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REVIEW ARTICLE

IRRITANT COMPOUNDS: RESPIRATORY IRRITANT GASES

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Summary

Respiratory irritants are substances which can cause inflammation or other adverse reactions in the respiratory system (lungs, nose, mouth, larynx and trachea) after being inhaled. Depending on the type and amount of irritant gas inhaled, victims can experience symptoms ranging from minor respiratory discomfort to acute airway and lung injury and even death. The lungs are susceptible to many airborne irritants. A common response cascade to a variety of irritant gases includes inflammation, edema and epithelial sloughing which, left untreated, can result in scar formation and pulmonary and airway remodeling. There are hundreds of substances that can pollute air and harm lungs. Harmful gases and chemicals are just one type of airborne pollutants that can adversely affect the lungs. Examples of respiratory irritants include, for example, chlorine, amonium, ozone, sulphur dioxide or nitrogen oxides. These substances, their sources of exposure, physical and other properties, and effects on the victim are summarized in this article.

Key words: respiratory irritants; irritant gases; inflammation; chlorine; hydrogen chloride; hydrogen fluoride; hydrogen sulfide; sulphur dioxide; nitrogen dioxide; ammonia; ozone.

INTRODUCTION

Irritant gases are those which, when inhaled, dissolve in the water of the respiratory tract mucosa and cause an inflammatory response. This biological effect is usually caused by the release of acidic or alkaline radicals. Irritant gas exposures predominantly affect the airways, causing tracheitis, bronchitis, and bronchiolitis. Irritant peak exposure during gassing episodes was a strong predictor of changing work due to respiratory problems, even after adjustment of asthma, chronic bronchitis, and chronic rhinitis (Murgia et al., 2011). Some inhaled agents may be directly toxic (eg, cyanide, carbon monoxide, perfluoroisobutene) or cause harm simply by displacing O2 and producing asphyxia (eg, methane, carbon dioxide).

The effect of inhaling irritant gases depends on the extent and duration of exposure and on the specific agent. Chemicals such as chlorine, sulfur dioxide, hydrogen chloride or sulfide, nitrogen dioxide, phosgene, ozone, and ammonia are among the most important irritant gases. Hydrogen sulfide is also

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a potent cellular toxin, blocking the cytochrome system and inhibiting cellular respiration.

A common exposure involves mixing household ammonia with cleansers containing bleach. This particular mixture forms intermediary chloramine that causes toxic pneumonitis (Reisz and Gammon, 1986). This article is dedicated to the toxicologically important industrial gases, which are used widely in various human activities. These are gases which are capable not only seriously harm human health, but also kill humans.

For some gases acute toxic gas standards were developed for occupational, military, and civilian use that predict or establish guidelines for limiting exposure to inhaled toxic gases. Nevertheless, large disparities between guidelines exist for similar exposure scenarios, such as: Acute Exposure Guidelines (AEGL), Immediate Danger to Life or Health (IDLH), Purser, International Organization for Standardization (ISO 13571), Federal Aviation Administration (FAA), or Agency for toxic Substance and Disease Registry (ATSDR) (Iyoho et al., 2011).

RESPIRATORY DAMAGE

Respiratory damage is related to the concentration of the gas and its solubility. Depending on the length of the inhalation, acute, subacute, or chronic disease may result. Exposure to high concentrations of toxic gas over a short time is characteristic to industrial accidents resulting from a faulty valve or pump in a gas tank or occurring during gas transport. Many people may be exposed and affected. (Henneberger et al., 1993). Acute toxic inhalational exposures may result in respiratory failure, multisystem organ dysfunction, and death (Chen et al., 2012). The release of methyl isocyanate from a chemical plant in Bhopal, India in 1984 killed more than 2000 people (Dhara and Dhara, 2002).

