

Occupational Poisonings and Toxicity

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Introduction

- **Poison:**
 - Any substance that, when administered to a living organism, causes a harmful effect.
- **Poisoning:**
 - The morbid condition produced by a poison.
 - Systemic effects of toxic materials
- **Toxic:**
 - Term used to describe a chemical that has the ability to cause harmful or fatal effects upon exposure to humans, animals, or plants.
- **Toxicity:**
 - The capacity of a substance to induce damage to living tissue. Toxicity can be *acute, chronic, local, or systemic*.

(Lewis' Dictionary of Occupational and Environmental Safety and Health)

Introduction

- Common occupational toxic substances can be divided into 4 groups:
 1. Heavy metals
 2. Pesticides
 3. Organic solvents
 4. Gases, vapours and particulates

Heavy metals

Heavy Metals

- What is a “heavy metal”?
- A metal of high specific gravity; esp. a metal having a specific gravity of 5.0 or over
- Examples:
arsenic, cadmium, chromium, lead, mercury, nickel, tin etc.
- Widely used
- Over exposure may lead to ill health

Schedule II, USECHH 2000

- Arsenic (As)
- Beryllium (Be)
- Cadmium (Cd)
- Chromium (Cr)
- Lead (Pb)
- Manganese (Mn)
- Mercury (Hg)
- Nickel (Ni)

Arsenic (As)

- Three forms: Inorganic, organic, arsine gas
- Used as insecticides and herbicides, in glassware, alloy and pigment production, and in the semiconductor industry
- Occupational exposure mostly to inorganic arsenic:
 - those involved in the processing of copper, gold, and lead ores.
 - Agriculture (pesticides)
- The organic arsenic[V] forms are less toxic than the inorganic arsenic[III] forms
- Toxicokinetic : $t_{1/2}$ (blood) \sim 60 hrs, eliminated via kidney

Acute Arsenic Poisoning

- May follow the ingestion of deliberately or accidentally contaminated food or drink
- Gastrointestinal: metallic or garlic taste, dry mouth, dysphagia, abdominal pain, profound vomiting, and diarrhea with rice water stools
 - Shock → multi organ failure → death
- Survivors often develop:
- Bone marrow suppression (anemia, leukopenia)
 - Hemolysis
 - Hepatomegaly
 - Melanosis
 - Polyneuropathy

Arsine gas (AsH_3)

- A colorless & odorless gas at low concentration but smell of “garlic” at high concentration
- Generated when arsenic containing metals contact with strong acid
- Intravascular hemolysis (abdominal pain, vomiting, hemoglobinuria, renal failure)

Chronic arsenic poisoning

- More common form of arsenic poisoning
- Skin : pigmentation, depigmentation, cancer
- Peripheral nerves: sensorimotor neuropathy
- Liver: Cirrhosis
- CVS: hypertension
- Blood: Megaloblastic anemia
- Others: nasal perforation

Cadmium (Cd)

- Used in electroplating, to make pigments, as a stabilizers in plastics & as alloy (cd-nickel batteries)
- Toxicokinetics:
 - Absorbed through GIT and lungs; 40% retained in the lungs, 70% bound to rbc ; accumulated in the liver & kidney; excreted in the kidney
 - Elimination of cadmium is a slow process, with a half-life of 16–33 years.

Acute effect

- Mainly due to inhalation to cadmium oxide fume
- Latency time : 10 hours
- C/f: Retrosternal pain, dyspnoea, cough, pulmonary edema (severe case)
- Recovery: within weeks

Chronic effect

- Principal target organ is kidney
- Kidney damage (proteinuria): This is due to proximal tubule damage and may be associated with hypertension.
- Itai-itai disease (Itai-itai byo @ ouch-ouch disease): osteomalacia, pain, nephropathy
 - observed in postmenopausal women in Japan, caused by a combination of cadmium contamination of diet and low calcium and vitamin D intake.
- Other effects include emphysema, chronic bronchitis and lung cancer.

