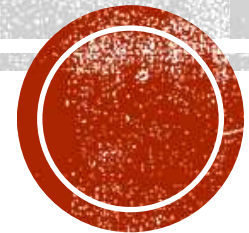


CHRONIC HEALTH EFFECTS OF EXPOSURE TO SULPHUR MUSTARD

Shahriar Khateri, MD. PhD

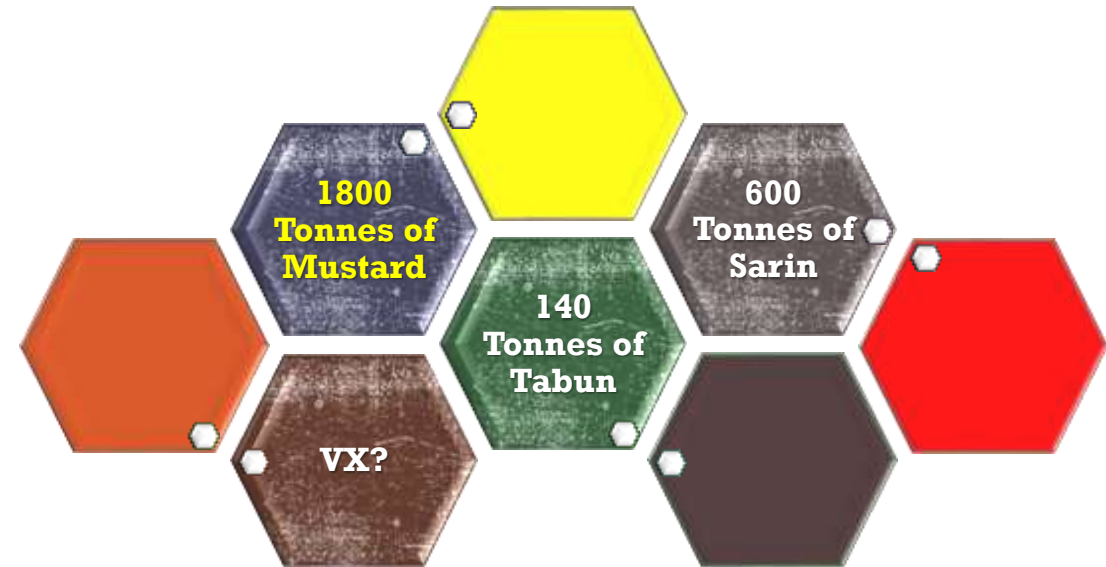
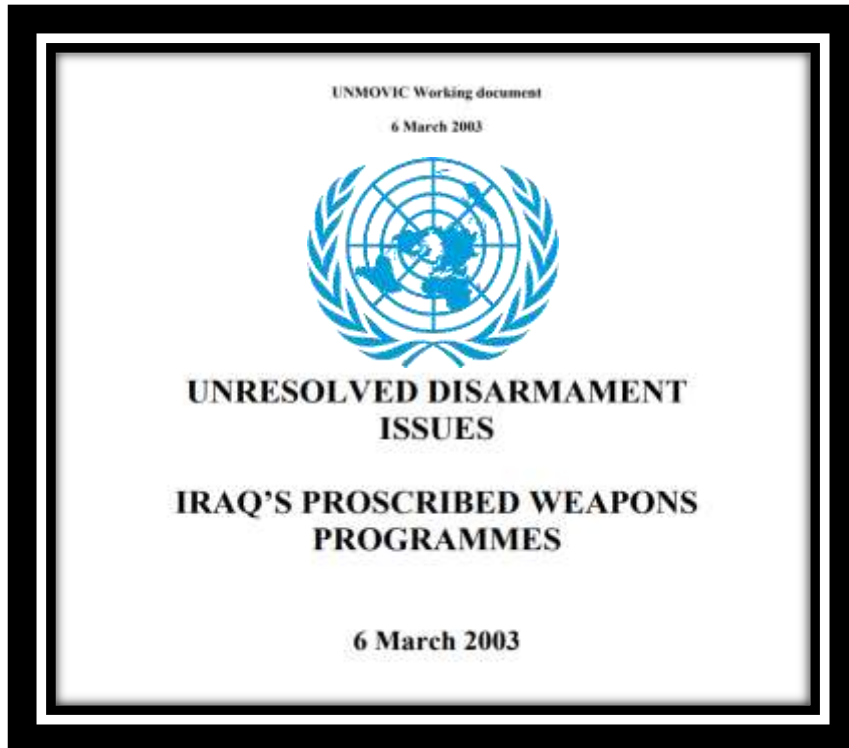
Medical Toxicologist



Background

This presentation is mainly based on the experience of Iranian Medical community following the 1980s use of Sulphur Mustard against Iran





The end of the Iraq-Iran War

The use of CW

The war with Iran ended in August 1988. By this time seven UN specialist missions had documented repeated use of chemicals in the war. According to Iraq, it consumed almost 19,500 chemical bombs, over 54,000 chemical artillery shells and 27,000 short-range chemical rockets between 1983 and 1988. Iraq declared that about 1,800 tonnes of Mustard, 140 tonnes of Tabun and over 600 tonnes of Sarin had been consumed during these years. Almost two-thirds of the



