European Module EMUTOM for Undergraduate Teaching of Occupational Medicine

Chapter 2.2: Toxicological agents & chemicals

Petar Bulat, MD, PhD, University of Belgrade, School of Medicine, Belgrade, Serbia
Last updated version 09/09/2012

Objectives

Knowledge objectives:

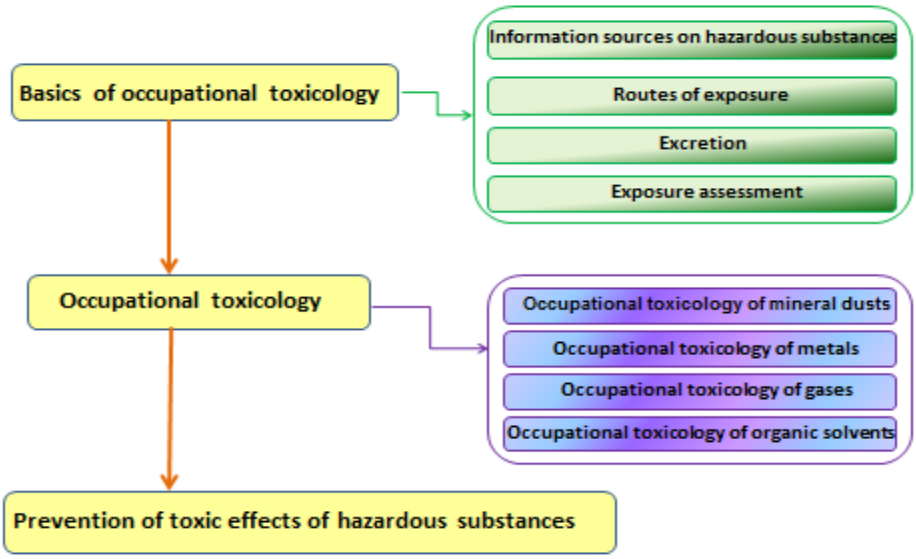
- The student identifies sources of chemical exposures at the workplace
- The student explains the basics of occupational toxicology
- The student summarizes the principles of environmental and biological monitoring
- The student gives examples how to manage potential cases of occupational poisoning

Skills/attitudes related objectives:

- The student recognizes adverse health effects of workplace exposure to chemicals
- The student recognizes and partially diagnoses case of occupational poisoning
- The student finds reliable sources of information on chemicals adverse health effects and prevention
- The student advices the worker on preventive measures related to chemical exposure

Concept Map

Framework



Glossary

Acute Exposure: Exposure to a chemical for a duration of 14 days or less.

Ambiental (environmental) monitoring: Measurement of an exposure to an agent in general workroom ambient, specific operation, worker's breathing zone.

Biological monitoring: Measurement conducted in biological sample that evaluate an exposure or biologic effect of that exposure.

Chronic Exposure: Exposure to a chemical for 365 days or more

Half-life: The time taken for the concentration of a substance, to decrease by half from a given point.

Metabolic biotransformation: Process of breakdown of hazardous substance with main objective to detoxify substance and to increase the water solubility of the substance to facilitate excretion by the kidney.

Occupational toxicology: Discipline of toxicology which identifies hazardous substances encountered in the work environment, recognizes adverse health effects of workplace exposures and establishes control measures to prevent or minimize exposures to hazardous substances.

Stochastic and non-stochastic toxic effects: Non-stochastic toxic effects are characterized by a threshold dose below which they do not occur. On contrary, stochastic toxic effects are not dose dependent so the event can randomly occur purely by chance.

Toxicology: The science discipline focused on 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.

Xenobiotic: A chemical or substance which is not normally found or produced in a human organism.

