Chapter 20

HAZARDOUS SUBSTANCES IN THE WORKPLACE

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INTRODUCTION

Military personnel are exposed to numerous metals, chemicals, and solvents in the workplace, many of which can have deleterious effects on human health. This chapter provides a short list of chemicals and other hazards common to many military installations. Included for each chemical is its use, exposure routes, toxicology, and in some cases, recommended medical surveillance. There are several governing bodies and organizations that publish standards for occupational exposures, which vary in some cases. Because the military uses different sources for exposure limits, which can vary by branch, the limits are not provided here. However, in many cases the military uses the most stringent guidelines recommended.

OCCUPATIONAL EXPOSURE LIMITS

Occupational exposure limits can be either legally enforceable standards established by regulatory agencies or guidelines determined by research groups. In either case, the goal of these exposure limits is to protect workers over their entire working lifetime. The most commonly encountered organizations are described below.

Occupational Safety and Health Administration

The Occupational Safety and Health Administration (OSHA) is a federal agency in the Department of Labor. OSHA issues workplace health and safety regulations, such as exposure limits, employee access to information, conditions governing the use of personal protective equipment, and requirements for safety procedures. It is also responsible for enforcing its standards.[1]

OSHA promulgates permissible exposure limits (PELs), which are legally enforceable standards.[2] PELs are set based on chronic exposure and indicate the maximum values for the "employee's average airborne exposure in any 8-hour work shift of a 40-hour work week which shall not be exceeded"; otherwise known as the 8-hour time-weighted average.[2] For certain substances, OSHA has also set ceiling limits, the concentration of the substance that should never be exceeded. The OSHA action level is set at half the PEL value and indicates the level at which medical surveillance should be initiated.

American Conference of Governmental Industrial Hygienists

The American Conference of Governmental Industrial Hygienists (ACGIH) is a professional association of industrial hygienists and related professionals that publishes exposure guidelines known as threshold limit values (TLVs) and biological exposure indices (BEIs).[3] Unlike OSHA PELs, these are recommendations and not legal standards. They are based solely on health factors with no consideration of economic or technical feasibility and, therefore, tend to be more stringent than OSHA levels. In addition to the time-weighted average and ceiling limit, for certain substances, the ACGIH defines a short-term exposure limit as the concentration below which workers can be exposed for a period of up to 15 minutes.

National Institute of Occupational Safety and Health

The National Institute of Occupational Safety and Health (NIOSH) is a federal agency under the Centers for Disease Control and Prevention. It is responsible for conducting research and making recommendations for the prevention of work-related injury and illness.[4] NIOSH publishes recommended exposure limits (RELs). As with TLVs and BEIs, RELs are generally updated more frequently and are stricter than PELs.

American Industrial Hygiene Association

The American Industrial Hygiene Association (AIHA) is a professional association, like the ACGIH. Its major goals are the advancement of the study and control of industrial health hazards, and the dissemination of technical knowledge.[5] AIHA publishes workplace environmental exposure levels (WEELs), which are health-based guidelines published annually. Like RELs, TLVs, and BEIs, WEELs are not legally enforceable.

METALS

Arsenic

Forms

Arsenic is a naturally occurring metal.[6] It exists in several forms: elemental, inorganic, organic, and gaseous. Elemental (or metallic) arsenic is a steel grey solid material. Arsenic more commonly exists as inorganic salts, in one of three oxidation states: -3, +3, or +5. Organic arsenic compounds can be further described as organometals, otherwise known as organoarsenic compounds, characterized by a chemical bond between arsenic and one or more carbon atoms. In inorganic form, arsenic generally combines with oxygen, chlorine, or sulfur. Arsine is the gaseous form of arsenic.

Uses

Elemental arsenic is used as an alloying agent in ammunition and solders, an antifriction additive for bearings, and a structural strengthening agent for lead batteries. Organoarsenic compounds, namely cacodylic acid, disodium methyl arsenate, and monosodium methyl arsenate, are used as pesticides. Other organoarsenic compounds are used as additives in animal feed to control intestinal coccidian parasites in some poultry and swine farms. Inorganic arsenics, such as arsenic acid, arsenic pentoxide, and arsenic trioxide, are also used as pesticides in the United States. Arsenic trioxide and arsenic acid are also decolorizers and fining agents used in the production of bottle glass and other glassware. Finally, arsine gas is used in the microelectronics industry for gallium-arsenide semiconductor production and as a source of dopant arsenic atoms.

Routes of Exposure

Arsenic compounds can be ingested, inhaled, and absorbed through the skin. The efficiency of absorption depends on the form of arsenic, its solubility, and the route of exposure. In general, both organic and inorganic forms of arsenic are well absorbed through the gastrointestinal tract, but dermal uptake is low. Inhalational exposure usually occurs only with trivalent arsenic oxide or arsine gas.

Toxicology

Inorganic arsenic compounds have been recognized as a human poison since ancient times.[7] Arsenic is an irritant to the skin and gastrointestinal tract and has numerous long-term health effects. Unfortunately, little is known about the effects of organoarsenic compounds in humans. Studies in animals show that most organoarsenic compounds are less toxic than the inorganic forms but still have toxic effects on the digestive and urinary tracts.

Acute toxicity. Acute arsenic poisoning commonly occurs when arsenic is ingested in large doses as inorganic arsenic. This occurs when arsenic has contaminated drinking water wells, but it does not routinely occur in the occupational setting. Individuals who ingest large quantities of inorganic arsenic will develop symptoms within minutes to hours after exposure. Symptoms can range from gastrointestinal discomfort, including nausea and vomiting, to severe abdominal pain, abdominal cramps, and profuse diarrhea. In the worst cases, hepatic necrosis associated with markedly elevated liver enzyme levels and acute renal failure can occur. Cardiovascular effects can also result from acute arsenic poisoning.[7] Seizures, coma, and circulatory collapse leading to death may result when individuals are exposed to more than 70 mg of arsenic. Persons who recover from acute arsenic poisoning may develop delayed peripheral neuropathy, which presents as symmetrical sensory loss in the distal lower extremities.

Arsenic dusts and vapors are both respiratory and eye irritants. Inhalational exposure of arsine gas results in intravascular hemolysis. The initial symptoms of exposure include headache, nausea, and chest tightness. Shortly afterward, the triad of abdominal pain, jaundice, and oliguria develop. Death can occur if exposures exceed 10 ppm.

Chronic toxicity. The skin is the major target organ in chronic inorganic arsenic exposure. Long-term ingestion produces characteristic skin changes on the palms of the hands and feet, including hyperkeratosis and hyperpigmentation with spots of hypopigmentation. Workers chronically exposed to arsenic also experience these dermal manifestations. Individuals who have a history of chronic arsenic ingestion have an elevated risk of skin cancer, including basal cell and squamous cell carcinoma.

Peripheral neuropathy can develop in individuals who have chronic low-level arsenic ingestion. The neuropathy is sensory in nature and includes paresthesia or numbness; in severe cases, the peripheral neuropathy can affect the motor neurons. Liver damage and peripheral vascular disease can also result from chronic low-dose exposure to arsenic. Individuals may be accidentally exposed to arsenic pesticides or they may drink arsenic-contaminated water. However, the most frequent source of arsenic poisoning in the United States is eating food contaminated with arsenic.[7]

The International Agency for Research on Cancer (IARC) classifies arsenic as a human carcinogen. In addition to skin cancer, arsenic exposure has been associated with an increased risk of developing bladder, lung, liver, kidney, and prostate cancer.[7]

Medical Surveillance

Arsenic compounds, both inorganic and organic, are excreted in the urine, making urinary testing the most reliable means of detecting arsenic exposures. Although most tests measure the total amount of arsenic present, organic and inorganic forms can be parsed. Because the half-life of arsenic in the body is only 10 hours, analysis of urine can only reveal recent exposures. Arsenic also accumulates in hair and nails, and testing either can detect exposures over the previous 6 to 12 months. However, the value of hair and nail testing is questionable in industrial settings because of the difficulty in removing all external contamination.[6]

The Department of Defense (DoD) recommends medical monitoring of persons with potential for arsenic exposure at or above the action level.[8] For arsenic, the DoD instruction recommends an annual exam, in addition to a baseline and termination exam. The exams focus on the respiratory system and include work history, medical history (particularly smoking and respiratory history), physical examination of the nasal tract, pulmonary system, and skin, and a chest x-ray.

