-like illness) and Legionnaires Disease. It enters into the body when fine droplets of contaminated water are inhaled. The bacterium is not transmitted from person to person.

Pontiac fever is a short 'self limiting' illness with a shorter incubation period and milder symptoms than Legionnaires disease. Pontiac Fever does affect a greater percentage of those exposed but has so far not been fatal.

Legionnaire's disease is an illness characterised mainly by pneumonia and flu-like symptoms. It is fatal in about 10 - 15% of cases. Men are more likely to develop the illness than women; other risk factors include age and general health status.

Legionella are widespread in natural fresh water including rivers, lakes, streams and ponds. There is a strong likelihood of very low concentrations of the bacteria existing in all open water systems, including those of building services. The most common sources of

outbreaks of Legionnaires disease have been cooling towers and water systems in large buildings, particularly hospitals and hotels.

The primary ways of preventing and controlling the spread of Legionnaires disease are to control the initial growth of the bacterium in water systems and prevent the generation of aerosols.

Areas most at risk include

- Cooling towers
- water storage tanks and calorifiers
- hot and cold water services in premises where occupants are particularly susceptible (homes for the elderly, hospitals etc.)
- humidifiers and or washers that create a spray of water droplets and in which water temperature exceed 20°C
- spa baths and pools
- fire sprinkler systems and fountains

Factors affecting growth include:

- Water temperature - Temperatures in the range of 20-45°C favour growth (optimum temperature 37°C). Proliferation of the bacteria is unlikely below 20°C, and the organism does not survive above 60°C.
- Water being stagnant favours multiplication
- The presence of sediment, scale and sludge
- The presence of other micro-organisms (algae, amoeba and bacteria) or a biofilm (a layer of micro-organisms contained in a matrix which may form a slime on surfaces).

Control:

- Measures must be taken to minimise the risk of exposure by preventing the proliferation of Legionella in the system or plant and to reduce exposure to water droplets and aerosol
- minimise the release of water spray

- avoid water temperatures between 20°C and 45°C (major control mechanism).
- avoid water stagnation
- avoid use of materials that can harbour or support the growth of bacteria and other organisms
- keep the system clean (avoid sediments etc..)
- use of suitable water treatment systems including biocides
- ensure that the system operates safely and correctly and is well maintained.

Sampling to assess water quality is an essential part of the water treatment regime and should include both chemical and microbiological tests.

### **12.2.2 Humidifier fever**

Humidifier fever is associated with exposure to many different types of micro-organisms including various bacteria and fungi found in humidifier reservoirs and air-conditioning units. The micro-organisms have been found in both large ventilation systems as well as in small units. Significant concentrations of these organisms can be dispersed into the environment in the aerosol mist generated by the humidifiers during normal operation.

Humidifier fever generally causes a flu-like illness with fever, chills, headache, muscle ache and fatigue. These symptoms usually occur a few hours after exposure and usually subside within a day or so. However, in some cases it may manifest as an allergic alveolitis.

Controls to prevent humidifier fever centre on ensuring that the bacteria and fungi do not multiply and reach high concentrations in the water reservoir. Approaches include regular cleaning and maintenance schedules, coupled with disinfection.

## 12.3 BLOOD BORNE DISEASES

Transmission in the workplace can occur through sharps injuries and contact of infected blood and other body fluids with mucous membranes or non-intact skin.

The risk of occupational acquisition of a blood borne virus relates to:

- The prevalence of the virus in the patient population
- The efficiency of virus transmission after a single contact with infected fluid / tissue
- The nature and frequency of occupational blood contact
- The concentration of the virus in the blood

Occupations at greater risk include health care and emergency service personnel as well as those who travel and work in countries which have high prevalence of the illness.

Protection comes from avoidance of blood to blood contact by precautions including:

- Wearing protective gloves and face masks
- Covering cuts and wounds with a waterproof dressing
- Care with sharps
- Ensuring all equipment is appropriately sterilized
- Safe disposal of infected material
- Control of surface contamination
- Good hygiene
- When appropriate immunisation of 'at risk' workers (e.g. hepatitis B)

### 12.3.1 Hepatitis B

Hepatitis B is a blood-borne and sexually transmitted virus which causes inflammation of the liver. Many infected people have no symptoms, but

others have a flu-like illness with nausea and jaundice. Hepatitis B can cause hepatitis (inflammation of the liver) and can also cause long term liver damage.

Hepatitis B is more common in parts of the world such as south-east Asia, Africa, the middle and Far East and southern and eastern Europe. WHO estimates that there are 350 million chronically infected people world-wide.

The virus may be transmitted by contact with infected blood or body fluids from an infected person. The failure to clear hepatitis B infection after six months leads to the chronic carrier state. Many people who become chronic carriers have no symptoms and are unaware that they are infected.

General precautions include protecting against blood to blood contact. In addition all healthcare workers should be immunised against hepatitis B infection and should be shown to have made a serological response to the vaccine. Universal precautions should be adhered to in the hospital setting.

