Military Toxicology

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ABSTRACT

This first edition of Military Toxicology, composed of three parts, is a survey of both basic and practical information on the essential facets of toxicology with military toxicology as its focus. The first part, including chapter 1 to 6, mainly introduces some important concepts, principles and methodologies which are the foundation of the science of toxicology. Chemical agents employed in war are primarily discussed in chapter 1 and interactions of chemicals and the body are examined in chapter 2 to 3. Chapter 4 to 6 are especially important in understanding the effects of chemical agents, as they deal with the issue of toxicity and factors influencing toxicity. The second part of the book consists of only one chapter, chapter 7, which focuses on the the work of risk assessment of potential adverse health effects resulting from hazardous agents or situations. It explores the principles and strategies of risk assessment, including decision making, hazard identification, risk characterization, risk perception and comparative analyses. Chemical agents reported up to now in the world are charted in detail in the last part of this book (chapter 8 ~ 13). It includes lethal agents, blister agents, incapacitating agents and other chemical agents used in foreign armed forces. With abundant information and authentic data, the present book may serve as a useful clue to further studies on toxicity, mechanism, treatment and prevention of chemical agents intoxication.

Editorial Board

Preface

Military toxicology, evolved from the needs of medical supports during the first and the second World War and developed during the later stage of 20 centuries, becomes a division of military medicine. It is designed to solve both academic and practical problems for a medical treatment system of the troops' chemical defense and security in peace and war. It plays a major role in the toxicological assessment of health and environmental hazards associated with substances that are used primarily by the military or that present an unusual type of exposure as a result of a unique military environment. It deals with the way that substances are absorbed, distributed or eliminated and studies the mechanism of a xenobiotic-induced intoxication. And it can even identify poisonous and hazardous chemicals from different sources such as air, soil, fruits, waters, urine or blood. As a classroom discipline it is to train the students for a wide range of toxicological issues so that the students may work under supervision of researchers in emergency medicine or participate in an active research project. Although there are some excellent references in toxicology, a textbook systematically elaborating the theoretical and practical problems encountered in military operations is not available until now. This void impelled the authors to produce the present textbook for students in military medical colleges and research institutes.

The first edition of Military Toxicology provides both basic and practical information on the many facets of toxicology and especially on the principles, concepts and modes of thought that are the foundation of the discipline. It also reflects the progress made in defenses of chemical agents and even in chemical hazard management. Graduate students and researchers will find this book an excellent reference when approaching problems encountered in areas of military medicine or peripheral interests.

CONTENTS

Chapter 1 INTRODUCTION

Zhaojun Dong

Key words: toxicology, poison, exposure, effect, response, genotoxicology, radiation, behavioral toxicology, reproductive toxicology, environmental toxicology, ecotoxicology, military toxicology, nerve agents, systemic agents, blister agents, asphyxiants, incapacitating agents, irritants

Toxicology is the scientific study of poisons on their actions, detections and treatments of the condition produced by them. A poison is generally considered to be any substance which can cause severe injury or death as a result of a physicochemical interaction with living tissues. All substances are potential poisons since all of them can cause injury or death following excessive exposure. If exposure of people or susceptible organisms is kept below defined tolerable limits, on the other hand, all chemicals can be used safely. The duty of a mechanistic toxicologist is concerned with identifying and understanding the cellular, biochemical, and molecular mechanisms by which chemicals exert toxic effects on living organisms. A descriptive toxicologist, however, is concerned directly with toxicity testing and provides information for safety evaluation and regulatory requirements. Evolved from needs identified during the World Wars, the Army, Navy and Air Force developed toxicological capabilities in response to their respective operational needs. These three previously separate efforts have been integrated into the military toxicology in response to the continually changing and growing operational needs of the foreign forces in the world.

