In the Name of GOD

Long-Term Dermatologic effect of MUSTARD Gas in IRANIAN Chemical War victims (14-20 years after Exposure)

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Skin

- largest organ in the body and makes 18% of the total mass body

- protect of the vital organs against chemical, physical, microbial and biological trauma

- Keep the vital substances, fluids and discharge or excrete of the toxins & unnecessary substances

- Control of the body temperature
Fig. 1.1 Marked regional variations of normal skin structures as seen in sections from (left) fingertip of young male and (right) abdomen of young female. Haematoxylin & eosin stains.

Fig. 1.2 Marked regional variations of normal skin structures as seen in sections from (left) nose of young female and (right) scalp of elderly female. H & E stains.
Epidermis

Papillary dermis

Periadnexal dermis

Reticular dermis

Subcutaneous fat layer

Rete ridge
Papilla
Papillary capillary loop
Superficial or sub-papillary plexus of blood vessels
Sebaceous gland
Dermal duct of eccrine sweat gland
Arrector pili muscle
Hair follicle
Deep plexus of blood vessels
Loose connective tissue of subcutaneous fat layer (connective tissue septa)
Lobules of adipose tissue

Papillary dermis and periadnexal dermis together are also referred to as adventitial dermis.
Sulfur Mustard

✓ Sulfur mustard [\(S(CH_2-CH_2-Cl)_2\) OR dichloro di-ethyl sulfide ]
✓ Alkilating,
✓ toxigen,mutagen,carcinogen,
✓ lipophil,nucleophil,
✓ low solubility in water
ENVIRONMENTAL EFFECTS

- Colourless, oily, stability, boiling temperature (228), freezing temp. (14), 5.5 times heavier than air
- Light
- Wind
- Rain
- Moist
- Temperature (activation of S.M, increased penetration to the skin)
Increased susceptibility for skin damage by SM poisoning

1. Female
2. Low age
3. White skin
4. moistness
5. Hyperhydrosis
6. Body areas with thin epidermis & flexures
7. Dependent and frictional parts
8. Infected areas
9. Greasy skin
10. Stress & emotional hydrosis
11. Extension and longer duration of skin involvement
Biology and acute effects of Sulfur-Mustard

✓ Early manifestations of Sulfur-Mustard Intoxication.

✓ Histopathology of Acute S.M Injuries
Early manifestations of Sulfur-Mustard Intoxication:

1. Incubation period: 1-4 hrs
2. Erythema, edema: 4-8 hrs
3. Vesicle & bulla: 6-12 hrs
4. Pigmentation: 3-8 weeks

6 important factor for skin damage

1- Dose of S.M
2- Duration of exposure
3- Frequency of exposure
4- Form of S.M (Liquid-vapor)
5- Location of exposure
6- Ability of immune systems
Histopathology of Acute S.M Injuries (Vogt, 1984)

Primary phase

- Injury to fibroblasts, endothelium & venules. Cellular infiltration, vascular leak, enzyme changes, lymphokines secretion, cell adhesion detachment leading to erythema, edema & bulla.

Secondary phase

- Epidermal cell death, DNA damage, heterophils immigration & dermal collagenosis leading to chronic ulcers, scars & neoplasms.
Sulfur Mustard and Skin Interactions:

- **Epidermis** (stratum corneum- basal layer- pigment loss- bulla formation)
- **Dermis** (infiltration- fluid- fibroblast- collagen- vascular changes-systemic absorption)
- **eccrine glands** (NaCl 5%- emotional perspiration hyperhidrosis-amunium and urea)
- **Melanocyte system** (hyperpigmentation-depigmentation- salt pepper 6 to 12 mo)
Evidence of long-term health effects of S.M in World

✓ animal studies: macnamara 1975
  high dose SM intradermal- papiloma, sarcoma, BCC, SCC

✓ Human studies: inada 1978, adams 1973, klehr 1984 in WWWw I - SCC, BCC due to erythema, edema, bulla

✓ Occupational exposure: butcher 1932, stone 1988, from 53 german labors 34% had skin tumors, 45% had ulcers from 488 okonajina island labors 22 bowen & BCC, after 31 to 46 yrs

✓ Medical therapeutic exposure: russian physicians, psoriasin cream 0.005%, in psoriasis treatment- hyperpigmentation & skin sensitivity

✓ Experimental exposure: 4000 US soldiers after www I
Treatment

✓ General measures (Environmental detoxification, Self protection shields, Irrigation with water)

✓ Prevention (hight, mask, moving against the wind, mercapto ethyl amin)