Thousands of persons experience accidental high-level irritant exposures each year but most recover and few die. Irritants function differently than allergens because their actions proceed non-specifically and by non-immunologic mechanisms. For some individuals, the consequence of a single massive exposure to an irritant gas, is persistent airway hyperresponsiveness and the clinical picture of asthma, referred to as reactive airways dysfunction syndrome (RADS). Repeated irritant exposures may lead to chronic cough and continual airway hyperresponsiveness. Cases of asthma attributed to repeated irritant-exposures may be the result of genetic factors (Brooks and Bernstein, 2011). The most serious immediate complication is RADS, which usually occurs within 24 h. Patients with significant lower airway involvement may develop bacterial infection (Costa and Orriols, 2005).

SYMPTOMS AND SIGNS

Soluble irritant gases cause severe burning and other manifestations of irritation of the eyes, nose, throat, trachea, and major bronchi. More water-soluble gases (e.g. chlorine, ammonia, sulfur dioxide, hydrogen chloride) dissolve in the upper airway and immediately cause mucous membrane irritation. The upper airway may be obstructed by edema, secretions, or laryngospasm. Permanent damage of the upper respiratory tract, distal airways, and lung parenchyma occurs only if escape from the gas source is impeded. Less soluble gases (e.g. nitrogen dioxide, phosgene, ozone) may not dissolve until they are well into the respiratory tract, often reaching the lower airways. These agents are less likely to produce early warning signs and are more likely to cause severe bronchiolitis, and often have a lag of $\geq$ 12 h before symptoms of pulmonary edema develop. Non-soluble gases cause fewer immediate symptoms but can cause dyspnea or cough (Turk et al., 2007).

Severe irritant gas inhalations, usually accidental due to human error or equipment failure, can result in immediate death from asphyxia or cause mild to severe respiratory distress from acute upper airways inflammation, delayed pulmonary edema, respiratory muscle dysfunction, or a combination of illnesses. Most patients are expected to survive and recover with little or no residual dysfunction regardless of the severity of the initial event. However, in some cases disabling long-term sequelae, some patients develop bronchiectasis, bronchiolitis, chronic airflow obstruction or bronchial hyperreactivity progressing to acute respiratory distress syndrome (ARDS) (Moldoveanu et al., 2009). Bronchiolitis obliterans with organized pneumonia can ensue when granulation tissue accumulates in the terminal airways and alveolar ducts during the body's reparative process. A minority of these patients develop late pulmonary fibrosis (Brautbar et al., 2003).

DIAGNOSIS

Diagnosis is usually obvious from the history. Patients should have a chest X-ray and pulse oximetry. Chest X-ray findings of patchy or confluent alveolar consolidation usually indicate pulmonary edema (Brooks and Bernstein, 2011). CT is used to evaluate patients with late-developing symptoms. Those with bronchiolitis obliterans that progresses to respiratory failure manifest a pattern of bronchiolar thickening and a patchy mosaic of hyperinflation (Mihălţan et al., 2001).

PROGNOSIS

Most people recover fully, but some have persistent lung injury with reversible airway obstruction or pulmonary fibrosis; smokers may be at a greater risk. There is also some disagreement as to the likely prognosis with this disorder. Currently, the diagnosis requires the assumption of normal premorbid pulmonary physiology and absence of bronchial hyperreactivity (Bardana, 1999).

THERAPY

Therapy of the respiratory effects of irritant gases should follow the general principles used for the treatment of upper and lower airway obstruction, non-cardiogenic pulmonary edema, and hemorrhagic pneumonitis while spontaneous healing and recovery occurs, because no specific therapy is available for direct chemical pulmonary injury (Heierli, 1989). Corticosteroids (e.g. prednisone 45 to 60 mg once/day for 1 to 2 wk) are frequently used and recommended, but their efficacy in altering the course and outcome of respiratory injury has not yet been properly documented (Cevik et al., 2009).

Management does not differ according to a specific inhaled agent but rather by symptoms. Patients should be moved into fresh air and given supplemental oxygen O_2. Treatment is directed toward ensuring adequate oxygenation and alveolar ventilation. Bronchodilators and O_2 therapy may suffice in less severe cases. Severe airflow obstruction is managed with inhaled racemic epinephrine, endotracheal intubation or tracheostomy, and mechanical ventilation. Because of the risk of ARDS, any patient with respiratory tract symptoms after toxic inhalation should be observed for 24 h. After the acute phase has been managed, physicians must remain alert to the development of reactive airways dysfunction syndrome, bronchiolitis obliterans with or without organized pneumonia, pulmonary fibrosis, and delayed-onset ARDS (Carron, 2009).