HUMAN COST

Morbidity and Mortality from Chemical Warfare Agents (CW) during Iran-Iraq War

Iranians exposed to CW agents	1,000,000*
Iranians who received medical treatment for heavy exposure	100,000
Iranian deaths from direct and immediate CW effects	7,500 4,000 nerve or blood agents 3,500 mustard agent
Iranians with chronic CW injuries, in registry	75,000
Iranians with chronic CW injuries, not in registry	40,000*
Iranian civilians with chronic CW injuries *registered & unregistered)	35,000*

*Estimate



Dealing with SM exposure is a serious challenge for medical responders

- Latency Period,
- Unknown Mechanism
- Long Hospitalization
- Slow Recovery
- Long Term Health Effects



Incidence of Lung, Eye, and Skin Lesions as Late Complications in 34,000 Iranians With Wartime Exposure to Mustard Agent

Shahriar Khateri, MD
Mostafa Ghanei, MD
Saeed Keshavarz, MD
Mohammad Soroush, MD
David Haines, PhD

Learning Objectives

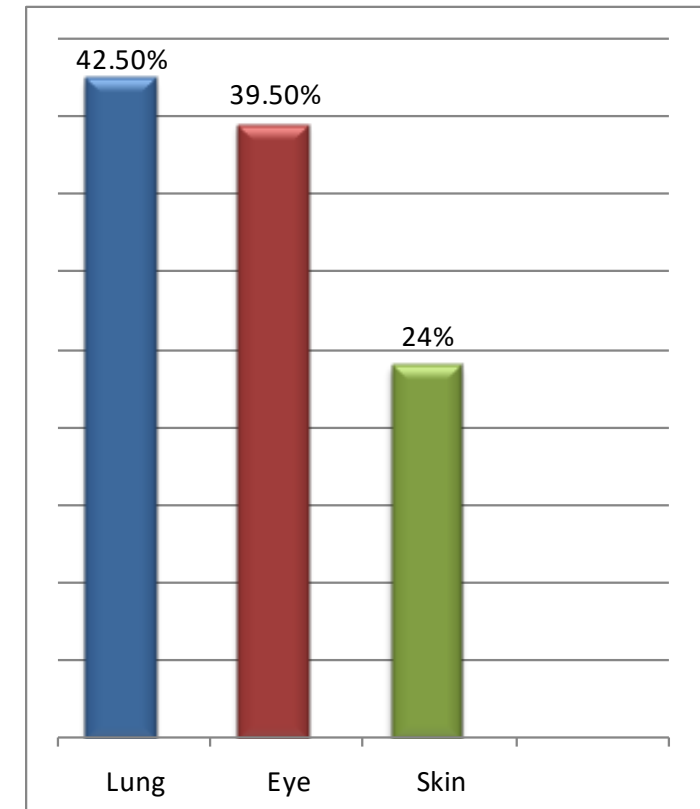
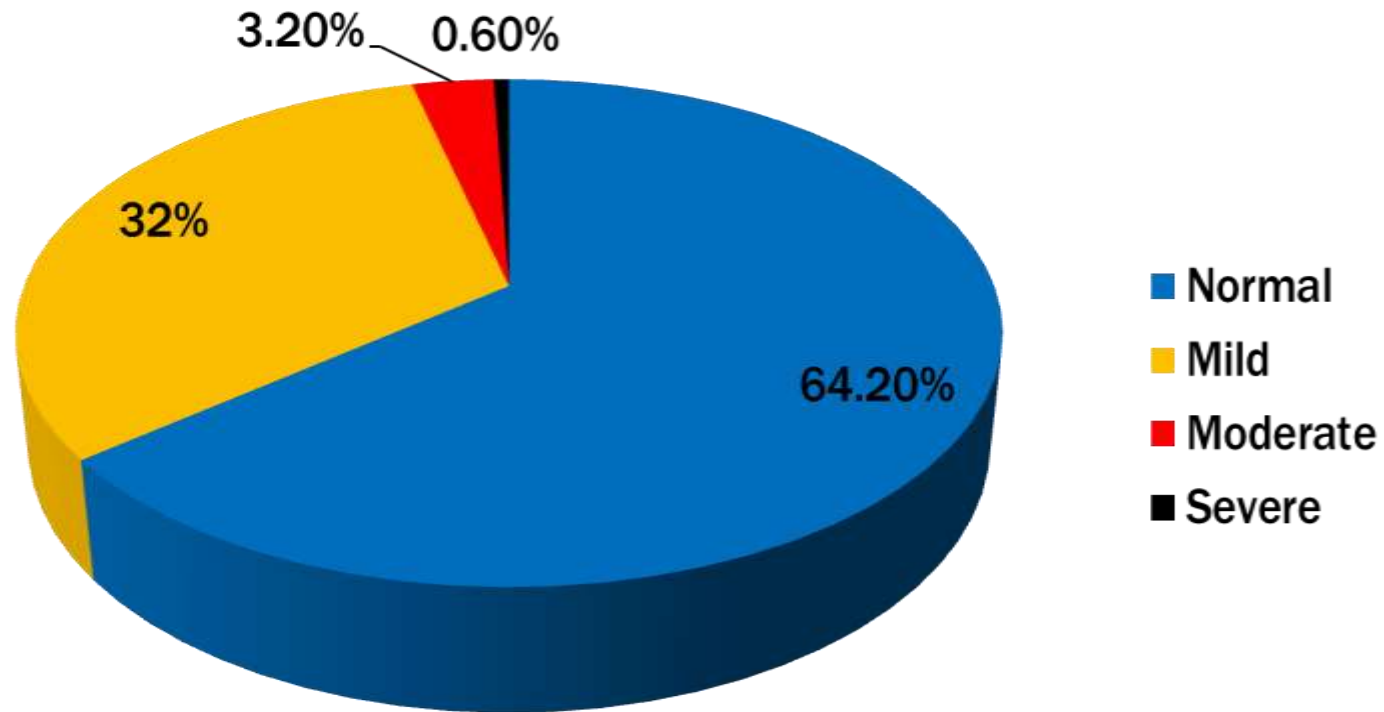
- Recall the frequency and severity of chronic pulmonary, ocular, and cutaneous lesions in this study of 34,000 Iranians exposed in war to mustard