Case

Mr. Jones, a 53 year-old worker in Ni-Cd battery production visited his physician due to coughing up blood several times during the previous day. Apart from the coughing up blood episode, Mr. Jones mentioned that he coughs every day for years and that he is a chain smoker, smoking more than 30 cigarettes per day for almost 15 years. He claimed that he had shortness of breath and that he could not manage physically demanding activities. He noticed that since he is living on the second floor in last three months he needs a break on the first floor in order to reach his apartment. During the history taking his physician got information that Mr. Jones is working in the Ni-Cd battery production for 31 years. The first 24 years he was working in the production and the last 7 years he is a foreman in Ni-Cd battery production. His job position includes mostly managing production workers and occasional work in production (in case of production problems). Data on workplace exposure were not available to the consulted physician.

Physical examination revealed that Mr. Jones has dyspnoea and chest wheezing during breathing. Laboratory findings indicate increased sedimentation rate, decreased number of erythrocytes and decreased blood iron levels. Spirometry indicates decreased FVC and FEV1. Based on anamnesis, physical examination and laboratory findings, the physician decided to perform a chest X-ray, which revealed a massive tumour in lower part of right lung with exudation in right lung.

After detailed examination (including CT, MRI, bronchoscopy etc) Mr. Jones underwent surgery and chemotherapy. Three years after the treatment Mr. Jones has been asked by his employer to continue his work as a foreman in Ni-Cd battery production. He visited the occupational health specialist which had several dilemmas.

1. Basics of occupational toxicology

1.1 Information sources on hazardous substances

Due to enormous developments of industry and technology in the last decades a very wide range of chemicals is offered. It is estimated that there are 3 to 4 million of chemicals available in the world. Of course not all of them are widely used and not all of them are hazardous[1]. Having in mind that there are so many different chemicals the question of finding reliable information on chemicals becomes essential. In case of workplace exposure usually the first source of information is the Material Safety Data Sheet (MSDS) since every employer should have one for the chemicals he is using. The quality and reliability of these MSDS vary a lot since they are prepared and provided by the chemical producer. Generally, MSDS may be a good starting point in exploring properties of a hazardous substance. Information available on internet is easy to get but one should be extremely cautious and use data only from websites with proven good reputation (eg: Toxicology Data Network (http://toxnet.nlm.nih.gov/), Haz-Map (http://hazmap.nlm.nih.gov/index.php), Chemical Carcinogenesis Research Information System (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?CCRIS), etc.)

1.2. Routes of exposure

The major routes (pathways) by which toxic agents gain access to the body are the gastrointestinal tract (ingestion), lungs (inhalation), skin (topical, percutaneous, or dermal), and other parenteral (other than intestinal canal) routes. Toxic agents generally produce the greatest effect and the most rapid response when given directly into the bloodstream (the intravenous route). An approximate descending order of effectiveness for the other routes would be inhalation, intraperitoneal, subcutaneous, intramuscular, intradermal, oral, and dermal.

To exert a systemic toxic effect, a hazardous substance 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.

[1] Of course we have to keep in mind a famous Paracelsus (1493-1541) sentence "All substances are poisons; there is none which is not a poison. The right dose differentiates a poison and a remedy…"

1.3. 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.

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 15 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.

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)

1.4. Exposure assessment

Exposure assessment is the process of estimating or measuring the magnitude, frequency and duration of exposure to an agent. It could be performed through two basic concepts:

- Ambiental (environmental) monitoring
- Biological monitoring

a. *Ambiental (environmental) monitoring* is a measurement of an exposure to an agent in general workroom ambient, specific operation, worker's breathing zone. It could be performed through one of the following three strategies:

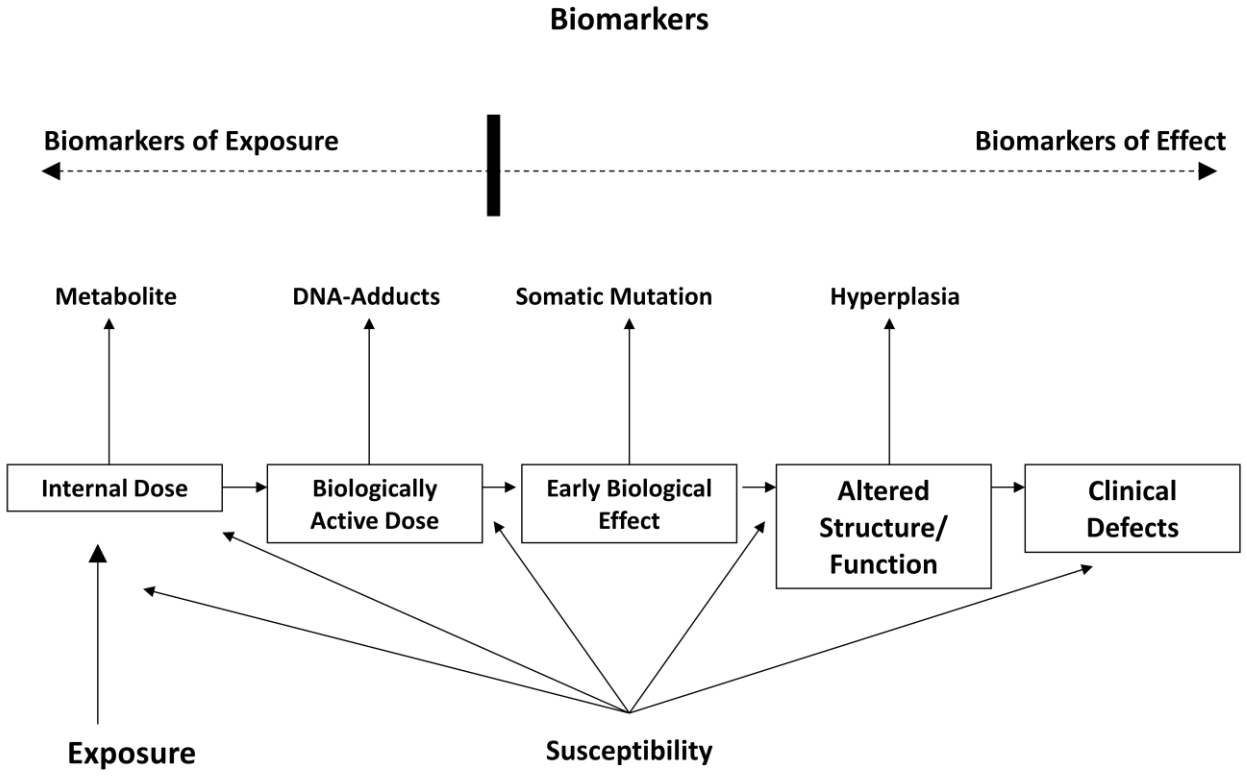
1. Continuous monitoring: provides real-time measurement of contaminant concentration in the workplace environment.
2. Integrated sampling: based on collection (and concentration) of samples over a period of time to obtain the average exposure in the sampling period (operation, whole shift…).

3. Grab (spot) sampling: based on the collection of samples at a point in time to evaluate peak exposures.

b. *Biological monitoring* is measurement conducted in biological sample that evaluate an exposure or biologic effect of that exposure. It could be performed through:

- Biological markers of exposure-measurements of toxin or its specific metabolite in a biological sample (like blood lead level; trans,trans-muconic acid as the benzene metabolite in urine and ethanol in exhaled air).
- Biological marker of effect-measurement of biological response leading to injury or disease caused by exposure (like acetyl-cholinesterase activity (in case of organophosphate pesticide exposure), erythrocyte protoporphyrine level (in case of lead exposure) and urine β2 microglobuline level (in case of cadmium exposure).
- Biomarkers of susceptibility, indicators signalling unusually high sensitivity to certain exposure like activity of enzymes involved in xenobiotic biotransformation (such as GST: glutathione *S*-transferase or NAT: N-acetyltransferase) and activity of cell DNA repair mechanisms.