### **12.3.2 Hepatitis C**

Hepatitis C is a bloodborne virus which causes inflammation of the liver. There is no vaccine available to prevent hepatitis C infection. Hepatitis C infection affects different people in different ways; many experience no symptoms at all while others experience extreme tiredness. Reported symptoms include fatigue, weight loss, nausea, 'flu like symptoms, problems concentrating, abdominal pain and jaundice.

It is estimated that around 15-20% of infected people clear their infections naturally within the first 6 months of infection. For the remainder, hepatitis C is a chronic infection that can span several decades and can be life-long

In the 80-85% of individuals who fail to clear their infections naturally, the outcome of infection is extremely variable. Many people never develop any

signs or symptoms of liver disease in their lifetime and may not even know that they have been infected. Other people go on to develop serious liver disease.

The World Health Organisation estimates that there are 170 million carriers of hepatitis C worldwide. The virus is spread when blood from an infected person gets into the bloodstream of another. Prevention is centred on stopping the blood from infected individuals from coming into contact with others.

Injecting drug users are at high risk of infection, sterile injecting equipment should always be used. In a health care setting, universal precautions should be adhered to; all blood and body fluids should be treated as potentially infectious at all times.

### **12.3.3 HIV - (Human Immuno-deficiency Virus)**

HIV is the infection which through progressive destruction of specific immune cells leads to AIDS. HIV is a sexually transmitted and blood-borne virus.

- People with HIV usually have no symptoms for a prolonged period of time, while the virus acts slowly to weaken the body's immune system
- When a person's immune system has been broken down, he or she is susceptible to other illnesses, especially infections (eg tuberculosis and pneumonia) and cancers, many of which are not normally a threat to a healthy person. At that severe stage of infection the person is often diagnosed as having AIDS. AIDS stands for Acquired Immunodeficiency Syndrome
- Usually the cause of illness and eventual death in a person with HIV is not the virus itself, but illnesses to which the virus has made the person vulnerable. With treatment a person with AIDS may recover

from an illness, but will usually succumb to another. People with HIV infection will almost certainly die prematurely.

HIV is a serious infection. Without treatment most people are expected to die from their infection.

Currently there is no vaccine or cure for HIV. However, there is now treatment called highly active antiretroviral treatment (HAART). The treatment suppresses the HIV virus and can reverse the damage to the immune system for some time, prolonging the lives of those infected. The virus is continually changing, sometimes becoming resistant to current drugs, so HAART may not be a long term solution and it is not a cure.

## 12.4 ZOONOSES

Zoonoses are infections that are naturally transmitted from animal to humans. There are over 150 known zoonoses which range from ring worm to anthrax and rabies. Zoonoses primarily affect people who work closely with animals and animal products such as farm workers, laboratory workers, vets, forestry workers and those working in the wool and tanning industries.

Infection can occur through contact with:

- Animal and animal products (meat, bone meal, fur, feathers, skins, wool)
- Animal tissue & body fluids (blood, saliva etc)
- Birth products (placenta etc)
- Waste products (urine, dung, faeces)
- Contaminated materials (ground, fencing, clothing etc)

Infection may occur via inhalation, ingestion or through broken skin or contact with mucous membranes



### 12.4.1 Anthrax (ACDP Group 3)

The disease is caused by the spore forming bacteria Bacillus anthracis. Many animals may carry the anthrax bacteria or spores including cattle, horses, goats and sheep. Spores on hides, wool and animal hair may be a problem for subsequent manufacturing processes using these products. The spores are very resistant and grazing land may remain infected for many years.

There are two main forms of anthrax disease that may occur in humans; cutaneous anthrax (a skin disease) or pulmonary anthrax (affecting the lungs).

- Cutaneous – the most common form following skin contact. A red spot at the site of the infection develops to a pustule with a black centre. Without treatment, the lesion normally begins to heal after about 10 days. In a small proportion of cases, bacteria from the lesion enter the blood stream producing a septicaemia which may be fatal.
- Pulmonary or inhalation anthrax - due to the inhalation of spore containing material. The spores enter the lungs and are taken up by the immune system. Initial symptoms are similar to those of influenza but these develop rapidly as the spores germinate in the lymphoid tissue, multiply and produce a powerful toxin. The disease progresses with breathing difficulty, skin discolouration and disorientation, leading to coma and death within 24 - 48 hours.

The main occupations at risk include agricultural workers, abattoirs, animal by product processing, vets and the wool and tanning industries.

Control measures include elimination of anthrax in farm animals, high standards of personal hygiene including the covering of cuts with

waterproof dressings and information and training.

#### **12.4.2 Leptospirosis (Hazard group 2)**

The main form of leptospirosis is Weil's disease which is a potentially life threatening illness caused by the *Leptospira* bacteria passed from rats via urine. Symptoms include flu-like symptoms such as fever, headache, vomiting, muscle pains, pneumonia and possible kidney failure and death.