Cadmium

Forms

In its pure form, cadmium is a soft, silver-white, electropositive metal.[9,10] It is found in the earth's crust, associated with zinc, lead, and copper ores. Cadmium also exists in various inorganic forms, such as cadmium oxide, cadmium chloride, and cadmium sulfate.[9,10]

Uses

The most common use for cadmium is as an active electrode material in nickel-cadmium batteries. Cadmium compounds are also used for electroplating and to impart corrosion resistance to other metals. Cadmium alloys are used in solder and jewelry. Cadmium sulfides and selenides are used in materials where heat stability and alkali resistance are desired, such as in pigmented rubber, inks, plastics, and ceramics. Cadmium is also used in photoelectric cells and semiconductors.[9,10]

Routes of Exposure

In the workplace, most cadmium exposure occurs via inhalation. Workers breathe in cadmium dusts and fumes during smelting, plating, and welding processes. Inhaled cadmium is relatively well absorbed, with about 10% to 40% reaching the bloodstream. The efficiency of absorption is based on particle size and chemical composition.

Non-occupational exposure is mainly through ingestion from dietary sources. Meat, shellfish, and vegetables are the primary sources of contamination. Cadmium is not as well absorbed through the gastrointestinal tract; only about 5% to 10% reaches the blood.[9,10]

Toxicology

Cadmium affects the kidneys, lungs, bones, and heart. Its acute effects target the pulmonary and renal systems.[7]

Acute toxicity. Acute cadmium poisoning results from inhalation of large doses of soluble cadmium compounds, such as cadmium oxide, chloride, or carbonate. This mainly occurs in the occupational setting from industrial accidents. Symptoms develop after a 4- to 10-hour latent period and generally consist of sore throat, headache, myalgia, nausea, and a metallic taste. Eventually cough and dyspnea develop, and death occurs 7 to 10 days after exposure from fulminant chemical pneumonitis and respiratory failure. Exposures to concentrations above 40 mg/m^3 for 1 hour or 9 mg/m^3 for 5 hours have resulted in fatalities. Acute toxicity from high-dose ingestion is rare but results in nausea, vomiting, headache, abdominal pain, and liver and renal failure.

Chronic toxicity. Chronic exposure results in kidney damage via tubular nephropathy with an increased urinary excretion of small proteins, such as β_2-microglobulin and retinol-binding protein. This can result in nephrolithiasis and eventually progress to Fanconi syndrome. The renal dysfunction impacts

calcium metabolism and, combined with effects on parathyroid function and vitamin D metabolism, leads to osteomalacia with resulting propensity for pathological fractures. Chronic inhalation of cadmium results in irreversible emphysematous lung injury. Other consequences of cadmium exposure are anemia, eosinophilia, yellow discoloration of the teeth, occasional ulceration of the nasal septum, and anosmia.

Long-term ingestion of cadmium can lead to itai-itai (or "ouch-ouch") disease. Itai-itai disease is characterized by severe osteomalacia and osteoporosis. The symptoms of itai-itai disease include back and joint pain, height loss, a broad-based or waddling gait, and, in severe cases, fatal renal failure.

Cadmium is classified as a human carcinogen. Occupational exposure to cadmium has been implicated in lung cancer. Cadmium accumulates in the kidney and pancreas and may be associated with cancer of both organs.

Medical Surveillance

OSHA requires medical monitoring of employees who are, will be, or have been exposed to cadmium at the action level, which is one half of the OSHA PEL of 15 mg/m^3. Employees who perform welding, cutting, brazing, burning, or grinding on surfaces that were painted with cadmium-containing paints; do electrical work using cadmium-coated conduit; use cadmium-containing alloys; perform fusing of reinforced steel by cadmium welding; maintain or retrofit cadmium-coated equipment; or perform wrecking and demolition where cadmium is present must be monitored.

The OSHA standard requires baseline, annual, and termination exams. The exams must include a medical and work history, emphasizing exposure, smoking history, reproductive status, and medication use, and any conditions of the cardiovascular, respiratory, renal, hematopoietic, and musculoskeletal systems; a physical exam with focus on blood pressure and the respiratory and urinary systems, including a prostate exam; a chest x-ray; pulmonary function tests; and lab work including complete blood count, blood urea nitrogen and creatinine, blood and urine cadmium levels, and urine β_2-microglobulin.[10] The DoD requirements for medical surveillance are the same as the OSHA regulations.[8]

Chromium

Forms

Chromium is a brittle, gray metal that exists as chromite or ferrochromium in the environment.[11] Forms of chromium used industrially include chromates, chromium alloys or compounds, and chromic acid. The valence state, or electric charge due to the ions present, is the essential factor in determining toxicity. Hexavalent chromium is the most toxic form.

Uses

Chromium compounds provide heat resistance and corrosion resistance. Chrome plating is used on automotive parts, household appliances, tools, and machinery for resistance against corrosion and heat as well as for decoration. In addition, chromate pigments are added to paints, dyes, textiles, rubber, plastics, and inks. Chrome-based orthopedic devices are used for joint replacement. Also, the radioisotope ^{56}Cr is used for erythrocyte labeling in nuclear medicine.

Routes of Exposure

Chromium may be absorbed via ingestion, inhalation, or dermal routes. The valence state influences degree and rate of uptake, with the soluble hexavalent forms absorbed most readily. Most facile absorption occurs via inhalation. Following inhalation, up to 80% of hexavalent chromium is absorbed into the bloodstream. After oral exposure, absorption of chromium through the gastrointestinal tract is low, estimated to be less than 5%. Chromium can penetrate the skin to some extent, but far less is absorbed compared to inhalation exposure.[11]

The greatest occupational hazards historically have been in chromate production, with exposure to hexavalent chromium. However, stainless steel workers and welders are also exposed to chromium fumes and compounds; production and arc welding of stainless steels releases chromium. Workers also may be exposed to chromates through their use in the paint, textile, leather, glass, and rubber industries and in lithography, printing, and photography. Electroplaters are exposed to chromic acid mists. Also, certain cements have a high chromium content.[11,12]

Toxicology

The water-soluble hexavalent chromium compounds, such as chromic acid or chromates, have an extremely high boiling point. However, they can be inhaled when chromium is dissolved in droplets and salt aerosols that easily penetrate the respiratory tract and act as severe irritants of the nasopharynx, larynx, lungs, and skin.[7,11]

Acute toxicity. Acute exposure to high concentrations of water-soluble chromium compounds, such as chromic acid or chromates, causes irritation of the

eyes, nose, throat, and respiratory tract. Acute oral exposure causes nausea, vomiting, and abdominal pain. Ingestion of high levels of chromium can result in acute renal failure and death from resulting uremia.

Chronic toxicity. Chronic inhalation of chromic acid or chromates may cause ulceration, bleeding, and erosion of the nasal septum. Cough, chest pain, dyspnea, and development of chromium-induced asthma are other sequelae of long-term inhalation toxicity. Chronic exposure to chromic mist results in conjunctivitis.[7,11]

Dermatologic manifestations are common in chromium workers. Chrome ulcers, penetrating lesions of the skin, occur chiefly on the hands and forearms. These ulcers are thought to result from a direct necrotizing effect of the chromate ion where there has been a break in the epidermis. The ulcer is relatively painless, heals slowly, and produces a characteristic depressed scar. Sensitization dermatitis, ranging from localized erythematous or vesicular lesions at points of contact to generalized eczematous changes, has also been reported.[7,11]

Chromium is a recognized by IARC as a human carcinogen. It is associated with cancer of the nasopharynx, trachea, bronchus, and lung. When hexavalent chromium is introduced into the cell, it can damage the genetic material and produce DNA adducts and strand breaks. Animal and cellular studies have revealed that hexavalent chromium causes mutagenesis, produces reactive oxygen radicals, and interferes with both cellular regulation of apoptosis and repair of DNA damage, which may arrest the cell cycle.[11]

Medical Surveillance

Urine chromium levels may be useful for assessing recent exposure. However, there are no practical laboratory methods for monitoring chronic exposure aside from monitoring changes resulting from end organ damage. For example, medical surveillance may detect changes in pulmonary function when workers develop respiratory disease due to exposure.