It is useful to envision the processes that link exposure, dose, and effect as a continuum, as shown in Figure 1 (Adapted from William N. Rom. Environmental & Occupational Medicine 1998).



The concepts of ambiental and biological monitoring have both advantages and disadvantages. Main advantages and disadvantages are shown in table 1.

Table 1: Ambiental vs. biological monitoring

	Ambiental monitoring	Biological monitoring
Includes all sources of exposure	-	++
Excludes exposure-modifying external factors	-	+
Accounts for individual differences in uptake	-	++
Influence of individual differences in the xenobiotic biotransformation	-	++
In case of multiple agents exposure could provide summary measure	+/-	+
Availability	++	+/-
Price	+	-
Specificity	++	+/-
Sensitivity	+	+/-
Integration of past exposure	-	+
Peak values	+	-
Active participation and collaboration of sampled worker	+	-
Sample falsification	+/-	+/-
Invasive	+	-/+
Immediate results	+	-

In occupational health exposure assessment, both types of monitoring have its place. Ambiental monitoring is relatively precise, inexpensive and a broadly available source of data for exposure

assessment. Biological monitoring is unsurpassing method for exposure assessment when dermal exposure is significant as well as in cases when interindividual variability might have an important role. Consider use of both, ambiental and biological, monitoring whenever it is possible.

2. Occupational toxicology

2.1. Occupational toxicology of mineral dusts

Asbestos is the term for a group of naturally occurring hydrated silicate minerals. 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 (Chrysotile, Amosite and Crocidolite) 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.

Route of exposure: 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.
Health effects: 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.
Mesothelioma: a malignant growth in the pleura or more rarely the peritoneum. Mesothelioma may develop any time from 15 to 50 years after the first exposure to asbestos.

Exposure and prevention: In the past the persons considered to be most at risk were those 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.

2.2. Occupational toxicology of metals

In the past occupational toxicology has been dealing a lot with occupational exposure to metals, especially to heavy metals. During the previous decades with the introduction of new technologies the exposure to metals has generally decreased. Lead, once a huge problem due to occupational and environmental exposure (gasoline, lead based paints, lead batteries etc.) has now more a historic role in developed countries. This is also the case with metal mercury (used in thermometers and barometers, batteries, mercury vapour fluorescent lighting, amalgams and pharmaceuticals) and other heavy metals.

Cadmium

Since cadmium is still in significant use in developed countries and since it has similar toxicological properties like other heavy metals, it is good example for heavy metal toxicology.

Cadmium occurs naturally as cadmium sulphide with zinc blende. It is produced as by-product in zinc, lead and copper production. Cadmium is used for electro plating of steel to impart corrosion resistance properties, in a number of steel alloys, in Ni-Cd batteries, and as a stabilizer and colorant in plastics.

The most important occupational exposures occur during cadmium smelting, steel alloys production and recycling of electronic waste. It should be mentioned that cigarette smoking is also a significant source of cadmium exposure in the general population.

Route of exposure: The main route of cadmium exposure is inhalation. In case of cadmium fumes absorption may reach 40-60% of inhaled cadmium. Through digestive system only 5% of ingested cadmium is absorbed (in children absorption through digestive system is significantly higher). Once taken up by the blood, the majority of cadmium is transported bound to proteins, such as Albumin and Metallothionein. After uptake cadmium is mainly stored in the liver and kidneys. In case of exposure cessation cadmium liver body burden tends to decrease by shifting to the kidneys. Cadmium has an extremely long half-life (15-30 years) so it may be detected a long time after exposure has occurred. Its toxic effects are linked with cadmium reaction with enzyme sulfhydryl groups and consecutive enzyme activity inhibition. Due to decreased activity of enzymes involved in metabolism and consecutive lack of energy a number of processes in cells are affected. It has to be mentioned that disturbances of cell metabolism leads also to free radical production and lipid peroxidation damage of cell membranes.

