A review on delayed toxic effects of sulfur mustard in Iranian veterans

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Abstract

Iranian soldiers were attacked with chemical bombs, rockets and artillery shells 387 times during the 8-years war by Iraq (1980–1988). More than 1,000 tons of sulfur mustard gas was used in the battlefields by the Iraqis against Iranian people. A high rate of morbidities occurred as the result of these attacks. This study aimed to evaluate the delayed toxic effects of sulfur mustard gas on Iranian victims. During a systematic search, a total of 193 (109 more relevant to the main aim) articles on sulfur mustard gas were reviewed using known international and national databases. No special evaluation was conducted on the quality of the articles and their publication in accredited journals was considered sufficient. High rate of morbidities as the result of chemical attacks by sulfur mustard among Iranian people occurred. Iranian researchers found a numerous late complications among the victims which we be listed as wide range of respiratory, ocular, dermatological, psychological, hematological, immunological, gastrointestinal and endocrine complications, all influenced the quality of life of exposed victims. The mortality rate due to this agent was 3%. Although, mortality rate induced by sulfur mustard among Iranian people was low, variety and chronicity of toxic effects and complications of this chemical agent were dramatic.

Keywords: Chemical injuries, Chemical victim, Chemical warfare agents (CWA), Sulfur mustard, Mustard gas, Toxic effects of sulfur mustard

Background and history

Mustard gas or sulfur mustard is a chemical warfare agent (King of the battle gases) [1] with cytotoxic, vesicant and blistering effects on exposed skin [2]. This agent can enter the body through various routes including the skin, the respiratory system, conjunctiva and the gastrointestinal system by contaminated foods [3]. It can cause both acute and delayed manifestations and late complications even 40 years after the exposure as reported for victims of the first worldwar [4]. People can be exposed to small or large amounts of mustard gas through terroristic actions, wars, leakage from the factories, and even activities like fishing [5].

Sulfur mustard can be easily produced. It has a delayed, extensive absorption, multi-organ effects and quick penetration. It is stable in the environment, has a low production cost, is easy to use and has the ability to debilitate soldiers [6,7]. After dissemination in an area, mustard gas remains in that area for a long time and makes that area non-habitable. Mustard gas victims temporarily lose their vision a few hours after exposure which is a critical strategy in warfare [7], and so far, it has been used in >10 military conflicts [8].

Human losses related to destructive effects from this agent in the World War I are as follow: the soldiers were only equipped with protective breathing masks and lack of skin protection resulted in the death of more than 90,000 soldiers and about 1.3 million injured people [8] and out of which, 400,000 people required long term medical care [9]. According to the other reports mustard gas caused 14,000 injuries in the first 3 months of use in World War I and a total of 120,000 injuries [10]. In the US army, out of the total of 36,965 chemical warfare victims, 27,711 (75%) were due to sulfur mustard gas, and according to a report from the contamination control unit of the British army, of a total of 160,970 chemically injured soldiers, 124,752 (77.5%) had been injured by sulfur mustard gas. The greatest damage by chemical warfare agents in World War I was done to the Russians resulting in 50,000 casualties and
500,000 injuries. Years after the application of mustard gas in World War I, its delayed progressive and destructive effects were recognized [7].

In the beginning of Iraq-Iran war in 1980, use of chemical warfare agents was limited but in March 1985, despite international conventions on prohibition of using chemical warfare agents, Iraqis extensively used these agents against Iran. They used nerve agents (Sarin & Tabun) and mustard gas against Iranian soldiers [11,12].

According to data reported by Veterans and Martyrs Affair Foundation (VMAF) which is responsible for taking care of the war victims in Iran, the Iranian people were 387 times attacked with chemical bombs, rockets and artillery shells during the 8-years war by Iraq (1980–1988) [13]. More than 1,000 tons of sulfur mustard was used in the battlefields [2] and about 100,000 of people were injured due to this agent [8], as at the present, after more than two decades, still about 30,000 of them are under treatment [14].

Sardasht is a city in north-west of Iran. Iraqis released four 250 kg bombs containing mustard gas on this city at 4 pm, July 27, 1987 injuring 4,500 civilians [15]. Use of mustard gas against Iranian soldiers by the Iraqis was reported to the international commissions by Iran in 1984 and in 1986 application of this agent by Iraqis was documented by the United Nations observatory team led by M. Dominguez [16]. They evaluated the battlefields, clinically examined the victims and performed some para-clinical tests and approved that Iraqis had used chemical bombs containing mustard gas and to a lesser extent organophosphorous nerve agents especially Tabun [17].

Mustard gas was used by the Iraqis in south and west of Iran many times and in 1988 the last chemical attack was performed on Oshnaviyeh city injuring 2,680 civilians [13-18].