The disease may be transmitted through contact with rat's urine or watercourses contaminated with it. It may enter the body through abrasions, cuts in the skin and through the lining of the mouth, nose and conjunctiva.

At risk occupations include farmers, farm workers, fish farmers, construction workers, water industry workers, leisure industry workers, sewer workers and laboratory workers

#### **12.4.3 Salmonellosis**

Salmonellosis is the name given to an infection caused by any of the *Salmonella* group of bacteria. *Salmonella* bacteria may be carried by most types of farm animal. Infections are usually associated with ingestion of contaminated food or may result from contact with farm animal dung e.g. using contaminated hands to eat, drink or smoke.

Symptoms develop suddenly about 12 to 24 hours after infection and include malaise, headache, nausea, abdominal pain, diarrhoea and fever. Symptoms normally last 2 to 3 days but can persist longer. Dehydration or septicaemia (blood poisoning) may also occur.

## 12.5 MOULDS

Moulds are microscopic fungi that grow in the form of branching threads or filaments. They reproduce by means of microscopic spores which can give rise to new mould growth which in turn can produce millions of spores.

If inhaled, fungal spores may cause allergic rhinitis or other allergic responses such as alveolitis.

Moulds can be found wherever there is moisture, oxygen and a source of nutrients. They grow on dead organic matter such as on rotting vegetation and dead leaves, especially in moist shaded areas.

In industrial situations bakeries, breweries, dairies and greenhouses are examples of ideal places for moulds to grow. Any areas where fresh food is stored are also potential sites where mould growth is possible. Well documented examples include grain stores or silos, particularly if the grain has been stored slightly damp.

Indeed, in any indoor environment, mould may grow in damp places such as in poorly ventilated basements, bathrooms, and humidifier and air-conditioning units. Indeed they can thrive in any area where surfaces or materials are damp. Reduction of moisture and humidity levels is the most important factor in mitigating mould growth.

## 12.6 PANDEMICS

A pandemic can be defined as an epidemic of an infectious disease that spreads over a wide geographic area (several countries, a continent or even worldwide) and affects a large proportion of the population.

A pandemic can start when the following conditions occur:

- Emergence of a disease, or a particular strain of a disease, new

to a population

- The agent affects humans, causing serious illness
- The agent spreads easily and sustainably among humans

There have been many pandemics in the past including those caused by typhoid, cholera, bubonic plague and influenza viruses. Bubonic plague killed tens of millions of people in Europe in the middle ages. The most severe influenza virus pandemic recorded occurred between 1918 and 1920 when 'Spanish Flu' was estimated to have killed at least 40 million people. More recently 'Hong Kong Flu' was estimated to have killed about 1 million deaths in the late 1960's.

New strains of the influenza virus continue to emerge in animals with the potential that any particular new strain could cause a future pandemic. These new strains of the influenza virus occur when they are transmitted to humans from another animal species such as pigs, chickens or ducks.

A recent example of a new variant strain of influenza virus is H5N1 ('Bird Flu') which was found in 2004 in birds in Vietnam. By 2007 numerous cases had been found across Asia and much of Europe. There have been human fatalities among people who have had close contact with infected birds. There has been no, or limited, transmission of the disease from person to person.

H5N1 bird flu is not categorized as a pandemic as the virus cannot yet spread easily or sustainably among the human population. However, if the virus combines with a human influenza virus strain a new sub-type may evolve that could be highly contagious in humans.

Another concern related to pandemics is that many micro-organisms are becoming resistant to many of the antibiotics currently in use. These antibiotic resistant micro-organisms (sometimes termed 'superbugs') may contribute to the re-emergence of many diseases which are currently well controlled e.g. tuberculosis.

A range of common bacteria are also becoming more resistant to antibiotics leading to a rise in the number of healthcare acquired infections. A well known example of this is methicillin-resistant *Staphylococcus aureus* (or MRSA).

## **12.7 GENETIC MODIFICATION**

Genetic modification is a technology developed in the past 30 years for altering the characteristics of living organisms, such as plants or animals. It involves the addition of new genetic material into an organism's genome.

Genetically modified organisms (GMO) have widespread applications. They are used in biological and medical research, production of pharmaceutical drugs and agriculture. So far the largest application of genetic modification has been in the production of food crops which are more resistant to disease, or to insect attack, or with increased crop yields.

The benefits of genetic modification are potentially enormous. Potential benefits in the future include new treatments for diseases, crops that are more resistant to pests and diseases, food of greater nutritional value and the production of pharmaceuticals from plants.

However, there are a number of concerns with regard to this technology. Some people have concerns in principle about the alteration of biological systems that have evolved naturally. In addition, many people are concerned that we are not yet able to understand all the potential ramifications of genetic manipulation.

A particular concern has been the possibility of genetically modified plants cross pollinating (or 'outcropping') with other 'natural' crop varieties to produce another variety whose properties have not been assessed. The safety of genetically modified organisms in the food chain has also been

questioned.

As a result of these concerns, strict controls have been implemented in the use and production of genetically modified organisms.

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