Chromium

- Used for chrome plating & in the manufacture of special steels, such as stainless steel
- Use as compounds: dyeing silk, wool & other textiles, tanning agents, pigments.
- Only the trivalent [III] and hexavalent [VI] compounds, are of practical importance. Of these, the hexavalent form is 100–1000 times more toxic than most common trivalent compounds (irritant, corrosive, carcinogenic).
- Toxicokinetic : absorption (lungs, GIT); excreted in the urine
- All chrome compound are sensitizers; may cause contact dermatitis (chrome ulcers) & occupational asthma

Lead (Pb)

- Lead is usually found in ores
- The richest ore is galena (lead sulphide)
- Uses:
 - used to make lead-acid batteries
 - used as the metal, for example, lead sheet, cable sheathing, solder, ammunition, alloys, weights, ballast, low melting alloys
 - Lead-based pigments have a long tradition of being used in paints (discontinued)
- Lead exists in both organic and inorganic forms:
 - Inorganic lead**
 - The lead found in old paint, soil, and various products described below is inorganic lead. Leaded gasoline exhaust contributed to ambient inorganic lead contamination. For this reason, the focus of this document is on inorganic lead.
 - Organic Lead**
 - Leaded gasoline contained organic lead before it was burned; however, since the elimination of lead from gasoline in the U.S. starting in 1976, exposure to organic lead is generally limited to an occupational context. However, organic lead **can be more toxic** than inorganic lead because the **body more readily absorbs** it. Potential exposures to organic lead should be taken very seriously.

Toxicokinetic:

- Absorption:
 - 5-10% via GIT
 - 50-70% via lungs
- Most recently absorbed lead is stored in rbc (half-life of about 20–40 days) and most long-term body lead (90%) is stored in bone tissue (half-life in the order of 20–30 years).
- Elimination mainly through the kidney.

Lead Poisoning

Neural effect

- CNS: lead encephalopathy, ataxia, vomiting, restless, seizure, unconscious
- Autonomic: lead colic, constipation
- PNS: lead palsy
- Brain - most sensitive target organ
- Children: ↓IQ, cognitive deficit, reading disabilities, ↓ motor skills
- Adults: Neurobehavioural changes

Extraneural effect

- haematopoietic system: disruption in porphyrin synthesis, anaemia)
- CVS: hypertension
- kidney: lesions of proximal tubule, Fanconi syndrome, chronic interstitial disease
- Endocrine: delayed puberty, ↓ Vit D
- Reproductive and developmental:
 - Readily cross placenta
 - Abortions, stillbirth
 - LBW, Premature
 - Males: ↓ sperm count and motility
- Carcinogen: IARC 2A - probably carcinogenic to humans (Lung, kidney, and brain cancer)

Laboratory evaluation

- Hct, Hb:
 - Slight or moderately low
- Peripheral blood film:
 - Normochromic normocytic or microcytic hypochromic
- Blood lead:
 - Indicate exposure – level above 10 micrograms/dL is considered positive and consequential
- Erythrocyte protoporphyrin level:
 - **Zinc protoporphyrin** (ZPP) is a compound found in rbc when heme production is inhibited by lead
 - Indirect measure of long term lead exposure (normal level < 35µg/dl)
 - Not sensitive to low levels of lead exposure
- Renal profile (Urea and Creatinine)
- Urine analysis
- Others: Blood ALAD, urine ALA, urine coproporphyrin

Lead Medical Surveillance

- PEL = 50 $\mu\text{g}/\text{m}^3$ (USECHH 2000)
- Biological monitoring (Lead Regulations, 1984)
 - At least every 6 months:
 - All exposed > Action level > 30 days a year
 - At least every 3 months:
 - Blood lead ($\mu\text{g}/100\text{g}$) at 40 to <60
 - Until 2 consecutive < 40
 - At least every month
 - Blood lead ($\mu\text{g}/100\text{g}$) at 60 to <80
 - Until 2 consecutive <60
 - During temporary removal period at 80 & above
 - Females of childbearing capacity