During the 8-year war between Iran and Iraq (1980–1988), Iraqi forces were known to have frequently used chemical weapons against Iranian targets, which included both military personnel and civilians in Iranian border towns. The agents used by the Iraqis fell into 2 major categories based on chemical composition and



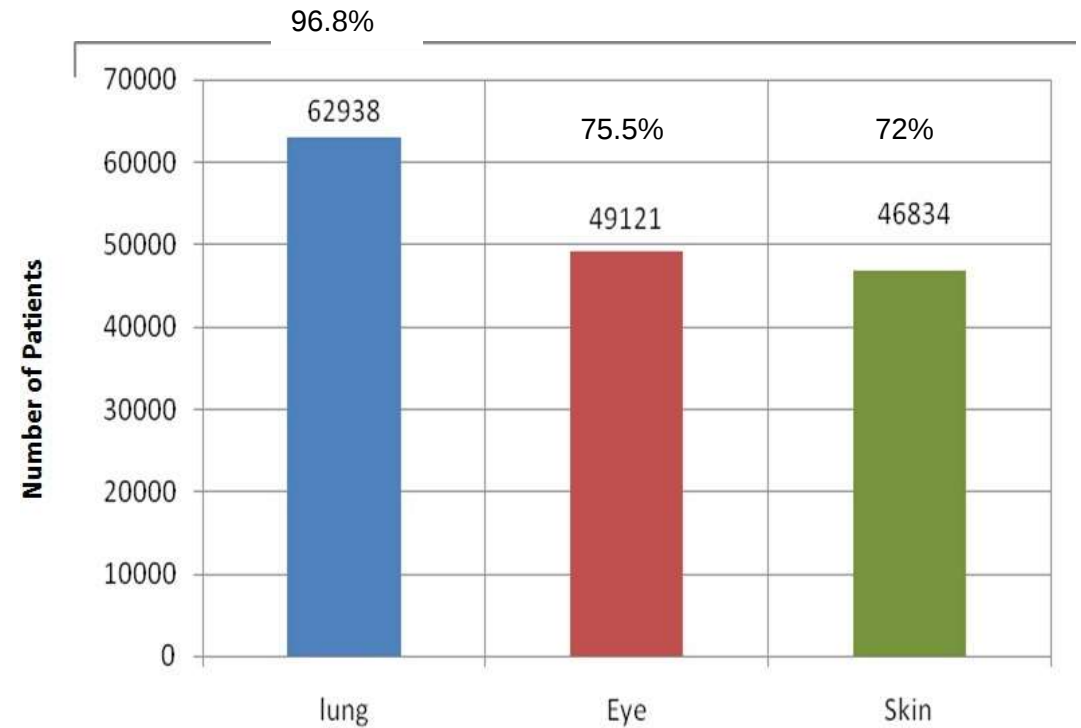
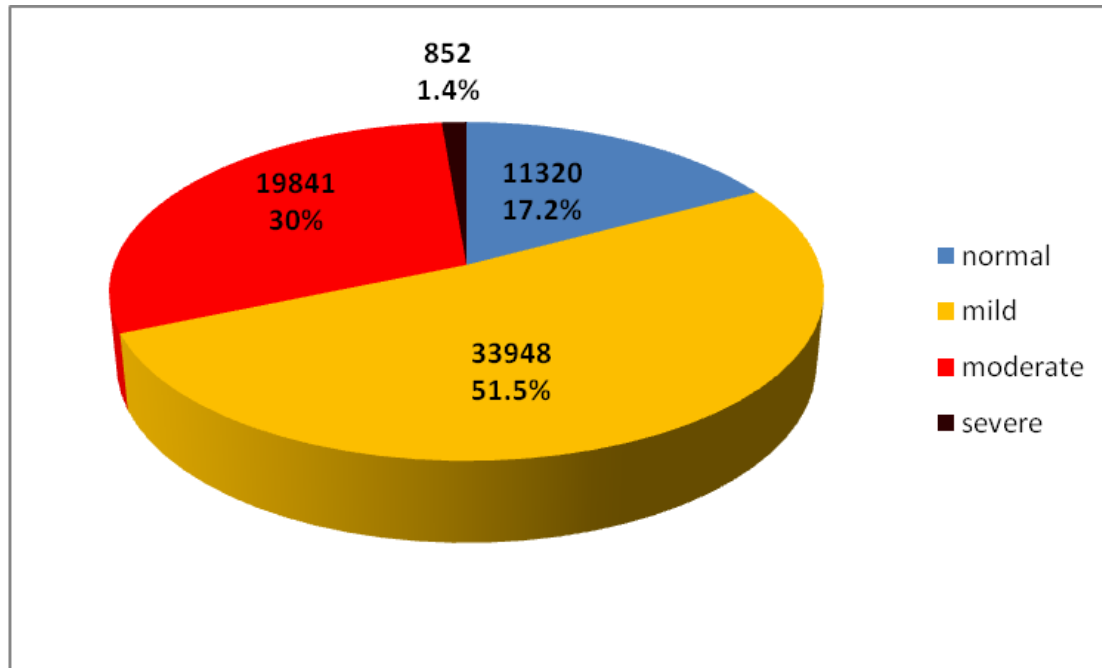
15 years after exposure

