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# Acute and Chronic Effects of Disturbance Control Factors, Complications and Treatment Method

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#### **Abstract**

The main aim of this study was to collect the experiences of Iranian researchers about different types of tear gases and pepper sprays, effects, treatment strategies and also to provide a guideline for the prevention of abuse of these dangerous agents. Tear gases include CS, CN, CA and OC sprays most common of which is CS. Tear gas that through the eyes of confusion (tearing and spasm) of the eyelids and closing the gases, and through upper respiratory tract irritation (sneezing and vomiting) temporary disables the person. Pepper spray, also known as OC spray (from "oleoresin capsicum"), OC gas, and capsicum spray, is a lachrymatory agent (a chemical compound that irritates the eyes to cause tears, pain, and temporary blindness). It is used in policing, riot control, crowd control, and personal self-defense, including defense against dogs and bears. Its inflammatory effects cause the eyes to swell, impairing the vision. The results also show that tear gas abstract by target tissues of the eyes, skin, and digestive system and affect the nerves. There is no effective antidote to common tear gases; however, decontamination is the first line of action. Once a person exposed to these agents, there is a variety of methods to remove as much chemical as possible and relieve the symptoms. The standard first aid for burning solutions in the eye is irrigation (spraying or flushing out) with water, and some evidence suggests that diphoterine solution, a first aid product for chemical sprays, may help with ocular burns or chemicals in the eye. As chemical gases are easily accessible and the risk of their being used threatens people, the proposed approach is necessary to control all gases. It is suggested that these gases and sprays be less available and less used. Furthermore, the proper administration route of these tools should be taught to people.

**Keywords:** Tear gas; Pepper spray; Debilitating agents; Skin conditions; Chemical injuries

#### Introduction

Tear gas and other chemical substances have gained widespread acceptance as a means of controlling civilian crowds and subduing barricaded criminals [1]. The most widely used forms of tear gas are o-Chlorobenzylidenemalononitrile [CS], Chloroacetophenone, [CN], dibenzoxazepine [CR] and Oleoresin capsicum [OC]. Proponents of their use claim that if used correctly, the noxious effects of exposure are transient and of no long-term consequences [2]. The use of tear gas in recent situations of civil unrest, however, demonstrates that exposure to this weapon is difficult to control and it is often not used correctly. Severe traumatic injuries from exploding tear gas bombs, as well as lethal toxic injuries, have been documented [3]. Moreover, available toxicological data are deficient as to the potential of tear gas agents to cause long-term pulmonary, carcinogenic, or reproductive effects. Published and recent unpublished in vitro tests have shown o-chlorobenzylidenemalononitrile to be both clastogenic and mutagenic. Sadly, the nature of its use renders analytic epidemiologic investigation of exposed persons difficult [3]. In 1969, eighty countries voted to include tear gas agents among chemical weapons banned under the Geneva Protocol [4]. There is an ongoing need for investigation into the full toxicological potential of tear gas chemicals and renewed debate on whether their use can be condoned under any circumstances

TEAR gas is a weapon that has become familiar to the world. Hardly a week goes by without press reports of tear gas being used in a public setting, typically for the dispersal of demonstrators or the subdual of a barricaded criminal [8]. Recent years have seen the use of large amounts of tear gas in several countries, including Chile; Panama; South Korea; and the Gaza Strip and West Bank, Israel. Liar gas is actually the common term for a family of chemical compounds that have been otherwise referred to as "harassing agents" because of their ability to cause temporary disablement. Some 15 chemicals have been used worldwide as tear gas agents. Six of these – chloroacetophenone [CN], o-chlorobenzylidenemalononitrile [CS], 10-chloro-5,l0-dihydrophenarsazine, bromo-tolunitrile, dibenzoxazepine [CR] and pepper spray [OC] have been used extensively. [8] In the United States,

Britain, and Europe, CN and CS have been employed most widely. o-Chlorobenzylidenemalononitrile [CS], in particular, is a weapon that has gained widespread acceptance as a means of controlling civilian populations during disturbances [9].

The widespread use of tear gas agents naturally questions their safety. Relatively little, however, has appeared in the mainstream medical literature regarding their toxicology. In general, authors of review articles have averred that, if used correctly, the noxious effects of exposure are transient and of no long-term consequence. [10-12]. Much emphasis has been given to the findings of the Himsworth Report, [13] the results of an inquiry by a committee appointed by the British Secretary of State for the Home Department following the use of CS in Londonderry, Northern Ireland, in 1969. In addition to investigating the use of CS in Londonderry, the committee reviewed a wide range of scientific data. Its main conclusion was that while exposure to CS can be lethal, most likely in the form of toxic pulmonary damage leading to pulmonary edema, such an occurrence would only be at concentrations that were several hundred times greater than the exposure dosage that produces intolerable symptoms [14]. Many questions remain, however, unanswered. Epidemiologic inquiry following the use of tear gas under actual field conditions has been almost completely absent [15,16].

The term tear gas, also called Lacrimator, can be used for any chemical substance that irritates the mucous membranes of the eyes, causing a stinging sensation and tears. These gases may also irritate the upper respiratory tract, causing coughing, choking, and general debility. Tear gas was first used in World War I in chemical warfare,

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but since its effects are short-lasting and rarely disabling, it came into use by law-enforcement agencies as a means of dispersing mobs, disabling rioters, and flushing out armed suspects without the use of deadly force.

The substances most often used as tear gases are synthetic organic halogen compounds; they are not true gases under ordinary conditions but are liquids or solids that can be finely dispersed in the air through the use of sprays, fog generators, or grenades and shells [3]. The two most commonly used tear gases are ω-chloroacetophenone, or CN, and o-chlorobenzylidenemalononitrile, or CS. CN is the principal component of the aerosol agent Mace and is widely used in riot control. It affects chiefly the eyes. CS is a stronger irritant that causes burning sensation in the respiratory tract and involuntary closing of the eyes, but its effects wear off more quickly, after only 5 to 10 minutes of breathing fresh air. Other compounds used or suggested as tear gases include bromoacetone, benzyl bromide, ethyl bromoacetate, xylyl bromide, and  $\alpha$ -bromobenzyl cyanide. The effects of tear gases are temporary and reversible in most cases. Gas masks with activated charcoal filters afford good protection against these gases. Different types of tear gas included CS, CN, CA and OC.

## CS and other tear gas agents

compound 2-chlorobenzalmalononitrile [also called o-chlorobenzylidene malononitrile] [chemical formula: C10H5ClN2], a cyanocarbon, is the defining component of a tear gas commonly referred to as CS gas, which is used as a riot control agent. Exposure to this agent causes a burning sensation and tearing of the eyes to the extent that the subjects cannot keep their eyes open. In addition, the burning irritation of the nose, mouth and throat mucous membranes causes profuse coughing, mucous nasal discharge, disorientation, and difficulty breathing, partially incapacitating the subject. CS gas is an aerosol of a volatile solvent [a substance that dissolves other active substances and evaporates easily] and 2-chlorobenzalmalononitrile, which is a solid compound at room temperature. CS gas is generally accepted as being non-lethal. It was discovered by two Americans, Ben Corson and Roger Stoughton [5] at Middlebury College in 1928, and the chemical's name is derived from the first letters of the scientists' surnames [6,8].

CS was developed and tested secretly at Porton Down in Wiltshire, England, in the 1950s and 1960s. CS was used first on animals, then subsequently on British Army servicemen volunteers. CS has less effect on animals due to under-developed tear-ducts and protection by fur [8].