Mercury

- Mercury is liquid at room temperature, and exists in elemental (metallic), inorganic (Hg, or mainly, Hg²⁺) or organic (Hg⁴⁺) forms (highly neurotoxic).
- Used in dentistry, battery, medical and scientific equipment manufacture, and in the production of chlorine and caustic soda
- Source: Mining, environment
- Toxicity: nephrotoxic, neurotoxic - “Mad Hatters” disease (paraesthesias, vision and hearing impairment, slurred speech, anxiety, hallucinations, irritability, depression, lack of coordination, and tremors).
- Facts – liquid ‘silver’ evaporates at room temperature. bacteria converts it to organic methyl



“Mad Hatter”

- Toxicokinetic:
 - Elemental mercury vapour is well absorbed by the lung but poorly absorbed by the gut
 - Inorganic mercury are absorbed by the gut (7–15%). These cause most cases of mercury poisoning. Systemic effects are possible from skin and lung exposure
 - Organic forms of mercury are extremely well absorbed across the gut, though dermal absorption does not appear to be great.
 - Excretion occurs in urine and faeces

Mercury Poisoning

Acute effect

- By ingestion: local corrosive effects; nausea, vomiting, severe abdominal pain, chemical colitis, renal damage
- By inhalation: chemical pneumonitis, pulmonary edema

Chronic effect

- Classic symptoms: tremor, gingivitis, erethism (greek erethismos = irritate)
- Renal & CNS damage
- Minamata disease - neurological syndrome caused by severe mercury poisoning

Nickel (Ni)

- 90% of nickel is used in alloys, mostly stainless steel. Others : aero engine, plating, foundry, catalyst, rechargeable battery, coating of fibers.
- Toxicokinetic:
 - GIT absorption of soluble nickel compounds is rapid, but only about 1–5% is absorbed.
 - Absorption and clearance of inhaled insoluble nickel compounds from the lungs is slow, occurring over months.
 - Dermal absorption of nickel and nickel compounds is minimal.
 - Absorbed nickel is rapidly excreted in the urine, with a half-life of 20–60 hours.

Acute effect:

- Lungs: Acute chemical pneumonitis with cough, dyspnea, tachycardia, and cyanosis. Slowly resolving and death may result from respiratory failure.
- Brain: Encephalopathy, due to cerebral edema and possibly hemorrhage
- Skin: Allergic dermatitis. 'Nickel itch'.

Chronic effect:

- chronic rhinitis, sinusitis, perforation of the nasal septum, and anosmia
- Lung and nasal sinus cancer

Medical management – Chelation Therapy

Properties

- Chelate is from the Greek word for claw
- Metal chelators accelerate the excretion of metal from the body
- Non-specific – can remove essential metals and elements

Examples:

- Dimercaprol or British anti-Lewisite (BAL) – one of the first, broad action but potentially toxic
- Calcium EDTA – lead
- Penicillamine – copper
- Desferrioxamine – iron
- DMPS – lead, mercury

Pesticides

Pesticides

- A pesticide is any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest.

(US EPA)

- Pesticides are often referred to according to the:
 - 1) Type of pest they control
 - 2) Derived from a common source or production method
 - chemical pesticides
 - biopesticides
 - antimicrobials
 - pest control devices

Chemical pesticides:

- **Organophosphate Pesticides** - These pesticides affect the nervous system by disrupting the enzyme that regulates acetylcholine, a neurotransmitter. Most organophosphates are insecticides. However, they usually are not persistent in the environment. (e.g. parathion, malathion, and methyl parathion)
- **Carbamate Pesticides** affect the nervous system by disrupting an enzyme that regulates acetylcholine, a neurotransmitter. The enzyme effects are usually reversible. There are several subgroups within the carbamates. (e.g. Bendiocarb, Carbaryl, Methomyl, and Propoxur)
- **Organochlorine Insecticides** were commonly used in the past, but many have been removed from the market due to their health and environmental effects and their persistence (e.g. DDT and chlordane).
- **Pyrethroid Pesticides** were developed as a synthetic version of the naturally occurring pesticide pyrethrin, which is found in chrysanthemums. They have been modified to increase their stability in the environment. Some synthetic pyrethroids are toxic to the nervous system. (e.g. permethrin, resmethrin, and sumithrin)