PREVENTION

Care in handling gases and chemicals is the most important preventive measure. The availability of adequate respiratory protection (e.g. gas masks with a self-contained air supply) for rescuers is also very important; rescuers without protective gear who rush in to extricate a victim often succumb themselves. Industrial air filters, adequate ventilation, and respirators in polluted work sites are now mandatory.

IRRITANT GASES CHARACTERISATION

Inhalation accidents frequently involve these irritant gases: chlorine, hydrogen chloride, hydrogen fluoride, hydrogen sulfide, sulphur dioxide, nitrogen dioxide, ammonia and ozone.

Chlorine (Cl_2, CAS Number 7782-50-5) is a chemical element from the halogen group. The ele-ment is a yellow-green gas under standard conditions, where it forms diatomic molecules. In industry, elemental chlorine is usually produced by the electrolysis of sodium chloride dissolved in water. This method, the chloralkali process industrialized in 1892, now provides essentially all industrial chlorine gases (Greenwood and Earnshaw, 1997). Principal applications of chlorine are in the production of a wide range of industrial and consumer products. Chlorine is mainly used to bleach paper and cloth and to make pesticides, chemicals, rubber, and organic solvents. It is used to kill bacteria in drinking water and swimming pool water. It is also used in the sanitation process for industrial waste and sewage, and as a disinfectant and fungicide.

Most people are generally not exposed to pure chlorine (Mangat et al., 2012). They may be exposed to non-toxic concentrations of chlorine through household products that are made from chlorine, such as disinfectants used in drinking water and swimming

pools (Odabasi, 2008). Household bleach does not contain pure chlorine. It is made from sodium hypochlorite, a chlorine-based chemical. However, human may be exposed to hazardous chlorine gas at home if you mix bleach containing sodium hypochlorite with ammonia or other cleaning products. Exposure to pure chlorine occurs primarily in industrial situations where chlorine is used.

Exposure to low levels of pure chlorine gas is irritating to the respiratory tract, eyes, and skin. Exposure can cause sore or swollen throat, coughing, choking, sneezing, pneumonia, chest tightness and pain, headache, dizziness, watery eyes, blurred vision, nausea, vomiting, vomiting blood, severe abdominal pain, skin blisters and irritation, difficult breathing, and pain or burning in the stomach, nose, eyes, ears, lips, or tongue. Exposure to extremely high levels of pure chlorine gas can cause lung collapse and death. Only few inspirations may be fatal (Patočka and Měrka, 2005). Exposure to high levels can cause pulmonary edema, rapid breathing, wheezing, blue coloring of the skin, vomiting, anxiety, accumulation of fluid in the lungs, severe eye and skin burns, loss of vision, and lung pain.

The current Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL) for chlorine is 1 ppm (3 milligrams per cubic meter [mg/m^3]) as a ceiling limit. A worker's exposure to chlorine shall at no time exceed this ceiling level. The National Institute for Occupational Safety and Health (NIOSH) has established a recommended exposure limit (REL) for chlorine of 0.5 ppm mg/m^3) as a time weighted average (TWA) for up to a 10-hour workday and a 40-hour workweek and a short-term exposure limit (STEL) of 1 ppm (3 mg/m^3) [NIOSH, 1992]. The lowest published toxic concenration (TCLo) of chlorine in human at inhalation exposure is 66 ppm/1hour (Shroff et al., 1988). The lethal effects of chlorine in humans are well documented (Das and Blanc, 1993; Becker and Forrester, 2008). An unusual case of human death after poisoning with chlorine in a swimming pool is even known (Rao and Hearn, 1988). Death is due to pulmunary edema (Mohan et al., 2010).