CS is synthesized by the reaction of 2-chlorobenzaldehyde and malononitrile via the Knoevenagel condensation.

$$\begin{array}{c} CN \\ CN \\ CN \\ -H_2O \end{array}$$

 $ClC_6H_4CHO + H_7C[CN]_7 \rightarrow ClC_6H_4CHC[CN]_7 + H_7O$ 

The reaction is catalysed with weak base like piperidine or pyridine. The production method has not changed since the substance was discovered by Corson and Stoughton [9]. Other bases, solvent free methods and microwave promotion have been suggested to improve the production of the substance [10]. The physiological properties had been discovered already by the chemists first synthesising the compound in 1928: "Physiological Properties". Certain of these dinitriles have the effect of sneeze and tear gases. They are harmless when wet but to handle the dry powder is disastrous [9].

Many types of tear gases and other riot control agents have been produced with effects ranging from mild tearing of the eyes to immediate vomiting and prostration. CN and CS are the most widely used and known agents, but around 15 different types of tear gas have been developed worldwide e.g., adamsite or bromoacetone, CNB, and CNC. CS has become the most popular due to its strong effect and lack of toxicity in comparison with other similar chemical agents. The effect of CS on a person will depend on whether it is packaged as a solution or used as an aerosol. The size of solution droplets and the size of the CS particulates after evaporation are factors determining its effect on the human body [11].

The chemical reacts with moisture on the skin and in the eyes, causing a burning sensation and the immediate forceful and uncontrollable shutting of the eyes. Effects usually include tears streaming from the eyes, profuse coughing, exceptional nasal discharge that is full of mucus, burning in the eyes, eyelids, nose and throat areas, disorientation, dizziness and restricted breathing. It will also burn the skin where sweaty and/or sunburned. In highly concentrated doses, it can also induce severe coughing and vomiting. Almost all of the immediate effects wear off within an hour [such as exceptional nasal discharge and profuse coughing], although the feeling of burning and highly irritated skin may persist for hours. Affected clothing will need to be washed several times or discarded.

People or objects contaminated with CS gas can cause secondary exposure to others, including healthcare professionals and police. In addition, repeated exposure may cause sensitisation [12]. Although described as a non-lethal weapon for crowd control, studies have raised doubts about the classification of CS. As well as causing severe pulmonary damage, CS can also significantly damage the heart and liver [13].

On 28 September, 2000, Prof. Dr. Uwe Heinrich released a study commissioned by John C Danforth, of the United States Office of Special Counsel, to investigate the use of CS by the FBI at the Branch Davidians' Mount Carmel compound. He concluded that the lethality of CS used would have been determined mainly by two factors: whether gas masks were used and whether the occupants were trapped in a room. He suggests that if no gas masks were used and the occupants were trapped, then, "...there is a distinct possibility that this kind of CS exposure can significantly contribute to or even cause lethal effects" [2].

At least one study has associated CS exposure with miscarriages [17]. This is consistent with its reported clastogenic effect [abnormal chromosome change] on mammalian cells.

In Israel, CS gas was reported to be the cause of death of three boys on 31 December, 2010, [18] although the Israel Defense Forces have questioned the veracity of the report. Other reports [19] suggest the cause of death was in fact the impact of a high-velocity CS gas canister to the chest. In Egypt, CS gas was reported to be the cause of death of several protesters in Mohamed Mahmoud Street near Tahrir square during the November , 2011 protests. The solvent in which CS is dissolved, methyl isobutyl ketone [MIBK], is classified as harmful by inhalation; irritating to the eyes and respiratory system; and repeated exposure may cause skin dryness or cracking [20].

CS is used in spray form by many police forces as a temporary incapacitant to subdue attackers or persons who are violently aggressive. Officers who are trained in the use and application of CS spray are routinely exposed to it as part of their training. Blank pistol cartridges carrying CS in powder form have been released to the public. These, when fired at relatively close ranges, fully expose the target to the effects of CS, and are employed as a potent defensive weapon in regions where blank firing pistols are legally permitted for such use [12]. Although predominantly used by police, it has also been used in criminal attacks in various countries [21].

Use of CS in war is prohibited under the terms of the Chemical Weapons Convention, signed by most nations in 1993 with all but 5 other nations signing between 1994 and 1997. The reasoning behind the prohibition is pragmatic: use of CS by one combatant could easily trigger retaliation with much more toxic chemical weapons such as nerve agents. Only 4 nations have not signed the Chemical Weapons Convention and are therefore unhindered by restrictions on the use of CS gas: Angola, Egypt, North Korea and Somalia. Domestic police use of CS is legal in many countries, as the Chemical Weapons Convention prohibits only military use [22-24].

Tear gas, formally known as a lachrymatory agent or lachrymator [from lacrima meaning "tear" in Latin], is a chemical weapon that stimulates the corneal nerves in the eyes to cause tears, pain, vomiting, and even blindness. Common lachrymators include pepper spray [OC gas], CS gas, CR gas, CN gas [phenacyl chloride], nonivamide, bromoacetone, xylyl bromide, syn-propanethial-S-oxide [from onions], and Mace [a branded mixture]. Lachrymatory agents are commonly used for riot control. Their use as chemical warfare agents is prohibited by various international treaties. During World War I, toxic lachrymatory agents were used increasingly.

Tear gas works by irritating mucous membranes in the eyes, nose, mouth and lungs, and causes crying, sneezing, coughing, difficulty breathing, pain in the eyes, and temporary blindness. With CS gas, symptoms of irritation typically appear after 20–60 seconds of exposure [1] and commonly resolve within 30 minutes of leaving [or being removed from] the area [2]. With pepper spray the onset of symptoms, including loss of motor control, is almost immediate [2]. There can be considerable variation in tolerance and response, according to the National Research Council [US] Committee on Toxicology [3].

The California Poison Control System analyzed 3,671 reports of pepper spray injuries between 2002 and 2011 [4]. Severe symptoms requiring medical evaluation were found in 6.8% of people, with the most severe injuries to the eyes [54%], respiratory system [32%] and skin [18%]. The most severe injuries occurred in law enforcement training, intentionally incapacitating people, and law enforcement [whether of individuals or crowd control] [4]. Lachrymators are thought to act by attacking sulfhydryl 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, mouth and lungs.

As with all non-lethal, or less-than-lethal weapons, there is some risk of serious permanent injury or death when tear gas is used [5,6]. This includes risks from being hit by tear gas cartridges, which include severe bruising, loss of eyesight, skull fracture, and even death [7]. A case of serious vascular injury from tear gas shells has also been reported from Iran, with high rates of associated nerve injury [44%] and amputation [17%], [8] as well as instances of head injuries in young people [9].

While the medical consequences of the gases themselves are typically limited to minor skin inflammation, delayed complications are also possible: people with pre-existing respiratory conditions such as asthma, who are particularly at risk, are likely to need medical attention [1] and may sometimes require hospitalization or even ventilation support [10]. Skin exposure to CS may cause chemical burns [11] or induce allergic contact dermatitis [1,2]. When people are hit at close range or are severely exposed, eye injuries involving scarring of the cornea can lead to a permanent loss in visual acuity [12].

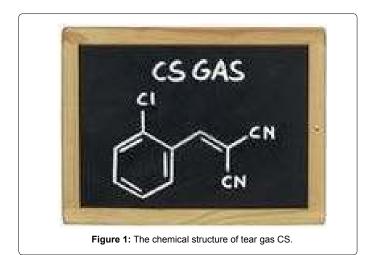
Use of tear gas in warfare [as all other chemical weapons] is prohibited by various international treaties [13] that most countries have signed. Police and private self-defense use is not banned in the same manner. Armed forces can legally use tear gas for drills [practicing with gas masks] and for riot control. First used in 1914, xylyl bromide was a popular tearing agent since it was easily brewed. The US Chemical Warfare Service developed tear gas grenades for use in riot control in 1919 [14].