OSHA requires medical monitoring of persons with chromium exposure at or above the action level, which is one half the OSHA PEL of 5 $\mu g/m^3$.[12] The OSHA regulation requires baseline, annual, and termination exams. The exams must include a medical and work history, emphasizing past chromium exposure, a smoking history, a history of respiratory disorders and skin disorders, and a physical exam focusing on the respiratory tract and skin. DoD requirements for medical surveillance align with the OSHA regulations.[8]

ORGANIC EXPOSURES

Cyanide

Forms

The cyano group is a negatively charged ion species with three molecular carbon-nitrogen bonds.[13] Hydrogen cyanide exists as a colorless gas at ambient temperature and has a bitter, almond-like odor. Cyanide salts, such as sodium cyanide and potassium cyanide, are white solids with a similar odor. In organic cyanides, the cyano group is bound to a carbon, such as methyl. Other forms of cyanide include the thiocyanates, which are cyanide compounds that contain sulfur. Ferrocyanides, such as sodium, potassium, and calcium ferrocyanide, have highly stable bonds with iron and do not easily break down to lethal compounds.

Uses

Cyanide is mainly used in gold and silver mining, where it helps dissolve the precious metals from the impure ores. Cyanide is also used in electroplating for stabilizing metal ions prior to their deposition. It is used in jewelry making and for sepia toning in photography. In some areas of the world, cyanide is used as pesticide.[13]

Routes of Exposure

Cyanide can be absorbed via inhalation, ingestion, and dermal uptake. Hydrogen cyanide is absorbed within seconds following inhalation exposure. Following ingestion, cyanide salts rapidly enter the bloodstream from the gastrointestinal tract. On the other hand, ferrocyanides are poorly absorbed due to the iron, and thus relatively nontoxic. Chronic dermal exposure to cyanide can occur in occupational settings. Case reports in humans and studies in animals have shown toxic effects following only dermal exposure, but little is known about the toxicokinetics of dermal absorption.[13]

Toxicology

The cyanide anion is an inhibitor of the enzyme cytochrome *c* oxidase, part of the electron transport chain. It disrupts the electron transport chain in aerobic respiration and interferes with adenosine 5′-triphosphate metabolism.[13] Tissues that depend highly on aerobic respiration, such as the central nervous system (CNS) and the heart, are particularly affected.

Acute toxicity. Acute inhalation, ingestion, or dermal absorption of high concentrations of cyanide results in neurological depression, convulsions, coma,

and death due to depression of the respiratory centers. Those who survive acute poisoning can develop parkinsonism and dystonia.[13]

Chronic toxicity. Chronic exposure to low concentrations has been associated with respiratory, endocrine, and CNS toxicities. Workers subjected to low levels of airborne cyanide reported dyspnea, presumably caused by a decrease in pulmonary phospholipids and loss of pulmonary surfactant. CNS effects include vague symptoms such as fatigue, dizziness, headaches, and tinnitus, and more severe symptoms such as paresthesia, syncope, hemiparesis, and hemianopia. Chronic cyanide exposure also results in adverse thyroid effects. In the body, cyanide metabolized to thiocyanate interferes with iodine uptake and utilization by the thyroid gland. Chronic exposure leads to reduced thyroid hormone levels, elevated thyroid stimulating hormone levels, and goiter. [13]

Medical Surveillance

If cyanide exposure is suspected, blood and urine levels of cyanide and thiocyanate can be measured. However, there are no formal OSHA or DoD regulations regarding routine medical surveillance for workers with potential for cyanide exposure.

Diesel Exhaust

Diesel exhaust is a mixture of gases and particulates produced during the combustion of diesel fuel. Gaseous components of the exhaust include carbon dioxide, oxygen, nitrogen, water vapor, carbon monoxide, nitrogen compounds, sulfur compounds, and low-molecular-weight hydrocarbons.[14]

Exposure

Uptake of diesel exhaust, and its constituents, occurs via inhalation. Workers in the following occupations have the greatest risk for exposure: mine workers, railroad workers, bus and truck drivers, truck and bus maintenance garage workers, loading dock workers, firefighters, heavy equipment operators, and farm workers.[14]

Toxicology

The primary organ system affected by diesel exhaust is the respiratory tract. Diesel exhaust particles become deposited in the airways and activate alveolar macrophages. These macrophages release cytokines and growth factors, leading to inflammation, epithelial cell injury and fibrosis, and goblet and alveolar lining cell proliferation.[14]

Acute toxicity. Acute exposure to diesel exhaust causes acute irritation of the eyes, throat, and respiratory tract, as well as neurophysiological symptoms (lightheadedness, nausea). Symptoms of acute exposure mostly consist of respiratory effects such as cough and phlegm.[14,15]

Chronic toxicity. While few studies of chronic exposure in humans have been published, extensive evidence from animal studies show that diesel exhaust poses a chronic respiratory hazard. Chronic animal inhalation exposure studies reveal dose-dependent inflammation and histopathological lung changes in several animal species including rats, mice, hamsters, and monkeys. Studies have also found a statistically significant correlation between long-term diesel exhaust exposure and an increased risk of lung cancer.[15]

Medical Surveillance

Several biomarkers correlate well with diesel exhaust exposure. Metabolomics studies of various polycyclic aromatic hydrocarbons found in diesel exhaust were also correlated with postdeployment serum studies of deployed personnel exposed to diesel exhaust. Serum immune mediators and microRNAs were also found to be elevated in these service members.[16–19]

OSHA has not established a standard for diesel exhaust as a unique hazard; however, exposures to various components of diesel exhaust are addressed in specific standards. Likewise, the DoD does not have specific regulations or recommendations for monitoring of workers exposed to diesel exhaust.

Diisocyanates

Isocyanates are a family of highly reactive chemicals. Diisocyanates are compounds of two isocyanate groups.[20,21]

Uses

Previously, military vehicles were painted with standard alkyl and acrylic paints, but these paints absorbed chemical warfare agents. To avoid this hazard, the military switched to polyurethane paints, which are chemical agent-resistant coatings (CARCs). There are three types or layers of coatings in the CARC system: an epoxy polyamide primer, an aliphatic polyurethane paint, and epoxy polyamide enamel. Each of the coatings is supplied as a two-component system. When the two components are combined, a chemical reaction converts them into an impermeable coating material. The polyurethane systems contain unreacted isocyanate or diisocyanate groups in the uncured resin, which irritate the

skin and sensitize the respiratory system. Once cured, polyurethanes no longer release isocyanates unless heated.[20,21]

Diisocyanates are also used in insulation, upholstery, and furniture. Spray-on polyurethane products containing isocyanates are used for protective coatings for truck beds, trailers, boats, foundations, and decks and to protect cement, wood, fiberglass, steel, and aluminum.

Routes of Exposure

Isocyanates can be ingested, inhaled, and absorbed through the skin. However, most occupational exposure occurs via inhalation when workers breathe in vapors, mist, or smoke released by uncured polyurethane products.[20,21]

Toxicology

Isocyanates are powerful irritants to the mucous membranes. They cause airway epithelial damage resulting from extensive inflammation and increased bronchial hyperresponsiveness.[7]

Acute irritation. Diisocyanates are severe irritants of the eyes and gastrointestinal and respiratory tracts. Direct skin contact can also cause marked inflammation. Symptoms include burning and watering of the eyes, burning sensations in the nose and throat, sore throat, productive cough, and in some cases tightness of chest, discomfort, a feeling of breathlessness, and a temporary reduction in lung function. The severity of symptoms depends on the extent of exposure, the tissue exposed, and individual susceptibility, but it is generally independent of the individual's exposure history. These acute symptoms are generally reversible if the victim is removed from the source of toxicant or, in cases of skin contact, the skin is decontaminated.

