

## INTERNATIONAL MODULE SYLLABUS

### W507 - HEALTH EFFECTS OF HAZARDOUS SUBSTANCES

**Aim:** To provide an introduction to the principles of toxicology, physiology and epidemiology. The main types of harmful effects to target organs from exposure to chemical hazards at work, and the hazards associated with common hazardous substances.

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

- Outcomes:**
- 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;
  - 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 and toxic and health effects for hazardous substances commonly encountered in the workplace.
  - basic interpretation of the results from epidemiological studies

Content:	Topic	Time Allocation
	<b>1 Basic Principles of Toxicology</b>	<b>25%</b>
	<b>2 Physiology and Target Organs</b>	<b>30%</b>
	<b>3 Epidemiology</b>	<b>15%</b>
	<b>4 Health Effects and Industrial Processes</b>	<b>30%</b>

#### Biological Agents (outlined as annex\*)

*[\* It should be noted that the outline of Biological Agents is provided as an Annex for reference purposes only as part of the course manual. The student's understanding of this section of the syllabus is not included in the assessment of this module. The inclusion of this section is simply to make students aware that consideration of exposures to Biological Agents could be important in certain workplace situations.]*

#### 1. Basic Principles of Toxicology (25%)

##### 1.1 Definitions

Acute, Chronic, Local, Systemic, Allergic reaction, Sensitiser, Carcinogen, Mutagen, Teratogen, Xenobiotic, Stochastic, Non-Stochastic.

##### 1.2 Basic Pharmacokinetics

- Absorption: Routes of absorption for substances, when ingestion can occur, situations where skin absorption and penetration can occur.
- Distribution: main distribution pathways, blood, lymphatic system.
- Storage: How chemical properties of a substance influence site of storage; common examples of where materials are stored (eg. solvents in fatty tissues, lead in bones, liver as a storage organ).
- Biotransformation: Meaning of biotransformation, where biotransformation occurs, how biotransformation can initiate or enhance toxic effects (examples - benzene, dichloromethane, methanol).
- Elimination: Definition of biological half life, wide variation of half lives, shape of curve.

### 1.3 Dose Response Relationships

- Meaning of dose response relationships
- Typical shape of dose response curve
- Concept of threshold and no-observed adverse effect level
- Dose response curves without threshold
- Importance of slope of curve.

### 1.4 Toxicity Testing

- Meaning of LD<sub>50</sub>, LD<sub>Lo</sub>, LC<sub>50</sub>, LC<sub>Lo</sub>, TD<sub>50</sub>, TD<sub>Lo</sub>, TC<sub>50</sub> and TD<sub>Lo</sub>
- Units used to express results of animal testing
- Types of toxicity testing – toxicokinetic studies, acute toxicity studies, sensitisation studies, repeated dose toxicity studies, genotoxicity studies, reproductive and developmental toxicity studies, carcinogenicity studies
- Uses of toxicological data and estimation of safe human dose
- Limitations of toxicity testing data.

### 1.5 Types of Combined Effects

- Addition, synergism, potentiation, antagonism, independent

### 1.6 General Health Effects

- *Asphyxia*
- *Irritation*
- *Narcosis*
- *Toxicity*
- *Carcinogens*
  - Basic mechanisms of Carcinogenicity [geneotoxicity, Irritant etc.]
  - Benign and malignant tumours
  - Difficulties in identifying causal agents, long latency periods
  - IARC classifications
- *Sensitisers*
  - How sensitisation affects individuals
  - Sensitisers (respiratory, animal allergy, skin - chromium).
  - Uncertainty about thresholds
  - Mechanisms of sensitisation and assessment methods
- *Reproductive Effects*
  - Teratogens

## 2 Physiology and Target Organs (30%)

### 2.1 Respiratory System

#### Structure

The main regions of the respiratory system:

- Head airways region: role of turbinates, filtration mechanisms
- Tracheobronchial region: Structure, dimensions of air passages
- Mucociliary escalator
- Alveolar region: Surface area, Retention time of particles, Lack of cilia

#### Particles

- Definition of aerodynamic diameter. Relevance of particle size.
- Particle deposition and clearance.
- Main deposition mechanisms; Interception, Impaction, Sedimentation, Diffusion.
- Particle size ranges from each of the three regions.
- Particles: Those deposited in the alveoli, fate of particles deposited elsewhere, including absorption via digestive tract
- ISO Curves: Inspirable, thoracic and respirable curves, Shape of respirable curve.