Certain lachrymatory agents are often used by police to force compliance, most notably tear gas [6]. In some countries [e.g., Finland, Australia, and the United States], another common substance is mace. The self-defense weapon form of mace is based on pepper spray, and comes in small spray cans, and versions including CS are manufactured for police use [15], Xylyl bromide, CN and CS are the oldest of these agents, and CS is the most widely used. CN has the most recorded toxicity [1].

Typical manufacturer warnings on tear gas cartridges state "Danger: Do not fire directly at person[s]. Severe injury or death may result" [16]. Such warnings are not necessarily respected, and in some countries, disrespecting these warnings is routine. In the 2013 protests in Turkey, there were hundreds of injuries among protesters targeted with tear gas projectiles [23]. In the Israeli-occupied territories, Israeli soldiers have been routinely documented by Israeli human rights group in firing direct tear gas canisters at activists, some of which resulted in fatalities [17]. However, tear gas guns do not have a manual setting to adjust the range of fire. The only way to adjust the projectile's range is to aim towards the ground at the correct angle. Incorrect aim will send the capsules away from the targets, causing risk for non-targets instead.

A variety of protective equipment may be used, including gas masks and respirators. In riot control situations, protesters sometimes use equipment [aside from simple rags or clothing over the mouth] such as swimming goggles and adapted water bottles [20]. There is no effective antidote to common tear gases [1]. Getting clear of gas and into fresh air is the first line of action [1]. Once a person has been exposed, there is a variety of methods to remove as much chemical possible and relieve symptoms [1]. The standard first aid for burning solutions in the eye is irrigation [spraying or flushing out] with water, [21] and some evidence suggests that diphoterine [22] solution, a first aid product for chemical sprays, may help with ocular burns or chemicals in the eye [23] shown in Figure 1.

The term "tear gas" is a misnomer. For one thing, "tear gas" seems to imply something innocuous you would think it's just a chemical that makes you tear up. In fact, tear gas is a dangerous, potentially lethal chemical agent which is outlawed under the Chemical Weapons Convention for use during wartime. As the Omega Research Foundation argues: "Less-lethal weapons are presented as more acceptable alternatives to guns; but these weapons augment rather than replace the more lethal weapons. Euphemistic labels are used to create the impression that these weapons represent soft and gentle forms of control. CS is never referred to by the authorities as vomit gas, in spite



of its capacity to cause violent retching." NGO Physicians for Human Rights believes that 'tear gas' is a misnomer for a group of poisonous gases which, far from being innocuous, have serious acute and longer-term adverse effects on the health of significant numbers of those exposed." We aim to change the conversation on tear gas by calling this so-called "nonlethal" weapon what it is: a chemical weapon. We view tear gas, pepper spray, and all "lachrymatory agents" and so-called "non-lethal weapons" as chemical weapons in the war on democracy.

It's important to note that "tear gas" is not actually a gas. The active chemicals in all different kinds of tear gas and pepper spray are solid at room temperature, and need to be mixed with other chemicals in order to produce what is called an aerosol— solid particles finely dispersed in the air, similar to smoke or a cloud. They can also be dissolved in liquid solution, which is how pepper spray is commonly used. This is significant since the symptoms and treatment for tear gas and pepper spray exposure can vary depending on the kind of aerosolizing agents or solvents used. For example, when silica gel is added to CS to form CS1 or CS2, the result is a stronger tear gas which is more water resistant. Methylene chloride, a known carcinogen, was used as a solvent in the tear gas and pepper spray against WTO protesters in Seattle in 1999. This is believed to have caused many health problems for protesters who were exposed.

## The history of chemical gas

As waves of popular uprising have spread across the globe, these disparate movements have all faced overwhelming repression from their own police or military forces. Beyond a general sense of popular power, what unites these popular revolts more than anything else is the tool used to quell mass protests: tear gas. But perhaps what is most striking is that the same handful of tear gas manufacturers ships their gas to repressive regimes around the world.

Widely regarded as a "non-lethal" technology—despite the counter-factuals we have known for quite some time the appeal of tear gas to state security is its effectiveness for blanket, indiscriminate crowd control. With the ability to quickly transform a bustling city boulevard overflowing with political energy into a desolate no-man's land, it is no wondered that those who oppose popular demonstrations of political will turn to tear gas as a means to crush dissent.

As a result of the Arab uprisings, the state security market in the Middle East has ballooned into a multi-billion dollar industry. But the ones profiting most from the stifling of political expression are tear

gas manufacturers, most of which are US-based [24]. In Egypt during late 2011, port workers in Suez took note of this and refused to unload a shipment of tear gas from Pennsylvania-based Combined Systems. Turkey, which came under criticism for excessive use of tear gas during the Diren Gezi movement of summer 2013, reportedly imported 628 tons of teargas in the period from 2000 to 2012. Muammer Guler, who recently resigned as Interior Minister of Turkey, confirmed that during the Gezi protests Turkish police added tear gas to the water used in the water cannons on armored riot control vehicles [25] (Figure 2).

Chemical weapons have, for at least the last century, been viewed as a dishonorable and offensive kind of weapon [26-38]. However, chemical weapons of some sort have been part of warfare as far back as Thucydides, when "the Peloponnesians tried to reduce the town of Plataea with sulphur fumes in the fifth century BC." The first international agreement aimed at restricting their use took place at the Hague Conference of 1899, where certain attendees agreed "to abstain from the use of projectiles the sole object of which is the diffusion of asphyxiating or deleterious gas." The two most significant military powers to refuse the above provision were the US [39,40] and the UK by the outbreak of World War I, a more universal taboo against the use of chemical weapons began to take hold. In the Great War, German forces "handed the allies a propaganda coup" by being the first to use lethal chemical munitions [41]. This first-to-act status enabled their adversaries to blame Germany for "the initiation of 'frightfulness' [as gas warfare was dubbed]." It is important to note that some of the chemical weapons used in WWI were RCAs, including, achrymators [tearproducing agents] like chloroacetophenone [CN], along with vomiting agents." Initially, CN gas was developed for domestic law enforcement use in France [42,43]. In fact, the first chemical munition brought to the front was a canister of CN gas carried by a French policeman [44,45].

The inter-war period saw a proliferation of international institutions and conventions. Among these newly founded agreements was the Washington Treaty, championed by the U.S. The Washington Treaty established that "the use in war of asphyxiating, poisonous or other gases, and all analogous liquids, materials or devices" is prohibited. This agreement is notable in that it did not prohibit the stockpiling or development of chemical weapons—simply their use [44,45]. Additionally, the U.S. did not consider RCAs "chemical weapons." The language of the Washington Treaty was reproduced in the 1925 Geneva Protocol, which the U.S. signed, though did not actually ratify until 1975 [46,47].

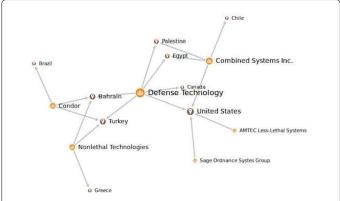


Figure 2: A network graph showing tear gas manufacturers and the countries in which their products are used.