- Route of absorption:
 - Skin penetration (most common)
 - Inhalation
 - Ingestion
 - Conjunctival membranes of the eye
 - Other mucous membranes
- Occupational exposure to pesticides occurs among manufacturers and formulators; during transport and storage; among mixers, loaders, and applicators working in fields, greenhouses, parks, and residential buildings

General principle in the management of acute pesticide poisonings

- Skin decontamination:
 - Remove clothes
 - Shower patient with water and soap
- Airway protection
- GIT decontamination:
 - Gastric lavage or Syrup of ipecac
 - If pt presents within 60 minutes
 - Contraindicated in hydrocarbon ingestion
- Catharsis (cleansing @ purging):
 - Sorbitol and magnesium citrate
 - It will increase gut motility to improve excretion
- Activated charcoal adsorption:
 - Effective adsorbent for pesticides

Organophosphate poisoning

- Symptoms of acute organophosphate poisoning develop during or after exposure, within minutes to hours, depending on the method of contact. (inhalation (fastest) > GIT > dermal route).
- All signs and symptoms are cholinergic in nature and affect muscarinic, nicotinic, and central nervous system receptors
- Signs and symptoms:
 - early symptoms - headache, nausea, dizziness, and hypersecretion (sweating, salivation, lacrimation, and rhinorrhea).
 - Muscle twitching, weakness, tremor, incoordination, vomiting, abdominal cramps, and diarrhea → signal worsening of the poisoned state.
 - Miosis is often a helpful diagnostic sign
 - Anxiety, restlessness, choreiform movements, depression, memory loss, and confusion have been reported.
 - Seizures, lethargy and coma were common in children

- Some organophosphorus insecticides (chlorpyrifos, dichlorvos, methamidophos, trichlorfon and trichloronat, isofenphos) caused a sensorimotor polyneuropathy known as **organophosphate-induced delayed polyneuropathy (OPIDP)**:
 - characterised by flaccid paralysis of the lower limbs (the upper limbs might also be affected in severe cases).
 - Sensory peripheral nervous system is affected to a lesser degree

Organophosphate poisoning

Lab investigation:

- Biochemical indicators:
 - ↓ plasma pseudocholinesterase level
 - ↑ red blood cell AChE level
- Urinary alkyl phosphate and phenol analyses can demonstrate organophosphate absorption at lower dosages

Tx of Organophosphate poisoning

- Airway protection
- Atropine sulfate:
 - Iv, im or via endotracheal tube
 - Aim is to antagonize the effects of excessive concentrations of acetylcholine at end-organs having muscarinic receptors
- Glycopyrolate:
 - an alternative to atropine using continuous infusion

Carbamate poisoning

- As with OP poisoning, the signs and symptoms are based on excessive cholinergic stimulation
 - but shorter duration because carbamates are more rapidly metabolized
- Early symptoms: Malaise, muscle weakness, dizziness, sweating, headache, salivation, nausea, vomiting, abdominal pain, and diarrhea.
- Serious toxicity:
 - CNS depression (coma, seizures, and hypotonicity)
 - Nicotinic effect – HPT and cardiorespiratory depression
 - Dyspnea, bronchospasm, bronchorrhea with pulmonary edema

Lab investigation:

- Biochemical indicators:
 - ↓ plasma pseudocholinesterase level
 - ↑ red blood cell AChE level
- Urine analysis for unique metabolites (e.g. Alpha-naphthol from Carbaryl, isopropoxyphenol from propoxur)

Treatment:

- Airway protection
- Atropine

Organochlorine poisoning

- Many of these chemically diverse insecticides have been banned or restricted in the developed world because they persist in the environment and concentrate in the food chain, damaging wildlife. (e.g. DDT)
- Acute toxicity reflects influence on neuronal membrane stability through interaction with either sodium channels or GABA receptors, resulting in hyperactivity in the central nervous system.
- Signs and symptoms:
 - Headache, nausea, dizziness, inco-ordination, confusion, tremor, paresthesias, and sudden seizures