Toxicology discipline is also one of the primary fields driving risk assessment and analysis. Once exposure has been established by such epidemiology as hydrogeology and environmental geology, the impact of such exposure is then evaluated and prioritized. Analytical chemistry is also important to provide the chemical data on the type and concentration of contaminants present in the environment samples. Thus, toxicology is a central discipline in such efforts as risk assessment, regulatory negotiations, litigation support, strategic planning, program development, and program management in the industrial arena.

1. HISTORY OF TOXICOLOGY

Toxicology can be dated back to the earliest humans, who used animal venoms and plants for hunting, warfare, and disease treatment. Shen Nong (2696 BC) is considered to be the father of Chinese agriculture—a legendary emperor, who taught his people how to cultivate grains as food, so as to avoid killing animals. He tasted 365 medicines which derived from plants, minerals, and animals. He wrote treatise On Herbal Medical Experiment Poisons and died of a toxic dose. Another well preserved medical document came from ancient Egyptian (1500 BC). That contains 110 pages on anatomy and physiology, toxicology, spells, and treatment recorded on papyrus. It recognized poisons such as hemlock, aconite and opium. With time, poisons became widely used and greatly sophisticated. Solon of Athens put hellebore roots in the drinking water of Kirrha in 600 BC. In 429 and 424 BC, the Spartans and their allies used noxious smoke and flame against Athenian-allied cities during the Peloponnesian War. About 200 BC, the Carthaginians used Mandrake root left in wine to sedate the enemy. The notable poisoning victims include Socrates (470 ~ 399 BC) and Cleopatra (69 ~ 30 BC). By the time of Renaissance and Age of Enlightenment, certain concepts fundamental to toxicology began to take shape. Noteworthy in this regard were the studies of Paracelsus (1493 ~ 1541) and Orfila.

Paracelsus is a physician-alchemist and the son of a physician. He determined that specific chemicals were actually responsible for the toxicity of plant or animal poison. He also documented that the body's response to those chemicals depend on the dose received. His studies revealed that small doses of a substance might be harmless or beneficial whereas larger doses could be toxic. This is now known as the dose-response relationship, a major concept of toxicology. Paracelsus is often quoted for his statement: "all substances are poisons; there is none which is not a poison. The right dose differentiates a poison and a remedy."

The classification of toxic substances was first systematized by Matthieu Orfila (1787 ~ 1853), who was the leading medico-legal expert of his time. Orfila demonstrated effects of poisons on specific organs by analyzing autopsy materials for poisons and their associated tissue damage. In 1814, he published his first work, *Traité des poisons*, in which he divided poisons into six classifications: corrosives, astringents, acrids, stupefying or narcotics, narco (tico) acids, and septica or putreficants.

Many German scientists contributed greatly to the growth of toxicology in the late nineteenth and early twentieth centuries. Among the giants of the field are Oswald Schmiedeberg (1838 ~ 1921) and Louis Lewin (1850 ~ 1929). Schmiedeberg is generally recognized as the founder of modern toxicology. He studied the effect of the chloroform in blood and the property of the chloral hydrate. In 1869, Schmiedeberg showed that muscarine evoked the same effect on the heart as electrical stimulation of the vagus nerve.

Organic chemicals became more widespread in the late nineteenth century. Benzene, toluene, and the xylems went into large-scale commercial production. The introduction of ether, chloroform, and carbonic acid led to several iatrogenic deaths. These unfortunate outcomes stimulated the research on the causes of the deaths and on the physiological mechanisms in the late nineteenth and the early twentieth centuries. In addition to clinical uses of the organic chemical, toxic compounds can also be employed by army for campaign. During the Crimean War (1853 ~ 1856), there were several proposals to initiate chemical warfare to assist the Allies, particularly to solve the stalemate during the siege of Sevastopol. Lyon Playfair, a British chemist, proposed a cacodyl cyanide artillery shell for use primarily against enemy ships. The British Ordnance Department rejected it as "bad a mode of warfare as poisoning the wells of the enemy." Playfair's response outlined a different concept, which was used to justify chemical warfare into the next century.