The fact that even today chlorine can be dangerous shows a case that happened in 2011 in Arkansas (CDC, 2011). A worker at a poultry processing plant began to pour sodium hypochlorite into a 55-gallon drum that contained residual acidic antimicrobial solution. When the sodium hypochlorite reacted with the solution, chlorine gas was released into the small room where the drum was located and then spread into the plant, where approximately 600 workers were present. These workers were promptly evacuated. Out of approximately 600 workers who were evacuated; 545 were later interviewed, 195 reported seeking medical treatment, 152 reported being hospitalized, and the plant nurse reported that five were admitted to intensive-care units. Centers for Disease Control and Prevention (CDC, 2011a) describe the results of that evaluation, including findings from two follow-up site visits conducted approximately 4 and 6 months after the release. Out of 545 workers who participated in the evaluation, three developed ARDS, an irritant-induced form of asthma that can persist for life. The worker who inadvertently mixed the two solutions indicated that the drum was labeled in English but he could only read Spanish. This incident underscores the danger posed by chlorine gas and the importance of employers providing adequate training and communication of health and safety precautions to employees.

Hydrogen chloride (HCl, CAS Number 7647-01-0) is a colorless gas at room temperature, which forms white fumes of hydrochloric acid upon contact with atmospheric humidity. Hydrogen chloride gas and hydrochloric acid are important in technology and industry. Hydrochloric acid, the aqueous solution of hydrogen chloride, is also commonly given the formulaHCl.

Exposure to hydrogen chloride can occur through inhalation, ingestion, and eye or skin contact (Sittig, 1991). Hydrogen chloride forms corrosive hydrochloric acid on contact with water found in body tissues. Inhalation of the fumes can cause coughing, choking, inflammation of the nose, throat, and upper respiratory tract. In severe case hydrogen chloride in high concentrations causes pulmonary edema, circulatory system failure, and death. Skin contact can cause redness, pain, and severe skin burns. Hydrogen chloride may cause severe burns of the eye and permanent eye damage (Kirsch and Drabke, 1982).

HCl is irritating and corrosive to the eyes, skin, and mucous membranes. Exposure to high concentrations can cause laryngitis, bronchitis, and pulmonary edema (Rom, 1983). Brief exposures to concentrations in the range of 1,300 to 2,000 ppm are lethal to humans (Braker and Mossman, 1980). In workers, exposure to 50 to 100 ppm for 1 hour was barely tolerable; short exposure to 35 ppm caused

irritation of the throat, and 10 ppm was considered the maximal concentration allowable for prolonged exposure. Hydrochloric acid causes burns of the skin and mucous membranes. Burns may progress to ulcerations and lead to keloid and retractile scarring (Kaplan et al., 1988). Frequent contact of the skin with aqueous solution may cause dermatitis. Contact of the eyes with aqueous solutions may produce reduced vision or blindness (Parmeggiani, 1983). Ingestion of hydrochloric acid causes severe burns of the mouth, esophagus, and stomach, with consequent pain, nausea, and vomiting (Hathaway et al., 1991).

As for acute toxicity data, the LD_{50} of HCl in mouse at intraperitoneal application is 40.142 mg/kg (Bienvenu et al., 1963) and LDLo in man at oral application is 2.857mg/kg (Henderson et al., 1993). The current OSHA PEL for hydrogen chloride is 5 ppm (7 milligrams per cubic meter (mg/m^3) as a ceiling limit. The NIOSH has established a REL for hydrogen chloride of 5 ppm (7 mg/m^3) as a ceiling [NIOSH, 1992].

Hydrogen fluoride (HF, CAS Number 74835-82-8 or 24993-08-6 or 24993-08-6) is a colorless gas and the principal industrial source of fluorine, often in the aqueous form as hydrofluoric acid. It is also the precursor to many important compounds including pharmaceuticals and polymers (e.g. Teflon). HF is widely used in the petrochemical and nuclear industry. Hydrogen fluoride boils just below room temperature (19.5 °C). Unlike the other hydrogen halides, HF is lighter than air and diffuses relatively quickly through porous substances.