Definition and etiology
When mustard plants with the Latin name, Synapsis is affected by the tyrosine glycoside Synacrine enzyme, a substance is produced that naturally does not exist in the seeds of this plant. This compound is isothiosyanate which is a vesicant agent [19]. Mustard compounds are classified among the alkylating agents that substitute hydrogen with an alkyl cation. A large group of these compounds such as nitrogen mustards (chlorambucil) is mainly used in medicine for treatment of cancers. The other group namely sulfur mustard is considered a chemical warfare agent used in many battlefields in the 20th century [3]. This agent is recognized with various abbreviations H, HD, HT, LOST, SM (sulfur mustard), MG (mustard Gas) and Y perit “H” and “HD” come from the words “Hun Stufse” and “Distilled”, HT is a combination of 6% HD and 40% of a substance called T and the LOST come from the name of the scientists Lommel and Stein kopf, who developed a method for the large-scale production of the agent for the German army. French say to this agent, Y perit because it was used in the Y pres at the first time [20].

Tables 1 and 2 indicate the history and properties of sulfur mustard based on literature [1,3,6-10,18,21-26].

Pathology and mechanisms of actions
In summary, this alkylating substance leads to DNA damage, cell membrane damage, decrease in glutathione, activation of nuclear factor kappa-light-chain-enhancer of activated B cells (NFkB), and caspase activation. DNA damage lead to Poly (ADP-ribose) polymerase (PARP) activation and nicotin adenine nucleotide (NAD) depletion and this process in turn will lead to necrosis. Glutathione decreasing produce reactive oxygen and these two phenomena may lead to necrosis and cell death [27]. In addition to cell death, SM has many other

Table 1 Historical evolution

| Year | Event | Reference no. |
|------|-------|---------------|
| 1822 | A type of Mustard gas was developed by César-Mansuete Despretz, the Belgian scientist. | [8] |
| 1860 | Frederick Guthrie noted its blistering properties | [1,8] |
| 1886 | Victor Meyer produced pure sulfur mustard. | [1] |
| 1917-1918 | First use in World War I by the German army - along 10 days about 1 million sulfur mustard shells were poured on Belgian soldiers. 1.3-2.5 million people in Belgium and France and thousands of British soldiers were injured. | [1,8,10] |
| 1919 | Production of mustard gas in American factories reached 19 tons a day. | [7] |
| 1925 | Use of these agents was banned in Geneva Gas Protocol. | [8] |
| 1935- 1936 | Italy breached the Geneva Protocol treaty and used sulfur mustard gas against Ethiopia when conquering the Ethiopian plane. | [8] |
| 1943 | A cargo ship carrying a large amount of sulfur mustard exploded in the harbor of Bari, Italy. The gas was disseminated in the area injuring more than 600 people. | [1] |
| 1937-1945 | Japan used sulfur mustard gas against China. | [8,10] |
| 1945-1948 | A large amount of sulfur mustard was poured in the Baltic Sea. Exposure of Scandinavian fishermen to this agent resulted in development of skin blisters | [1] |
| 1963-1967 | Egypt used sulfur mustard bombs against Yemeni pro-monarchy supporters. | [1,8] |
| 1983-1988 | Iraq extensively used SM and nerve agents against Iran and injured more than 50,000 victims. | [8,9] |
| 1988 | Iraqi army killed 5,000 Iraqi civilians in Halabcheh using SM. In this attack, nerve agents like sarin were also used. | [1,8] |
### Table 2 Physical properties of sulfur mustard