Health effects: Acute inhalation of cadmium oxide fumes 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 cadmium exposure leads to emphysema caused by decreased activity of α1-antitripsine. Also, longterm exposure to cadmium leads to kidney damage. Due to accumulation of cadmium in tubular cells and consecutive lack of energy and damage of tubular cells membranes occurs, leading to damage of tubular reabsorption of calcium, phosphate, amino acids, and some low molecular weight proteins (α1-microglobuline and β2-microglobuline). Cadmium induced calcium loss and decreased activation of vitamin D in kidney, leads to bone decalcification and consecutive bone damages. According to data from the WHO International Agency for Research on Cancer (IARC) cadmium is a human carcinogen causing lung cancer.

Biological monitoring is based on biological markers of exposure blood and urine cadmium. Blood cadmium levels are principally indicative of recent exposure to cadmium rather than whole-body burdens. Urine cadmium levels primarily reflect total body burden of cadmium, although urine levels do respond somewhat to recent exposure. According to American Conference of Governmental Industrial Hygienists (ACGIH) recommendation urine cadmium should be below 5 µg/g creatinine and blood cadmium below 5 µg/L.

Therapy: Some of the chelating drugs that are beneficial for other toxic metals actually increase cadmium toxicity by mobilizing the cadmium and substantially increasing the renal concentrations and toxicity. It seems that Monoisoamyl meso-2,3-dimercaptosuccinate (Mi-ADMS) was an effective chelating agent for reduction of kidney and liver cadmium when administered either parenterally or orally.

2.3. Occupational toxicology of gases

For the purpose of occupational toxicology gases are divided in the following groups:

- Asphyxiants
    - Simple asphyxiants: Nitrogen, Methane, Argon.
    - Chemical asphyxiants: Carbon monoxide, Carbon dioxide, Hydrogen cyanide
- Irritants
    - Upper respiratory tract irritants : Chlorine, Ammonia
    - Lower respiratory tract irritants : Nitrous oxides

a) Simple asphyxiants

As the name indicates these gases cause adverse health effects by simple asphyxia. Their effects are the consequence of decreased oxygen level in local atmosphere caused by increased concentration of one of the gases from this group. If the level of oxygen in the air is reduced below 14% it will cause rapid breathing and tissue damage followed by loss of consciousness and death as oxygen levels reduce further.

Patients intoxicated by simple asphyxiants should be treated with oxygen therapy.

b) Chemical asphyxiants

Chemical asphyxiants are a heterogenous group and each member has its own mechanism of action which at the end leads to asphyxia.

Carbon monoxide is a typical representative for the whole group.
Exposure: Carbon monoxide is a colorless, odorless gas that is produced by the incomplete combustion of organic compounds. It is produced as a by-product in 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.
Health effects: Acute health effects include giddiness, headache and muscle weakness. In case of fatal carbon monoxide intoxications victims are quite often found on the ground near doors or windows. It is due to their attempt to open a door or window but due to extreme muscle weakness they could manage it. In heavily exposed patients hypoxia causes brain damage with memory loss. Also, hypoxia could cause acute heart failure.
Therapy: Patients intoxicated by carbon monoxide should be treated with oxygen therapy as well as other symptomatic and supportive therapy.

c) Irritants

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

Chlorine (Cl_2), upper respiratory tract irritant, is a greenish-yellow gas of pungent odour, over twice as dense as air. It is used in chemical and pharmaceutical production, water disinfection in swimming pools and water supply as well as in plastics manufacture. Chlorine reacts with tissue water forming hydrochloric acid, which can cause severe tissue damage in high concentrations. The hydrochloric acid is responsible for most of the symptoms in case of chlorine intoxication.
Health effects: 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.
Therapy: Patients intoxicated by chlorine should receive supportive therapy including bronchodilatator therapy. In case of pulmonary oedema high-flow oxygen therapy should be administered.