The concept of creating a toxic gas from chemical cylinders was credited to Fritz Haber of the Kaiser Wilhelm Physical Institute of Berlin in late 1914. Owing to shortages of artillery shells, Haber thought a chemical gas cloud negate the enemy's earthworks without the use of high explosives. In addition, gas released directly from its storage cylinder would cover a far broader area than that dispersed from artillery shells. Haber selected chlorine for the gas since it was abundant in the German dye industry and would have no prolonged influence over the terrain. On 10 March 1915, under the guidance of Haber, Pioneer Regiment 35 placed 1600 large and 4130 small cylinders containing a total of 168 tons of chlorine opposite the allied troops defending Ypres, Belgium. Haber also supplied the entire regiment with Draeger oxygen breathing sets, used in mine work, and a portion of the surrounding German infantry with small pads coated with sodium thiosulfate. Once the cylinders were in place, the Germans then waited for the winds to shift to a westerly direction. On 22 April 1915, the Germans released the gas with mixed success. The attack was more significant than the Germans expected, and they were not ready to make significant gains despite the breakthrough. In addition, fresh allied troops quickly restored a new line further back. The Allies claimed that 5000 troops were killed in the attack, but this was probably an inflated number for propaganda purposes.

Sulfanilamide was a chemical used to treat streptococcal infections and was shown to have dramatic curative effects. It has been used safely for some time in tablet and powder form. In June 1937, however, a salesman in Bristol reported a demand in the southern states for the chemical in liquid form. The company's chief chemist and pharmacist experimented and found that sulfanilamide would dissolve in diethylene glycol. The company control lab tested the mixture for flavor, appearance, and fragrance and found it satisfactory. Immediately, the company compounded a quantity of the elixir and sent shipments all over the country. During September and October 1937 this chemical produced more than 100 deaths of people in 15 states, as far east as Virginia and as far west as California. The patients died of acute kidney failure resulting from the metabolism of the glycol to oxalic acid and glycolic acid. This tragic event led to the passage of the bill involving the formation of the Food and Chemical Administration (FDA), which played a critical role in the further development of toxicology.

Dichlorodiphenyltrichloroethane (DDT) was first prepared in 1874 by the reaction of chloral with chlorobenzene in the presence of sulfuric acid. Its insecticidal properties were discovered in 1939 by a Swiss chemist, Paul Hermann Müller. During and after World War Ⅱ (WW Ⅱ), DDT was found to be effective against lice, fleas, and mosquitoes (the carriers of typhus, of plague, and of malaria and yellow fever, respectively) as well as the Colorado potato beetle, the gypsy moth, and other insects that attack valuable crops. Other examples of this series are BHC, lindane, chlorobenzilate, meth oxychlor, and the cyclodienes (which include aldrin, dieldrin, chlordane, heptachlor, and endrin). Some of these compounds are quite stable and have a long residual action;

they are, therefore, particularly valuable where protection is required for long periods. Their toxic action is not fully understood, but they are known to disrupt the nervous system. Soon after the BHC, organophosphates were developed as the largest and most versatile class of insecticides. Parathion, malathion, Diazinon, naled, methyl parathion and dichlorvos are widely used throughout the world. These compounds kill insects by inhibiting the enzyme cholinesterase and are generally much more toxic than the chlorinated hydrocarbons. With the development of the organophosphous insecticides, some were selected as military agents, the nerve gases, in the US and the Soviet Union during the 1960s.

The history of toxicology has been interesting and varied but never dull. Perhaps as a science that has grown and prospered by borrowing from many disciplines, it has suffered from the absence of a single goal, but its diversification has allowed for the interspersion of ideas and concepts from higher education, industry, and government. As an example of this diversification, one now finds toxicology graduate programs in medical schools, schools of public health, and schools of pharmacy as well as programs in environmental science and engineering and undergraduate programs in toxicology at several institutions. Surprisingly, courses in toxicology are now being offered in several liberal arts undergraduate schools as part of their biology and chemistry curricula. This has resulted in an exciting, innovative, and diversified field that is serving science and the community at large.

