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REVIEW ARTICLE

IRRITANT COMPOUNDS: MILITARY RESPIRATORY IRRITANTS. PART II. STERNUTATORS

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Summary

Sternutators are substances that irritate the nasal and respiratory passages and cause coughing, sneezing, lacrimation, and sometimes vomiting. They are organoarsenic compounds and some of them were used as warfare toxic gases in World War I, namely diphenylaminochloroarsine, diphenylchloroarsine, diphenylcyanarsine, and phenyldichloroarsine. The effect of these irritants is in principle non-lethal.

Key words: irritant compounds; sternutators; organoarsenic compounds

INTRODUCTION

Irritant incapacitants, also called irritant compounds, riot control agents (RCAs), lacrimators or tear gases, are aerosol-dispersed chemicals that produce eye, nose, mouth, skin and respiratory tract irritation. Tear gas is the common name for substances that, in low concentrations, cause pain in the eyes, flow of tears and difficulty in keeping the eyes open. Historically, irritant incapacitans were categorized as lacrimators, sternutators, and vomiting agents based upon their predominant toxicity on the eyes, lungs, or digestive tract. All of these irritants were used in World War I (WWI) with different results. Lacrimators were summarized in our previous paper [1] and this review is focused on sternutators. These are substances that irritate the nasal and respiratory passages and causes coughing, sneezing, lacrimation, and sometimes vomiting.

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STERNUTATORS

WWI marked the birth of irritants as well as the modern age of CWAs. Both German and French forces used a wide variety of irritating agents, such as chloroacetone, bromoacetone, acrolein, benzoyl chloride, etc. [1]. The sternutator gases or nasopharyngeal irritants were also used in a wide scale [2]. They were capable, however, of producing extreme irritation of the nose, throat, and eyes, caused severe headache and nausea [3]. The symptoms were comparatively short in duration, and the gases were

Table 1. Irritant Chemical Agents with a Predominant Effect on the Upper Respiratory System (Sternites, Sternutators) Used in World War I

Chemical name CAS Registry Number (CAS RN)	Code	German name	Production
Diphenylaminochloroarsine 578-94-9	DM	Adamsite; D.M.	USA, GB
Diphenylchloroarsine 712-48-1	DA	Clark I; Blaukreuz	Germany
Diphenylcyanarsine 23525-22-6	DC	Clark II; Cyan Clark	Germany
Phenyldichloroarsine 696-28-6	PD	PFIFFIKUS	Germany France

not effective when the mask was worn [4]. The effect of these agents is in principle non-lethal, but it is very annoying and very difficult for soldiers to carry out combat operations [5]. The inhalation of these gases before the application of the mask made mask wearing very uncomfortable and was apt to cause its premature removal and thus to subject the wearer to the effect of the more important gases which usually accompanied or immediately followed the use of the sternutators [6]. This type of gas usually arrived in the nature of a surprise, since it was used in high explosive shells. Because of this it was difficult for the troops to recognize immediately the presence of the gas. A good example of this type of gas is diphenylchlorarsine, which was long and extensively used at the front. Overview of poison gases used in WWI as sternutators is shown in Table 1.

PHYSICAL, CHEMICAL AND BIOLOGICAL PROPERTIES OF STERNUTATORS

All known sternutators used in WWI as chemical warfare agents are organoarsenic-based compounds. These are all solid and for military use were dispersed in various smoke forms [7]. Arsenic in sternutators is in trivalent forms, which are more toxic than pentavalent forms. Sternutators are also known as nasal irritants and cause sneezing, malaise, headache, nausea, vomiting, sense of tightness in the chest etc. Symptoms were comparatively short in duration, and the gases were not effective when the mask was worn. The effect lasts for one to two hours [8]. Newerheless, the inhalation of these gases before the application of the mask made mask wearing very uncomfortable and was apt to cause its premature removal and thus to subject the wearer to the effects of the more important gases which usually accompanied or immediately followed the use of the sternutators.

Diphenylaminochloroarsine

Diphenylamine chloroarsine (Adamsite, DM, 10-Chloro-5,10-dihydrophenarsazinine, CAS RN: 578 -94-9) is an organoarsenic compound that was first synthesized in Germany by Heinrich Otto Wieland in 1915 and it was independently developed by the US chemist Roger Adams in 1918 [9].