Sensitization. Sensitization, however, is a systemic response and is not limited to the area of contact. Sensitization usually does not occur on initial exposure but can develop within the first few months of exposure to an isocyanate environment. Sensitization may develop as a result of repeated overexposure or a large single dosage from a spill or other accident. Once sensitized, subsequent exposures can cause very strong allergic reactions. A sensitized individual may react to extremely low airborne levels. The response is similar to asthma, that is, coughing, wheezing, tightness in the chest, and shortness of breath. The skin sensitization reaction is allergic dermatitis, which includes symptoms such as rash, itching, hives, and swelling of the arms and legs. If an individual is sensitized to isocyanates, complete removal of the individual from area of potential exposure to isocyanate vapor or mist is necessary.

Medical Surveillance

There are no practical biological methods for monitoring chronic exposure to diisocyanates aside from screening for antibody production, indicating sensitization, and changes due to end organ damage. While OSHA has set the PEL for isocyanate exposure at 0.02 ppm, it has not developed a required medical surveillance program.[21] However, it does provide general guidance on medical surveillance for employers. Likewise, the DoD does not have specific regulations or recommendations regarding monitoring of workers exposed to isocyanates.

Methylene Chloride

Form

Methylene chloride is a member of the chlorinated hydrocarbon family. It is a colorless liquid with a pleasant odor. It evaporates readily but has low flammability.[22]

Uses

Widely used as an industrial solvent and paint stripper, methylene chloride is also an ingredient in some aerosol and pesticide products, spray paints, automotive cleaners, and other household products. It is also used in the production of photographic film.[22]

Routes of Exposure

Methylene chloride can enter the body via inhalation, ingestion, or dermal absorption. Due to its high volatility, inhalation is the major route of exposure, followed by dermal uptake. Inhalation is an efficient method of absorption, with up to 75% of inhaled methylene chloride reaching the bloodstream.[22]

Occupational exposure to methylene chloride occurs in numerous industries. Workers may be exposed during a variety of industrial activities including spray painting, spray gluing, metal painting, paint stripping, and aerosol packing. Most occupational exposure occurs during metal cleaning, industrial paint stripping, and ink solvent use.[22,23]

Toxicology

Methylene chloride gets metabolized to carbon monoxide.[7] The toxic effects are secondary to carbon monoxide and its subsequent binding to hemoglobin, producing carboxyhemoglobin. The pulmonary, hematopoietic, and nervous systems are the major targets of exposure to methylene chloride.[22]

Neurotoxicity. The nervous system is the most important target of acute methylene chloride toxicity. Methylene chloride is a mild CNS depressant, and the accompanying hypoxia from carboxyhemoglobin aggravates the CNS effects. Symptoms include dizziness, nausea, peripheral paresthesia or anesthesia, and a subjective feeling of drunkenness. With high enough exposure, usually above 8,000 ppm, unconsciousness and death result.[22]

Hematologic toxicity. Inhalation and ingestion of methylene chloride result in increased blood carboxyhemoglobin, as previously described. In some studies, in persons with chronic occupational exposure, increases in the red cell count, hemoglobin, and hematocrit were seen, believed to be compensatory hematopoiesis from chronic hypoxia.[22]

Pulmonary toxicity. Acute inhalation of high concentrations of methylene chloride damages the Clara cells of the bronchioles. This damage can result in pulmonary infiltrates, congestion, hemorrhage, and death.[22]

Carcinogenicity. While there is no clear evidence in humans that methylene chloride exposure causes cancer, a number of animal studies have demonstrated its potential as a carcinogen. Lung and liver tumors have developed in mice with chronic overexposure. As a result, IARC has classified methylene chloride as a possible human carcinogen.[22]

Medical Surveillance

Measurements of parent methylene chloride and its metabolites in expired air, blood, and urine have been used as indicators of exposure. But because it is cleared from the body very rapidly, these methods are useful for monitoring recent exposures only.

OSHA requires medical monitoring of persons with methylene chloride exposure at or above the airborne action level of 12.5 ppm.[23] The OSHA regulation requires full medical surveillance at baseline and termination, with periodic surveillance as determined by the employee's age. The full surveillance exam must include a medical and work history (updated annually), emphasizing neurological symptoms; history of skin, hematologic, hepatic, and cardiac disorders; risk factors for cardiac disease; and methylene chloride exposure. The physical exam should focus on the respiratory tract, lungs, cardiovascular system (including blood pressure and pulse), liver, nervous system, and skin.[23] DoD requirements for medical surveillance align with the OSHA regulations.[8]

Methyl Ethyl Ketone

Form

Methyl ethyl ketone is also known as 2-butanone. It is a colorless liquid with a sharp, sweet odor. It is highly volatile and water soluble.[24]

Uses

Methyl ethyl ketone is used mainly as an industrial solvent. Most of its use is in paints, glues, and other coatings because of its rapid evaporation and ability to dissolve many substances. It is used in the manufacturing process of the following products: fabric coatings, synthetic resins, surface coating, artificial leather, lacquer and varnish, pharmaceuticals, cosmetics, synthetic rubber, lubricating oils, vinyl coatings, adhesives, acrylic coatings, hardwood pulps, and ink. Methyl ethyl ketone is also a naturally occurring substance produced by some trees, fruits, and vegetables.[24]

Routes of Exposure

Occupational exposure to methyl ethyl ketone mainly occurs via inhalation during the production, formulation, use, or transport of this compound. Approximately 50% of the inhaled compound is absorbed into the bloodstream. It can also be ingested or absorbed dermally, but less is known about the rate and efficiency of these routes of exposure.[24]

Exposure occurs when workers apply commercial coatings containing methyl ethyl ketone, especially in enclosed, unventilated spaces. It is also released into the air as a component of car and truck exhausts.[24]

Toxicology

While methyl ethyl ketone is an irritant to the eyes, mucous membranes, and skin, serious health effects have only been seen in study animals under high-concentration exposure conditions. Inhalation causes irritation of the nasal passages and respiratory tract, with symptoms of sore throat, dry nose, and cough. Exposure to the vapor can also cause conjunctival

irritation manifested as redness, tearing, and blurred vision. There have been some reports of inhalation exposure resulting in mild skin irritation, but no studies or reports of dermal exposure causing skin inflammation in humans has been reported. Animals exposed to extremely high concentrations of inhaled or ingested methyl ethyl ketone have been reported to exhibit severe respiratory, hepatic, renal, and neurological effects generally culminating in death.[24]

Medical Surveillance

Methyl ethyl ketone can be detected unchanged in the blood, urine, and exhaled air. Its metabolites, 3-hydroxy-2-butanone and 2,3-butanediol, can be detected in the urine. However, methyl ethyl ketone is metabolized and excreted rapidly, with a half-life of only 90 minutes, so testing is only good for very acute exposures. Furthermore, alcohols, hydrocarbons, and other ketones also break down to 2-butanone and its metabolites, so testing is not specific for 2-butanone exposure.[24]

While OSHA has set the PEL for methyl ethyl ketone exposure at 200 ppm or 590 mg/m^3, it has not developed specific medical surveillance program requirements. Likewise, the DoD does not have specific regulations or recommendations regarding monitoring of workers exposed to methyl ethyl ketone.