Few disciplines can point to both basic sciences and direct applications at the same time. Toxicology, the study of the adverse effects of xenobiotics, may be unique in this regard.

2. SUBDISCIPLINES OF TOXICOLOGY

Toxicology has been defined as the study of the adverse effects of chemical on living organisms and assesses the probability of their occurrences. The main goals of toxicology are to elucidate the toxic properties of chemicals, to evaluate the hazards of chemicals to organisms in relation to the concentration of these substances in the environment and to advise society in measures to control or prevent the harmful effects of chemicals. Molecular toxicology is a subdiscipline interested in clarifying the cellular, biochemical, and molecular mechanisms of these adverse effects of chemicals. Because of the fact that a lot of toxic chemicals have been employed in arms for military operations, another subdiscipline named as military toxicology has been growing up in the later 20^{th} century.

Other areas evolved during the second half of the twentieth century are genotoxicology, neurotoxicology and behavioral toxicology, reproductive toxicology, etc. Methodologies and strategies become more precise along with developments of biological, biochemical, pathological and molecular analysis.

2.1 GENOTOXICOLOGY

Genotoxicology as a subdiscipline of toxicology focuses on the study of interactions between DNA and various substances known as genotoxic agents (ionizing radiation, solar radiation, etc.), as well as on the DNA lesions caused by these agents. Research in this field aims to identify cell mechanisms used to detect and then repair such lesions in order to restore genome integrity. In higher organisms, DNA is organized within cell nuclei in complex structures, known as chromatin. The functional integrity of the genome is intimately dependent on the preservation of this structure. During processes such as DNA replication and repair, chromatin undergoes disassembly followed by reassembly. Factors contributing to this dynamic chromatin assembly process are presently being subjected to detailed analysis.

2.2 BEHAVIORAL TOXICOLOGY

Behavioral end points are being used with greater frequency in neurotoxicology to detect and characterize the adverse effects of chemicals on the nervous system. Behavioral measures are particularly important for neurotoxicity risk assessment since many known neurotoxicants do not result in neuropathology. The chlorinated hydrocarbon class consists of a wide variety of chemicals including polychlorinated biphenyls, clioquinol, trichloroethylene, hexachlorophene, organochlorine insecticides (DDT, dicofol, chlordecone, dieldrin, and lindane), and phenoxyherbicide, etc. Each of these chemicals has effects on motor, sensory, or cognitive function that are detectable using functional measures such as behavior. Furthermore, there is evidence that if exposure occurs during critical periods of development, many of the chlorinated hydrocarbons are developmental neurotoxicants. Developmental neurotoxicity is frequently expressed as alterations in motor function or cognitive abilities or changes in the ontogeny of sensorimotor reflexes.

2.3 REPRODUCTIVE TOXICOLOGY

Reproductive toxicology encompasses reproductive and developmental biology, toxicology, teratology, and pharmacology, in addition to epidemiology, occupational and environmental health and medicine. It is vital for considering the development and function of the male and female reproductive systems, including fertilization, implantation, embryonic and fetal development, parturition and postnatal adaptation. In general, the survival of any species depends on the integrity of its reproductive system. Genes located in the chromosomes of the germ cells transmit genetic information from previous generations and control cell differentiation and organogenesis. Under normal situations germ cells ensure the maintenance of structures and functions in the organism in its own lifetime and from generation to generation. The adverse effects of exogenous chemicals on the human reproductive system have become a major issue; incidence of chemically induced germ cell damage and sterility appear to be on the increase. According to a reproductive investigation in battery factories, the male workers occupationally exposed to lead has a higher rate of abnormal sperm, congenital epilepsy, and heart disease of children than that of the unexposed controls. The developments of children's intelligence were hindered significantly. Another study indicated that the carbon disulfide may cause sexual dysfunctions and impairment of spermatogenesis among male workers so exposed.

