

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

1. **Q:**Title: Chloracne induced by 3, 5, 6-Trichloropyridin-2-ol sodium is still a disease worthy of great attention----case report Suggest the title be changes to reflect the focus or the report as well as the fact that these cases further confirming the putative toxicity of STCP (Richardson 1995) in 3 males post unprotected exposure; such as “Neuropathy and chloracne induced by 3, 5, 6-trichloropyridin-2-ol sodium. Report of 3 cohort cases.”

A: Thank you very much for your advice. The title of the manuscript is to highlight chemical induced acne. The emphasis is on chemicals.

I have changed the title to “Neuropathy and chloracne induced by 3, 5, 6-trichloropyridin-2-ol sodium. Report of 3 cohort cases”.

2. **Q:**Core tip: My need to be rewritten... May be shortened. Omit sentence 2. Rewrite sentence 3 (“development of science”, not sure what the authors mean).

A: I have omitted sentence 2 and rewritten sentence 3. “In recent years, new chloracnogens are emerging with the increasing number of new chemical compounds”

3. **Abstract:** Suggest focusing the Background on the known neurotoxicity

and chloracne of STCP as well as halogenated aromatic insecticides for a more general audience.

A: Thank you for your advice. I added the following background knowledge: Sodium 3,5,6-trichloropyridin-2-ol (STCP) is a necessary precursor compound for the production of chlorpyrifos and triclopyr, which are extensively used as pesticide and herbicide. It is a chlorophenol which has been associated with chloracne. STCP poisoning could induce mild myelin sheath damage

4. Suggest the case summary include the age, sex, and time to symptoms post exposure for each case. (Note the photos shows multiple lesions mostly in the genital area not the scrotum).

A: Thank you very much for your advice. I have made the corresponding changes

5. Treatment is confusing; Suggest... The patients were prescribed oral viaminate capsules, topical adapalene gel and regular hematologic follow up for AST (spell out acronym as aspartate transaminase- first reference) and lipids. In the absence of a specific pathologic mechanism, but advances in treatment options the conclusion should underscore the importance of physician awareness of neuropathy and chloracne associated with STCP exposure.

A: Thank you very much for your advice. I have made the corresponding changes: All these also reminds us that the treatment of chloracne caused by STCP is difficult, and we should attach great importance to this new

compound related with the neuropathy and chloracne.

6. .Background: Recommend shortening by about a third by consolidating the chronologic reports of the incidence of chloracne associated with occupational exposure to related halogenated aromatic compounds.

A: Thank you very much for your advice. I have made the corresponding changes: According to a report in 1974, the patients who were exposed to pentachlorophenol, Trichlorobenzene (TCB) and 2, 3, 7, 8-tetrachlorodibenzop-dioxin (TCDD) developed chloracne in different proportions of poisoning cases.

7. Case presentation: The authors can make the text flow more smoothly if the individual cases are referenced in Table 1 and the common symptoms of all cases are presented. Then address differences in symptoms and coordinate the Figure 1 images with the correctly identified case. Note the clinical symptoms in Table 1 of patient 1 do not include the genital lesions shown in Figure 1. Specifically identify the patient having the persistent symptoms.

A: Thank you very much for your advice. I rechecked the patient's clinical symptoms in picture 1 and table 1, and revised them accordingly. The patient with persistent symptoms is patient 1

8. Discussion: What are some other possible explanations in addition to lack of PPE and physical condition (all the same) for the diversity in incubation period, symptoms, labs, and persistence after short exposure.

See dose effect (Albers et al., 2007)

A: Thank you very much for your reference. After reading the references, I think that the incidence of chloracne may be related to the increased exposure time of STCP, age, height and low education level.

9. Suggest the following change to Discussion line 8-11... Based on the history of unprotected acute exposure to chloracnegenic substances, clinical manifestations, dermoscopic findings, biopsy results, and career identification results at our hospital, a diagnosis of chloracne due to STCP toxicity was made in these 3 patients. However, toxic levels of STCP...

A: Thank you very much for your advice. I have revised it as you said in Discussion line 8-11.

10. Table: Add distribution of lesions to patient 1's narrative.

A: I have added distribution of lesions to patient 1's narrative.

11. Figures 2 and 3 do not identify the specific patient(s) providing the image or pathology.

A: Thanks for you advice. The three patients came to the clinic together, and their rash was similar. As the patient 1 in Fig 1 was the most serious patient, extensive photography and pathological biopsy were carried out on the patient. The clinical symptoms of the patients 2 and 3 were milder than patient 1 in Figure.1, so only exposed parts were photographed. Figures 2 and 3 are the relevant examinations of patient 1. According to the clinical photos of patients 2(G) and 3(H), they are obviously different from our

common acne vulgaris. In my opinion, we want to emphasize that STCP is a chemical that causes chloracne, and we should be alert to this chemical. Although there is no pathological examination on the patient 2 and 3, clinical manifestation of these two patients can also prove that the occurrence of chloroacne is a fact.

12. Additional references for consideration: Wu N, Hao F, Yu X. Peripheral nerve and skin damage associated with working in a STCP factory: report of four cases. *Clin Toxicol (Phila)*. 2012 Jul;50(6):514-7. doi: 10.3109/15563650.2012.696200. Epub 2012 Jun 18. PMID: 22702901. Albers JW, Garabrant DH, Mattsson JL, Burns CJ, Cohen SS, Sima C, Garrison RP, Richardson RJ, Berent S. Dose-effect analyses of occupational chlorpyrifos exposure and peripheral nerve electrophysiology. *Toxicol Sci*. 2007 May;97(1):196-204. doi: 10.1093/toxsci/kfm028. Epub 2007 Feb 25. PMID: 17324952. Richardson RJ. Assessment of the neurotoxic potential of chlorpyrifos relative to other organophosphorus compounds: a critical review of the literature. *J Toxicol Environ Health*. 1995 Feb;44(2):135-65. doi: 10.1080/15287399509531952. PMID: 7531775. Bock KW. Toward elucidation of dioxin-mediated chloracne and Ah receptor functions. *Biochem Pharmacol*. 2016;112:1-5. Doi: 10.1016/j.bcp.2016.01.010.

A: Thank you very much for your advice. I get new inspiration from these references, and I have added them to the manuscript

Science editor:

1. I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

A: I have provide the original pictures in PPT according to your requirements.

2. please don't include any *, #, †, §, ‡, ¥, @....in your manuscript;

A: I have revised the relevant content in the full text according to what you said

3. please provide the audio core tip file where the content of core tip is recorded.

A: OK. I've recorded this file.