| Properties | Description | References |
|------------|-------------|------------|
| Formulation | C4H8Cl2S | [1,18] |
| | 2 side chains of dichloroethyl/sulfide or bis (2-chloro-ethyl) sulfide | |
| Color | Colorless, lucent, or pale yellow (pure) to yellow, brown, dark brown or black color (impure) | [8,18] |
| Odor | Sulfur mustard has a slight garlic, horseradish, addled egg or fried vegetables or mustard type odor. | [8,14,18] |
| Form | Oily substance, liquid (in room temperature), solid, powder (decontamination is much more difficult), gas or vapor. It transforms into aerosols in 105°C. | [3,8,18,21] |
| Chemical reaction | Neutral | [8] |
| Solubility | Lipophilic substance and highly fat soluble (it can easily disseminate into skin, mucosa, brain, kidneys, muscles and liver), negligible solubility in water, may be hydrolyzed in water and soluble in acetone. Water solubility 0.092 g/100 g at 22°C. | [3,8,22] |
| Stability | In low temperatures, sulfur mustard remains stable in clothing and soil for months. It remains in the battlefields (for example beside the moats in World War I) and can be found in the amount of 1–25 mg/m³ in 6–12 inch depth of the soil. In moderate temperatures with mild winds sulfur mustard can remain stable for more than a week. Different forms of SM can be stored in the soil for up to 10 years. | [8,23] |
| Boiling point | 215 - 227°C | [1,8] |
| Melting point | 13-14°C | [1] |
| Freezing point | 14°C (its freezing point is decreased by chlorobenzene) | [8] |
| Volatility | 610 mg/m³ in 20°C | [8] |
| Specific Gravity | 1.27 (in liquid form than water and in gas form is heavier than air) | [21,24] |
| Vap. Pres. | 0.072 mmHg at 20°C | [8] |
| Molecular weight | 159.08 | [1] |
| Evaporation degree | SM evaporates at 15°C, in warm temperatures becomes less stable and its vapor form increases, and at night it sediments because of decreased temperature. | [7] |
| Density | SM is heavier than water when in the form of liquid and heavier than air when in the form of vapor or gas. Liquid density (1.274g/ml), Vapor Density (5.4), Solid Density (Crystal) 1.37 g/ml at 20°C | [1,8] |
| Half life | 5 min in 37°C | [3] |
| Permeability | SM penetrates the porous clothing and food and plants, easily penetrates into the cell membrane of most tissues, wood, leather (it an permeate leather and regular clothing in a few minutes and reach body tissues), rubber, plastics (can easily pass through regular or plastic breathing masks and rubber or plastic clothing can protect the body for a few hours) and remains active for a long time in cold or moderate temperatures. | [1,8,26] |
| Absorption in the body | Eighty percent of the SM gas is evaporated and the remaining 20% penetrates the body. Of the 20%, 12% remains on the skin and 8% is absorbed systemically. Absorption is done through moist tissues like respiratory system, axillary area, genital area/groins and eyes. Tissues with higher metabolism are more sensitive to this toxic gas. | [1,8,26] |
| Metabolites | The main metabolite of SM in the urine is 2-chloroethyl sulfide which can be detected by chromatography with1ng /ml sensitivity. | [3] |
| Excretion | Fifty percent of the absorbed SM in the body is conjugated with aminoacid lecithin producing di-cystylethyl sulfone which is excreted through the kidneys. | [22] |
| Anti-toxin | Unfortunately there is no specific antitoxin for SM gas | [6] |
| Applications | Except for chemical warfare, a nitrogen analogue of SM is now being used in chemotherapy for treatment of leukemia. This therapeutic agent is called Mustargen | [1] |

### Table 2 Physical properties of sulfur mustard (Continued)

Adverse effects on cells such as alklylation effects, mitosis inhibition (effects on hematologic system, immunologic system, epithelial and germinal tissues), mutagenesis, carcinogenesis, and colinomimetic effects [28].

On the basis of Kehe et al. study, in summary, mustard gas in the molecular level induces the releasing of cytokines, prostaglandines, matrix metalloproteinases (MMPs) and serine proteases, and increases DNA damages, oxidative stress, and impaired energy metabolism. Following to these molecular changes, cellular infiltration, apoptosis and necrosis occur that is continued by erythema and pain and formation of vesicles, blisters, ulcer and impaired wound healing [27].

Regarding above mechanisms, some authors suggest use of antioxidants, antiinflammatoriy, PARP inhibitors and N-acetyl-cystein (NAC) in treatment of SM toxicity.

### Methods

During a systematic search, a total of 193 medical articles related to SM were reviewed using known international medical databases such as Scopus, Medline, ISI, and Iranian medical databases such as Iranmedex, SID, and Irandoc. One hundred and nine articles were more relevant to the main aim. Eight articles were on general aspects of SM effects, 36 articles were related to respiratory effects, 16 articles were on dermatologic effects, 15 articles were on ophthalmologic effects, 11 articles on psychological effects, 10 articles on endocrinology & reproductive health effects, 4 articles related to quality of life and 9 articles were related to other items such as:
neurologic, oncologic, hematologic, cardiologic, laboratory. No special evaluation was conducted on the quality of the reviewed manuscripts and the credit of journal was considered sufficient. Our study had been handled in accordance with the rules of the ethical review board of Tehran University of medical sciences.

**Results**

**Initial description of victims**

Some Iranian soldiers described their first encounter with SM as follows: immediately after exposure to the SM bomb, we smelled a garlic odor and had a bitter taste in our mouth. A few hours later, we became dizzy, with a headache and we could not breathe. A short time after the explosion, we developed small bleeding areas and inflamed small lesions (macules and papules) on our skin. Then we felt hoarseness in our voice and this condition has been going on and off so far [28,29]. Also, some other victims described the events at the exposure time as follows:

We were exposed to SM gas delivered through bomb explosion from 5 to 30 meters distance. We smelled a strong smell of garlic, addled egg or fried vegetables. A bluish-grayish cloud and a white dust appeared in the sky. We had no protection. In the first hours following the attacks, we washed our faces and hands with waters which we did not know the water may be contaminated with SM [14]. Gradually, ocular, dermatologic and respiratory symptoms developed. We are still suffering from the related respiratory symptoms.

