sure to CO and/or solvents. CO levels from all sources, including cigarette smoking, are additive to CO inhaled at the workplace.

Exposure to levels of CO and/or solvents that are high enough to cause sudden death is most likely to occur in enclosed spaces, such as in a reactor vessel.

The following principles from animal studies need to be considered: (a) The threshold for initiation of an arrhythmia is independent of duration of exposure but dependent on dose. (b) The heart remains sensitized until the solvent level in the blood is reduced below the threshold of initiation—not until exposure in the air ceases. (Therefore, arrhythmias after work may be due to elevated levels of workplace chemicals in the blood.) (c) Halogenated solvents are more arrhythmogenic than aliphatic solvents. (d) Other stresses, such as noise, lower the initiation threshold for arrhythmias. (See also chapters on Stress and Work Organization.)

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Arsenic, Adverse Effects

ICD-10 J57.0

Rose H. Goldman

Acute arsenic poisoning can occur after the ingestion of arsenic trioxide or lead arsenate, or after the inhalation of the toxic arsine gas (AsH_3). Acute symptoms can begin minutes to hours following ingestion of contaminated

food or drink, and include vomiting, abdominal pain and cramping, diarrhea, sometimes gastric hemorrhage. These initial symptoms can then lead to dehydration and leg cramps, followed by irregular pulse, cardiac toxicity, shock, and, in extreme cases, death. If those poisoned survive the initial illness, they usually develop hepatitis and pancytopenia within 1 week, and may also experience peripheral neuropathy 1-3 weeks after the exposure. The blood changes are usually reversible once exposure ceases.

Arsine gas is highly toxic. It has been reported that one half-hour of exposure to 25-50 ppm can be lethal. A patient may present initially with dizziness, headache, abdominal pain, hemolysis, hyperbilirubinemia, jaundice, and kidney failure.

The diagnosis of acute arsenic poisoning is supported with urine confirmation of arsenic exposure. In an emergency situation, a spot urine sample is sufficient. In the setting of acute symptoms due to poisoning, the spot urine samples would be expected to exceed 1000 μg/L reference values usually are less than 50 μg/L or 50 μg/gram creatinine). Recent ingestion of seafood may elevate total urinary arsenic levels markedly for the subsequent 48 hours due to the presence of a relatively nontoxic organic form of arsenic, so a diet history is critical. If diet information is not available, then the total urine arsenic can be speciated into total and elemental arsenic. Whole blood arsenic may be elevated early in an acute poisoning event, but will decline faster than the urine levels.

Most human problems with arsenic are due to chronic ingestion or inhalation, rather than to acute poisoning. One of the characteristic developments is that of a sensorimotor peripheral neuropathy. In mild cases, the patient may present with paresthesias. In more serious cases, there may be stocking-and-glove sensory deficits, painful dysesthesias (painful burning sensations in the soles of the feet), loss of vibration, and positional sense, gait disorders, motor weakness, and loss of deep tendon reflexes. Some central nervous system effects have been reported, including confusion, delirium, encephalopathy, and seizures. More severe cases of chronic intoxication can cause hematological effects, kidney damage, and liver disease. Skin manifestations of chronic exposure, particularly after long-term ingestion of arsenic in drinking water or for medicinal purposes, include chronic eczema, patchy hyperpigmentation, keratoses (raised warty lesions especially on palms and soles), and skin cancers (squamous and basal cell carcinomas). Nails may be marked by horizontal white bands known as Mees lines. Recent studies and analyses have suggested that chronic ingestion of arsenic is associated with an increased incidence of bladder and lung cancer at arsenic concentrations in drinking water that are below 50 μg/L (50 ppb), which was the previous EPA maximum contaminant level (MCL) for arsenic in drinking water. In early 2002, the EPA adopted a new standard for arsenic (10 ppb) to replace the previous 50 ppb standard; water systems must comply with the new 10 ppb standard by January 23, 2006.

Chronic inhalation of arsenic compounds can cause conjunctivitis, inflammation of the mucous membranes, and sometimes perforation of the nasal septum at very high exposure levels. Human studies have reported that inhalation of inorganic arsenic is strongly associated with lung cancer.