### *Gases and Vapours*

- Absorption through the lungs.
- Gases; Importance of solubility.

### *The Lung as a Target Organ*

- Gaseous contaminants: Acute irritancy, Role of solubility in determining region affected, Chronic effects.
- Causes and consequences of inflammation.
- Benign pneumoconiosis: Definition, Main agents (iron, tin, barium).
- Fibrosis: Definition. ( Crystalline Silica, Asbestos etc.)
- Emphysema (Cadmium Oxide etc.)
- Cancer ( Rubber fume, Arsenic, Hexavalent Chromium etc.)
- Allergic Conditions:
  - Rhinitis - symptoms, non specific nature, wide range of agents.
  - Asthma - symptoms, common causes (isocyanates, solder fume, metals, latex, vegetable dusts, animal proteins, and enzymes { industrial and food utilisation}).
  - Allergic alveolitis - symptoms, causative agents for farmers lung and other moulds.
  - Byssinosis - symptoms, main stages of textile process associated with disease.

Assessment methods – Lung function testing, Challenge testing, Skin prick testins, Blood iGe analysis etc.

## 2.2 *Skin*

### *Structure*

The structure and function of the different layers and components:

- Stratum corneum and epidermis
- Dermis
- Hair follicles
- Sweat glands
- Nerves
- Fat

Mechanisms of cutaneous protection against chemical penetration and biological agents.

The skin as a target organ.

Definitions, main mechanisms and common causes of irritant contact dermatitis, allergic contact dermatitis (nickel, epoxy resins), folliculitis, pigment disturbances, Ulceration, Cancer.

## 2.3 *Nervous System*

Central and peripheral nervous systems: Definitions, Roles, Structure of nerve cells, Transmission of nerve impulses; Transmission along cells, Transmission across synaptic gap.

Nervous system as a target organ.

Role of volatile organic compounds as depressants.

Definitions, main mechanisms and common causes of:

- Damage to nerve cells (lead, mercury, n-hexane, manganese.)
- Deactivation of cholinesterase (organophosphates)

## 2.4 *Circulatory system*

Composition of blood and role of constituents.

Blood as a target organ.

Definitions and common causes of:

- Haemolysis (arsine and stibene).
- Carboxyhaemoglobin formation (carbon monoxide - from direct exposure and from metabolism of dichloromethane).
- Methaemoglobin formation (aromatic amines).
- Anaemia (lead, benzene).

- Leukaemia (benzene).

#### 2.5 *Liver*

Position of liver in the circulatory system.

Role in biotransformation and consequent vulnerability to toxic agents.

Structure of liver lobules.

Main agents which can cause liver damage (eg. alcohol, chlorinated hydrocarbons, metal compounds).

#### 2.6 *Kidney*

Structure and function.

Role in homeostasis and excretion.

Link to circulatory system.

Structure and role of nephrons.

Kidney as a target organ: Effects of Cadmium, Lead, Mercury, Organic compounds.

#### 2.7 *Reproductive System*

Effects on unborn child: Heredity, Teratogenicity. Interference with the male and female systems.

### 3 **Epidemiology (15%)**

Types of epidemiological study,

Importance of study design,

Definitions of cohort/case-referent, retrospective/prospective, cross-sectional/ longitudinal designs, mortality/morbidity ratios

Use of epidemiological data, limitations and restrictions, confounding factors.

Bradford Hill criteria

Limitations of epidemiological studies, importance of study size, link to exposure standards

### 4 **Health Effects and Industrial Processes (30%)**

#### 4.1 *Risk and Safety Phrases*

International system for Risk and safety phrases

#### 4.2 *Sources of information*

Safety data sheets.

Literature

National data bases including REACH

#### 4.3 *Gases*

Use a **selection** of the gases given below to illustrate the principal toxic effects (simple asphyxiation, chemical asphyxiation, upper and lower respiratory tract irritation, blood effects, lung damage, cancer) from exposure to gaseous substances. The occurrence of these gases and their common applications should be included.