- Distribution of late toxic effects of SM among 34000 registered CW survivors



25 years after exposure

- Distribution of late toxic effects of SM among 75000 registered CW survivors



MUSTARD LUNG (CLINICAL PATTERN)



Acute:

- ☐ Severe Tracheobronchitis
- ☐ Pseudo membrane formation
- ☐ Alveolar Hemorrhage
- ☐ ARDS (Acute Respiratory Distress Syndrome)

Late:

- ☐ **COPD**
- ☐ Chronic Bronchitis
- ☐ **Bronchiolitis Obliterans**
- ☐ Bronchiectasis
- ☐ Tracheomalacia
- ☐ Bronchomalacia
- ☐ Bronchospasm
- ☐ Tracheobronchial stenosis
- ☐ Fibrosis ??
- ☐ Organized Pneumonia
- ☐ **CANCER**

* *Mustard gas toxicity: the acute and chronic pathological effects.*

Ghabili K, Agutter PS, Ghanei M, Ansarin K, Shoja MM. J Appl Toxicol. 2010 Oct;30(7):627-43

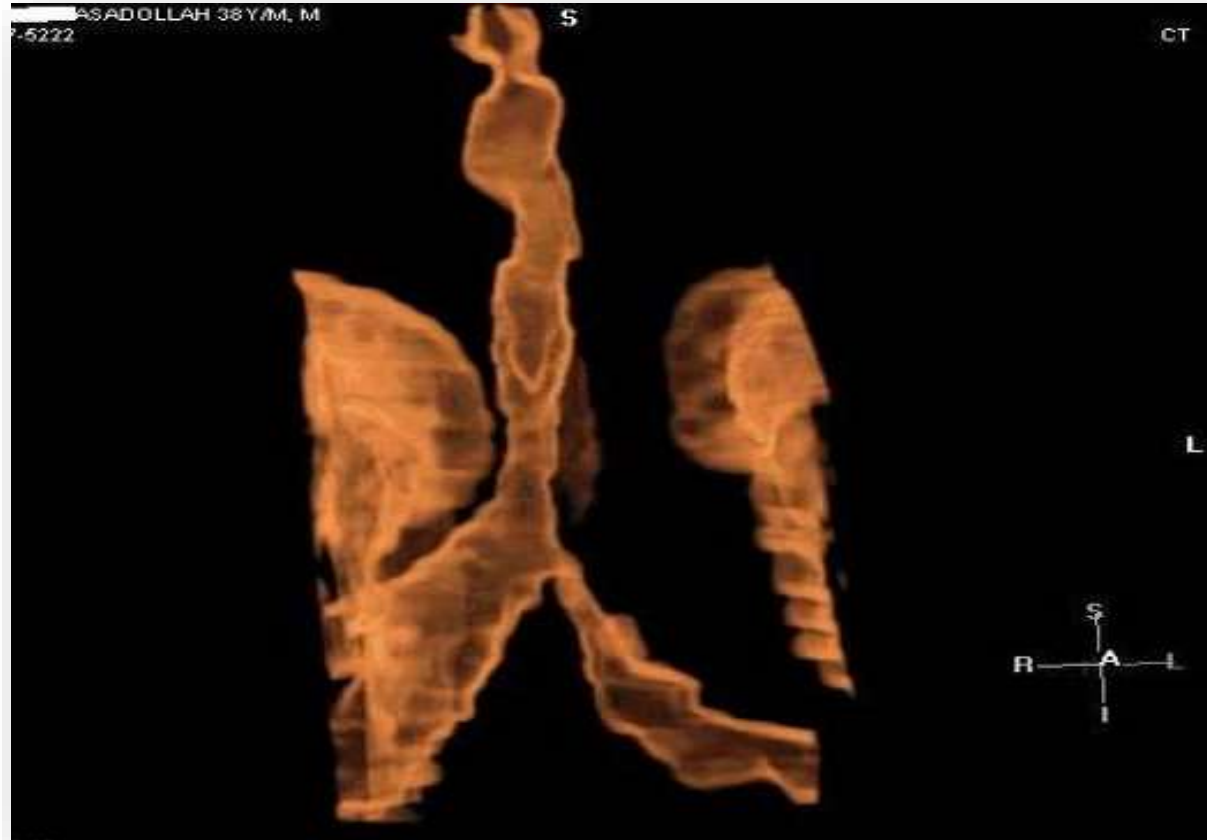
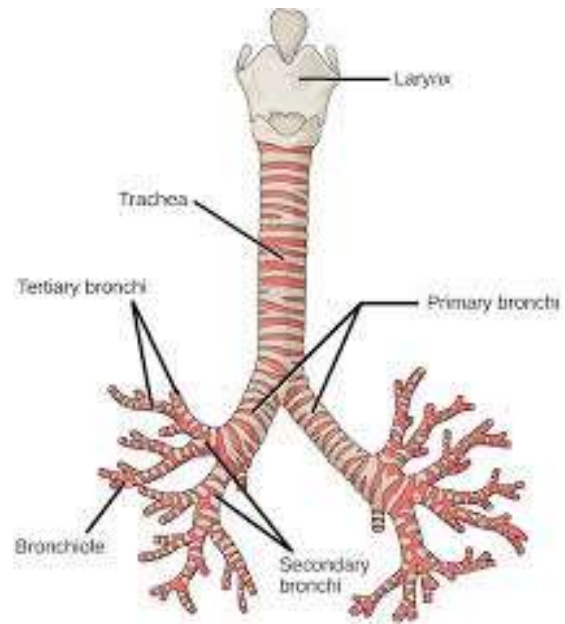