Mustard Agents

Forms

Sulfur mustards are oily, clear or yellow to brown liquids with an odor like garlic, onion, or mustard. They are liquids at room temperature but will vaporize over the course of days to weeks and at faster rate at higher temperatures. They are not water soluble but dissolve easily in oils, fats, and other solvents. HD is the most common mustard agent used. Agent H is chemically distinct from the more common HD and contains about 20% to 30% impurities. HT is a mixture of 60% HD and 40% H.[25]

Uses

Sulfur mustard agents are blister or vesicant agents developed for chemical warfare. They were first used during World War I and have been used as recently as the Iran-Iraq War (1980–1988). Sulfur mustard is no longer being produced by the United States, and Congress has mandated that all stockpiles be destroyed. It is now used only for research purposes in the United States.[25]

Routes of Exposure

Sulfur mustard gas or vapor is readily absorbed through the lungs, via inhalation, or the skin. Liquid sulfur mustard is absorbed readily through the skin. Occupational exposure may occur on Army bases where sulfur mustard was previously released and has persisted in the soil, or where old containers are currently stored. Construction workers or other such laborers are most at risk at these sites. Persons involved in the storage and destruction of this compound could also be exposed during accidental release. Researchers may be exposed to sulfur mustard, and soldiers are still at risk for exposure if it is used as a chemical warfare agent. Service members who deployed to Iraq after the first and second Gulf wars occasionally encountered buried and partially buried projectiles containing sulfur mustard. Most rounds were intact, but many were leaking and exposed unprotected service members to sulfur mustard. Finally, there have been reports of fishermen being exposed by inadvertently snaring discarded canisters containing sulfur mustard in areas of historical ocean dumping with subsequent puncturing of the canister.[25]

Toxicology

Sulfur mustard has many biological actions, but the exact mechanism of tissue injury is not known.[25] Several studies have shown that sulfur mustard can produce biochemical alterations consistent with free-radical-mediated oxidative stress, such as lipid peroxidation, antioxidant enzyme activities, and depletion of glutathione. However, DNA is the most functionally sensitive biomarker of mustard gas exposure.[25,26] Mustard gas causes DNA alkylation and crosslinking in rapidly dividing cells, leading to cellular death and inflammatory reactions resulting in large fluid-filled blisters on skin and excretion of fluid in the respiratory track (which causes breathing difficulty or asphyxiation). The main effects of sulfur mustard agents are in the eyes, airways, and skin.[25]

Dermal toxicity. Mustard agent causes erythema of the skin, along with itching, burning and stinging pain. The skin is most sensitive where it is thinnest, in the warm, moist areas around the eyes and genitalia. Small vesicles form in the erythematous areas, which may later coalesce to form bullae. Bullae look like large, domed-shaped, thin-walled, translucent bubbles on the surface of the skin.[25]

Pulmonary toxicity. Mustard agent that gets into the lungs causes necrosis of the mucosa and potential damage to the airway musculature. The damage begins in the bronchus and upper airways. As the exposure continues, the lower airways and bronchioles become

affected. The alveoli are the last part of the lung affected. When the mustard causes severe lung injury, hemorrhagic pulmonary edema develops. Respiratory failure or secondary bacterial pneumonia is the usual cause of death from mustard exposure. If the mustard poisoning is less severe, chronic respiratory effects can develop, including chronic bronchitis, cough, and diminished lung volumes.[25]

Ocular toxicity. The eyes are the organ most sensitive to mustard vapor. Conjunctivitis, with reddening and irritation, is the earliest symptom of exposure. As the exposure level increases, the severity of clinical conjunctivitis symptoms increases, causing photophobia, blepharospasm, pain, and corneal damage. Swelling and loosening of corneal epithelial cells lead to corneal edema and leukocyte clouding. There may also be scarring between the iris and lens, which can restrict pupillary movement and predispose victims to glaucoma.[25]

Medical Surveillance

Although tests are available to detect metabolites of sulfur mustard in blood and urine, they are not readily available in most clinical settings. Rather, samples must be sent to the Centers for Disease Control and Prevention or the Army Medical Research Institute of Chemical Defense for analysis. Also, while the tests can confirm sulfur mustard exposure, they are of little use in preventing onset or treating clinical disease.[26]

OSHA has no standards or regulations regarding medical surveillance for persons with possible exposure to sulfur mustard. However, the DoD requires workers with access to chemical, biological, and nuclear materials, such as mustard agents, to be enrolled in a "surety" medical program.[8] Surety programs place added emphasis on safety, security, and personnel reliability. The Army has published recommendations for medical surveillance programs for persons with potential exposure to sulfur mustard agents, which have subsequently been adopted by the DoD.[26]

Organophosphate Nerve Agents

Organophosphates comprise a group of chemicals that were developed for home and industrial applications. These diverse chemicals are used as insecticides and anthelmintics in agriculture, as ingredients in ophthalmic medical applications, and as chemical warfare agents by several countries. Given their relevance to military personnel, the remainder of this section will focus on organophosphate use in nerve agents. The US chemical warfare agent stockpile contains the nerve agents sarin (GB) and VX.

Forms

Nerve agents are liquids under ambient conditions. The G-type agents such as sarin are more volatile and readily vaporize and disperse as vapors under normal conditions. They are clear, colorless, and tasteless liquids that are soluble in water and most organic solvents. Sarin is the most volatile nerve agent and evaporates at the same rate as water. VX is the least volatile of the nerve agents and is a clear, amber-colored, odorless, oily liquid.[27]

Uses

Organophosphates were originally developed as pesticides, but they were repurposed as chemical weapons. Sarin was developed in 1938 by Germany, and VX was synthesized in England in 1952. After World War II, organophosphates were reintroduced as pesticides as well as medicinal and pharmaceutical agents. Organophosphate pesticides reversibly inhibit acetylcholinesterase, whereas nerve agents irreversibly inhibit acetylcholinesterase. The deadly effects of these nerve agents result from a buildup of acetylcholine, which can lead to muscle fasciculations, seizures, flaccid paralysis, apnea, and copious secretions.[27]

Routes of Exposure

Nerve agents are readily absorbed via inhalation, ingestion, and through the skin.[7] Inhalation is the usual route of exposure in combat settings, but dermal exposure is the primary route of occupational exposure. Vapors are not absorbed through the skin except at very high concentrations. Ingestion of nerve agents is relatively rare compared to inhalation exposure or skin contact; however, nerve agents are readily absorbed from the gastrointestinal tract.[27]

Toxicology

Nerve agents are cholinesterase inhibitors.[27] They inhibit the carboxyl ester hydrolases in plasma, red blood cells, and cholinergic receptors, particularly acetylcholinesterase. Once acetylcholinesterase has been inactivated, acetylcholine accumulates, resulting in overstimulation of muscarinic and nicotinic receptors of the affected organ and the CNS. Onset of symptoms occurs soon after high-level exposure, but little is known about chronic low-level exposure.[27]

Central nervous system toxicity. Nerve agents cause behavioral and psychological effects, such as irritability, nervousness, fatigue, insomnia, memory loss, impaired judgment, slurred speech, and depression.

The CNS signs of a large exposure are loss of consciousness, seizures, and apnea. Symptoms usually begin within a minute of exposure to a large amount of vapor or skin contact, but may be preceded by a latent period of up to 30 minutes after exposure. CNS effects such as fatigue, irritability, nervousness, and memory impairment may persist for as long as 6 weeks after recovery from acute effects.[27]

Pulmonary toxicity. Nerve agent vapor causes bronchoconstriction and increased secretions of the glands in the airways, manifesting as excessive rhinorrhea and bronchial secretions. The exposed person may feel a slight tightness in the chest after exposure to a small amount of agent and may be in severe distress after a large amount of agent. Respiratory failure may occur due to CNS depression.[27]

Cardiovascular toxicity. Exposure to organophosphate pesticides and nerve agents can result in bradycardia due to vagal nerve stimulation, or tachycardia, due to ganglionic stimulation and hypoxia. Hypertension may also result in response to the bradycardia.[27]

Gastrointestinal toxicity. Organophosphate pesticide and nerve agent exposure may stimulate nerve cells, which increases motility and secretions by the glands in the wall of the gastrointestinal tract. Nausea and vomiting are early signs of nerve agent exposure, and diarrhea may occur with large exposures.[27]