Dipehylaminochlorarsine is a yellow-to-brown crystalline solid with very low vapour pressure, melting at 1950C and boiling at 410°C. The colour of the crystals depends on the purity. In vaporous form it appears as canary yellow smoke. It is readily soluble in some organic solvents (e.g. acetone, dichloromethane), but nearly insoluble in water (0.064 g/dm^3).

Adamsite is not a typical sternutator. It is intensely irritating to the nose, throat and respiratory tract, but also peripheral sensory nerves are affected. Adamsite is usually dispersed as an aerosol, making the upper respiratory tract the primary site of action. Lower dosages affect the upper respiratory tract; higher dosages cause deeper lung irritation. Symptoms are apparent 2 - 3 minutes after initial exposure. Recovery is usually complete in 1 - 2 hours if exposure is not prolonged.

Together with these symptoms, there is oppressive pain in the chest, shortness of breath, nausea and vomiting, unsteady gait, vertigo, weakness in the legs and all-over trembling. Mental depression may occur as symptoms progress. Very high dosages may damage the lungs. Deaths have been reported and lethal dosages are estimated to be some 15 000 mg.min/m^3.

Inhalation LCLo (Lethal Concentration Low) for human was estimated to 54 ppm for 30 minutes exposition. Lethal dose for acute toxicity in intravenous application was 35 mg/kg for mouse and 6 mg/kg for rabbit [10]. Adamsite is now regarded as obsolete. It has been widely replaced by riot control agents such as CS (o-chlorobenzalmalonitrile) which are less toxic and more rapid in onset of symptoms.

Adamsite has no odour, therefore symptoms are the first indication of exposure. Nevertheless, rapid detection using GC-MS is now available [11] as well as many other methods for detecting arsenic in biological samples, including X-ray fluorescence and neutron activation [12].

Diphenylchloroarsine

Diphenylamine chloramine (DA, Clark I, CAS RN: 712-48-1) is a low-melting solid organoarsenic compound with a melting point 44°C, boiling point 337°C, and density 1.55 g/cm^3. Its solubility in water is 2.72 mg/L and partition coefficient is log $P_{oct./wat.}$ is 4.520. It was first produced in 1878 by Michaelis and La Coste by the reduction of diphenylarsonic acid with sulfur dioxide [13]. Diphenylchlorarsine is known to cause sneezing, coughing, headache, salivation, and vomiting. The inhalation LCLo in human is estimated at 55 ppm for 30 minutes according to the National Technical Information Service. Vol. PB214-270.

Diphenylchloroarsine was used as a chemical weapon on the Western front during the trench warfare of World War I [14]. It belongs to the class of chemicals classified as vomiting agents. Also Japan used organoarsenic weapons including chlorodiphenylarsine after Japan's numerous invasions of China [15, 16] and Italy in Italo-Ethiopian War [17].

Diphenylchloroarsine could penetrate the gas masks of that period and irritated violently, forcing removal of the protecting device. The Germans called it "Maskenbrecher", "mask breaker", together with other substances with a similar effect: Adamsite, diphenylarsincyanide, and diphenylaminarsincyanide [18].

Diphenylcyanarsine

Diphenyl cyanarsine (DC, Clark II, CAS RN: 23525-22-6) is a low-melting solid organoarsenic compound with a melting point 33 - 35°C and boiling point 346 - 350°C (decomposition temperature). It forms colorless crystals with slight odor, resembling a mixture of bitter almonds and garlic [19]. Its solubility in water is low, like diphenylchloroarsine, and is hydrolyzed with release of hydrogen cyanide. Diphenylcyanarsine is the most toxic sternutator [20].

Phenyldichloroarsine

Phenyl dichloroarsine (Phenyl disk, Pfiffikus, CAS RN: 696-28-6) is colorless liquid, turns yellow slowly, and has a boiling point 255°C. It is a sternutator and lung irritant, but also vesicant [21]. Phenyldichlorarsine was used as a solvent for diphenylcyanarsine in war gases and mixed with 40% diphenylchloroarsine as Sternite [22].