MUSTARD LUNG (PATHOPHYSIOLOGY)

- ❑ Imbalance between Oxidative Stress and anti-oxidants
- ❑ Inflammation
- ❑ Proteolysis
- ❑ Apoptosis



Airway Stenosis



Credit: Dr. M Ghanei



MUSTARD LUNG: TREATMENT

- ❑ Antioxidants (NAC)
- ❑ Bronchodilators / Corticosteroid Inhalers
- ❑ Macrolide Antibiotics
- ❑ Respiratory Rehabilitation



Mustard Eye (Ocular lesions)

Complicated mechanism / Progressive

- Dry eye
- Delayed Keratopathy
- Corneal opacity, ulcer, melting, perforation
- Loss of vision



MUSTARD EYE: TREATMENT

Complicated treatment

❑ Medical (Artificial tear, Lubricants, topical steroid,..)

❑ Surgical

❑ Corneal graft (Lamellar Keratoplasty / Penetrating K)

❑ Tarsorrhaphy,

❑ Allograft Limbus Transplant - ALT

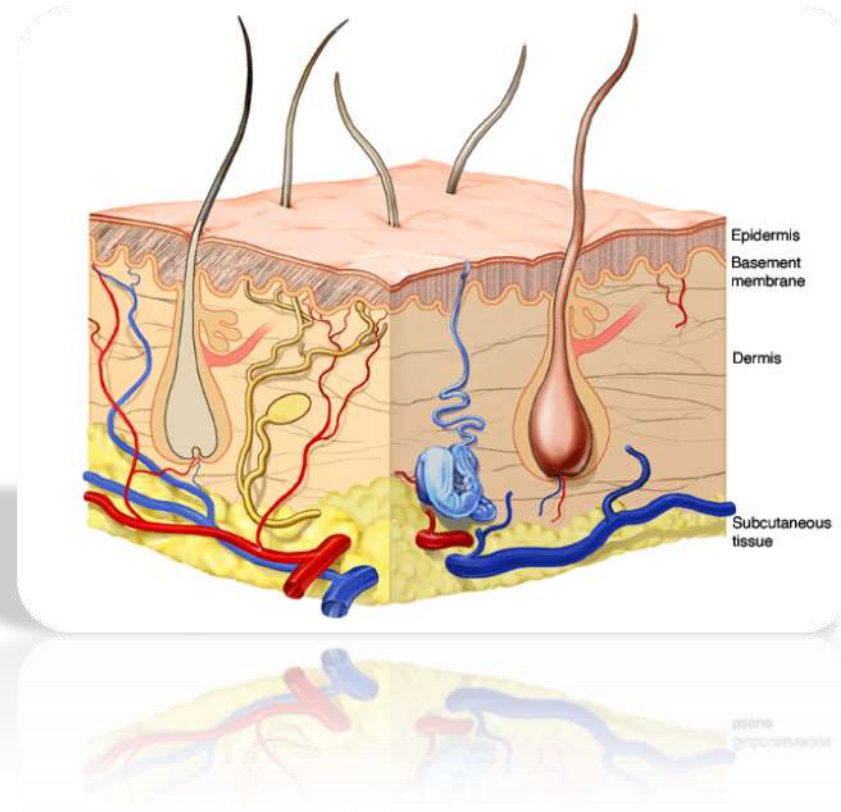
❑ Stem Cell Transplant - ACT

❑ Amniotic Membrane Transplant - AMT



Late Skin lesions (Mustard Skin)

- Dry skin (damaged sebaceous glands)
- Itching
- Pigmentation disorder
- Mustard Scar
- Other non-specific lesions



MUSTARD SKIN : TREATMENT

- Local emollients
- Systemic antihistamines
- Topical Corticosteroids



Carcinogenicity

Cancer Causes Control

DOI 10.1007/s10552-012-0094-8

ORIGINAL PAPER

Incidence of cancer in Iranian sulfur mustard exposed veterans: a long-term follow-up cohort study