2.4 ENVIRONMENTAL TOXICOLOGY

Environmental toxicology is the study of the ecological effects of anthropogenic substances released into the environment. It is a relatively diverse feld addressing impacts to aquatic and terrestrial organisms and communities. The determination of potential risk associated with toxic agents is of interest to government regulators, industry, researchers, private organizations and citizen groups. In assessing the ecological risk associated with a chemical stressor, it is important to establish linkages between likely exposure concentrations and adverse effects to ecological receptors.

2.5 ECOTOXICOLOGY

Ecotoxicology is the science devoted to the study of the production of harmful effects by substances entering the natural environment, especially effects on populations, communities, and ecosystems; an essential part of ecotoxicology is the assessment of movement of potentially toxic substances through environmental compartments and through food webs. As a new subdivision of toxicology, "ecotoxicology" has emerged following observations that some persistent chemicals can exert toxic effects at several points in an ecosystem. The appearance of a chemical or the manifestation of a toxic effect may occur far away from its initial point of introduction into the environment. Methods for assessing the extent and significance of the movement of pollutants and their degradation products through the environment to target systems are discussed in a recent publication

2.6 MILITARY TOXICOLOGY

Military toxicology as a subdiscipline of toxicology focuses on the study of chemicals used in warfare and military operations. A chemical agent is a substance intended for use in military operations to kill, seriously injure or incapacitate people because of its physiological effects. Excluded from this definition are riot control agents, herbicides, smoke and flame. The first chemical warfare agent used in 1915 is chlorine which produced 5000 deaths with severe edema of lung. The chemical agents used in WWI comprised 24 species in 4 types including the so called mustard gas, a vesicants which produced cytotoxicity by a function of DNA alkylation. During the Iraq-Iran war in 1980s, nerve agents were widely used. This kind of agents exerts its toxicity by inhibiting the acytylcholinestease, an enzyme that catalyzes the hydrolysis of acetylcholine to choline and acetate. In the central nervous system (CNS), this enzyme plays a role in the function of peripheral neuromuscular junctions. During Operations Desert Shield and Desert Storm, Intelligence estimates were reinforced by the knowledge that Iraq had used chemical weapons during its war with Iran. Coalition forces defensive measures included issuing to individuals protective masks and overgarments, pretreatment tablets (pyridostigmine bromide), and mark-1 antidote kits (atropine and pralidoxime). Preparations also included employment of detector alarms, detector kits, Fox reconnaissance vehicles, and personnel and units trained in the detection of, and response to, the presence of chemical weapons in the field.

3. CLASSIFICATION OF TOXIC AGENTS

A poison could be defined as any agent capable of producing a deleterious response in a biological or a physiological system, seriously injuring function or producing death. Depending on the interests and the needs, toxic agents can be classified in terms of: (a) their target organ/site; (b) their practical use, such as irritants, riot control agents, warfare agents, smokes and other agents; (c) their source; (d) their effects; (e) their physical state; (f) their chemical structure; (g) their poisoning potential. The toxic agents can also be classified by characterizing their adverse response such as: (a) temporal duration with acute toxicity (generally a sudden onset for a short period of time); (b) long or permanent duration with chronic toxicity (usually constant or continuous exposure). In this book, we mainly discussed the military toxic agents in terms of their holistic healthy effects and target organs such as nerves, blood and lungs. In some parts the physiological states (gas, dust, liquid, etc.) and chemical structures are involved.