Hydrogen fluoride is a highly dangerous, toxic, and potentially lethal gas, forming corrosive and penetrating hydrofluoric acid upon contact with tissue (Lund et al., 2002; Kawaura et al., 2009; Zierold and Chauviere, 2012). While acute symptoms include skin or nail burns, chronic ones involve systemic toxicity, eye injuries (the gas can also cause blindness by rapid destruction of the corneas), inhalation and ingestion-related symptoms that can be even fatal. HF can be harmful and particularly aggressive to soft tissues, but symptoms may not be apparent immediately after exposure (Skolnik, 2010). The hazardous effects are not based on the pH value, but on the toxicity of HF (Makarovsky et al., 2008). Potential hazards of HF known from other applications than dentistry should be considered also in dental applications. Especially the clinicians, who often deal with adhesive cementation or repair of glass ceramics, should take necessary precautions for possible hazards of HF (Ozcan et al., 2012).

Hydrogen sulfide (H_2S, CAS Number 7783-06-4) is a colorless, flammable, extremely hazardous gas with a "rotten egg" smell. H2S is produced by bacterial breakdown of organic materials and human and animal wastes. Approximately 90 % of the sources that emit hydrogen sulfide into the air are natural (EPA, 1993). Anthropogenic releases of H_2S into the air result from industrial processes, primarily from the extraction and refining of oil and natural gas and from paper and pulp manufacturing. H_2S is heavier than air and may travel along the ground. It collects in low-lying and enclosed, poorly-ventilated areas. For work within confined spaces, use appropriate procedures for identifying hazards, monitoring and entering confined spaces.

The primary route of exposure is inhalation and the gas is rapidly absorbed by the lungs. People can smell the "rotten egg" odor of hydrogen sulfide at low concentrations in air, however, with continuous low-level exposure, or at high concentrations, a person loses ability to smell the gas. This can happen very rapidly and at high concentrations, the ability to smell the gas can be lost instantaneously. In addition, hydrogen sulfide is a highly flammable gas and gas/air mixtures can be explosive. It may travel to sources of ignition and flash back. If ignited, the gas burns to produce toxic vapors and gases, such as sulfur dioxide.

Human health effects of exposure to H_2S depend on the concentration of the gas and the length of exposure. This gas is both an irritant and a chemical asphyxiant with effects on both oxygen utilization and the central nervous system. Because most organ systems are susceptible to its effects, hydrogen sulfide is considered to be a broad spectrum toxicant (Glass, 1990). The organs and tissues with exposed mucous membranes (eyes, nose) and with high oxygen demand (lungs, brain) are the main targets of hydrogen sulfide (Legator et al., 2001). Hydrogen sulfide acts similarly to hydrogen cyanide, interfering with cytochrome oxidase and with aerobic metabolism. Essentially, hydrogen sulfide blocks cellular respiration, resulting in cellular anoxia, a state in which the cells do not receive oxygen and die (Knight and Presnell, 2005).

Low concentrations irritate the eyes, nose, throat and respiratory system. Asthmatics may experience breathing difficulties. The effects can be delayed

for several hours, or sometimes several days, when working in low-level concentrations. Repeated or prolonged exposures may cause eye inflammation, headache, fatigue, irritability, insomnia, digestive disturbances and weight loss (Legator et al., 2001). Moderate concentrations can cause more severe eye and respiratory irritation, headache, dizziness, nausea, vomiting, staggering and excitability. High concen-trations can cause shock, convulsions, inability to breathe, extremely rapid uncon-sciousness, coma and death. Effects can occur within a few breaths, and possibly a single breath (Balletta et al., 2011).

The current OSHA workplace standard for H2S exposure is 10 ppm. The OSHA regulations do not specify an 8-hour TWA for H_2S. Exposure to these concentrations even for the seemingly short duration of 10 minutes can nevertheless result in eye and respiratory irritation, according to several sources. The NIOSH recommended exposure limit to the OSHA 10 ppm standard is 10 minutes, and Immediately Dangerous to Life or Health (IDLH) H_2S concen-tration is 100 ppm (Guidotti, 1994).

