

Long-term Effects of Exposure to Mustard Gas on Male Infertility

Dear Editor,

Sulfur mustard (mustard gas) is the most important vesicant agent, and among all chemical warfare agents it has caused the greatest number of casualties of particularly, during the Iran-Iraq War (1980-1988).¹ The designation of chemical weapons as "weapons of mass destruction" emphasizes their potential catastrophic effect on the health of a large number of population.²

According to Iraq's declarations, some 105,000 munitions filled with chemical warfare agents were supplied to their armed forces during the Iran-Iraq war from 1981 to 1988.³ Iraq also declared that about 1,800 tons of mustard gas were consumed during these years.⁴ There are numerous studies regarding late pulmonary, ophthalmic, dermatologic, immunologic, hematologic or carcinogenic complications of mustard exposure following the Iran-Iraq war,⁵⁻¹⁰ but the role of mustard exposure in the survivors' fertility is still unclear.

Recently, we came across an article in your journal entitled "Long-term effect of exposure to mustard gas on male infertility," which reported a 44% infertility rate among subjects who were "highly suspicious of being exposed to mustard gas during the Iran-Iraq war".¹¹ The study's findings contrast markedly with the findings of the studies of mustard-exposed survivors at the Janbazan Medical and Engineering Research Center (JMERC). In order to better understand this subject, the following notes should be considered: The authors neither specified how they drew their sample nor when the study took place. 1. It is difficult to draw conclusions about a causal relationship between mustard exposure and male infertility when the exposure is "highly suspected" rather than confirmed and when no data are presented on the level of exposure. 2. Although previous reports have demonstrated the ability of sulfur mustard to cause adverse reproductive effects,^{12,13} few correlations have been established between mustard exposure and human infertility. In 2004, a study on sulfur mustard exposed survivors of Sardasht reported that the

infertility rate was 8.3% among the exposed victims with confirmed exposure, which compares with a worldwide rate of 10-15%.¹⁴

Numerous clinical studies in the JMERC on mustard gas exposed survivors did not support the theory of reproductive toxicity of sulfur mustard. 2. In our recent work, a collective examination program as a part of the national health monitoring project run by the Iranian Veterans' and War Victims' Organization,¹ and JMERC, 419 victims with documented exposure to sulfur mustard now suffering from severe respiratory or ophthalmic complications were investigated for cumulative or lifetime infertility. Of these, 402 were married of whom 10 survivors (2.5%) were reported to have fertility problems. Of these 10 cases with fertility problems, 8 needed to use IVF or other assisted reproductive therapies and 4 were childless. Other than the four who had no child, the subjects who were married had 1 to 13 offspring (mean: 3.5 ± 1.8).

We have found that, in contrast with previously reported laboratory studies^{11,12} in the long term (21.2 ± 1.6 years after their exposure), there is no evidence of clinical life-time infertility among survivors with high dose mustard exposure. Because unverified reports of infertility after exposure to sulfur mustard could possibly lead to unfortunate consequences among chemical warfare victims, we would be grateful for your kindness in considering this letter as an opening to discussion on this subject.

Conflict of interest: None declared.

Janbazan Medical and Engineering Research Center (JMERC), P.O.Box: 19615/616, Tehran, Iran

MR Soroush*, E Modirian, Sh Khateri

*Correspondence: Mohammad Reza Soroush, MD, Director of Janbazan Medical and Engineering Research Center (JMERC) NO.25, Farrokh St., Moghaddas Ardebili Ave., Chamran Highway, P.O.Box: 19615/616, Tehran, Iran. Tel: +98-21-22412114, Fax: +98-21-22412502, e-mail: msoroush@jmerc.ac.ir
Received: July 28, 2008 Accepted: September 7, 2008

References

- 1 Hurst CG, Smith WJ. Chronic effects of acute, low-level exposure to the chemical warfare agent sulfur mustard. In: Somani SM, Romano JA Jr, eds. Chemical warfare agents: toxicity at low levels. Boca Raton, Fla.: CRC Press, 2001; pp. 245-60.
- 2 Macintyre AG, Christopher GW, Eitzen E, Gum R, Weir S, DeAtley C, Tonat K, Barbera JA. Weapons of mass destruction events with contaminated casualties: effective planning for health care facilities. *JAMA* 2000;**283**(2):242-9. [10634341] [10.1001/jama.283.2.242]
- 3 The United Nations Monitoring, Verification and Inspection Commission (UNMOVIC). Iraq's storage, handling and deployment of chemical and biological munitions. UN document S/2004/693, August 2004, Appendix I, p. 7.
- 4 The United Nations Monitoring, Verification and Inspection Commission (UNMOVIC) Working document, 6 March 2003. UNRESOLVED DISARMAMENT ISSUES. IRAQ'S PROSCRIBED WEAPONS PROGRAMMES. PP 145-6.
- 5 Shohrati M, Peyman M, Peyman A, Davoudi M, Ghanei M. Cutaneous and ocular late complications of sulfur mustard in Iranian veterans. *Cutan Ocul Toxicol* 2007;**26**(2):73-81. [17612976] [10.1080/15569520701212399]
- 6 Ghanei M, Harandi AA. Long term consequences from exposure to sulfur mustard: a review. *Inhal Toxicol* 2007;**19**(5):451-6. [17365048] [10.1080/08958370601174990]
- 7 Balali-Mood M, Hefazi M. Comparison of early and late toxic effects of sulfur mustard in Iranian veterans. *Basic Clin Pharmacol Toxicol* 2006;**99**(4):273-82. [17040211] [10.1111/j.1742-7843.2006.pto_429.x]
- 8 Hefazi M, Maleki M, Mahmoudi M, Tabatabaee A, Balali-Mood M. Delayed complications of sulfur mustard poisoning in the skin and the immune system of Iranian veterans 16-20 years after exposure. *Int J Dermatol* 2006;**45**(9):1025-31. [169 61503] [10.1111/j.1365-4632.2006.03020.x]
- 9 Zargar M, Araghizadeh H, Soroush MR, Khaji A. Iranian casualties during the eight years of Iraq-Iran conflict. *Rev Saude Publica* 2007;**41**(6): 1065-6. [18066475] [10.1590/S0034-89102007000600025]
- 10 Khateri S, Ghanei M, Keshavarz S, Soroush 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**(11):1136-43. [14610394] [10.1097/01.jom.0000094993.20914.d1]
- 11 Shakeri S, Yazdani M, Kheradpezhoh E. Long-term effect of exposure to mustard gas on male infertility. *IRCMJ* 2007;**9**(2):59-62.
- 12 Azizi F, Keshavarz A, Roshanzamir F, Nafarabadi M. Reproductive function in men following exposure to chemical warfare with sulphur mustard. *Med War* 1995;**11**(1):34-44. [7731411]
- 13 Safarinejad MR. Testicular effect of mustard gas. *Urology* 2001;**58**(1): 90-4. [11445486] [10.1016/S0090-4295(01)01085-8]
- 14 Ghanei M, Rajaei M, Khateri S, Alaeddini F, Haines D. Assessment of fertility among mustard-exposed residents of Sardasht, Iran: a historical cohort study. *Reprod Toxicol* 2004;**18**(5):635-9. [15219625] [10.1016/j.reprotox.2004.03.003]