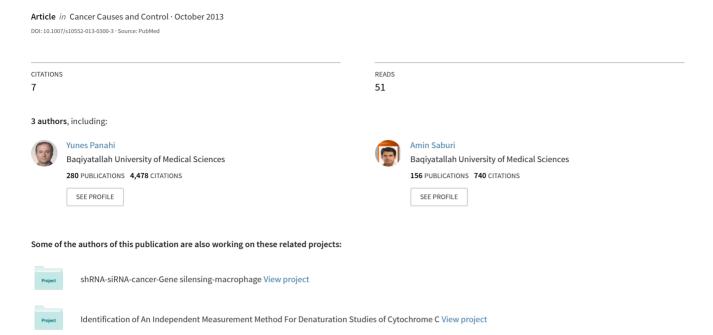
## Other considerations about carcinogenicity of sulfur mustard



## LETTER TO THE EDITOR

## Other considerations about carcinogenicity of sulfur mustard

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Dear Editor in Chief,

We read with great interest a recently published article by Zafarghandi et al. [1] in Cancer Cause and Control journal. In this long-term follow-up cohort study, the incidence of cancer in Iranian sulfur mustard (SM)-exposed veterans was assessed and reported in comparison with a matched control group. They reported that the incidence of cancer in exposed cases was significantly higher than controls (the incidence rate ratio of cancer = 1.81, the age-adjusted incidence rate ratio = 1.64, and the hazard ratio was 2.02). They also finally concluded that "present study suggests carcinogenesis of SM following acute exposure during war." Though it is one of the rare and moreover interesting articles in this field, we would like to draw the authors' attention to some points that can help to release a more valid conclusion about the carcinogenicity of SM:

It was approved that patients with chronic inflammatory diseases are susceptible to neoplasm [2, 3].
 Therefore, the role of chronic inflammatory conditions (bronchiolitis, bronchitis, dermatitis, recurrent pulmonary infections, etc.) should be considered in these patients [4]. It would be better concluded if findings were reported and separated in terms of the presence or

absence of chronic inflammatory conditions in these patients.

- These patients have an imbalance in oxidant-antioxidant levels in addition to increased levels of inflammatory substance. Therefore, some oxidative stressors such as NO may be escapes from cell defense due to decreased levels of antioxidant supply (such as NAD+) [5]. Hereupon, these reactive oxygen species (such as NO) can damage DNA in long term [6]. On the other hand, it was observed that DNA repair mechanisms are impaired in these patients [5, 6]. In addition to the above mechanism, these patients use long-term medications such as corticosteroid, which can make a defect in repair of damaged DNA [7] in addition to inhibition of p53dependent apoptosis [8]. So, injured cells can progress to neoplastic cells. Therefore, this mechanism can shed new light on the molecular mechanisms by which chronic inflammatory disorders may initiate or enhance carcinogenesis in these cases [9]. Moreover, treatment can have impact on some neoplasm; it was reported that pure risk of cancer increase in prolonged use of glucocorticoids and NSAIDs [10, 11]. Also, it was demonstrated that "glucocorticoids may play a significant role in regulating tumor cells gene expression and cell growth" [12]. It was better if these results have been analyzed based on treatment groups.
- 3. It was constantly approved that chronic psychological stress (for example, PTSD in these patients) promotes tumorigenesis. Feng et al. [13] showed that tumorigenesis could be due to "the attenuation of p53 function as an important part of the underlying mechanism." Consistet with this issue, the mental health of veterans who have been exposed to SM could be affected because of long-term adverse consequences [14]. Therefore, if the authors have compared SM-exposed case findings

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- with a control group of non-SM-disabled veterans, it would be more helpful.
- 4. More broadly, research is also needed to determine whether there was any screening program for these patients or not. It can justify the higher incidence of cancer due to more accessible diagnostic protocols.
- 5. These cases were susceptible to comorbid disorders such as coronary artery diseases, obesity, and musculoskeletal disorders [15]. The mortality in SM-exposed cases is actually higher than that on non-exposed cases because they have some disability such as prolonged pulmonary sequels affecting their lifestyle, physical activity, and psychological status [14, 16]. On the other hand, some malignancies do not present in these cases because the patients die due to the mentioned comorbidities before presentation of these in situ neoplasm. Therefore, if these patients be alive for much time, it is possible to present.
- Furthermore, it is suggested to separate and arrange incidence and prevalence of neoplasm based on years after exposure. It can be more helpful to conclude about pure or mediated carcinogenesis impacts of SM.

Finally, we concluded that there are some confounding factors that can distort the conclusion about the "pure" carcinogenicity impact of single exposure with SM.

**Conflict of interest** There is no conflict of interest to be declared.

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