✓ Classification of victims first 48 hrs (poor prognosis), after 48 hrs

✓ Specific measures (soap washing, N-Acethyl cystein lavage, gavage & injection or sodium thio-sulfate, forced diuresis, calamin lotion for blisters,)

✓ Patient follow-up (longterm effects: skin injury)
History of Sulfur mustard usage

- world
- Iran – Iraq war
- Comparison of these two
1. Synapis plant-hipocrat-vegetable
2. 1822-despretz
3. 1887-meyer(blistere formation)
4. 1894-Sulfur gas-krime war(ENGLAND)
5. 1915 april 27th-cholor gas-Ypr-5000 victims(Belgium)
6. 1917-the first mustard attack in WWW I in Ypr-400,000 poisoned due to SM(www I)
7. 1943-american navy ss.john harrey containing 100 tons of SM- collapsed in italy by german forces
8. WWW II-1945 to 1948-christian islands in denmark,
9. goateland in sweden-( 1984- 23 fishers injured )
Chemical attacks to IRAN 1983 - 1988
Iran-Iraq

1. 1359-susangerd-first CW
2. 63/12/3-kheibar op.5 tons of SM- 2100 vic
3. 63/12/22-majnoon- nerve & SM- 2231 vic
4. 64/12/24-faav- cianide & SM- 8500 vic
5. 64/12/8-hazrate zahra hospital accident
6. 65/10/10-sumar hospital- 420 vic
7. 66/1/21-khoramshahr-katiusha- nerve & SM
8. 66/4/7-sardasht- SM- 7000 vic
9. 67/4/4-majnoon- nerve & cianide- capturing
10. 66/12/27-halabcheh- nerve,SM & cianide-12000 vic
11. 67/5/11-oshnaviyyeh- the last attack-2680 vic
Comparison of WWI with IRAN

WWI
1. 400,000 poisoned-20,000 killed
2. Skin lesions- 80 to 90%
3. Occular lesions- 86%
4. Respiratory lesions-75%

IRAN
1. 100,000 poisoned- 15000 killed
2. Respiratory lesions-95%
3. Occular lesions-92%
4. Skin lesions-82%
The reason for these differences

1. higher temperature in IRAN than Europe
2. Higher frequency of attacks & gas persistence in the environment
3. Incorrect use of protections by Iranian forces
4. Iranian’s beards causing the masks not to fit properly
Classification of
Long-Term Dermatologic effect of MUSTARD Gas in IRANIAN Chemical victims
Classification of S.M Lesions

1. Definitely caused by S.M: scar due to sulfur mustard gas and Neoplasm at the site of scar

2. Probably caused by S.M: xerosis, seborrheic dermatitis, itching, vitiligo, vascular abnormalities, folliculitis, urticaria & tinea versicolor

3. Atypical forms by S.M: DLE, cherry angioma, seborrheic dermatitis, versicolor, xerosis, skin cancer
### Prevalence of long term skin lesions in 800 victims

<table>
<thead>
<tr>
<th>lesion</th>
<th>percent</th>
<th>location</th>
<th>Relationship with SM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xerosis</td>
<td>33/1</td>
<td>Limbs, trunk</td>
<td>Probable</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>14/93</td>
<td>Face, trunk, upper limb</td>
<td>Probable</td>
</tr>
<tr>
<td>Cherry angioma</td>
<td>24/67</td>
<td>Trunk, abdomen</td>
<td>Probable</td>
</tr>
<tr>
<td>Dermatitis seborrh</td>
<td>11/03</td>
<td>Face, scalp, chest</td>
<td>Probable</td>
</tr>
<tr>
<td>Eczema</td>
<td>9/1</td>
<td>Limbs</td>
<td>Probable</td>
</tr>
<tr>
<td>Acneiform lesions</td>
<td>5/84</td>
<td>Back, limbs</td>
<td>Probable</td>
</tr>
<tr>
<td>Tinea versicolor</td>
<td>6/49</td>
<td>Trunk, neck, upper limb</td>
<td>Probable</td>
</tr>
<tr>
<td>Melanocytic nevi</td>
<td>6/1</td>
<td>Trunk, face</td>
<td>Probable</td>
</tr>
<tr>
<td><strong>Malignant Neoplasms</strong></td>
<td>1/94</td>
<td>Scalp, face, on sulfur mustard’s scar</td>
<td>Possible</td>
</tr>
<tr>
<td>Mustard scar</td>
<td>40/84</td>
<td>Upper &amp; lower limb, folds</td>
<td>definite</td>
</tr>
</tbody>
</table>
SM SCAR

Definition:
It refers to a localized patch and plaque with pigmentory, vascular and trophic cutaneous changes due to erythema, edema, bullae from months or years ago.