During World War II, none of the belligerents used chemical weapons, though all maintained capabilities in the area. The reasons for the non-use of chemical weapons varied, but in part it was based on the fear of alienating neutral parties, fear of retaliation in kind, and the limited utility of chemical weapons in a fast-moving war. The next major use of chemical weapons came in Vietnam, where the US used chemical defoliants to destroy ambush-friendly jungles and riot control agents, including ortho-chlorobenzylidene-malononitrile [CS], to force enemy combatants out of hiding in order to facilitate lethal targeting. The use of such chemicals in Vietnam stirred outrage in much of the international community and within the U.S. In response, the General Assembly of the United Nations in 1969 passed Resolution 2603A, "which purportedly gave its definitive interpretation of the [Geneva] Protocol to include tear gas?" However, the status of tear gas, RCAs, and other chemical agents remained unresolved [47].

## Pepper spray [OC]

Pepper spray, also known as OC spray [from "oleoresin capsicum"], OC gas, and capsicum spray, is a lachrymatory agent [a chemical compound that irritates the eyes to cause tears, pain, and temporary blindness] used in policing, riot control, crowd control, and personal self-defense, including defense against dogs and bears [1,2]. Its inflammatory effects cause the eyes to close, impairing vision. This temporary blindness allows officers to more easily restrain subjects and permits people using pepper spray for self-defense an opportunity to escape. Although considered a less-than-lethal agent, it has been deadly in rare cases, and concerns have been raised about a number of deaths for which pepper spray may have been a contributing factor.

The active ingredient in pepper spray is capsaicin, which is a chemical derived from the fruit of plants in the Capsicum genus, including chilis. Extraction of oleoresin capsicum from peppers requires capsicum to be finely ground, from which capsaicin is then extracted using an organic solvent such as ethanol. The solvent is then evaporated, and the remaining wax-like resin is the oleoresin capsicum. An emulsifier such as propylene glycol is used to suspend the OC in water, and pressurized to make it aerosol in pepper spray. The High performance liquid chromatography [HPLC] method is used to measure the amount of capsaicin and major capsaicinoids within pepper sprays.

Determining the strength of different manufactures of pepper sprays can be confusing and difficult. Statements a company makes about their product strength are not regulated. A method using the capsaicin and related capsaicinoids [CRC] content of the product is unreliable as well, because there are 6 different types of Capsaicinoids, varying in different levels of heat [Capsaicin], which manufacturers do not state which particular type of Capsaicinoids are used. Personal pepper sprays can range from a low of 0.18% to a high of 3%. Most law enforcement pepper sprays use between 1.3% and 2%. The federal government of the United States has determined that Bear Attack Deterrent Sprays must contain at least 1.0% and not more than 2% CRC. CRC does not measure the amount of Oleoresin Capsicum [OC] within the formulation. Instead, CRC is the heat bearing and pain producing components of the OC.

The federal government of the United States makes no mention of SHU [Scoville heat units] or OC in their requirements, only CRC [only for Bear Attack Deterrent Sprays]. But, there are countries [Italy, Portugal and Spain – see below, under "Legality"] and a few states within the US [Michigan and Wisconsin with a 10% OC limit] that do mention OC limitations. Some manufacturers may show a very high percentage of OC [Oleoresin Capsicum] and, although OC is the active

ingredient within the formulation, it does not indicate pepper spray strength. High OC percentage also indicates that a spray has more oil content; which, can possibly use lower grade pepper oils [but, more of it], or lower grade Capssaicinoids [within the Major CRC] and also has less ability to soak and penetrate skin than a formula with a less, but higher-quality, pepper oil, because oil has hydrophobic properties.

The OC percentage only measures the amount of peppers contained in the defense spray, not the strength, pungency or effectiveness of the product. Other companies may show a high SHU. The SHU is measured at the base resin and not by what comes out of the aerosol. The rated high heat of the resin may be diluted down depending on how much of it is put in the can. There are several counterparts of pepper spray developed and legal to possess in some countries for example Brazil, Russia and United Kingdom.

Pepper spray is an inflammatory agent which causes immediate closing of the eyes, difficulty breathing, runny nose, and coughing [48]. The duration of its effects depends on the strength of the spray but the average full effect lasts around thirty to forty-five minutes, with diminished effects lasting for hours. In 1998, The European Parliament Scientific and Technological Options Assessment [STOA] published "An Appraisal of Technologies of Political Control" [49] with extensive information on pepper spray and tear gas. They write: The effects of pepper spray are far more severe, including temporary blindness which lasts from 15–30 minutes, a burning sensation of the skin which lasts from 45 to 60 minutes, upper body spasms which force a person to bend forward and uncontrollable coughing making it difficult to breathe or speak for between 3 to 15 minutes.

For those with asthma, taking other drugs, or subject to restraining techniques that restrict the breathing passages, there is a risk of death. The Los Angeles Times reported in 1995 at least 61 deaths associated with police use of pepper spray since 1990 in the USA [50]. The American Civil Liberties Union [ACLU] documented 27 people in police custody who died after exposure to pepper spray in California since 1993 [7]. However, the ACLU report counts any death occurring within hours of exposure to pepper spray. In all 27 cases, the coroners' report listed other factors as the primary cause of death, though in some cases the use of pepper spray may have been a contributing factor [51].

In a 1993 Aberdeen Proving Ground study, the US Army concluded that pepper spray could cause mutagenic and carcinogenic effects, sensitization, cardiovascular, neurological and pulmonary toxicity, as well as possible human fatalities. There is a risk in using this product on a large and varied population" [52]. However, the pepper spray was widely approved in the US despite the reservations of the US military scientists after it passed FBI tests in 1991. As of 1999, it was in use by more than 2,000 public safety agencies [53].

Special Agent Thomas W. W. Ward, the head of the FBI's Less-Than-Lethal Weapons Program at the time of the 1991 study, was fired by the FBI and sentenced to two months in prison for receiving payments from a pepper gas manufacturer while conducting and authoring the FBI study that eventually approved pepper spray for FBI use. Prosecutors said that from December 1989 through 1990, Ward received about \$5,000 a month for a total of \$57,500, from Luckey Police Products, a Fort Lauderdale, Florida-based company that was a major producer and supplier of pepper spray. The payments were paid through a Florida company owned by Ward's wife [54].

Pepper spray has been associated with positional asphyxiation of individuals in police custody. There is much debate over the actual "cause" of death in these cases. There have been few controlled clinical

studies of the human health effects of pepper spray marketed for police use, and those studies are contradictory. Some studies have found no harmful effects beyond the aforementioned effects [55].

Direct close-range spray can cause more serious eye irritation by attacking the cornea with a concentrated stream of liquid [the so-called "hydraulic needle" effect]. Some brands have addressed this problem by means of an elliptically cone-shaped spray pattern.

For individuals not previously exposed to OC effects, the general feelings after being sprayed can be best likened to being "set alight." The initial reaction should the spray be directed at the face, is the completely involuntary closing of the eyes [sometimes described as leading to a disconcerting sensation of the eyelids "bubbling and boiling" as the chemical acts on the skin], an instant sensation of the restriction of the airways and the general feeling of sudden and intense, searing pain about the face, nose, and throat. Coughing almost always follows the initial spray. Subsequent breaths through the nose or mouth lead to ingestion of the chemical, which feeds the feeling of choking. Police are trained to repeatedly instruct targets to "breathe normally" if they complain of difficulty, as the shock of the exposure can generate considerable panic as opposed to actual physical symptom. Capsaicin is not soluble in water, and even large volumes of water will not wash it off. In general, victims are encouraged to blink vigorously in order to encourage tears, which will help flush the irritant from the eyes.