- Inert gases
- Carbon dioxide and carbon monoxide
- Hydrogen cyanide
- Ammonia
- Chlorine
- Hydrogen sulphide
- Oxides of nitrogen and ozone
- Acid gases (sulphur dioxide, hydrogen chloride, hydrogen fluoride)
- Metal hydrides

#### 4.4 *Vapours*

Describe the generic hazards of organic vapours (ie. Narcosis, respiratory irritation, skin irritation and dermatitis, skin absorption, organ damage) and use **some** of the substances given below to illustrate these: The occurrence of these vapours and their common applications should be included.

- Anaesthetic gases eg. Halothane, Nitrous oxide
- Aniline and phenol

- Benzene, toluene and xylene
- Formaldehyde
- Isocyanates
- Styrene
- Halogenated hydrocarbons
- vinyl chloride
- N-hexane
- Glycol ethers
- Acetone/MEK

#### 4.5 *Dusts and particulate materials*

##### *Minerals*

Use the minerals given below to illustrate the principal toxic effects of such substances: The occurrence of these minerals and their common applications should be included.

- Crystalline silica (quartz, cristobalite and tridymite)
- Asbestos (serpentine and amphibole)
- Machine-made mineral fibres (glass, rock, refractory ceramic fibre)

##### *Organic and other dusts*

Nanoparticles

Flour and other food components [Industrial and manufacturing]

Diesel fume

Latex [Manufacturing and use]

Enzymes [detergents and food industries]

Physiological active materials [Pharmaceuticals]

#### 4.6 *Metals and their compounds*

Use **some** of the metals given below to illustrate the principal toxic effects (nuisance, respiratory effects, organ damage, lung damage, fibrosis, skin irritancy/sensitisation, systemic effects, cancer) from exposure to such metals and their compounds. The occurrence of these metals and their common applications should be included.

- Arsenic
- Aluminium
- Beryllium
- Cadmium
- Chromium and nickel
- Cobalt
- Iron
- Lead (including differences between inorganic and organic lead compounds)
- Mercury
- Manganese
- Vanadium
- Zinc and copper

#### 4.7 *Common Industrial processes*

- Working with metals [Grinding, Machining, Welding]
- Surface coating and treatments [Chromium plating, galvanising etc.]
- Soldering
- Handling and processes involving solvents [open and closed systems. Degreasing, painting etc.]
- Handling of solids and powders

#### 4.8 *Specific industry profiles*

## **Biological Agents** (Outline as Annex\*)

Describe the principal toxic effects and sources of:

- Legionella and humidifier fever
- Infections of blood borne diseases (hepatitis and HIV)
- Zoonoses; definition, how infection can occur, common examples (anthrax, leptospirosis, salmonellosis).
- Bloodborne infections
- Moulds
- Pandemics
- Genetic modification

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## **Overall Assessment Method**

The overall assessment for this module consists of an “open book” written examination paper and satisfactory results from the formative practical assessment.

### **Written Examination**

40 short answer questions to be answered in 120 minutes. The questions require candidates to write short answers which will require no more than the box provided but may include multiple answers. Some questions may require calculations.

### **Formative Practical Assessment**

All candidates must participate in the practical case studies and demonstrate the required skills.

The case studies should be designed by the course tutor(s) to test the basic skill and knowledge of each of the candidates.

One study should be an evaluation of available data to advise on a suitable exposure limit to be applied for a material [Safety data sheets etc.] the other study should be a scenario study to evaluate potential exposure routes and the potential health consequences from a selected process.

Full details of the practical requirements and the individual candidate reporting forms etc. are available in document JG.2.

## **Relevant Documentation**

- i WHO Guidelines on the prevention of toxic exposures
- ii Patty's Industrial Hygiene and Toxicology
- iii NIOSH, IARC and WHO criteria documents
- iv Computer databases (RTECS, MEDLINE, TOXLINE, HSDB, HSELINE, CDROMS)
- v Controlling Skin Exposure to Chemicals and Wet-Work' by Rajadurai Sithamparanadarajah, ISBN 978-1-906674-00-7
- vi Introduction to Toxicology, 3<sup>rd</sup> edition, J.A.Trimbrell, Taylor and Francis
- vii Industrial Toxicology, P.L.Williams and J.L.Burson eds., Van Nostrand Reinhold
- viii Basic Epidemiology [WHO] second edition 2006 Bonita, Beaglehole and Kjeellstrom ISBN 92 4154707 3. [Also available as e-book]

*NOTE: This list is indicative only. Students should be encouraged to read as widely as possible on relevant topics.*