- The diagnosis of acute poisoning is made by a history of exposure in the appropriate clinical setting.
- Although the tests are not routinely available, organochlorines and their metabolites may be found in the blood or in fat.
- Treatment:
 - Supportive
 - Anti seizure
 - Diazepam
 - Pentobarbital
 - Cholestyramine (Questran) was found to be effective in increasing elimination and ameliorating hepatic effects in chlordecone poisoning

Pyrethroid poisoning

- They are relatively less toxic
- Toxicity is thought to be mediated through functional changes in sodium channels.
- Signs and symptoms:
 - salivation, nausea, vomiting, diarrhea, irritability, tremor, inco-ordination, and seizures
 - Allergic: asthma, allergic rhinitis, contact dermatitis
- Treatment:
 - Treatment of acute poisoning is non-specific and supportive, including administration of activated charcoal and a cathartic following gastric aspiration and lavage.

Organic solvents

Organic solvents

- What is organic solvent?
 - Organic solvent is a general term for organic chemicals characterized by their ability to dissolve oils, fats, resins, rubber, and plastics and etc.
 - Share important physical characteristics
 - Nearly all volatile liquids at room temperature
 - Strongly lipophilic

Organic solvents classification by chemical formula

Aliphatic HCs	n-Hexane
Aromatic HCs	Benzene, Toluene, Xylene, Styrene
Halogenated HCs	Dichloromethane, Trichloromethane
Esters	Ethyl acetate
Ethers	Ethyl ether, Tetrahydrofuran
Ketones	Acetone
Alcohols	Methanol, Isopropanol
Glycol esthers	2-Ethoxyethanol, 2-Ethoxyethyl acetate
Miscellaneous	Carbon disulfide, dimethyl formamide
Petroleum distillates	Petroleum benzine, White spirit

Table 14.2 Uses of solvents

<i>Application</i>	<i>Percent use</i>
Surface coatings	43.3
Metal cleaning (degreasing)	10
Household products	8.1
Adhesives	6.7
Pharmaceuticals	6.1
Dry cleaning	3.9
Other	20

Source: adapted from Collings and Luxon 1982.

General effects of organic solvents

Respiratory system:

- Asphyxiation
- Irritation – asthma, bronchitis, pneumonitis
- Sensitisation and allergy – bronchoconstriction
- Cancer – Lung

Skin:

- Irritant contact dermatitis
- Allergic contact dermatitis

The nervous system:

- Short-term effects - tiredness, disorientation, a sense of intoxication, drowsiness, euphoria, dizziness, confusion and eventually, unconsciousness.
- Long-term effects - memory impairment, coordination impairment, deterioration of personality and depression

General effects of organic solvents

Liver: Damage

Kidney: The most well-established solvent risk factors for kidney damage are the glycol ethers and some chlorinated solvents.

Cancer: Leukemia, liver, lung, Kidney, etc

General effects of organic solvents

Reproductive systems:

Table 14.9 Reproductive effects of solvents

<i>Reproductive effects</i>	<i>Solvent(s)</i>
Menstrual disorders	Toluene, styrene, benzene
Abortion or infertility	Formaldehyde, benzene
Testicular atrophy	2-Ethoxyethanol
Decreased libido and impotence	Vinyl chloride
Decreased foetal growth, low birth weight	Toluene, formaldehyde, vinyl chloride

Gases, vapours and particulates

Gases, vapours and particulates

Definitions:

- **gas** is a term usually applied to a substance that is in the gaseous state at room temperature and pressure
- **vapour** is applied to the gaseous phase of a material that is ordinarily a solid or liquid at room temperature and pressure
- **aerosol** is applied for a relatively stable suspension of solid particles in air, liquid droplets in air or solid particles dissolved or suspended in liquid droplets in air
- **mists and fogs** are aerosols of liquid droplets formed by condensation of liquid droplets on particulate nuclei in the air
- **fumes** are solid particles formed by combustion, sublimation or condensation of vaporised material
- **dusts** are solid particles in air formed by grinding, milling or blasting
- **fibres** are solid particles with an increased aspect ratio (the ratio of length to width); they have special properties because of their ability to be suspended in air for longer periods than dusts and other aerosols.