Sulphur dioxide (SO_2, CAS Number 7446-09-5) is a colorless toxic gas with a pungent, irritating smell, that is released by volcanoes and in various industrial processes. Further oxidation of SO_2, usually in the presence of a catalyst such as NO_2, forms H_2SO_4, and thus acid rain (Pelley, 2006). Acid rain damages trees and other plants, and it can also affect the soil. SO_2 emissions are also a pre-cursor to par-ticulates in the atmosphere (Lehman et al., 2008).

Sulfur dioxide can affect the body if it is inhaled or if it comes into contact with the eyes or skin. At inhalation exposure SO_2 can cause severe irri-tation of the nose and throat. Its irritant properties are due to the rapidity with which is forms H_2SO_4 on contact with moist membranes (White and Martin, 2010). At high concentrations it can cause life-threatening accumulation of fluid in the lungs (pulmonary edema). The SO_2 is very toxic and can cause death. Symptoms may include coughing, shortness of breath, difficult breathing and tightness in the chest. A single exposure to a high concentration can cause a long-lasting condition like asthma. Symptoms may include shortness of breath, tightness in the chest and wheezing (ARDS) (van Thriel et al., 2010). The gas irritates or burns the eyes. Permanent eye damage or blindness can result (Doyle et al., 1961).

The current OSHA standard for SO2 is 5 ppm (13 mg/m^3) averaged over an 8-hour work shift (Wilczek and Zimowski, 1989).

Nitrogen dioxide (NO2, CAS Number 10102-44-0) is one of several nitrogen oxides. This reddish-brown toxic gas has a characteristic sharp, biting odor and is a prominent air polutant. NO_2 is an intermediate in the industrial synthesis of nitric acid, millions of tons of which are produced each year. Emission of NO_2 in the atmosphere is an important contri-bution to the quality of indoor and outdoor air (Pilotto and Douglas, 1993).

Nitrogen dioxide is toxic by inhalation (Kelly and Fussell, 2011). However, as the compound is easily detectable by smell at low concentrations, inhalation exposure can generally be avoided. Symptoms of poisoning (lung edema) tend to appear several hours after inhalation of a low but potentially fatal dose (Di Giampaolo et al., 2011). Also, low concen-trations (4 ppm) will anesthetize the nose, thus creating a potential for overexposure. Spanish study (Esplugues et al., 2011) showed that children are more susceptible to respiratory disease and more vulnerable to ambient pollution, because their lungs and immune system are not completely developed and that exposure to outdoor, but not indoor, NO_2 during the first year of life increases the risk of per-sistent cough.

Also other studies show that even low concen-trations of NO_2 can be very dangerous to human health. As an example, a remark may be made about acute respiratory symptoms in a group of ice hockey players after exposure to nitrogen dioxide in an indoor ice arena in New Hampshire in 2011. The symptoms, which included cough, shortness of breath, hemoptysis, and chest pain or tightness, were consistent with exposure to nitrogen dioxide gas, a byproduct of combustion (CDC, 2011b).

Reported LCLo doses of inhaled NO_2 are 123 mg/m^3 (8 hr) in dog and monkey (Steadman et al., 1966), 315 ppm (15 min) in rabbit (Carson et al., 1962), and 200 ppm (1 min) (Mason, 1974), respectively 90 ppm (40 min) (Norwood et al., 1966) or 2 ppm (4 hr) (Devlin et al., 1999) in human. In literature reported LC50 of inhaled NO_2 were 30 ppm (1 hr) in guinea pig (Buckley and Balchum, 1965) and 315 ppm (15 min) in rabbit (Carson et al., 1962). The OSHA PEL of NO2 is 5 ppm (9 mg/m^3) ceiling and NIOSH recommended exposure limit (REL) is 1 ppm (1.8 mg/m^3) (OSHA, 2012a).