3.1 NERVE AGENTS

Nerve agents are a class of phosphorus-containing organic chemicals. As their name suggests, nerve agents attack the nervous system of the human body. The disruption is caused by interrupting the breakdown of the neurotransmitters that signal muscles to contract, preventing them from relaxing. Poisoning by a nerve agent leads to contraction of pupils, profuse salivation, convulsions, involuntary urination and defecation and eventual death by asphyxiation as control is lost over respiratory muscles. Some nerve agents are readily vaporized or aerosolized and the primary portal of entry into the body is the respiratory system. Nerve agents employed by foreign military are tabun (GA), sarin (GB), soman (GD) and VX. These agents can also be absorbed through the skin, requiring that those likely to be subjected to such agents wear a full body suit in addition to a respirator.

3.2 SYSTEMIC AGENTS

Systemic agents are the agents of hydrogen cynide and cyanogen chloride (CK). These agents are highly volatile and toxic chemical asphyxiants that interfere with the body's ability to use oxygen. Exposure to systemic agents can be rapidly fatal. It has whole-body effects, particularly affecting the CNS, the cardiovascular system and the pulmonary system. Systemic agents have strong irritant and choking effects. Its vapors are extremely irritating and corrosive. They are chemical warfare agents. Also, they are used commercially in chemical synthesis and fumigation.

3.3 BLISTER AGENTS

Blister agents are chemicals that can damage skin, eyes and lungs. Some examples of blister agents include sulfur mustard, lewisite and nitrogen mustard. They are named for their ability to cause severe chemical burns, resulting in large, painful water blisters on the bodies of those affected. Although these compounds have been employed on occasion for medical purposes, their most common use is as chemical warfare agents. These agents are liquids that can form vapor that floats into the air. People can be exposed by touching a liquid blister agent or breathing the vapor. Sulfur mustard harms the body within minutes of being exposed but symptoms may not start until 1 ~ 24 hours after coming into contact with it. Lewisite irritates the skin, eyes, nose and lungs immediately but the more serious symptoms appear 1 ~ 24 hours later.

3.4 ASPHYXIANTS

Asphyxia is a condition in which an extreme decrease in the concentration of oxygen in the body accompanied by an increase in the concentration of carbon dioxide leads to loss of consciousness or death. Asphyxia can be induced by choking, drowning, electric shock, injury, or the inhalation of toxic gases. Chlorine, phosgene and diphosgene are chemical asphyxiants. They irritate the alveoli in the lungs and cause the constant secretion of fluid into the lungs. The lungs slowly fill with fluid and the victim dies from the lack of oxygen. Thus, these agents are also called lung irritants or choking agents. There is no antidote for the intoxication of these agents.

3.5 INCAPACITATING AGENTS

Incapacitating agents are agents producing temporary physiological or mental effects, which will render individuals incapable of concerted effort in the performance of their assigned duties. They are nonlethal agents. Lethal agents are primarily intended to kill, but supposedly nonlethal agents can not kill many of those exposed to them. The term "incapacitation", when used in a general sense, is not equivalent to the term "disability" as used in occupational medicine and denotes the inability to perform a task because of a quantifiable physical or mental impairment. Although incapacitation may result from physiological changes such as mucous membrane irritation, diarrhea, or hyperthermia, the term "incapacitating agent" as militarily defined refers to a compound that produces temporary and nonlethal impairment of military performance by virtue of its psychobehavioral or CNS effects.

Following WW Ⅱ, the United States military investigated a wide range of possible psychobehavioral, chemical incapacitating agents to include psychedelic indoles such as lysergic acid diethylamide (LSD-25) and the marijuana derivative DMHP, certain tranquilizers, as well as several glycolate anticholinergics. One of the anticholinergic compounds, 3-quinuclidinyl benzilate, was assigned the NATO code BZ and was weaponized beginning in the 1960s for possible battlefield use. Although BZ figured as the compound responsible for hallucinations and violent deaths, this agent never saw operational use.