Clinical manifestations:
Pigmentory changes (leukomelanoderma or salt & pepper) • Vascular changes (telangiectasia, cherry angioma, spider angioma) • Trophic changes (reticulated atrophic and hypertrophic changes) •

Location:
Face, neck, axilla, antecubital, back, lumbosacral, genital •

Histopathology:
partial flattening of rete ridges, variable hyperpigmentation, depigmentation in flattened , rete ridges, partial to total loss of skin appendages, sclerotic reaction with collagenous deposits in papillary and mid-dermis(sclerodermoid changes)
SM SCAR

clinical grading (in order of severity of exposure to SM)

- Grade 1- (pigmentory disorders)
  - by low dose of S.M
- Grade 2- (P.D + vascular alterations)
  - by medium dose of S.M
- Grade 3- (P.D + V.A + trophic skin changes)
  - by high dose of S.M

Several environmental, individual factors and location, in addition to the concentration and form (liquid, vapor) of SM, determine the sequence and severity of manifestations in the injured organ.
Discussion
- During chemical attacks every body needs full protection

-( face mask, protective clothes for the whole body, gloves and boots)

- But we experienced many Iranian soldiers who used only face masks and upper body protective clothes
Incomplete protection during chemical attacks
Forms & Effects of S.M

1. S.M has 2 forms: liquid (below 14 °C) & vapor (above 14 °C)

2. Vapor form causes mainly lung & eye problems and minimal effects on the skin (warm weather)

3. Liquid form causes mainly skin problem and minimal effects on the lung & eyes (cold weather)

4. Liquid form in cold weather can penetrate and remain in the environment, on things (clothes) and especially wet ground
How is S.M transferred from wet ground to clothes & skin and then to the lungs & eyes?

1- Lying in the decubitus for protection or crawling for movement are common war positions for soldiers. The wet ground exposes the unprotected body to the activated S.M

2- So liquid form of S.M on the wet ground can penetrate through the clothes to the anterior aspects of the body (thighs & perineum)

3- On the other hand the thickness of palms epidermis in the unprotected hand which is more active than the other part of the body can retain a lot of S.M without any sign & symptoms can be a vector in transferring the S.M to the genitalia when urinating.

4- Remaining and effectiveness of S.M can cause serious problems in the groin and genitalia due to thin epidermis hence the likelihood of S.M penetrating in to the urethra(mea) and can cause severe destruction.

5- The victims with wet and polluted clothes when in an enclosed warm space with above 14 °C(car, home, health care center) produce condition for converting the liquid form of S.M on the body & clothes in to vapor and then with removing of the face mask, creates favorable condition for developing lung & eye problems.
Recommended safety measures for sulfur mustard

1- Use of full protection (facemask, full body cover)
2- Providing protection for the genitalia

3- Rapid & frequent urination to clear the urethra off S.M
4- Avoid urethral catheter to prevent deep penetration of S.M

5- Before entering any closed area the clothes must be removed to prevent inhaling of vapor form of S.M arising from the clothes
6- With attention to vector role of the hand, suggested washing of hands before & after contact with the body and remove the clothes
Summary

➢ There is significant association between S.M intoxication and type, location and severity of skin lesions.

➢ Mild to moderate injuries with S.M have no long-term skin lesion after 2 decades.

➢ Acute injury with High-Concentrate S.M and long-term chronic exposure with S.M can cause prominent scar, skin ulcers, dermatitis, pigmentation disorders and opportunistic neoplasms.
Suggestions

1. Accurate and complete Revision of all data

2. Data collection according to severity, location and duration of exposure and type of acute and chronic skin lesions

3. Classification of patients according to severity, location and duration of exposure and type of acute and chronic skin lesions.

4. Regular and serial examination of all victims and comparing them with matched control groups
روز اول

روز سوم تا پنجم

روز پنجم تا هفتم

15 سال بعد از تماشای گاز شیمیایی

17 سال بعد از تماشای گاز شیمیایی
severe restriction in range of motion due to S.M scar in hands & feet

1986 Iran
ضایعات جادویی و مزمن در مصدومان شیمیایی
How to find who is real chemical victim

1- Having strong documents
2- Finding SM scar on the common area
3- Reliable history of exposure at war time and later
4- Reliable past medical history of treatment and follow up
5- Starting skin illness from the exposure time or a few month later
6- Comparing histopathology finding with clinical presentation at once
7- Finding an atypical and severe form of disease in an unusual age or …
8- Referring and matching with the comments from lung and eye specialist
THANK YOU FOR YOUR ATTENTION

More detailed reports on late skin lesions of SM exposed victims will be published soon

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