Mustard effects on body organs are divided into acute and chronic phases. Most of the reviewed articles were performed in chronic phase of exposure which they are summarized in Table 3.

Percentage of organ involvement has been reported differently in various Iranian studies. For example, Balali and colleagues (1992) in their study evaluated the delayed toxic effects of mustard gas on 1,428 chemical victims 3–9 years after exposure and reported the most prevalent complications to be respiratory complications (90%), dermatologic complications (88%), ocular complications (78%), neural complications (71%), GI complications (55%), genital complications (52%) and hematopoietic system complications (38%) [32].

In a study conducted on 100 Iranian chemical warfare victims, 94% had dermatologic, 94% had ophthalmic, 75% had pulmonary, 5% had GI and 10% had hematologic complications as the result of chemical exposure [16].

In another study, delayed toxic effects of mustard gas were evaluated in 236 Iranian chemical victims 2 to 28 months after exposure and complications were as follows: respiratory complications in 78%, CNS in 45% and dermatologic complications in 24.5% of cases [35].

Table 3 shows distribution of pulmonary, ophthalmic and dermatologic complications in several studies in Iran [10,15,30-34].

According to report of Khateri and colleagues, the pulmonary, ophthalmic and dermatologic complications were the most common in 34,000 victims observed [30].

**Complications**

Mustard gas complications in Iranian victims were as follows:

**Respiratory system complications among Iranian Veterans include**

Obstruction of upper airways, chronic bronchitis, bronchiolitis, bronchiectasis [10,36], asthma [2,10], COPD [37,38], emphysema, stenosis of large airways, pulmonary fibrosis [10,39], thickening of the bronchial walls, air trapping, bronchiolitis obliterans organizing pneumonia

| Reference | First author     | After exposure time (years) | Agent               | Under studied population | Number | Ocular complications (%) | Pulmonary complications (%) | Dermatologic complications (%) |
|-----------|------------------|-----------------------------|---------------------|--------------------------|--------|--------------------------|-----------------------------|-----------------------------|
| [30]      | Khateri          | 13 - 20                     | Mustard             | Veterans                 | 34000  | 93.3                     | 42.5                        | 245                         |
| [30]      | Khateri          | 14                          | Mustard             | Children                 | 50     | 86                       | 100                         | 98                          |
| [31]      | Ghassemi Broumand| 19                          | Mustard             | Civilian population     | 600    | 37.7                     | 45.8                        | 31.5                        |
| [32]      | Balali Mood      | 3 - 9                       | Mustard + Nerve agents | Veterans             | 1428  | 88                       | 90                          | 78                          |
| [10]      | Ghassemi Broumand| 17 - 22                     | Various chemical agents | Militaries + civilian | 479    | 26                       | 321                         | 23.3                        |
| [33]      | Etezad Razavi    | 16 - 20                     | Mustard             | Veterans                 | 40     | 65                       | 95                          | 90                          |
| [15]      | Ghanei           | 15                          | Mustard             | Civilian population     | 108    | *                        | 100                         | *                           |
| [34]      | Emadi            | 14 - 20                     | Mustard + Nerve agents | Veterans             | 800    | *                        | *                           | 100                         |
Tabatabai and colleagues [49], behavior (80%), thought process (14%), and members of consciousness (2%), attention (54%), emotion (45%), nervousness (46%) [50].

Social activities (44%), loss of confidence (55%), paranoia (40%), bad mood and anger (40%), lack of interest in life among exposed patients as follows: irregular sleep [49]. Madarshahian has reported some changes in current psychopathological formation about the psychological disorders were: anxiety (15%), depression 46%, personality disorders 31%, psychosis 3% [32], post-traumatic stress disorder (PTSD) [10].

According to one study based on general health questionnaire, which were conducted on 206 victims from Sardasht city (a city which were on direct attacks), 95.1% of them, did not have a healthy psychological status [10]. Other information about the psychological disorders were: anxiety (15%), depression (46%), personality disorders (31%), psychosis (3%) [32], post-traumatic stress disorder (PTSD) [10].