Mohammad Reza Zafarghandi · Mohammad Reza Soroush · Mahmood Mahmoodi ·
Kourosh Holakouie Naieni · Ali Ardalan · Amir Dolatyari · Farahnaz Falahati ·
Majid Mirmohammadkhani · Batool Mousavi · Mostafa Ghanei

Received: 15 July 2012 / Accepted: 31 October 2012

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Abstract

Introduction It is estimated that during the Iraq–Iran war of the 1980s, over 100,000 Iranians (military or civilian)

Results Cancer incidence was significantly increased with exposure to SM. The incidence rate ratio of cancer for SM exposure was 1.81 (95 % CI 1.27–2.56), and the age-

* *SM has been categorized as Group 1 carcinogen to humans by the International Agency for Research on Cancer (IARC)*



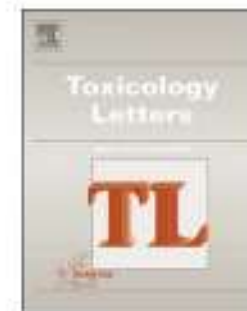


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Toxicology Letters

journal homepage: www.elsevier.com/locate/toxlet



DNA damage and repair proteins in cellular response to sulfur mustard in Iranian veterans more than two decades after exposure



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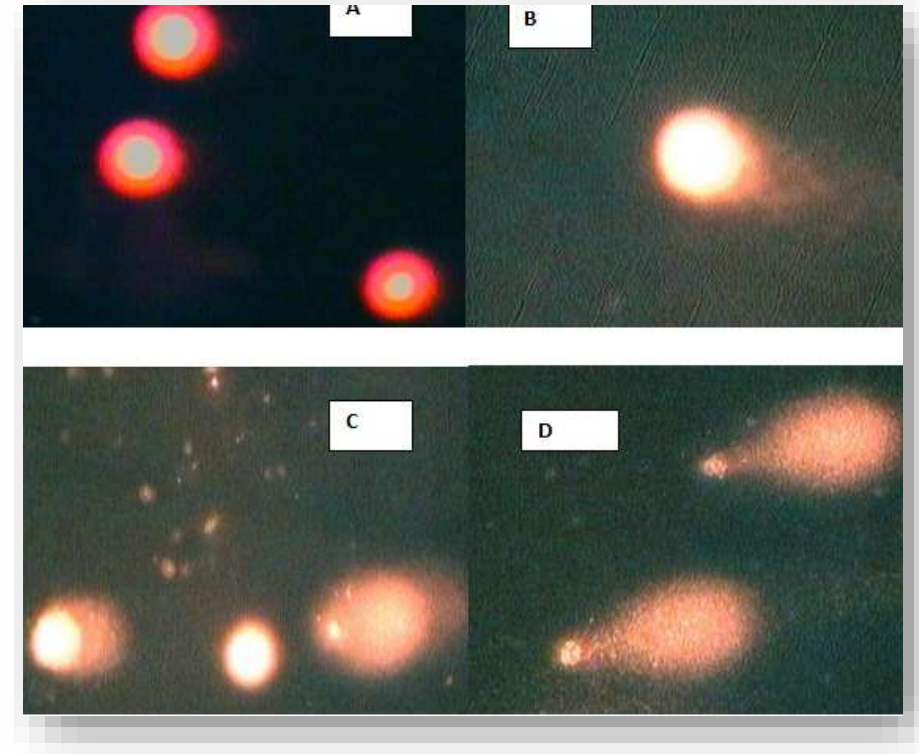
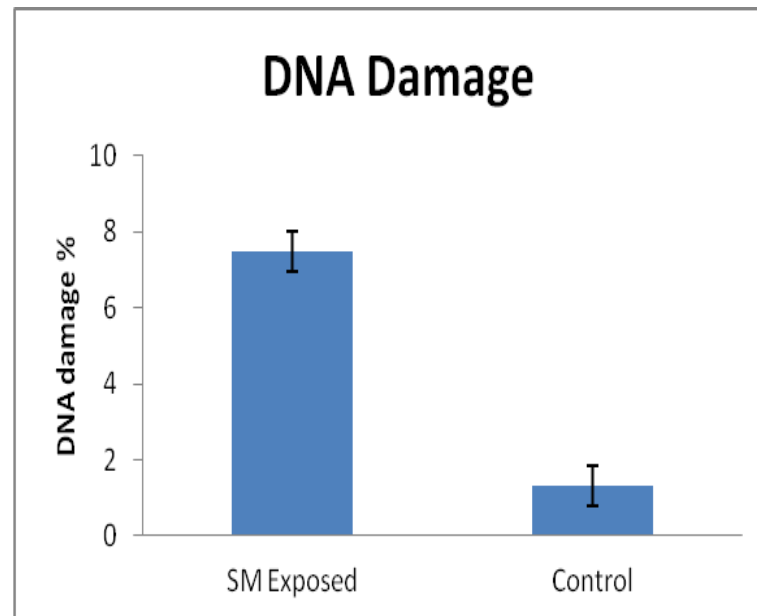
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ABSTRACT