A formal study of five often-recommended treatments for skin pain [Maalox, 2% lidocaine gel, baby shampoo, milk, or water] concluded that there is no significant difference in pain relief provided by five different treatment regimens. Time after exposure appeared to be the best predictor for decrease in pain [56]. To avoid rubbing the spray into the skin, thereby prolonging the burning sensation, and, in order to not spread the compound to other parts of the body, victims should try to avoid touching affected areas. There are also wipes manufactured for the express purpose of serving to decontaminate someone having received a dose of pepper spray. Many ambulance services and emergency departments use baby shampoo to remove the spray which has been reported to be generally of good effects. Some of the OC and CS will remain in the respiratory system, but the recovery of vision and the coordination of the eyes can be expected within 7 to 15 minutes [19]. Some "triple-action" pepper sprays also contain "tear gas" [CS gas], which can be neutralized with sodium metabisulfite [Campden tablets, used in home brewing], though it is not water-soluble either and must be washed off using the same procedure as for pepper spray.

#### Methods

A community medicine specialist and an expert with bachelor degree performed the literature search. They searched English and Farsi databases including MEDLINE, ISI and Scopus and Iranian databases including Iran Medex and Iran doc. The keywords were chemical gas, pepper spray and tear gases in the two languages. The titles and abstracts were evaluated and those with irrelevant base on both topics were excluded. The full texts of other articles were assessed according to the project goals. No specific evaluation was conducted on the quality of the reviewed manuscripts and their publication in accredited journals [according to The Commission for Accreditation and Improvement of Medical Journals affiliated to Iranian Ministry of Health & Medical Education]. Most of the evidences used were in the first 4 levels of 7 defined levels for evaluation of documents. In other words, the included articles were randomized controlled trials, cohort and historical cohort, case - control, case series and case reports and correlational studies [4,5].

#### Results

We found 100 articles in regard to chemical warfare against Iranian people which were published in approved medical journals. Most of these articles focused on the effects and treatment of tear gas complications. We collected the information and concluded from performed investigations and presented a preventive guideline containing 5 parts about 5 stages [before, at the time, and after the incident and also on early and late biological effects of the victims].

#### How does tear gas work?

Typical RCAs [Riot Control Agents] such as tear gas are delivered by either sprays or grenade canisters fired from baton guns. The canisters themselves can be hazardous as they usually generate a lot of heat and will cause nasty burns. If they are fired at close range, they can cause serious damage to the body and even result in death [41,42].

When chemicals used in tear gas react with moisture, they cause a burning sensation, meaning that the eyes, skin and lungs are extremely susceptible. Oil-based creams, sunscreens and make-up will also absorb tear gas and should not be worn in occasions where they might be used. Tear gas attacks the lungs, so those suffering from any respiratory diseases, including asthma should seriously consider the potentially dangerous effects this may have on their condition [45].

Streaming and burning of eyelids and throat as well as excessive coughing are all reactions to tear gas. An excessive amount of mucus coming from the nose, eyelids and throat is also common. People often report that they feel disorientated and dizzy just after breathing it in. The effects usually wear off within an hour, although the feeling of burning and highly irritated skin may persist for hours [40-42].

#### Preventive points

Preventive measures before the incident are as follows:

To provide the necessary infra-structures such as:

Strengthening the hardware and software facilities for rapid health-related reactions; Prediction of required preventive equipment and devices in the stocks of passive defense organization and update them with a checklist periodically; Designing and manufacturing the standard protective equipment against chemical agents in the factories throughout the country; Preparation of the new standard containers equipped with experienced trained personnel and portable emergency defense sites particularly for washing and decontaminating the victims [the current checklist should be revised];

Educating people, especially military and passive defense forces properly. The content of such training can be focused on early detection of chemical attacks signs, the first necessary critical measures, self-protection, properly transferring the injured victims, patient resuscitation and communicating with agencies and authorities for coordinated actions. It should be noticed that people should not be exposed to unnecessary distress during these educations; strengthening the passive defense scientific network; Implementing effective training exercises and periodic organized educational maneuvers particularly for passive defense volunteers and military forces.

Some researchers have used calcium chloride and magnesium oxide powder as anti-gas powder for skin exposures;

Use of the standard protective devices, particularly standard masks and wind wards; Ghasemi Boroumand et al. a descriptive study conducted on 189 selected male victims from 6 provinces in Iran, evaluated the protective effects of both wind wards and masks

in preventing ocular and pulmonary complications. They stated that the use of protective equipment [masks and wind wards] reduced the severity of lung and eye lesions. Namely, when the using rate of the protective equipment rose, severity of ocular and pulmonary lesions reduced significantly [11].

Gas masks [often called a respirator] are the best tool to protect from the chemical gases. A gas mask consists of a rubber mask with a canister and filter fitted to the side. It is fitted to the size and shape of your face, and you should not assume that yours will fit someone else. Ensure you have a spare canister, as they do need changing after several hours [this depends on the make and model of the gas mask as well as how long it has been used].

Those who already have a gas mask should make sure it is working properly and is correctly fitted. Any masks purchased online or in military surplus stores should be checked by an expert to ensure they work correctly. The next best thing after a gas mask is an escape hood, which is cheaper and is not subject to the same export rules. You can also use a builder's respirator that covers your nose and mouth – but make sure that you use appropriate filters. Failing that, a dust mask for building and airtight goggles will provide some degree of protection.

If only a gas mask, or a mask and goggles are available, they should be used. This might enable the user to continue working in the gas. However body and clothes decontamination are still needed.

If no protection is available, mouth and nose should be covered using a handkerchief or cloth or the inside of the coat to protect the airway [the outside of your jacket is likely to be contaminated].

Standing in the fresh air allows the breeze to carry away the CS gas.

Keeping both arms outstretched would help CS gas to come off the clothing.

As most RCAs are heavier than air and the highest concentrations tend to sit nearer to the ground, getting to higher grounds is recommended.

It should be remembered that the gas will impregnate clothing for many months, so any clothing that may have been contaminated should be immediately washed several times or discarded.

Any exposed skin should be washed with soap and water. Showering firstly in cold water, then warm water should be considered. However, bathing should be avoided.

Rubbing eyes or face should be avoided or this will reactivate any crystals.

## Use of the fine and thin texture and if possible, plastic clothes

According to published researches, mustard gas can penetrate ordinary or even leather clothing and thus, after a few minutes can reach the body tissues. This is while the rubber sheath can, at least for a few hours, protect the body. Also this agent can percolate from ordinary and plastic masks [12].

## Going to a high altitude area

Because tear gases are heavier than air, at the time of release, victims should climb to a height of at least 10 meters above the ground in the attacked area [18]. This comment also was recommended by Iranian researchers [57-58]. Removal of clothes as soon as possible: Sulfur mustard may remain in the liquid form on contaminated clothing and other devices for many hours or even days and it may affect the biological tissues [24,25]. Therefore, when exposure occurs,

all contaminated clothes should be removed from the body in the shortest possible time and should be destroyed. Plastic gloves can be used to remove the clothing. Rescuers and medical personnel are at risk of adverse effects, especially for skin blistering, if their bodies or their clothes come in contact with contaminated victims [20,21].

## Immediate body wash

Affected people should wash their body with plenty of fresh and clean water as soon as possible. During chemical attacks on Iran, some of the Iranian victims had washed their hands and faces by the water available in the area, while they were not aware that the water was contaminated by the SM toxin. This was a reason for eye and skin problems in these victims. Thus, water contamination should be considered before using it for eye and skin irrigation [16]. In these conditions, using mobile tanks or vehicles carrying clean water and showers will be very useful. Also, field centers equipped with healthy water should be established at the nearest safe place for treatment and rehabilitation facilities around the affected areas. Washing the skin with 0.5% household bleach is also useful [10].