Other complications include Decreased quality of life and sleep disorders as the result of several physical (ophthalmologic injuries, pruritus, COPD and ...) and mental complications [9,54], contamination of the wives of exposed soldiers [3,55]. Mustard gas can also cause liver and kidney failure, skin cancer, and bone marrow depression [56]. McNamara and colleagues in their study on rats found that using 0.5 to 2 mg/kg mustard gas through the stomach tube in days 6 and 15 of pregnancy caused no evidence of teratogenicity [15,57].

The most prevalent GI complications in Iranian victims were nausea, vomiting, loss of appetite, stomach pain and diarrhea. Mustard gas can cause stomach cancer, basal cell carcinoma, Bowen's carcinoma and spino-cellular carcinoma [1]. Mustard gas can eventually cause death. However, the mortality rate is low (2 – 3%) [8,58].

Discussion According to initial description of the victims, there is a latent phase between the exposure and appearance of symptoms. This time interval increases the morbidity of exposed victims. Victims at first are not aware of their exposure/contamination and as the result they do not attempt to clean themselves which consequently results in greater absorption of the toxic agent into the tissues. This phase usually takes between 30 minutes to 8 hours [8].

To deal with this phase soldiers should train on how to deal with chemical terrorism, especially with mustard gas. For example, they should avoid washing their hand,
face and body with water in the area that was attacked because it may be contaminated with the poison.

Longitudinal studies showed that those exposed to mustard gas suffer from long term complications causing significant morbidity [8]. There are 2 types of complications: early and late. Early complications appear in the first week following exposure but late complications may manifest in the next 50 years following exposure [10]. In chronic phase, patients may be suffering from various diseases.

During World War I, scientists found that mustard gas can cause bone marrow aplasia, dissolution of lymphoid tissue and GI ulcers. Later many more complications were reported due to mustard gas including respiratory, dermatologic, ocular, GI, hematopoietic, endocrine, neural, psychological, ear-nose-throat (ENT), genital, reproductive and immune system [21] involvement which can manifest as early or delayed complications.

In Iranian studies, all the above mentioned effects have been reported. Moreover, there are some studies about sleep disorders [59], immunologic disorders [1,60], oncologic diseases [61], cardiology diseases [62], exposed military and civilian rights [63], abnormal lab examination results [64] and death among Iranian victims [56].

Mustard gas is a chemical warfare agent that is detrimental for the earth and has a significant toxic effect on microorganisms in the soil. It also inhibits the enzymatic activity of the soil [65]. On the other hand, SM can remain in the battlefields (for example beside the moats in World War I) and can be found in the amount of 1–25 mg/m3 in 6–12 inch depth of the soil. In moderate temperatures with mild winds SM can remain stable for more than a week [8]. Different forms of SM can be stored in the soil for up to 10 years [10]. Considering all the above facts, since the war zones in our country now are major tourist areas, and every year a large number of people travel to these areas, healthy soil-building, should strictly be placed on the agenda of the popular visits.

There are different reports about the prevalence of death and its causes in Iranian veterans. Ghanei et al., in their study have stated that, the rate of death among 1,005 people who died during their study period, were 72% by trauma, 16.1% due to unintentional accidents, 2.3% due to suicide, and 0.8% caused by intentional accidents. The causes of deaths in 2.8% were uncertain and 12.1% of deaths were related to chemical agents effects [66].

Tavallai et al., in their study conducted on 1239 Iranian veterans also reported that 65.4% of deaths were due to diseases, and 24.7% were due to accidents [67].

In summary, reported fatality rates in exposed soldiers in World War I were less than 2% and among Iranian victims were 3-4% and disabling potential of SM is much greater than lethality of this agent [68]. According to Tavallai report, the most common causes, had led to death were cardiac diseases and this according to an other report, in Iranian victims 75% of deaths were due to respiratory complications [18], and many of Iranian soldiers lost their lives in a chemical battle scene and probably the cause of death was pulmonary edema induced by chemical agents (29).

Conclusion
Although, mortality rate induced by sulfur mustard among Iranian people was low, the variety and chronicity of adverse effects and complications of this chemical agent were dramatic.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
SWR theorized, designed and interpreted the data and drafted the manuscript. PS abstracted, designed, acquired the data and revised the manuscript. MS theorized the data, drafted and revised the manuscript. MA revised data and revised the manuscript. All authors read and approved the final manuscript.

Acknowledgements
The authors would like to thank Mrs. Ghadiri for typing the manuscript. Mohammad Abdollahi is a member of scientific advisory board in OPCW.