Urine arsenic levels are useful for documenting recent exposures within the last few days after exposure, but are less useful for documenting more distant exposures. Screening urine tests are typically measured for total arsenic, so persons should be advised to eat no fish or shellfish for at least 48 hours in order to eliminate measurement of organic (nontoxic) forms of arsenic found in fish. In that way, the urine arsenic is more reflective of the more toxic inorganic forms of arsenic. Inorganic arsenic is also bound in hair and nails and may persist for months after urine arsenic values have returned to baseline. However, hair and nail assessments are problematic as a reflection of internal dose because of the difficulty in removing the exogenous arsenic and problems with reliability of testing in commercial laboratories.

Occurrence

The number of cases of adverse effects of arsenic and the proportion that is occupationally related are not known.

Causes

Arsenic is a naturally occurring element found in the earth's crust and is found in numerous ferrous and nonferrous ores. It is classed as a metalloid, or transition element (Group V in the periodic table) because it complexes with metals but also reacts with other elements such as oxygen, hydrogen, chlorine, carbon, and sulfur. Arsenical compounds can be grouped as inorganic, organic, and arsine gas. The most common valence states are the metalloid (elemental, 0), arsenite (trivalent, +3), and the arsenate (pentavalent, +5). Toxicity of these arsenical compounds vary, with the most toxic being the inorganic trivalent arsenic compounds followed by organic trivalent arsenic compounds, inorganic pentavalent arsenic compounds, organic pentavalent compounds, and elemental arsenic. Some fish and crustaceans contain large amounts of forms of organic arsenic ("fish arsenic")—arsenobetaine (a trimethylated arsenic compound) and arsenocholine, both of which are thought to be of negligible toxicity.

Exposures come from naturally occurring and human-made sources. Natural sources include volcanic eruptions, and leaching of arsenic from rocks and soil into drinking water. Arsenic compounds are used in a number of commercial and industrial endeavors. Metallic arsenic is used as an alloy, such as for hardening lead in bearings and to improve the toughness and corrosion resistance of copper. Arsenic trioxide and arsenic pentoxide are used in the manufacture of calcium, copper, and lead arsenate pesticides. Arsenic

compounds are also used in herbicides. Sodium arsenate is used in ant killers and in animal dips acting as insecticides. Arsenic and arsenic trioxide are used in the manufacture of low-melting glasses. Fowler's solution (sodium arsenite) was used in the past to treat leukemia, psoriasis, and other diseases; arsanilic acid is still used in some veterinary medicines. Some arsenic compounds are found in Chinese and Indian traditional medicines. Copper acetoarsenite is used as a wood preservative, and exposure can occur from burning plywood treated with an arsenic wood preservative or from dermal contact with treated wood. Arsenic has been used in some pigments ("Paris green") and also in preservatives in tanning and taxidermy. Recent new uses for arsenic compounds have been found in the semiconductor industry. Crystals of gallium arsenide (GaAs) have been found to be better superconductors than silicon, and so are being used in semiconductors, integrated circuits, and scientific instruments. The highly toxic arsine gas (AsH_3) is used to make gallium arsenide.

Occupational exposure to arsenic can occur during metal smelting, where arsenic occurs as a contaminant or when heated ores give off arsenic trioxide (As_2O_3, or "white arsenic"). Dust can gather in flue dust, and therefore furnace and flue maintenance operations have a high risk of exposure. Fly ash in coal boilers may also contain arsenic, and thus present a hazard during maintenance. Workers involved in the manufacture or use of arsenic-containing pesticides may also be exposed. Persons who handle wood treated with chromated copper arsenate, such as in making house decks or playgrounds, may be exposed. Inhalation of fumes from burning arsenic-treated wood has caused arsenic poisoning. Epidemiolgic studies of pesticide production workers, sprayers, smelter workers, residents near polluting industries, and patients treated with arsenicals have demonstrated an association between respiratory exposure to arsenic and an increased risk of lung cancer. A current episode of mass arsenic poisoning recently began in West Bengal, India, in which high levels of arsenic have been leaching from natural underground sources to contaminate newly drilled wells, leading to more than 1 million people drinking arsenic-contaminated water (above 50 µg/L). Thousands have been found to have arsenic-related skin lesions and liver problems.