Nitrogen dioxide (NO_2), lower respiratory tract irritant - 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.
Health effects: 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.
Therapy: Patients intoxicated by nitrogen dioxide should be carefully monitored at least 48 hours after the exposure. They should receive symptomatic and supportive therapy. In case of pulmonary oedema high-flow oxygen therapy should be administered.

2.4. Occupational toxicology of organic solvents

Solvents are substances that are capable of dissolving or dispersing one or more other substances. The term 'organic' refers to substances whose molecular structure is based on a number of carbon atoms. So, organic solvents are solvents containing carbon in their molecular structure. A number of workers around the globe are exposed to organic solvents that are used in such products as paints, varnishes, lacquers, adhesives, glues, and degreasing/cleaning agents, and in the production of dyes, polymers, plastics, textiles, printing inks, agricultural products, and pharmaceuticals. One might assume that almost there is no profession which has not occasional exposure to organic solvents. We should keep in mind that apart from occupational exposure to organic solvents environmental exposure has also an important role since we are literally surrounded with organic solvents. Many organic solvents are recognized by regulatory agencies (IARC) as carcinogens (e.g., benzene, carbon tetrachloride, trichloroethylene), reproductive hazards (e.g., 2-ethoxyethanol, 2-methoxyethanol, methyl chloride), and neurotoxins (e.g., n-hexane, tetrachloroethylene, toluene).
Organic solvents are actually a heterogeneous group of substances including:

- Aliphatic hydrocarbons
- Aromatic hydrocarbons
- Alcohols
- Amines
- Esters
- Ethers
- Ketones
- Nitrated or chlorinated hydrocarbons
- Other

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.

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.

Health effects: The organic solvents adverse health effects may occur on exposure to any organic solvent and can be divided into acute and chronic effects.

Acute health effects are like in acute alcoholism. In the first phase, excitation: the exposed person is hyperactive; he is laughing and singing. It should be noted that in extremely high exposures the first phase might be so short that there are no symptoms of excitation. In the second phase, depression symptoms like headache, drowsiness, nausea and dizziness occurs. In case that exposure continues the person will lose consciousness. Most severe intoxication is followed by coma and might be fatal.

Chronic exposure to organic solvents leads to its chronic adverse health effects. In case of dermal exposure, skin manifestation may include dermatitis, hyper or hypopigmentation of skin, allergic manifestations etc. Chronic exposure to organic solvents may cause liver and kidney damage; almost all kinds of haematological changes (decreased or increased number of erythrocytes, leucocytes and thrombocytes). Quite often as manifestation of peripheral nervous system damage patients are suffering from peripheral neuropathy. Brain damage is developing insidiously through years of organic solvents exposure. First symptoms like sleepless, nervousness, light depression are rarely recognized. Usually, organic solvents adverse health effects are recognized when more prominent symptoms like irritability, sleep disorders, dementia occurs.

Since the exposure to organic solvents in developed countries is decreasing more attention is directed towards other chronic effects like carcinogenesis, mutagenesis and effects on reproductive system.

There are a number of organic solvents identified as carcinogens. One of the most common is benzene, responsible for leukemia and probably non Hodgkin Lymphoma.

(http://monographs.iarc.fr/ENG/ Classification/ClassificationsGroupOrder.pdf).

3. Prevention of toxic effects of hazardous substances

Prevention of toxic effects of hazardous substances is extremely important. This process demands multidisciplinary team work and occupational health specialists have an important role in this process. In occupational health and safety prevention there is a universally accepted hierarchy of measures:

1. Elimination
2. Substitution
3. Isolation
4. Segregation
5. Engineering controls
6. Administrative controls
7. Personal protective equipment
8. Housekeeping : provide training, signage – warning

3.1 and 3.2. Elimination – Substitution

The most effective form of prevention is simply elimination of the hazardous substance or the whole process in which it is used. However, this is not often applicable, but quite often a hazardous substance can be substituted with a less toxic one. The most well known substitutions are:
Benzene replaced with toluene
Trichloroethylene replaced with Perchloroethylene or *n*-propyl bromide
Carbon tetrachloride replaced with methyl chloroform
Asbestos replaced with synthetic and ceramics materials

3.3. Isolation

Wherever it is possible processes or operations in which exposure to hazardous substances might occur should be completely enclosed.