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Received: 4 July 2012 Accepted: 5 October 2012
Published: 9 October 2012

References
1. Balali M, Hefazi M. The pharmacology, toxicology and medical treatment of sulfur mustard poisoning. Fundam Clin Pharmacol 2005, 19:297–315.
2. Agin K: Comparison of serum magnesium values among sulfur mustard induced asthma with non-chemical asthmatic in Iranian war victims. J Army Univ Med Sci I.R. Iran 2005, 8:499–495. Persian.
3. Ketabchi AA: Urogenital and fertility complications in victims of chemical war residing in Kerman province. J Kerman Univ Med Sci 1998, 5:72–77. Persian.
4. Javadi M, Yazdani S, Sagjadi H, Jadidi K, Karmian F, Einiollahi B, JafariNSab MR, Zare M. Chronic and delayed-onset mustard gas keratitis. Ophthalmology 2005, 11:617–625.
5. Mirmadraee M, Attaran D, Boshkady M, Towhidi M. Airway hyperresponsiveness to methacholine in chemical warfare victims. Respiration 2005, 72:S23–528.
6. Roushan N, Abtahi HR, Daneshfar G, Akhlaghpour S, Arjmand Shabestari A, Youvari MR. Long term pulmonary complications of war related sulfur mustard exposure. J Mid Med 2003, 10:143–150. Persian.
7. Moosavi SA, Safarinejad MR. Ocular injuries caused by mustard gas: diagnosis, treatment and medical defense. Kowsar Med J 2000, 4:289–295. Persian.
8. Wattana M: Mustard gas or sulfur mustard: an old chemical agent as a new terrorist threat. Pre hospital and Disaster Medicine 2009, 24:19–29.
9.oustab B, Sarooch M, Montazer A. Quality of life in chemical warfare survivors with ophthalmologic injuries: the first results from Iranian chemical warfare victims health assessment study. Health Qual Life Outcomes 2009, 7:1–8.
10. Ghasemi Broumand M, Karamy G, Pourfarzam S, Erndi SN, Ghasemi H: Late concurrent ophthalmic, respiratory, cutaneous and psychiatric
complications of chemical weapons exposure in 479 war patients. Daneshvar Med 2007, 70:81–92.

11. Mansoor Ghaeili F, Alizadeh A: Chest X-ray findings in Guilanian chemical warfare victims. J Babol Univ Med Sci 1999, 1:13–18. Persian.

12. Balali-Mood M, Balali-Mood K, Daei G, Ghaeminejad E: Organophosphorous nerve agents poisoning. J Biomed Sci Uni Med 2006, 8:135–24.

13. Hashemian F, Khoshnoody N, Desai MM, Falahati F, Kasel S, Southwick S: Anxiety, depression, and posttraumatic stress in Iranian survivors of chemical warfare. JAMA 2006, 296:560–566.

14. Kehe K, Thiermann H, Balzszweft F, Eyer F, Steinzitz D, Zilker T: Acute effects of sulfur mustard injury – Munich experiences. Toxicology 2009, 256:3–14.

15. Ghaemi M, Aslani J, Khateri S, Harandanzadeh K: Public health status of the civil population of Sardasht 15 years following large-scale wartime exposure to sulfur mustard. J Burns Surg Wound Care 2003, 2(7):Serial Online.

16. Holisaz MT, Raigany SM, Hafezy R, Bakhshandeh H: Chest X-ray findings in Guilanian war victims living in Kermanshah. Daneshvar Med 2007, 70:215–217. Persian.

17. United Nations Security Council: document S 16433: “Report of the specialists appointed by the secretary general to investigate allegations by the Islamic Republic of Iran. New York, U.S.A.; 1984.

18. Dadpaye M, Ghaemian L: Respiratory complication of mustard gas in Iraq-Iran war victims living in Kermanshah. J Army Univ Med Sci I.R. Iran 2007, 5:1331–1335. Persian.

19. Shohrati M, Davoudi M, Ghaemi M, Peyrman M, Peyman A: Cutaneous and ocular late complications of sulfur mustard in Iranian veterans. Cutan Ocul Toxicol 2007, 26:73–81.

20. Shakerjani MP, Heck DE, Gray JP, Sinko PJ, Gordon MK, Casillas RP, Heindel ND, Grezeich DR, Laskin DL, Laskin JD: Mechanisms mediating the vesicant actions of sulfur mustard after cutaneous exposure. Toxicol 2010, 11:45–19.

21. Maleki M, Javid Z, Soofi-Zadeh V, Ebrahim Zadeh S: Multiple large cherry angiomas after exposure to sulfur mustard gas in Iranian veterans in Iraq-Iran war; A historical cohort study. Iran J Dermatol 2006, 9:40–45. Persian.

22. Ghaemi M, Panahi Y, Aslani J, Mojhatehedzadeh M: Successful treatment of pulmonary obliterative lesion in chemical warfare casualties with Gamma-interferon. Kowsar Med J 2003, 2(1):151–157. Persian.

23. Ghasemi Boroumand M, Amiri Z: Delayed ocular complications of mustard gas on 500 veterans. J Rehab 2008, 8:67–74. Persian.