Pathophysiology

Arsenic and its compounds enter humans through ingestion or inhalation. The rate of absorption is highly dependent on the solubility of the compound, and also on the valence state of the arsenic. After absorption, arsenic is initially bound to proteins in blood, but then rapidly cleared from blood as it is redistributed to the liver, spleen, kidneys, lungs, and gastrointestinal tract within about 24 hours. A major mechanism of toxicity is through trivalent arsenic binding to SH-groups (such as proteins, glutathione, and cysteine) and interfering with numerous enzyme systems, including those

involved in cellular respiration and DNA repair. Another mechanism of toxicity is through "arsenolysis," in which pentavalent arsenate substitutes for phosphate in biochemical reactions, leading to an uncoupling of oxidative phosphorylation, disruption of cellular oxidative processes, and consequently endothelial cellular damage. The clinical manifestations of these cellular changes are loss of capillary integrity, increased permeability of blood vessels, generalized vasodilation, transudation of plasma, hypovolemia, and shock. Pentavalent arsenic (+5) and arsine are converted to trivalent arsenic (+3) in vivo.

Most trivalent arsenic is metabolized to dimethylarsinic acid (DMA) and monomethylarsonic acid (MMA). DMA, MMA, and unchanged inorganic arsenic are then excreted in the urine, with an overall half-life of about 10 hours. Organic arsenic compounds are excreted unchanged in the urine.

Ingested inorganic arsenic crosses the placenta in humans. Studies of women who work in, or live near, metal smelters have shown an association between arsenic and higher than normal spontaneous abortion rates, but these studies may be limited because of methodological questions.

Prevention

Engineering controls can be used to control fumes in smelting and manufacturing. Personal protective equipment and clothing should be worn when performing maintenance work. Environmental exposures can be controlled by regulations/and or guidelines that limit the amount of arsenic in air and water. Since some forms of arsenic are carcinogens, there is no totally safe level. In 1993, WHO adopted a provisional guideline value of 10 μg/L as a realistic limit, given measurement capabilities. In 2001, EPA lowered the maximum level of arsenic permitted in drinking water to 10 μg/L. The current acceptable levels for reducing adverse health effects due to air exposures are the ACGIH TLV of 0.01 mg/m^3, the OSHA PEL of 0.01 mg/m^3 TWA, and the NIOSH REL of 2 μg/m^3 (ceiling limit for 15 minutes).

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Asbestos-Related Diseases

ICD-10 J61, J92.0

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Exposure to asbestos causes asbestosis, nonmalignant pleural disease, lung cancer, and mesothelioma. Exposure has also been associated with increased risk of cancer of the larynx, and pharynx and certain cancers of the gastrointestinal tract. Some studies have also associated cancer of the kidney with asbestos exposure, but other studies have not. Adverse effects of asbestos have been known since about the late 19th century. The purpose of this chapter is to describe disease control measure common to all asbestos-related diseases. (See Asbestosis, Laryngeal Cancer, Lung Cancer, Mesothelioma, and Pleural Diseases, Asbestos-Related.)

Asbestos is a naturally occurring class of silicate fibers mined primarily by open-cast mining. More than half of the world's production comes from mines in the Soviet Union and Canada. Other producing countries include South Africa, Zimbabwe, the United States, Italy, China, and Australia. Worldwide production peaked at about 6 million tons in 1973. Currently, U.S. production and consumption has declined dramatically because of regulation of the use of asbestos and litigation because of the health effects of asbestos exposure. The U.S. no longer mines asbestos, and U.S. consumption of imported (mostly Canadian) asbestos was down to 9000 tons in 2002. Despite what is known about the devastating effects of asbestos exposure, use has continued and even expanded in many developing countries.

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Cover photographs by Earl Dotter illustrate airborne, ergonomic, safety, and physical hazards at work, all of which are preventable.

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