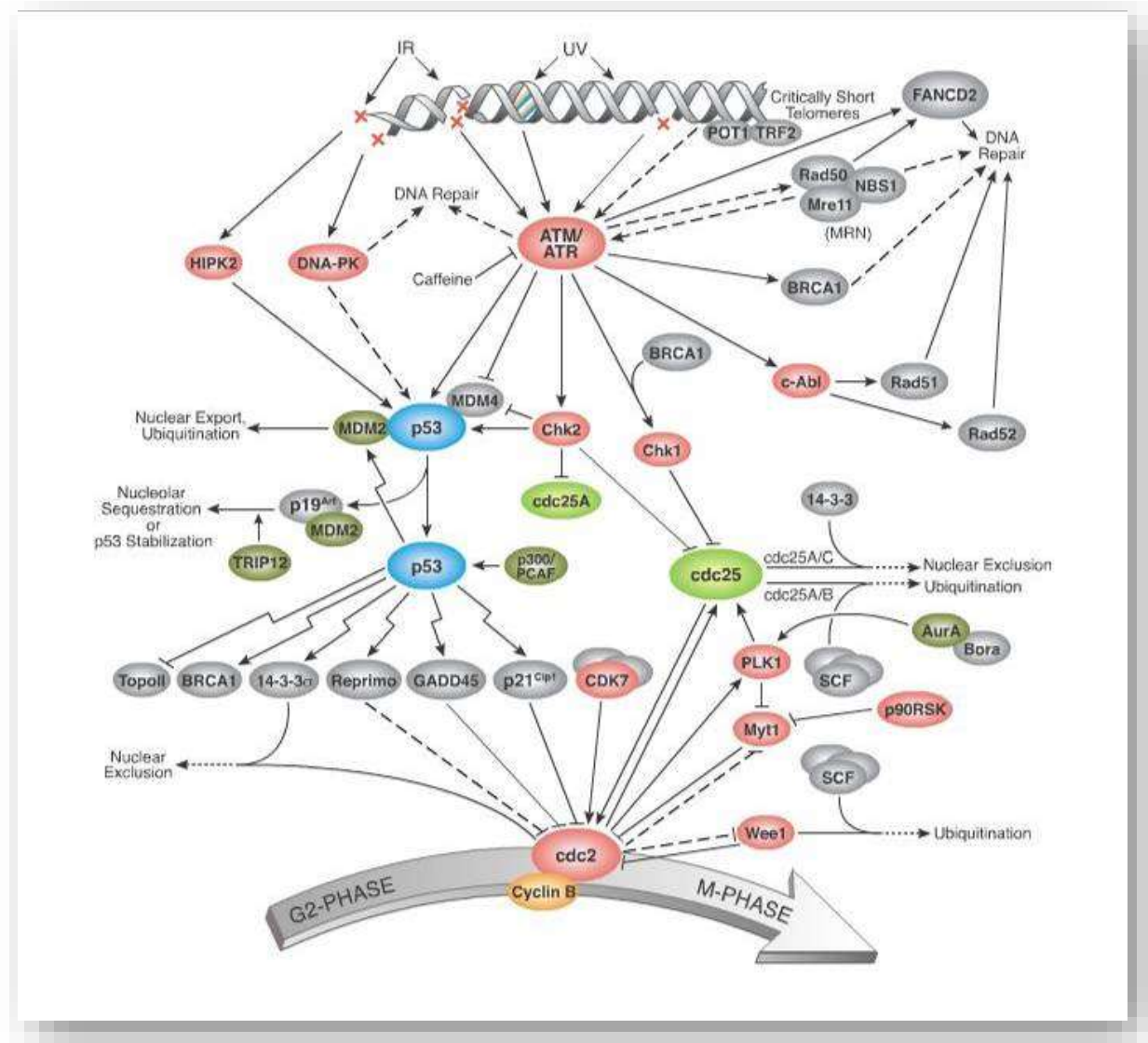


Disorders in cellular level

- DNA damage (Chronic)
- DNA damage signaling defect
- DNA repair impairment?



Disorders in DNA Repair pathways



- Cell cycle: G2/M DNA damage checkpoints and role of proteins in DNA damage/repair pathways (Cell signaling technology, 2010)



Chronic Psychological effects

Subjects\ symptom	Severe Depressive Symptoms	major anxiety symptoms
CW Exposed population	41.2%	64.7%
Conventional weapons victims	12%	13%
Non-Exposed to CW or war	5.9%	9%

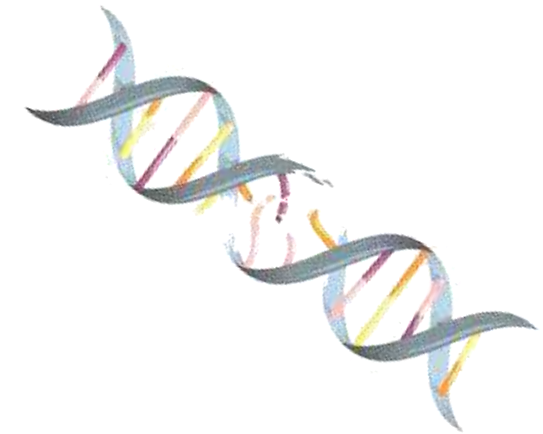
■ Poor Quality of Life

*Hashemian F, Khoshnood K, Desai MM, Falahati F, Kasl S, Southwick S. Anxiety, depression, and posttraumatic stress in Iranian survivors of chemical warfare. *JAMA*. 2006 Aug 2;296(5):560-6. doi: 10.1001/jama.296.5.560. PMID: 16882962.