THE FATE OF ARSENIC-CONTAINING CHEMICAL WARFARE AGENTS

Arsenic-containing chemical warfare agents (CWAs) were produced in large amounts during the WWI and World War II (WWII). After WWII the production sites and filling plants were destroyed and the CWAs were sunk in the North Sea and the Baltic Sea or deposited in the production sites and filling plants [23]. Residues of these chemicals are still present and contaminate soil and water [24, 25]. Several studies show an elevated arsenic content in dumpsite areas compared to reference areas [26, 27].

CHEMSEA PROJECT

Chemical Munitions Search and Assessment (CHEMSEA) is a flagship project of the Baltic Sea Region. The project lasts from the fall 2011 until 2014 is partly financed by the European Union. CHEMSEA is a transnational collaboration including project partners and associated organizations, including governmental agencies and international organizations. Ocean waters are in a constant flux, making the study of effect of CWAs on fish and other marine biota a challenging task. For the evaluation of the risks of dumped CWAs, triphenylarsine (TPA), sulphur mustard (H), Adamsite (DM) and Clark I (DA) are thought to pose the highest realistic risk to marine biota [28].

CHEMICAL ANALYSIS

Rapid detection using GC-MS, the most specific technique, is now available. Many other methods

for detecting arsenic in biological samples, including X-ray fluorescence and neutron activation, have been described [29, 30].

MAIN CLINICAL SYMPTOMS

Sternutators are solids which are highly dispersed in the form of smokes, and which are therefore more apt to collect in the upper respiratory passages rather than in the alveoli. Sufficient concentration or deep breathing incident to heavy work, however, will carry the particles into the deeper portions of the respiratory tract [31]. The phenylchloroarsines are the typical examples of this group. These compounds irritate the nerve endings in the nose and throat, producing violent sneezing or vomiting and coughing [32].

In parallel with these symptoms, there is oppressive pain in the chest, shortness of breath, nausea and vomiting, unsteady gait, vertigo, weakness in the legs and all-over trembling. Mental depression may occur as symptoms progress [5]. Very high dosages may damage the lungs. Deaths have been reported and lethal dosages are estimated to be some 15 000 mg.min/m^3 [2]. Inhalation LCLo for human was estimated to 54 ppm for 30 minutes exposition (National Technical Information Service, Vol PB214-270). Lethal dose for acute toxicity in intravenous application was 35 mg/kg for mouse (U.S. Army Armament Research & Development Command, Chemical Systems Laboratory, NIOSH Exchange Chemicals, Vol. NX11444) and 6 mg/kg for rabbit [10].

The mode of action of these smokes is not known definitely, though they are probably protoplasmic poisons per se, and on decomposition yield phenyl and arsenic groups as well as acid [33]. The fact that they are not gaseous prevents their affecting tissues to any large extent and this fact limits their field of impor-tance. They can be rather easily removed from the inspired air by a filtering device attached to the mask.

LONG-TERM HEALTH EFFECTS

There is some concern about neurotoxic effects [34], but these have not been documented in humans following topical application. There is equivocal evidence on mutagenicity, and both positive and negative results have been reported for different test systems [34-36]. The evidence available is not sufficient to evaluate human carcinogenicity [37].

MEDICAL MANAGEMENT

Principles of medical management are based on the rapid exit from the source of exposure. Clothing may be contaminated and should be removed with care to avoid spreading [38, 39].

PROTECTION, PROPHYLAXIS AND TRATMENT

A military-type gas mask provides protection. Breathing may be relieved by inhaling low concentrations of chlorine, e.g. from a bottle of bleach. Dust particles in the eye and on the skin should be removed with copious amounts of water. Treatment, by and large, is symptomatic [40]. If the inhaled dose is significant, the patient may require treatment for arsenic poisoning.

DECONTAMINATION AND NEUTRALIZATION

Oxidation with solutions of hypochlorite (bleach), chloramine or potassium permanganate is effective [40].

CONSLUSIONS

The group of poisonous substances known as saternutator is currently of no greater importance. They are capable, however, of producing extreme irritation of the nose, throat, and eyes and can cause severe headache and nausea. Although these compounds are not effective when a gas mask is used, they can be misused as terrorist agents.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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