Muscular toxicity. Nerve agent exposure stimulates skeletal muscle, which produces muscular fasciculations and twitching. Prolonged exposure to nerve agents produces fatigue and muscle weakness, rapidly followed by muscular flaccidity.[27]

Glandular toxicity. Nerve agent vapor causes the lacrimal, nasal, salivary, and bronchial glands to increase secretions. Localized sweating also occurs around the site of liquid agent contact on the skin, and generalized sweating occurs after a large liquid or vapor exposure.[27]

Ocular toxicity. Miosis, a characteristic sign of nerve agent vapor exposure, is a contraction of the muscles of the eye, causing the muscles of the iris to constrict, narrowing the opening. Miosis is accompanied by pain, blurred vision, conjunctival injection, and occasionally nausea and vomiting.[27]

Medical Surveillance

Organophosphate nerve agent toxicity is a clinical diagnosis that is made using an occupational history of exposure and physical examination that includes noting signs and symptoms of exposure. Laboratory testing is possible at chemical depots to confirm nerve agent exposure. The drop in blood pH following a nerve agent exposure reflects altered red blood cell cholinesterase activity in response to the exposure. Organophosphate pesticide applicators can also be monitored by checking red blood cell cholinesterase levels, which rise following pesticide exposure.

There are no OSHA regulations for nerve agent exposure or recommendations for medical surveillance of persons exposed to nerve agents. However, the DoD requires workers with access to nerve agents to be enrolled in surety medical programs, as described above.[8] The Agency for Toxic Substances and Disease Registry has published recommendations for medical surveillance for persons with potential exposure to nerve agents.[27]

Pentachlorophenol

Forms

Pure pentachlorophenol is a synthetic, colorless crystal. Impure varieties are dark brown or gray dust, beads, or flakes. When heated, pentachlorophenol releases a sharp, sweet, or "benzene-like" odor, but at room temperature, it produces very little odor. It exists in two forms: pentachlorophenol itself, and the sodium salt of pentachlorophenol. The sodium salt form is very water soluble compared to the other form.[28]

Uses

Pentachlorophenol is only used industrially. It is mainly used as a wood preservative for power line poles, fence posts, and similar structures. Sodium pentachlorophenol is used in plywood and fiberboard waterproofing, and in termite control. Previously it was a widely used pesticide and herbicide.[28]

Routes of Exposure

Pentachlorophenol is efficiently absorbed via inhalation, oral, and dermal exposure.[28] In the workplace, most exposure is from inhalation or skin absorption. Based on human and animal studies, over 70% of inhaled pentachlorophenol is subsequently absorbed. Oral absorption is even more efficient, with virtually all ingested chemical entering the bloodstream. Dermal uptake is the least efficient method of absorption. However, dermal absorption is based on the solution; pentachlorophenol in an oily solution is better absorbed, at approximately 60%, compared to pentachlorophenol in an aqueous solution, with less than 20% uptake.[28]

Occupational exposure occurs in the gas, electric, and wood preservative industries. Acute exposures occur in the production and application of

pentachlorophenol, when opening pressurized vessels, cleaning tanks, or application to lumber. Non-occupational exposure occurs by handling treated lumber.[28]

Toxicology

Pentachlorophenol is an irritant, affecting the eyes, nasal and oral passages, airways, and skin. Exposure to concentrations above 1 mg/m^3 causes upper airway pain and cough, but persons can become acclimatized to pentachlorophenol. Acclimatized persons can tolerate concentrations up to 2.4 mg/m^3. Systemic toxicity of pentachlorophenol results from uncoupling of oxidative phosphorylation and disruption of electron transport, leading to stimulation of cell metabolism and hyperthermia.[28]

Acute toxicity. Exposure to high concentrations of pentachlorophenol can cause skin irritation. Systemic intoxication is characterized by rapid onset of diaphoresis, elevated temperature, tachycardia, tachypnea, weakness, nausea, vomiting, abdominal pain, headache, intense thirst, and pain in the extremities. Symptoms culminate in progressive coma and death within hours after onset of symptoms.

Chronic toxicity. Repeated, dilute skin exposure also leads to irritation. Chloracne has been reported after direct skin exposure, most likely the result of dioxin contaminates in commercial-grade pentachlorophenol. Chronic exposure is also connected with conjunctivitis, sinusitis, bronchitis, and polyneuritis.[28]

Carcinogenicity. IARC has determined that pentachlorophenol is a possible human carcinogen. An increased risk of non-Hodgkin lymphoma has been observed in individuals exposed to pentachlorophenol.

Medical Surveillance

Pentachlorophenol and its metabolites can be measured in the blood, urine, and tissue. Since it is excreted in the urine largely unchanged, urinalysis is a noninvasive and useful method for determining exposure. However, other compounds such as hexachlorobenzene and lindane are metabolized to pentachlorophenol in the body, and thus it is a not a specific biomarker. Also, because pentachlorophenol is cleared from the body relatively quickly, these methods are only useful for monitoring exposures that occurred in the past few days.[28]

While OSHA has set the PEL for pentachlorophenol exposure at 0.5 mg/m^3, it has not developed a required medical surveillance program. Likewise, the DoD does not have specific regulations or recommendations regarding monitoring of workers exposed to pentachlorophenol.

Trichloroethylene

Forms

Like methylene chloride, trichloroethylene is a chlorinated hydrocarbon. It is a colorless liquid at room temperatures and has both a sweet odor and taste. It is fairly volatile at room temperature but nonflammable.[29]

Uses

Trichloroethylene is a solvent and is mainly used as a degreaser. It is also used as an intermediate to make other chemicals, particularly hydrofluorocarbons. Although its use is declining, trichloroethylene is also used in dry cleaning operations. Trichloroethylene can also be found in some household products, including typewriter correction fluid, paint removers, adhesives, and spot removers.[29]

Routes of Exposure

Trichloroethylene can enter the body via inhalation, ingestion, or dermal absorption. Inhalation is the major route of exposure; trichloroethylene is rapidly absorbed into systemic circulation following inhalation, with between 60% and 80% reaching the bloodstream. Although virtually all ingested trichloroethylene is absorbed by the gastrointestinal tract, this is not a common occupational route of exposure. Occupational exposure occurs in workers in the degreasing industry, as well as in those involved in trichloroethylene production or in industries using it as an intermediate.[29]

Toxicology

The toxicity associated with trichloroethylene is caused by its metabolites. Like other chlorinated hydrocarbons, trichloroethylene causes CNS and hepatic effects.[29]

Nervous system toxicity. Trichloroethylene is a CNS depressant. It causes headache, vertigo, fatigue, short-term memory loss, decreased word associations, and anesthesia. It is also associated with trigeminal neuralgia. Like other solvents, trichloroethylene is implicated in sensorineural hearing loss, especially in settings of noise exposure.[29]

Hepatic toxicity. Liver dysfunction has been noted in workers exposed to trichloroethylene. It causes acute, reversible hepatitis and fatty liver infiltrates.[29]

Degreaser's flush. Exposure to trichloroethylene and alcohol can lead to alcohol intolerance and

potentiation of the trichloroethylene's effects. This presents as transient redness or flushing affecting the face and neck.

Medical Surveillance

Biological monitoring for exposure to trichloroethylene is possible by measuring levels of the compound or its metabolites in exhaled air, blood, or urine. However, metabolites of trichloroethylene may also come from other sources; they are not specific to trichloroethylene exposure alone.[29]

While OSHA has established the PEL for trichloroethylene exposure at 100 ppm, it has not developed a required medical surveillance program. Likewise, the DoD does not have specific regulations or recommendations regarding monitoring of workers exposed to trichloroethylene.