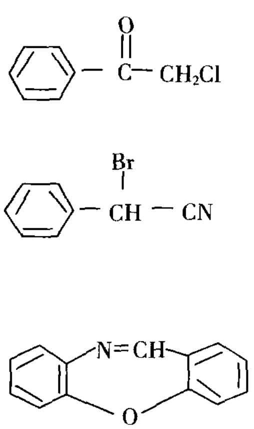
3.6 IRRITANTS

Irritants are chemicals that produce irritating or disabling effects when in contact with eyes, or when inhalled. These compounds are more properly defined in the west as riot-control agents. This group comprises compounds of divergent chemical structure, but all has the following characteristics: (a) active in low concentrations; (b) very low toxicity; (c) little or no latent period after contamination; (d) only local and temporary effects. These chemicals are very effective for putting troops temporarily out of action without being lethal, and their irritating actions are transient. On account of their reaction on the human body the compounds of this group can be subdivided into lachrymators (tear agents) and sternutators (nose agents).

3.6.1 LACHRYMATORS (TEAR AGENTS)

A lachrymatory agent or lachrymator (commonly referred to as tear gas) is a chemical compound that stimulates the corneal nerves in the eyes to cause tearing, pain, and even temporary blindness. Common lachrymators include CS, CR (Fig. 1-1 and Tab. 1-1), CN, nonivamide, bromoacetone, phenacyl bromide, xylyl bromide and syn-propanethial-S-oxide (from onions). Lacrymators often share the structural element Z = C-C-X, where Z = carbon or oxygen, and X = bromide or chloride. Lachrymators are thought to act by attacking sulphydryl functional groups in enzymes. One of the most probable protein targets is the TRPA1 ion channel that is expressed in sensory nerves (trigeminal nerve) of the eyes, nose and mouth.

During WW I (first in 1915) more toxic lachrymatory agents were used. Certain lachrymatory agents are often used by police to assist in bringing targeted persons under control, most notably tear gas, but also in some countries (Finland, Australia, and the USA). Another issued substance is Mace, which is used as a personal attack repellent.



CN(chloroacetophenone)

CA

CR

Fig. 1-1 Structure of lachrymators

3.6.2 STERNUTATORS (NOSE AGENTS)

A sternutator is a chemical substance that irritates the nasal and respiratory passages and causes coughing, sneezing, lacrimation, and sometimes vomiting. Adamsite was developed as a sternutator during the First World War. It is intensely irritating to the nose, throat and respiratory tract. Peripheral sensory nerves are affected, and eye, and to a lesser extent, skin irritation may occur. Lower dosages affect the upper respiratory tract; higher dosages cause deeper lung irritation.

Tab. 1-1 Physical & chemical properties for lachrymators

	CN	CA	CR
Appearance	Clear to yellowish-brown solid	Yellow, solid	Yellow, solid
Melting point	58 ~ 60℃	25℃	72℃
Boiling point	244 ~ 246℃	227 ~ 242℃	
Specific weight	1.31	1.52	
Solubility in water	Poor	Poor	Poor
Solubility in organic solvents	Good	Good	Good
Volatility at 20℃	105 mg/m^3	130 mg/m^3	
Smoke vapor odor	Apple-blossom	Rotting fruit	
Color	White	White	
Minimal irritant concentration (mg/m^3)	0.3	0.3	0.0047
Stability	Quite stable Not hydrolysed by water	Stable Decompose on heating at 160℃	Stable

People exposed to irritant agents may experience some or all of the following symptoms immediately after exposure: (a) eyes-excessive tearing, burning, blurred vision, redness; (b) nose-runny nose, burning, swelling; (c) mouth-burning, irritation, difficulty swallowing, drooling; (d) lungs-chest tightness, coughing, choking sensation, noisy breathing (wheezing), shortness of breath; (e) skin-burns, rash; (f) other-nausea and vomiting.

Long-lasting exposure or exposure to a large dose of irritants, especially in a closed setting, may cause severe effects such as the following: a. blindness, glaucoma (a serious eye condition that can lead to blindness); c. immediate death due to severe chemical burns to the throat and lungs; d. respiratory failure possibly resulting in death.

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