Ammonia (NH_3, CAS Number 7664-41-7) is a colorless gas with a characteristic pungent smell. Ammonia, either directly or indirectly, is a building-block for the synthesis of many pharmaceuticals and is used in many commercial cleaning products. Ammonia gas can be dissolved in water. This kind of ammonia is called liquid ammonia or aqueous ammonia. Once exposed to open air, liquid ammonia quickly turns into gas. Although in wide use, ammonia is both caustic and hazardous. Ammonia is produced worldwide at a rapid rate. The global production of ammonia for 2012 is anticipated to be 198 million tons and encountering it is possible in many places. It is therefore not surprising that ammonia poisoning is fairly common (Price et al., 1983; Woto-Gaye et al., 1999; Dilli et al., 2005).

Ammonia is applied directly into soil on farm fields, and is used to make fertilizers for farm crops, lawns, and plants. Ammonia does not last very long in the environment. It is rapidly taken up by plants, bacteria, and animals. Ammonia does not build up in the food chain, but serves as a nutrient for plants and bacteria. Many household and industrial cleaners contain ammonia.

Reported LCLo doses of inhaled NH_3 are 5000 ppm (5 min) (Tabulae Biologicae, 1933) and TDLo 15 µL/kg at oral administration (Klein et al., 1985) in human. The OSHA PEL of NH3 is 50 ppm (35 mg/m^3) ceiling and NIOSH recommended exposure limit (REL) is 25 ppm (18 mg/m^3) (OSHA, 2012b).

Ozone (O_3, CAS Number 10028-15-6) is a triatomic molecule, consisting of three oxygen atoms. It is an allotrope of oxygen that is much less stable than the diatomic allotrope (O_2), breaking down in the lower atmosphere to normal dioxygen. Ozone is formed from dioxygen by the action of ultraviolet light and also atmospheric electrical discharges, and is present in low concentrations throughout the Earth's atmosphere. In total, ozone makes up only 0.6 ppm of the atmosphere (Horvath et al., 1985).

Ozone is a powerful oxidant, much more than O_2, and has many industrial and consumer applications. This same high oxidizing potential, however, causes ozone to damage mucus and respiratory tissues in animals, and also tissues in plants. This makes ozone a potent respiratory hazard and pollutant near ground level. However, the so-called ozone layer, i.e. a portion of the stratosphere with a higher concentration of ozone (from two to eight ppm) is beneficial, preventing damaging ultraviolet light from reaching the Earth‘ surface, to the benefit of both plants and animals (Rowland, 2006).

When inhaled, ozone reacts with target molecules in pulmonary surfactant, a lipid-rich material that lines the epithelial cells in the airways. Phospholipids containing unsaturated fatty acyl groups and cholesterol would be susceptible to attack by ozone, which may lead to the formation of cytotoxic products (Pulfer and Murphy, 2004). The mechanism of ozone-induced lung cell injury is poorly understood. One hypothesis is that ozone induces lipid peroxidation and that these peroxidated lipids produce oxidative stress and DNA damage. Oxysterols are lipid peroxides formed by the direct effects of ozone on pulmonary surfactant and cell membranes (Kosmider et al., 2010). Exposure of the lungs to concentrations of ozone found in am-bient air is known to cause toxicity to the epithelial cells of the lungs and can also damage some other organs such as the heart (Einecke, 2012).

The current OSHA standard for ozone is 0.1 ppm (0.2 mg/m^3), averaged over an eight-hour work shift and 0.2 ppm (0.4 mg/m3), as a limit for an exposure time of 10 min (OSHA, 2012c).

CONCLUSIONS

Irritant gases are chemicals, which dissolve in the water of the respiratory tract mucosa and cause an inflammatory response. Irritant gas exposures predominantly affect the airways, causing tracheitis, bronchitis, and bronchiolitis. The effect of inhaling irritant gases depends on the extent and duration of exposure and on the specific agent. The chronic or acute irritant gas exposures cause asthma or a variant condition, reactive airways dysfunction syndrome (RADS). Among the most important irritant gases belong chlorine, hydrogen chloride, nitrogen dioxide, ammonia, ozone and others.

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