These can be divided into two main types of contaminant:

- those that are **dissolved in air, such as gases and vapours**
 - Dissolved contaminants will reach, and can have effects in, all parts of the respiratory system.
- those that are **suspended in air, such as fumes, dusts, mists, aerosols, fibres (also called particulates).**

Toxicity of Gases and vapours

- Asphyxiation:
 - ability of a gas or vapour to displace oxygen from air by dilution (simple asphyxiation) or;
 - Carbon dioxide
 - Nitrogen (N₂)
 - Inert gases such as helium, argon and neon.
 - by interfering with the ability of the body to transport oxygen (toxic asphyxiants).
 - Carbon monoxide
 - Cyanides
 - Hydrogen sulfide
- Irritation to the tissues in respiratory system
 - Ammonia
 - Chlorine
- Sensitisation – asthma

Particulates

Classification of particles by size:

1. Non-inhalable particle

- Larger than $200\ \mu\text{m}$ (0.2mm)

2. Inhalable particle (nasopharyngeal region)

- Smaller than $200\ \mu\text{m}$ (0.2mm)
- Deposit in nose or trachea
- Dissoluble particles are hazardous (e.g. lead fume)

3. Respirable particle (alveolar region)

- Smaller than $10\ \mu\text{m}$ (0.01mm)
- Deposition in alveolar area (e.g. pneumoconiosis)

Particulates

Table 15.3 Common particulate toxicants

<i>Particulate</i>	<i>Sources</i>	<i>Toxic effects/diseases</i>
Asbestos	Mining, manufacture of asbestos products, construction, ship building	Asbestosis, pleural plaques, lung cancer, mesothelioma
Aluminium dust and abrasives	Manufacture of aluminium products, ceramics, paints, electrical goods, fireworks, abrasives	Aluminosis, alveolar oedema, interstitial fibrosis
Beryllium	Mining and extraction, alloy manufacture, ceramics	Berylliosis, pulmonary oedema, pneumonia, granulomatosis, lung cancer, cor pulmonale
Cadmium (oxide)	Welding, manufacture of electrical goods, pigments	Pneumonia, emphysema, cor pulmonale
Chromium[VI]	Manufacture of chromium compounds, pigment manufacture, tanneries	Bronchitis, fibrosis, lung cancer
Coal dust	Coal mining	Fibrosis, coal miner's pneumoconiosis
Cotton dust	Textile manufacture	Byssinosis
Iron oxides	Hematite mining, iron and steel production, welding, foundry work	Siderosis, diffuse fibrosis-like pneumoconiosis
Kaolin	Pottery manufacture	Kaolinosis, fibrosis
Manganese	Alloy production, chemical industry	Manganism, manganese pneumonia

Nickel	Mining, production, electroplating	Pulmonary oedema, lung cancer, nasal cavity cancer
Silica	Mining and quarrying, stone cutting, construction, sand blasting	Silicosis, fibrosis, silicotuberculosis
Talc	Rubber industry, cosmetics	Talcosis, fibrosis
Tantalum carbide	Manufacture and sharpening of cutting tools	Hard metal disease, hyperplasia of bronchial epithelium, fibrosis
Tin	Mining, tin production	Stenosis
Tungsten carbide	Manufacture and sharpening of cutting tools	Hard metal disease, hyperplasia of bronchial epithelium, fibrosis
Vanadium	Steel manufacture	Irritation, bronchitis

Effects of inhaled airborne contaminants

- Physical and chemical properties of the chemicals
- The dose
- Duration of exposure
- The particles size
- Solubility
 - Phosphene gas is relatively insoluble that affect the deep lung; while the very soluble ammonia gas affects the upper respiratory tract

Thank you