INORGANIC OR ELEMENTAL EXPOSURES

Asbestos

Forms

Asbestos is the generic name given to a group of hydrated mineral silicates that occur naturally in the environment. There are two classes of asbestos, serpentine and amphibole. The most common forms used in the United States are amosite and crocidolite (amphiboles) and chrysotile (serpentine), with chrysotile making up the majority of asbestos use. All forms of asbestos are toxic, but amphibole forms of asbestos are considered to be more hazardous.[30]

Uses

Asbestos was once used widely for its insulation and fire-resistant properties. It was used in building insulation, floor and ceiling tiles, and ship-building, but its use is currently less than one-tenth of the amount consumed during the 1970s. Despite its decline, asbestos is still used in roofing products, gaskets, and friction products (such as automobile clutches, brakes, and transmission components).[30]

Routes of Exposure

Most asbestos uptake occurs via inhalation. The deposition and fate of the fiber in the lungs is largely dependent on its diameter and length. Fibers with larger diameters cannot penetrate the peripheral lung, while smaller diameter fibers can infiltrate to the pleural surface. Likewise, shorter fibers can be completely phagocytized and removed from lung by a mucociliary clearance mechanism, while longer fibers are incompletely ingested and become trapped in the alveoli.[30]

After ingestion, the majority of asbestos fibers are excreted within a few days. A small number penetrate and become embedded along the gastrointestinal tract, but very few will be fully absorbed. Similarly, while asbestos fibers can penetrate the skin, it has never been demonstrated that they can subsequently enter the bloodstream.[30]

Since asbestos is a naturally occurring product found in vermiculite and talc, persons using or exposed to these products, such as miners or gardeners, may be subject to asbestos exposure. Custodial, insulation, maintenance, and asbestos abatement workers who make repairs at installations with old buildings containing asbestos may also be exposed.

Toxicology

Because most exposure results from inhalation and absorbed asbestos stays isolated within the respiratory tract, the toxic effects of asbestos target the lungs. No acute toxic effects have been reported following exposure; rather, a latency period of 10 to 20 years is typical between exposure and development of clinical signs of early disease.[7]

Asbestosis. Workers who get asbestosis following asbestos exposure develop a diffuse interstitial pulmonary fibrosis that takes between 20 and 40 years to develop. It results from a slow build-up of scar-like tissue along the lung. Fibrotic pleural changes and calcification also occur, and pulmonary function may be restricted. Studies have suggested a difference in potency based on fiber morphology, but the results are inconclusive.[30] The amount of fiber present in the lung will also affect the degree of pulmonary fibrosis. The clinical examination may note fine rales, finger clubbing, dyspnea, dry cough, and cyanosis. The chest x-ray shows granular changes, chiefly in the lower lung fields starting 20 to 40 years after first exposure. Unfortunately, asbestosis continues to progress, even after exposure to asbestos has ceased.[30]

Pleural plaques. Workers exposed to asbestos will often develop pleural plaques. Pleural plaques are almost always asymptomatic, but there may be a small but significant reduction in lung volume. Pleural plaques serve as a marker of asbestos exposure and are associated with an increased risk for developing other asbestos-related lung disease. They are visible on standard radiographs, especially if calcified. They are not premalignant and do not require treatment.[30]

Cancer. Bronchogenic carcinoma and mesothelioma are causally associated with asbestos exposure. There is also some evidence that asbestos increases the risk of cancer in the stomach, intestines, esophagus, pancreas, and kidneys.[30]

Mesothelioma is a cancer of the pleural lining. These tumors are relatively rare in the general population but are often observed in asbestos workers. Dyspnea and chest wall pain are the most common presenting symptoms. Fatigue, fever, sweats, and weight loss are other associated symptoms. Patients may be asymptomatic, however, with only a pleural effusion as an incidental finding on chest x-ray.[30]

Cigarette smoking is strongly implicated as a co-carcinogen among asbestos workers. The incidence of lung carcinoma is much higher in asbestos workers who smoke. Cigarette-smoking asbestos workers have approximately 15 times the risk of developing lung cancer compared with nonsmoking asbestos workers. There are several proposed mechanisms for this synergism. One theory is that asbestos attracts pulmonary alveolar macrophages, which then metabolize polycyclic hydrocarbons into carcinogens. Another theory is the asbestos fibers absorb and concentrate the carcinogens in tobacco smoke and then slowly release them into the lung.[7,30]

Medical Surveillance

OSHA requires medical monitoring of persons with potential for asbestos exposure at or above the OSHA PEL of 0.1 fiber/cm^3 as an 8-hour time weighted average.[31] The OSHA regulation requires an annual exam, as well as a baseline and termination exam. The exams must include a medical and work history using a standardized questionnaire; a complete physical examination of all systems with emphasis on the respiratory system, the cardiovascular system, and digestive tract; a chest x-ray; and pulmonary function tests.[9] The DoD requirements for medical surveillance align with the OSHA regulations.[31]

Crystalline Silica

Forms

Silica refers to the chemical compound silicon dioxide. Silicon dioxide is found in either crystalline or noncrystalline amorphous form. Crystalline silica can be found in multiple forms, with the most abundant naturally found form being quartz. Quartz exists as colorless, odorless crystals.[32]

Uses

Crystalline silica is a component of sand, stone, rock, concrete, brick, block, and mortar, as well as of nearly every mineral deposit. Industrial silica is used in glass-making, foundry work, metallurgy, abrasive work, fillers, ceramics, water filtration, petroleum manufacture, gravel, and recreational sand.[32–34]

Routes of Exposure

Silica can be ingested or inhaled. Ingested silica is virtually nontoxic except at extremely high quantities. However, silica dust is easily inhaled and lodged in the airways.

Occupational exposure to crystalline silica often occurs in operations involving cutting, sawing, drilling, and crushing of concrete, brick, rock, and stone products. Processes historically associated with increased silica exposure include sandblasting, sand-casting foundry operations, mining, tunneling, cement cutting and demolition, masonry work, and granite cutting.[32–34]

Toxicology

Silica particles are engulfed by macrophages, leading to cytokine release, fibroblast proliferation, and collagen production. This process results in the formation of silicotic nodules and fibrosis.[32]

Silicosis. Workers exposed to crystalline silica can develop silicosis, a disabling, progressive, and sometimes fatal pulmonary disease that includes fibrosis and development of lung nodules. Silicosis onset can be extremely rapid at high doses of silica exposure. If exposure levels are low, onset can take 20 to 30 years. In simple silicosis, symptoms develop 10 to 30 years following exposure and include cough, dyspnea, and wheezing. There is also a progressive deterioration in pulmonary function. Early radiographic evidence of silicosis includes small opacities, 1 to 3 mm in diameter, that appear in the upper lung fields. The opacities increase in number and size as the disease progresses, and appear in the lower lung fields. Characteristic "eggshell calcifications" are seen on the chest x-rays of workers with silicosis.[32–34]

Exposure to high concentrations of silica over a short period in sandblasting and silica flour production has produced accelerated silicosis, a more rapidly progressive form of the disease. The symptoms are the same as those of chronic silicosis, but the clinical findings and radiological evidence develop more rapidly. In acute silicosis, the lungs on x-ray have a diffuse ground-glass appearance.[32–34] There is at least one instance of an

acute form of silicosis developing after workers were exposed to extremely high concentrations of silica over a very short period. The workers developed progressive dyspnea, fever, cough, and weight loss, and, in the most severe cases, death occurred within 1 to 2 years.[33,34]

Tuberculosis. Silicosis seems to increase the risk of developing mycobacterial and fungal infections. Silica dust tends to overwhelm the macrophages and they can no longer kill tuberculosis bacilli. The progression of silicosis when tuberculosis is present is much more rapid than uncomplicated silicosis.[32–34]

Carcinogenicity. IARC has determined that silica is a human carcinogen. Silicosis also increases the risk of developing bronchogenic carcinoma.

Other diseases. Epidemiologic studies have shown that occupational exposure to respirable crystalline silica is associated with the development of chronic obstructive pulmonary disease, including bronchitis and emphysema. Silica also stimulates the immune system via an adjuvant mechanism to cause scleroderma.