Other complications

- Immune system dysfunction
- Impaired pathways in cellular level
- Infertility?
- Congenital malformation?



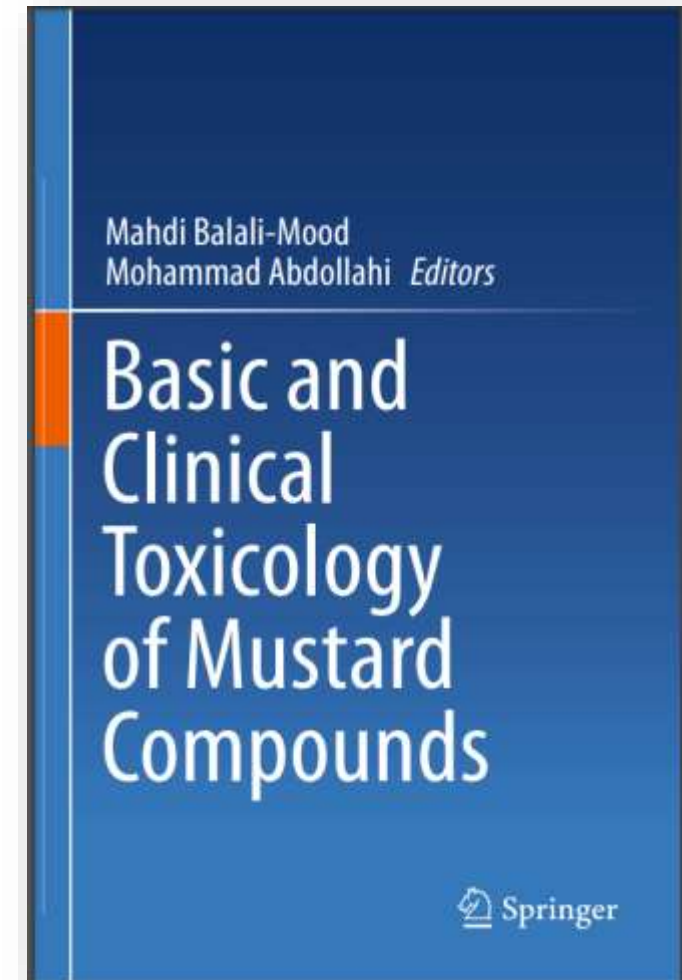
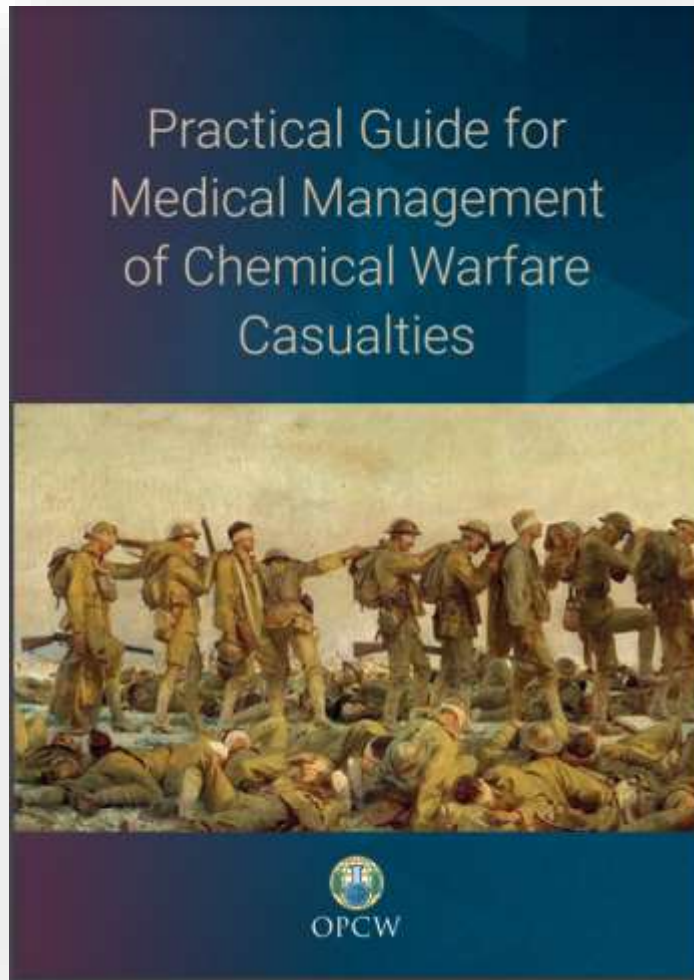


- ✓ SM targets all organs, it has no antidote
- ✓ Protection is the top priority
- ✓ **Removal of all clothing & Early /full body decon ASAP is crucial**
- ✓ Late effects of SM Injuries are high cost : Medical, Psychological, Social, Economic
- ✓ More in depth studies are needed to understand the mechanism of Injury / novel therapeutic methods for such late complications
- ✓ Medical management of the patients in long term needs a holistic approach



Further reading:

www.opcw.org



Thanks for your attention
ilginiz için teŝekkür ederiz