## Transport the injured people

With usage of adequate protective equipment, injured people should be transferred to areas with humid climates [17].

# Post preventive measures after the incident

**Decontamination of the area:** To reduce environmental pollution, Calcium hypochloride, stilbestrol or permanganate can be used to decontaminate the polluted areas [10,11].

## Protective measures for residence in contaminated area

The environmental sustainability of sulfur mustard is high. Hence, the agent is able to remain in soil for at least 10 years [17] and it can persist in the clothes and be active in soil even for months at low temperatures. It can be found with the concentrations of 1 to 25 milligrams per cubic meter in 6 to 12 inches in the soil around the affected zones. In addition, on the basis of the available researches, people who live in polluted areas, even with no obvious symptoms at the time of exposure, may eventually develop mustard-induced complications, especially pulmonary complications [18]. Therefore, residence in high traffic areas should be prohibited in coming to the polluted area, until complete decontamination of area is performed.

#### Early preventive measures for injured people

In cases of severe acute respiratory problems, a pseudo-membrane may form in the upper respiratory tract which may cause laryngospasm and stridor. This complication may lead to asphyxia and death. For prevention of death, an urgent tracheostomy and immediate treatment in the ICU might be required [19].

After chemical attacks, even exposed people without symptoms should irrigate their eyes for 5–15 minutes with copious amounts of healthy water, as soon as possible [9,10,15]. Solutions other than clean water that are recommended for washing the eyes include: normal saline, sodium bicarbonate solution 1.5%, Dichloramine T 0.5%, sodium sulfate or magnesium sulfate, and zinc or boric acid [20-22]. Also, diluted infant shampoo has shown to be useful for eye decontamination [9]. Application of topical anesthetic eye drops should be avoided for both healthy and damaged corneas [23].

Local steroids should also be avoided except in the presence of chemosis and epithelial edema [23]. Pads and bandages should not be used for eye lesions, as the toxic effects of sulfur mustard may exacerbate its effect due to raised temperature in the injured eye leading to ocular lesions [21]. In the case of skin exposure, initially, calcium chloride or magnesium oxide powder as the anti-gas agents should be used immediately on the exposed areas of skin followed by washing with soap and water [20]. In case of Gastrointestinal [GI] involvement, emesis should not be induced. After feeding 100 to 200 ml of milk, gastric lavage would be indicated. Activated charcoal is not of proven efficacy but is not contraindicated either [9].

## Post preventive measures for injured people

Acute effects of sulfur mustard-induced lesions gradually turn into the chronic phase. In this phase, our efforts should be focused on preventing from further complications. For this purpose, the following points are suggested: In the late phase, scarring and stenosis of the airways may occur. In these cases, removing debris by bronchoscopic maneuvers would be very useful and life-saving [24]. In the treatment of chronic lesions caused by sulfur mustard, corticosteroids are widely used. The long-term use of these drugs may cause undesirable effects such as growth inhibition, diabetes, muscle atrophy, osteoporosis, salt retention, dementia and opportunistic infections. Therefore, during the application of these medications, the injured victims should be made aware of these complications [35]. More than two-thirds of the chemical veterans with chronic bronchiolitis are overweight or obese. These patients should reduce their weights to prevent superimposing complications [46]

Treatment of magnesium deficiency in sulfur mustard induced asthmatic patients can decrease the side effects of asthma [37]. Some of the common medications used in lung diseases such as Theophylline have negative impact on the quality of sleep for the victims [58]. Therefore, such drugs should be substituted with other appropriate medications. In patients with photophobia, using dark sunglasses is recommended [59].

The use of petroleum jelly to prevent sticking of the eyelid edges is useful. To prevent corneal perforation, victims with the mustard eye injuries should not stay in hot and dry areas and use artificial tears. In addition, exposed people should avoid jobs such as sewing and driving for long hours since these conditions exacerbate the dryness of the eyes and increases the risk of corneal perforation [29].

Some complications such as COPD, pruritus, visual problems and mental disorders affect the quality of life in exposed people. In addition, quality of life in victims who exercise improves compared to those who are not active enough [60-62]. Depression is very common among the victims and the most important complication is suicide which could be prevented to some extent. Tavallai et al. in a retrospective study conducted on 1463 deaths among the chemical victims, investigated the causes of suicide [62,63]. The route of suicide was self-hanging, intentional self-poisoning, suffocation and use of firearms. These researchers stated that suicide is one of the causes of death among the victims which mostly occurs at younger ages [less than 40 years] [64]. Therefore, in order to prevent the suicide in victims with chemical injuries, especially those suffering from depression, they should be monitored regularly. Strengthening religious behaviors, patriotism and social supports are useful in prevention of wide variety of the mental complications [65,66].

#### Discussion

Unfortunately, most studied articles have emphasized on diagnostic and therapeutic implications in chemical victims, with little preventive measures to recommend. Centers for disease control and prevention [CDC] in the United States has emphasized on immediate departure

from the area where the sulfur mustard is released, sealing the contaminated clothing in a plastic [Polyethylene] bag, and then keeping that bag inside another plastic bag, going to a higher ground, removing the clothes, immediate washing of the body [particularly skin and eyes], not using bandages for eye lesions, using dark glasses, and not to induce vomiting in GI involvement [67,68]. All these recommendations are compatible with the aforementioned points in conducted studies. In addition, disposable clothing kits should be available [69]. According to Iranian reports, there were no such disposable clothes available to the victims. Cutting off contaminated hair is recommended, too [70], but there were not any reports regarding this in Iranian reports. Polk County Health Department has emphasized on removing the shoes, and even the contact lenses [71], but similarly, there were not any recommendations for these points in considered studies. According to published articles, during chemical attacks to Iran, contaminated clothes were burnt in some medical centers. Nevertheless, while the fire may destroy the agent, breathing the fumes is very dangerous and contact of the agent with liquid or vapor may be fatal. Thus, burning the material should be avoided [72].

Iranian researchers emphasized on transportation of the victims to an area with humid climates [72]. In CAMEO [Computer Aided Management of Emergency Operations] chemicals software there has been emphasis on the movement of the victims to fresh air area, as soon as possible [73]. Ghasemi Boroumand et al. pointed the mask as a preventive tool. Moreover, Zarchi et al., in a retrospective cohort study conducted on 1337 Iranian victims with a history of mustard gas exposure, estimated that the risk of pulmonary complications were increased among those not having worn masks [70]. These researchers have not mentioned the specific type of the masks required. In encyclopedia Britannica, a typical gas mask for protection of sulfur mustard toxicity is described as having a tightfitting face piece equipped with filters, an exhalation valve, and transparent eye pieces [67]. Based on papers, probably the masks used in Ghasemi's study were ordinary masks and lacked the essential specifications. According to the fact sheets on Chemical and Biological Warfare Agents report, masks alone do not provide adequate protection against sulfur mustard [68]. The most useful preventive recommendations suggested by Iranian researchers are the points for preventing the exacerbation of sulfur mustard-induced chronic complications.