3.4. Segregation

When isolation is not an appropriate measure, hazardous processes or operations can be segregated from lower risk ones by placing them in a separate room, or in a separate building thereby minimizing the number of workers at risk.

3.5. Engineering Controls

In case that in processes it is impossible to implement the above mentioned measures or in case that they are insufficient there is always possibility to implement engineering controls based on local and general ventilation.
Local Exhaust Ventilation
Local Exhaust Ventilation is based on capturing contaminants near to the source of emission or application and its elimination to a safe location or further processing and in some cases returning to a

process. This measure is particularly valuable for situations that involve a point source release of toxic contaminants.

General / Dilution Ventilation

Dilution Ventilation is widely used throughout industry for the ventilation of processes with low risk for hazardous substance exposure. It is not suitable for the control of dust, mist of fume or for substances of moderate to high toxicity, or in situations where the rate of generation of contamination is non-uniform or high.

3.6. Administrative Controls

Administrative controls relate to how the interaction between personnel and the process/operation are organised. Great care is needed to ensure that procedures, once adopted, are observed; particularly in the longer term, as shortcuts and non-observance can become „custom and practice" over time, and once established can be difficult to overcome. Sometimes the hazardous operation can be conducted during the evening or night shift when fewer workers are around to be exposed. Job rotation is another method of „protecting" personnel, through controlling work patterns. The workers can often influence the extent to which they are exposed to airborne contaminants, e.g. for welding, via stance and/or working upwind of the weld.

3.7. Personal Protective Equipment (PPE)

PPE is normally considered to be the last measure in prevention of adverse health effects of hazardous substances. In case that all preceding measures are insufficient or not reasonably practicable in achieving a satisfactory workplace environment personal protective equipment should be implemented. Careful consideration must be given to the choice of the personal protective equipment. It is important that the protection is effective and comfortable; most personal protective equipment is not comfortable for extended use.

3.8. Housekeeping

Good housekeeping is particularly important in processes and laboratories where hazardous materials may be handled. Clear labelling, with relevant health and safety advice, careful and appropriate storage and good work techniques all need to be addressed. Proper preventative maintenance schedules and regular inspection/leak detection of process plant; plus frequent maintenance, examination and testing of engineering controls are essential if effective control is to be achieved and kept.

Education of employees on health hazards in the workplace and the importance of correctly using all the control measures provided, adopting recommended operating procedures and wearing personal protection, if required, is needed in order to minimise the risk to health.

References and further reading

1. Occupational toxicology (second edition). Winder C & Stacey N (eds.). CRC Press 2004.

2. Occupational Industrial, and Environmental Toxicology (second edition). Michael I. Greenberg, Richard J. Hamilton, Scott D. Phillips, Gayla J. McCluskey. Elsevier Health Sciences 2003.
3. ATSDR (Agency for Toxic Substances and Disease Registry) 2008. Public Health Statement for Cadmium. Available: http://www.atsdr.cdc.gov/phs/phs.asp?id=46&tid=15
4. DeCaprio, Anthony P. (1997). Biomarkers: Coming of Age for Environmental Health and Risk Assessment. Environmental Science and Technology, 31(7); 1837-1847.
5. International Agency for Research on Cancer (IARC) http://www.iarc.fr/
6. American Conference of Governmental Industrial Hygienists (ACGIH) http://www.acgih.org/home.htm
7. Where to find Material Safety Data Sheet (MSDS) online http://www.ilpi.com/msds/index.html