24. Rice P: Sulfur mustard injuries of the skin, pathophysiology and management. Toxicol Rev 2003, 22(11):118–11.

25. Saffarnejad MR: Ocular injuries caused by mustard gas: diagnosis, treatment and medical defense. Mil Med 2001, 166:67–70.

26. Chauhan RS, Murty LV: Effect of topically applied sulphur mustard on guinea pig liver. J Appl Toxicol 1997, 17:415–419.

27. Kehe K, Blazszweft F, Emmler J, Kreppel H, Jochum M, Thiermann H: Sulfur mustard research – strategies for the development of improved medical therapy. Eplasty 2008, 10:e32.

28. Foroutan A: Medical notes on the chemical warfare: Part II. Kowsar Med J 1997, 1:159–177. Persian.

29. Freitag L, Firasat N, Stamatis G, Geschurucha D: The role of bronchoscopy in pulmonary complications due to mustard gas inhalation. Chest 1997, 100:1436–1441.

30. Khateri S, Ghaemi M, Kheshvar S, Sorouch M, Haines D: Incidence of lung, eye, and skin lesions as late complications in 34,000 Iranians with wartime exposure to mustard agent. J Occup Environ Med 2003, 45:1136–1143.

31. Ghasemi Boroumand M, Aslani J, Emadi SN: Delayed ocular, pulmonary, and cutaneous complications of mustard gas in patients in the city of Sardasht, Iran. Cutan Ocul Toxicol 2008, 27:295–305.

32. Balali M: The evaluation of the toxic effects of sulfur mustard poisoning in 1428 Iranian veterans. In: proceedings of the seminar on late complications of chemical warfare agents in iranian veterans. Edited by Veteran Foundation. Tehran, Iran; Persian; 1992:15–31.

33. Etezad-Razavi M, Mahmoudi M, Hefazi M, Balali-Mood M: Delayed ocular civilian mustard gas poisoning and the relationship with respiratory and cutaneous complications. Clin Experiment Ophthalmol 2006, 34:342–346.

34. Emadi SN, Mortazav M, Mortazav H: Late cutaneous manifestations 14 to 20 years after wartime exposure to sulfur mustard gas: a long-term investigation. Arch Dermatol 2008, 144:1059–1061.

35. Balali Mood M: First report of delayed toxic effects of Yperite poisoning in Iranian fighters. In: proceedings of the second world congress on new compounds in biological and chemical warfare, 21–25 May 1984. Rijksuniversiteit. Edited by Heydrimck B, Ghent, Belgium; 1986:489–495.

36. Bagheri MH, Hosseini SK, Mostafavi SH, Aliay SA: High-resolution CT in chronic pulmonary changes after mustard gas exposure. Acta Radiol 2003, 44:241–245.

37. Ghaemi M, Amini S, Akbari H, Kosani F, Hosseini Khalili AR, Aladedin F, Aslani J, Giardina C, Haines DD: Correlation of sulfur mustard exposure and tobacco use with expression (immune reactivity) of p53 protein in bronchial epithelium of Iranian military lung patients. Mil Med 2007, 172:780–784.

38. Etezad-Razavi M, Jaddi K: A study of ophthalmic complications due the Mustard gas in the chemical war injured. Kowsar Med J 2000, 4:285–287. Persian.

39. Ghaemi M, Harandi AA: Long term consequences from exposure to sulfur mustard: a review. Int J Toxicol 2007, 19:451–456.

40. Alavian SM, Fallyhian F, Shohrati M, Fakher-Yaseri H, Zaman F: Long term effects of mustard gas on Iranian veterans. Shiraz E Med J 2009, 10:1–10.

41. Ghaemi M, Moqadam FA, Mohammadpour P, Toosi S: Skin lesions in 880 Iranian victims of mustard gas, 14–20 years after exposure, Iran J Dermatol 2005, 8:177–189. Persian.

42. Feiki AR, Janghorbani M: Late cutaneous complications in chemical warfare victims in kerman province. J Kerman Univ Med Sci 1995, 2:108–119. Persian.

43. Momeni AZ, Eshraeili S, Meghdadi M, Amindjadiwaher M: Skin manifestations of mustard gas, a clinical study of 535 patients exposed to mustard gas. Archiv Dermatol 1992, 128:775–780.

44. Tavallaee SM, Javadi Vashi R: Study of mental health of chemically injured people in Sardasht in 2001, MD Thesis.: Baqiatallah University of Medical sciences; 2002. Persian.

45. Fath Artashini A, Tavallaii A, Azizbodi Farahani M, Moghani Lankarani M: Association of psychological symptoms and self-esteem in chemical warfare agent exposed veterans. Iran J Med Sci 2009, 22:273–282. Persian.