#### Conclusion

This is the first systematic review in medical literature aiming to evaluate the health hazards of CS which is used for both riot control and military/police training. A significant function of a systematic review is the establishment of further research needs. In this review, we assembled and discussed 39 studies [74-76]. The majority of them were case reports and there were few descriptive studies and only one analytical study. It is of note that the analytical study revealed long term clinical effects with Attack Rates ranged from 25%-30%. Also a considerable part of case reports failed to include essential information [e.g., latency period or duration of symptoms]. Moreover, long term and life threatening health effects have been recorded. Police officers, demonstrators, bystanders, health care workers and surgical patients could be harmed from exposure to CS. The establishment of surveillance schemes for the registration of the health effects and conditions of exposure among subjects exposed to CS and the completion of cohort studies among exposed populations [e.g., police officers, demonstrators, health care workers] would further illuminate the full health consequences of exposure to CS.

Performed studies on chemical gases in Iran are mainly focused on

tear gas and treatment of induced complications. Although the issue of prevention is very important, the literature related to this topic was limited to scattered facts within published papers. It is suggested that more research is needed in relation to preventive measures against sulfur mustard attacks.

#### References

- Health Aspects of Chemical and Biological Weapons. Geneva, Switzerland: World Health Organization; 1970.
- 2. Ballantyne B. Riot control agents. Med Annu 1977/1978: 741.
- Beswick FW (1983) Chemical agents used in riot control and warfare. Hum Toxicol 2: 247-256.
- Danto BL (1987) Medical problems and criteria regarding the use of tear gas by police. Am J Forensic Med Pathol 8: 317-322.
- Himsworth H (1971) Report of the Enquiry Into the Medical and Toxicological Aspects of CS [Orthochlorobenzylulene Malononitrile], II: Enquiry Into Toxicological Aspects of CS and Its Use for Civil Purposes. Her Majesty's Stationery Office, London, England.
- Ballantyne B, Callaway S (1972) Inhalation toxicology and pathology of animals exposed to o-chlorobenzylidene malononitrile (CS). Med Sci Law 12: 43-65.
- Chapman AJ, White C (1978) Death resulting from lacrimatory agents. J Forensic Sci 23: 527-530.
- Kaczmarek B, Gaszyński W (1977) Ultrastructure of the rabbit's lung tissue after administration of the CS preparation. Acta Med Pol 18: 327-328.
- Krapf R, Thalmann H (1981) [Acute exposure to CS tear gas and clinical studies]. Schweiz Med Wochenschr 111: 2056-2060.
- Park S, Giammona ST (1972) Toxic effects of tear gas on an infant following prolonged exposure. Am J Dis Child 123: 245-246.
- Sanford JR (1976) Medical aspects of riot control [harassing] agents. Annu Rev Med 27: 412-429.
- 12. Wiegand DA (1969) Cutaneous reactions to the riot control agent CS. Milit Med 134: 437-440.
- Sidel VW, Goldwyn RM (1966) Chemical and biologic weapons--a primer. N Engl J Med 274: 21-27.
- Ballantyne B, Swanston DW (1978) The comparative acute mammalian toxicity of 1-chloroacetophenone (CN) and 2-chlorobenzylidene malononitrile (CS). Arch Toxicol 40: 75-95.
- Gaskins JR, Hehir RM, McCaulley DF, Ligon EW Jr (1972) Lacrimating agents (CS and CN) in rats and rabbits. Acute effects on mouth, eyes, and skin. Arch Environ Health 24: 449-454.
- Cucinell SA, Swentzel KC, Biskup R, Snodgrass H, Lovre S, et al. (1971) Biochemical interactions and metabolic fate of riot control agents. Fed Proc 30: 86-91
- Jones GR, Israel MS (1970) Mechanism of toxicity of injected CS gas. Nature 228: 1315-1317.
- 18. Jones GR (1971) Verdict on CS. Br Med J 4: 170.
- Chung CW, Giles AL Jr (1972) Sensitization of guinea pigs to alphachloroacetophenone (CN) and ortho-chlorobenzylidenemalononitrile (CS), tear gas chemicals. J Immunol 109: 284-293.
- 20. Holland P, White RG (1972) The cutaneous reactions produced by o-chlorobenzyl-idenemalononitrile and -chloroacetophenone when applied directly to the skin of human subjects. Br J Dermatol 86: 150-154.
- Shmunes E, Taylor JS (1973) Industrial contact dermatitis. Effect of the riot control agent ortho-chlorobenzylidene malononitrile. Arch Dermatol 107: 212-216.
- Brooks SM, Weiss MA, Bernstein IL (1985) Reactive airways dysfunction syndrome (RADS). Persistent asthma syndrome after high level irritant exposures. Chest 88: 376-384.
- Upshall DG (1973) Effects of o-chlorobenzylidene malononitrile (CS) and the stress of aerosol inhalation upon rat and rabbit embryonic development. Toxicol Appl Pharmacol 24: 45-59.
- 24. Jones GRN (1971) CS in the balance. New, Scientist 50: 690-692.

- 25. [No authors listed] (1971) Toxicity of CS. Lancet 2: 698.
- von Däniken A, Friederich U, Lutz WK, Schlatter C (1981) Tests for mutagenicity in Salmonella and covalent binding to DNA and protein in the rat of the riot control agent o-chlorobenzylidene malononitrile (CS). Arch Toxicol 49: 15-27.
- 27. McGregor DB, Brown A, Cattanach P, Edwards I, McBride D, et al. (1988) Responses of the L5178Y tk+/tk- mouse lymphoma cell forward mutation assay. II: 18 coded chemicals. Environ Mol Mutagen 11: 91-118.
- Zeiger E, Anderson B, Haworth S, Lawlor T, Mortelmans K, et al. (1987) Salmonella mutagenicity tests: III. Results from the testing of 255 chemicals. Environ Mutagen 9 Suppl 9: 1-109.
- Rietveld EC, Delbressine LP, Waegemaekers TH, Seutter-Berlage F (1983)
   Chlorobenzylmercapturic acid, a metabolite of the riot control agent
   chlorobenzylidene malononitrile (CS) in the rat. Arch Toxicol 54: 139-144.
- Wild D, Eckhardt K, Harnasch D, King MT (1983) Genotoxicity study of CS (ortho-chlorobenzylidenemalononitrile) in Salmonella, Drosophila, and mice. Failure to detect mutagenic effects. Arch Toxicol 54: 167-170.
- Barry DH, Chasseaud LF, Hunter B, Robinson WE (1972) The suppression of non-specific esterase activity in mouse skin sebaceous gland by "CS" gas. Nature 240: 560-561.
- Chasseaud LF, Hunter B, Robinson WE, Barry DH (1975) Suppression of sebaceous gland non-specific esterase activity be electrophilic alpha betaunsaturated compounds. Experientia 31: 1196-1197.
- 33. McNamara BP, Renne RA, Rozmiarek H, Ford DF, Owens EJ (1973) CS: A Study of Carcinogenicity. Edgewood Arsenal, Md: National Technical Information Service Publication FB-TR-73027.
- 34. Marrs TC, Colgrave HF, Cross NL, Gazzard MF, Brown RF (1983) A repeated dose study of the toxicity of inhaled 2-chlorobenzylidene malononitrile (CS) aerosol in three species of laboratory animal. Arch Toxicol 52: 183-198.
- 35. Riot Control Manual. Saltsburg, Pa: Federal Laboratories; 1988.
- 36. Israel and the Occupied Territories (1988): The Misuse of Tear Gas by Israeli Army Personnel in the Israeli Occupied Terrifies. London, England: Amnesty International.
- 37. Penneys NS, Israel RM, Indgin SM (1969) Contact dermatitis due to 1-chloroacetophenone and chemical mace. N Engl J Med 281: 413-415.
- 38. Gonzales TA, Vance M, Helpern M, Umberger CJ (1957) Legal Medicine: Pathology and Toxicology. Appleton-Century-Crofts, East Norwalk, Conn.
- Stein AA, Kirwan WE (1964) Chloracetophenone (Tear Gas) Poisoning: A Clinico-Pathologic Report. J Forensic 9: 374-382
- Beswick FW, Holland P, Kemp KH (1972) Acute effects of exposure to orthochlorobenzylidene malononitrile (CS) and the development of tolerance. Br J Ind Med 29: 298-306.
- Busker RW, van Helden HP (1998) Toxicologic evaluation of pepper spray as a
  possible weapon for the Dutch police force: risk assessment and efficacy. Am
  J Forensic Med Pathol 19: 309-316.
- National Institute of Justice (2003) The Effectiveness and Safety of Pepper Spray. NIJ, Washington, DC:.
- Lumb RC, Friday PC (1997) Impact of pepper spray availability on police officer use-of- force decisions. Policing 20: 136-148.
- Panama (1987) Health Consequences of Police and Military Actions. Physicians for Human Rights 1988.
- Bazell RJ (1971) CBW ban: Nixon would exclude tear gas and herbicides. Science 172: 246-248.
- International Bill of Human Rights: Universal Declaration of Human Rights. New York, NY: United Nations; 1978. Articles 19 and 20.
- Bruera E, Seifert L, Watanabe S, Babul N, Darke A, et al. (1996) Chronic nausea in advanced cancer patients: a retrospective assessment of a metoclopramidebased antiemetic regimen. J Pain Symptom Manage 11: 147-153.
- Mystakidou K, Befon S, Liossi C, Vlachos L (1998) Comparison of the efficacy and safety of tropisetron, metoclopramide, and chlorpromazine in the treatment of emesis associated with far advanced cancer. Cancer 83: 1214-1223.
- Perkins P, Dorman S (2009) Haloperidol for the treatment of nausea and vomiting in palliative care patients. Cochrane Database Syst Rev 2: CD006271.