Medical Surveillance

OSHA requires medical monitoring of persons with potential for respirable crystalline silica exposure at or above the OSHA PEL of 50 $\mu g/m^3$ as an 8-hour time weighted average on 30 or more days per year.[35] The OSHA regulation requires a baseline exam and a periodic exam at least every 3 years, or more frequently if recommended by the examiner. The exams must include a medical and work history using a standardized questionnaire; a complete physical examination of all systems with emphasis on the respiratory system; a chest x-ray (including an interpretation and classification per the International Labour Office International Classification of Radiographs of Pneumoconioses by a NIOSH-certified B reader); pulmonary function testing; and tuberculosis testing. The DoD requirements for medical surveillance align with the OSHA regulations.[35]

Tritium

Tritium is a radioisotope of hydrogen, containing one proton and two neutrons. It is also called hydrogen-3.[7]

Forms

The most commonly encountered forms of tritium are tritium gas and tritium oxide (or "heavy water"). Tritium is a gas at ambient temperature and pressure. It combines with oxygen to form a liquid called tritiated water.

Uses

Tritium is used to make self-powered lighting devices called betalights, which are now used in firearm night sights, watches, exit signs, map lights, and other devices. Tritium is also an important component in nuclear weapons. It enhances the efficiency and yield of fission in bombs in a process known as "boosting."[7]

Routes of Exposure

Tritium is readily taken into the body via inhalation, ingestion, and dermal absorption. Skin and pulmonary absorption occur readily and are equally important as routes of entry.

Toxicology

Tritium is a beta radiation emitter. Beta particles are a charged form of ionizing radiation with moderate penetrating ability; they penetrate the skin down to the germinal layer and are a radiation hazard when internalized. They contain enough energy to alter structures with which they collide, and hence, are potential mutagens or carcinogens. The beta radiation emitted during tritium decay is very weak (6 keV), but produces essentially whole-body radiation injury because of the distribution of heavy water.[7]

Medical Surveillance

Workers routinely exposed to tritium should be enrolled in a medical surveillance program and are normally required to submit periodic urine samples for bioassay. The sampling frequency is determined based on the exposure potential and may be daily, weekly, monthly, or a longer interval.

Urine bioassay samples are required after each exposure incident as well. The urine bioassay should be collected 1 to 2 hours after exposure, and the worker should empty their bladder. The sampling protocol is located in Army Public Health Command Technical Guide 211, *Radiobioassay Collection Labeling and Shipping Requirements*.[36] A sample taken 2 hours after exposure should be reasonably representative of the body water concentration. An early sample may still be useful to confirm tritium exposure.

Tritium-labeled molecules can be found in the skin due to contact with metal surfaces contaminated with HT. These molecules, which interact with organic hydrogen, have a longer half-life in the body than tritium oxide. Airborne metal tritides may be taken into the lungs and then slowly released into the blood. When

this is the case, medical surveillance should carefully follow the elimination data and look for organically bound tritium in the urine.[37] The results of the bioassay measurements should be documented in the health record and shared with the worker, like other medical surveillance results.

White Phosphorus

Forms

White phosphorus is a waxy solid with a garlic-like smell. It is white in its pure form, but commercial white phosphorus is usually yellow. It is spontaneously combusts at temperatures l0° to 15° above room temperature.[38] Because of its high reactivity with oxygen, white phosphorus is generally stored under water.

Uses

White phosphorus is used in the production of phosphoric acid and other phosphates, which are used in fertilizers, food and drink additives, industrial cleaning compounds, and waste and water treatments. It is also used as a rat and roach poison and a component in fireworks. In the military, white phosphorus is used in incendiary mortar and artillery shells and grenades. When ammunitions containing white phosphorus are combusted, they produce smoke containing some unburnt phosphorus. In military operations, white phosphorus smoke is used as an obscurant to conceal troop movements and to identify targets or the locations of friendly forces.[38]

Routes of Exposure

White phosphorus enters the systemic circulation via ingestion. Studies in animals reveal that it is almost fully absorbed through the gastrointestinal tract. While white phosphorus and its smoke can be inhaled, there is no evidence that it penetrates through the respiratory tract. Its inhalation effects result from local contact with the particles. There is no evidence that white phosphorus can be dermally absorbed.[38]

Occupational exposure occurs in persons who work in phosphorus production or in industries using phosphorus, such as grain fumigation and other previously mentioned uses. Military personnel handling munitions or involved in warfare may also be exposed. Non-occupational exposure can occur in persons who live near white phosphorus production sites and artillery training sites. White phosphorus can also bioaccumulate slightly in fish and waterfowl, so people can be exposed by eating contaminated game or fish.[38]

Inhalational exposure. Inhalation of white phosphorus or white phosphorus smoke results in respiratory tract irritation, leading to cough and laryngitis at low levels, and wheezing, dyspnea, and pneumonia at high levels. Chronic inhalation exposure can result in "phossy jaw," a progressive degeneration or necrosis of the soft tissue, teeth, and bones of the oral cavity, particularly the maxilla and mandible. The condition is thought to be caused by the direct effects of white phosphorus contact. The presenting symptoms are toothache and increased salivation, and the oral mucosa becomes red and dull. This is followed by tooth loss from bone degeneration, poor healing of the resulting socket, and infection.[38]

Oral exposure. Ingestion of white phosphorus results in gastrointestinal, hepatic, renal, and musculoskeletal effects. In severe cases, ingestion can result in death. The earliest effect of white phosphorus ingestion, beginning within hours of exposure, is vomiting. Other gastrointestinal effects include abdominal pain and cramping. These symptoms are caused by local irritation of white phosphorus on the gastrointestinal mucosa. Hepatic dysfunction and injury occur in most persons following ingestion. Signs and symptoms include jaundice, hepatomegaly, and elevated bilirubin and liver-associated enzymes. Liver biopsies reveal necrosis, degeneration, fibrosis, hemorrhages, and fatty infiltration. White phosphorus is a renal toxin. After ingestion, the following renal effects have been detected in patients: proteinuria, albuminuria uremia, and oliguria. There are two possible mechanisms of the renal insufficiency, direct injury to the kidney or fluid loss and shock resulting in acute tubular necrosis. "Phossy jaw" is also a result of white phosphorus ingestion.[38]

Dermal exposure. Dermal exposure to white phosphorus can result in a second- or third-degree burn. White phosphorus damages the skin via corrosion and heat. It is also oxidized into a hygroscopic metabolite that further damages the skin.[38]

Medical Surveillance

Currently there are no biomarkers to indicate whether a person has been exposed to white phosphorus. While OSHA has set the PEL for white phosphorus at 0.1 mg/m^3, it has not developed a required medical surveillance program. Likewise, the DoD does not have specific regulations or recommendations regarding monitoring of workers exposed to white phosphorus.

SUMMARY

Military members have the potential to face a greater number and variety of exposures, both "traditional" occupational hazards as well as those encountered in combat zones. As described, these exposures can occur via multiple routes and can result in acute and chronic illnesses, thereby impacting both immediate missions and long-term operations. By recognizing all possible hazards, persons who may be at risk, and how the toxicities manifest, military commanders can mitigate or even prevent their effects.

ADDITIONAL RESOURCES

Copies of the various standards or recommendations regarding exposure levels can be obtained by contacting the following agencies:

- **Permissible Exposure Levels (PELs)**
  The OSHA standards are available for public access at https://www.osha.gov/dsg/annotated-pels.
- **Threshold Limit Values (TLVs)**
  Copies of ACGIH recommendations can be purchased by calling ACGIH at 513-742-2020 and referencing Publication #0113 or Publication #0114. They can also be ordered online at http://www.acgih.org.
- **Recommended Exposure Levels (RELs)**
  The NIOSH guidelines can be accessed online at http://www.cdc.gov/niosh/npg/. Hard copies or CD-ROM versions can be ordered by at the NIOSH website.
- **Workplace Environmental Exposure Levels (WEELs)**
  The AIHA recommendations can be accessed at https://www.aiha.org/get-involved/AIHAGuidelineFoundation/WEELs.

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