46. Madarshahian F: Comparison of coping with direct and indirect consequences of war stress in later life between chemical and physical war injured. J Mil Med 2003, 5:117–120. Persian.

47. Ranjbar Shayan H, Ahmadi K, Raeesi F: Sexual dysfunctions in chemical injured veterans. J Mil Med 2008, 10:99–106. Persian.

48. Azizi F, Jalali N, Nafarabadi M: The effect of chemical weapons on serum concentrations of various hormones. Iran J Med Sci 1989, 14:46–50.

49. Anslove WP, Houk CR: Systemic pathology and pharmacology of sulphur and nitrogen mustard In: Chemical warfare agents and related chemical problems. Washington DC, USA: National Defense Research Committee; 1946:440–478.

50. Attaran D, Khajedalouie M, Jafarzadeh R, Mazloomi M: Health – related quality of life in patients with chemical warfare - induced chronic obstructive pulmonary disease. Arch Iran Med 2006, 9:339–343.

51. Pourjafari H: Congenital malformations in the progenies of iranian chemical victims. Vet Hum Toxicol 1994, 36:562–563.

52. Akhavan A, Ajjaloueyan M, Ghaemi M, Mohramzad Y: Late laryngeal findings in sulfur mustard poisoning. Clin Toxicol 2009, 47:142–144.

53. McNamara BP, Owens EJ, Christensen MK, Voice FJ, Ford DF, Rozmarenik: Toxicological basis for controlling levels of mustard in the environment. EB 59: 7403. Edgewood Arsenal Aberdeen proving grounds, MD; 1975.

54. Karimi Zarchi AA, Holakouie Naieni K: Long-term pulmonary complications in combatants exposed to mustard gas: a historical cohort study. Int J Epidemiol 2004, 33:579–581.

55. Tavalaie A, Asari S, Habbibi M: Subjective sleep quality in chemical warfare veterans. Iran J Psychiatry Clin Psychol 2006, 12:263–269. Persian.
60. Pourfarzam S, Ghazanfari T, Yaraee R, Ghasemi H, Hassan ZM, Faghhizadeh S, Ardestani SK, Kariminia A, Fallahi F, Soroush MR, Merasizadeh J, Mahlojirad M, Naghizadeh MM: Serum levels of IL-8 and IL-6 in the long term pulmonary complications induced by sulfur mustard: Sardasht – Iran cohort study. *Int Immunopharmacol* 2009, 9:1482–1488.

61. Glasi HR, Holakouie Naeni K, Zafarghandi MR, Mahmoudi M, Ghanei M, Soroush MR, Dowlatyari A, Ardalan A: Relationship between mustard gas and cancer in Iranian soldiers of imposed war in Isfahan Province: A Pilot Study. *J Sch Public Health Inst Public Health Res* 2006, 4:15–23. Persian.

62. Jalali Farahani AR, Naeni MH, Lal Dolatabadi H, Arab Salmani E, Jonaidi Jafari N, Teimouri M: Comparative study of cardiovascular risk factor between military patient and non-military patient in Shahid Rajae and Bajiyatallah hospital. *J Mil Med* 2008, 10:137–142. Persian.

63. Madar Shahian F: Observance of patient rights in war chemical victims. *J Mil Med* 2005, 7:109–112. Persian.

64. Hooshiar E, Mohammad Hassan Z, Salek Moghadam AR, Shaker Z, Ebtekar M: Study of the effects of chemical warfare (Mostly Sulfur Mustard) on neutrophils in chemical injuries ten years after exposed war. *RJMS* 2004, 11:165–172. Persian.

65. Medvedeva N, Polyak Y, Kuzikova I, Orlova O, Zharikov G: The effect of mustard gas on the biological activity of soil. *Environ Res* 2007, 106:289–295.

66. Ghanei M, Assari SH, Alaeddini F, Tavallaie SA: Pattern of delayed mortality in I.R.IRAN veterans exposed to chemical warfare agents. *Military Medicine* 2005, 6:233–239.

67. Tavallaie SA, Assari S, Ghanei M, Khedmat H, Alaeddini F, Naderi Z: Study of causes of mortality and correlated variables in deceased Iranian veterans – 1979 – 2004. *J Iran Univ Med Sci* 2005, 47:29–37. Persian.

68. Maynard RL, Meredith TC, Vale JA: Management of war injuries. *Lancet* 1991, 337:122.

doi:10.1186/2231-051

Cite this article as: Razavi et al.: A review on delayed toxic effects of sulfur mustard in Iranian veterans. *DARU Journal of Pharmaceutical Sciences* 2012 20:51.

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