- Ezzo JM, Richardson MA, Vickers A, Allen C, Dibble SL, et al. (2006) Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting. Cochrane Database Syst Rev: CD002285.
- 51. Clark K, Agar MR, Currow D (2010) Metoclopramide for chronic nausea in adult palliative care patients with advanced cancer [Protocol] Cochrane Database Syst Rev.
- 52. Walkembach J, Brüss M, Urban BW, Barann M (2005) Interactions of metoclopramide and ergotamine with human 5-HT(3A) receptors and human 5-HT reuptake carriers. Br J Pharmacol 146: 543-552.
- 53. De Maeyer JH, Lefebvre RA, Schuurkes JA (2008) 5-HT4 receptor agonists: similar but not the same. Neurogastroenterol Motil 20: 99-112.
- 54. Cuomo R, Vandaele P, Coulie B, Peeters T, Depoortere I, et al. (2006) Influence of motilin on gastric fundus tone and on meal-induced satiety in man: role of cholinergic pathways. Am J Gastroenterol 101: 804-811.
- Schuurkes JAJ, Helsen LFM, Ghoos ECR, Eelen JGMG, van Nueten JM (1986) Stimulation of gastroduodenal motor activity: dopaminergic and cholinergic modulation. Drug Dev Res 8: 233-241.
- Magueur E, Hagege H, Attali P, Singlas E, Etienne JP, et al. (1991) Pharmacokinetics of metoclopramide in patients with liver cirrhosis. Br J Clin Pharmacol 31: 185-187.
- Bateman DN, Gokal R, Dodd TR, Blain PG (1981) The pharmacokinetics of single doses of metoclopramide in renal failure. Eur J Clin Pharmacol 19: 437-441
- Santucci G, Mack JW (2007) Common gastrointestinal symptoms in pediatric palliative care: nausea, vomiting, constipation, anorexia, cachexia. Pediatr Clin North Am 54: 673-689.
- 59. Hardy J, Daly S, McQuade B, Albertsson M, Chimontsi-Kypriou V et al. (2002) A double-blind, randomised, parallel group, multinational, multicentre study comparing a single dose of ondansetron 24 mg p.o. with placebo and metoclopramide 10 mg t.d.s. p.o. in the treatment of opioid-induced nausea and emesis in cancer patients. Support Care Cancer 10: 231-236.
- Corli O, Cozzolino A, Battaiotto L (1995) Effectiveness of levosulpiride versus metoclopramide for nausea and vomiting in advanced cancer patients: a double-blind, randomized, crossover study. J Pain Symptom Manage 10: 521-526.
- 61. Kim SW, Shin IS, Kim JM, Kang HC, Mun JU, et al. (2006) Mirtazapine for severe gastroparesis unresponsive to conventional prokinetic treatment. Psychosomatics 47: 440-442.

- Koutsoumbi P, Epanomeritakis E, Tsiaoussis J, Athanasakis H, Chrysos E, et al. (2000) The effect of erythromycin on human esophageal motility is mediated by serotonin receptors. Am J Gastroenterol 95: 3388-3392.
- Abrahamsson H (2007) Treatment options for patients with severe gastroparesis. Gut 56: 877-883.
- 64. Barone JA (1999) Domperidone: a peripherally acting dopamine2-receptor antagonist. Ann Pharmacother 33: 429-440.
- Osborne RJ, Slevin ML, Hunter RW, Hamer J (1985) Cardiotoxicity of intravenous domperidone. Lancet 2: 385.
- Puisieux FL, Adamantidis MM, Dumotier BM, Dupuis BA (1996) Cisaprideinduced prolongation of cardiac action potential and early afterdepolarizations in rabbit Purkinje fibres. Br J Pharmacol 117: 1377-1379.
- 67. Enger C, Cali C, Walker AM (2002) Serious ventricular arrhythmias among users of cisapride and other QT-prolonging agents in the United States. Pharmacoepidemiol Drug Saf 11: 477-486.
- Stacher G, Gaupmann G, Steinringer H, Schneider C, Stacher-Janotta G, et al. (1989) Effects of cisapride on postcibal jejunal motor activity. Dig Dis Sci 34: 1405-1410.
- Twycross R, Wilcock A, Charlesworth S, Dickman A (2002) Palliative care formulary (2ndedn.) Radcliffe Medical Press, Oxford, UK.
- McCallum RW, Prakash C, Campoli-Richards DM, Goa KL (1988) Cisapride.
   A preliminary review of its pharmacodynamic and pharmacokinetic properties, and therapeutic use as a prokinetic agent in gastrointestinal motility disorders. Drugs 36: 652-681.
- 71. Richelson E (1985) Pharmacology of neuroleptics in use in the United States. J Clin Psychiatry 46: 8-14.
- Kudo S, Ishizaki T (1999) Pharmacokinetics of haloperidol: an update. Clin Pharmacokinet 37: 435-456.
- Skinner J, Skinner A (1999) Levomepromazine for nausea and vomiting in advanced cancer. Hosp Med 60: 568-570.
- Panahi Y, Ghanei M, Ghabili K, Ansarin K, Aslanabadi S, et al. (2013) Acute and chronic pathological effects of sulfur mustard on genitourinary system and male fertility. Urol J 10: 837-846.
- Ghabili K, Shoja MM, Golzari SE, Niyousha MR (2013) Mustard gas keratitis: a common misnomer. Cornea 32: 382-383.
- 76. Ghabili K, Shoja MM, Golzari SE, Ansarin K (2012) Serum testosterone level and semen indices in sulfur mustard exposed men: comment on "sperm chromatin structure assay analysis of Iranian mustard gas casualties: a longterm outlook". Curr Urol 6: 112.