

Although duration of exposure was defined as the time between the first and last prescription for a TCN agent (doxycycline, minocycline or tetracycline), with our approach, and even though an interruption is unlikely to have occurred with continuous prescribing, we cannot verify that there was or was not any isolated period of interruption in TCN exposure. Certainly, cumulative dose may, or may not, ultimately be proven to correlate with carcinogenicity, and this idea is of interest, but such correlation requires even larger sample size and is also well beyond the scope of work for our project.

The aim of our study, as stated in our report, was to simply determine if there was an association between exposure to TCNs and non-melanoma skin cancer (NMSC), namely basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), being an unmet need, given that prior literature focused on NMSC associations for other phototoxic drugs.^{3–5} In focusing on NMSC for our study design, we did not collect data for precancers such as actinic keratosis, nor did we collect data for malignant melanoma, all of which may inform future exploration within research designed as such.

It is agreed that a limitation to our study includes the potential for an immunomodulating effect from TCNs that could very well contribute to the study observations, but this cannot be ascertained from the data collection for our project. Moreover, based on the abundant prior evidence for TCN-related phototoxicity compared to the lower level of evidence regarding immunomodulating activity, it seems that the association with NMSC identified in our report is likely to be more attributable to phototoxicity than to an immunomodulating effect, yet both may apply.^{6–8}

Regardless, and relevant to the point, the association for TCNs with NMSC, as found in our large patient population, seems to well support what we have concluded: that awareness and enhanced sun protection education seem justified as part of therapeutic decision-making in these patients when an association such as this is found in a large patient population.

P.P. Vakharia,¹ B. Nardone,^{1,*} B.J. Schlosser,¹ D. Lee,¹
L. Serrano,¹ D.P. West^{1,2}

¹Department of Dermatology, Northwestern University Feinberg School of Medicine, 676 N. Saint Clair Street, Suite 1600, Chicago, 60611, IL, USA,

²Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, 676 N. Saint Clair Street, Suite 1600, Chicago, 60611, IL, USA

*Correspondence: B. Nardone. E-mail: b-nardone@northwestern.edu

References

- Vakharia PP, Nardone B, Schlosser BJ, Lee D, Serrano L, West DP. Chronic exposure to tetracyclines and subsequent diagnosis for non-melanoma skin cancer in a large Midwestern US patient population. *J Eur Acad Dermatol Venereol* 2017. <http://doi.org/10.1111/jdv.14399>.
- Nwabudike LC, Tatu AL. Response to 'Chronic exposure to tetracyclines and subsequent diagnosis for non-melanoma skin cancer in a large Mid-Western US population'. *J Eur Acad Dermatol Venereol* 2017. <http://doi.org/10.1111/jdv.14657>.
- Jensen AO, Thomsen HF, Engebjerg MC, Olesen AB, Sorensen HT, Karagas MR. Use of photosensitising diuretics and risk of skin cancer: a population-based case-control study. *Br J Cancer* 2008; **99**: 1522–1528.
- Karagas MR, Stukel TA, Umland V et al. Reported use of photosensitizing medications and basal cell and squamous cell carcinoma of the skin: results of a population-based case-control study. *J Invest Dermatol* 2007; **127**: 2901–2903.
- Robinson SN, Zens MS, Perry AE, Spencer SK, Duell EJ, Karagas MR. Photosensitizing agents and the risk of non-melanoma skin cancer: a population-based case-control study. *J Invest Dermatol* 2013; **133**: 1950–1955.
- Henehan M, Montuno M, De Benedetto A. Doxycycline as an anti-inflammatory agent: updates in dermatology. *J Eur Acad Dermatol Venereol* 2017; **31**: 1800–1808.
- Hasan T, Kochevar IE, McAuliffe DJ, Cooperman BS, Abdulah D. Mechanism of tetracycline phototoxicity. *J Invest Dermatol* 1984; **83**: 179–183.
- Stern RS. Photocarcinogenicity of drugs. *Toxicol Lett* 1998; **102–103**: 389–392.

DOI: 10.1111/jdv.14662

A severe case of mango dermatitis

Editor

A 27-year-old Japanese woman visited our hospital with eruptions on the lips, which had appeared 2 days after she took acetaminophen. At day 15, her lips were severely swollen with erosions, most of which were covered with dense crusts (Fig. 1). Clinically, Stevens–Johnson syndrome due to acetaminophen was suspected. However, the drug-induced lymphocyte stimulation test for the reagent was negative (stimulation index: 156%; normal: <179%), and the eruption did not recur after she resumed acetaminophen. The cause of the eruption was uncertain, but the same eruptions recurred 2 months later. The patient took time-lapse clinical pictures by herself, in which the eruptions were seen to initially develop on the lips before spreading to the face (Fig. 2). From the clinical manifestations,



Figure 1 Clinical manifestations of the lips at day 15. The lips are swollen and covered with dense crusts. Erosions are also noted.



Figure 2 Time-lapse clinical features 1 day after eating mango. Irregularly shaped itchy erythema is noted on the face.

allergic contact dermatitis was suspected, and a detailed clinical inquiry revealed that she had eaten unpeeled mango 1 day before developing the eruption. A patch test using 0.02% of urushiol was positive (+, assessed by International Contact Dermatitis Research Group criteria)¹ at days 2 and 3 (not shown). From these findings, the diagnosis of allergic contact dermatitis due to mango contact was made.

Mangoes are among the most common fruits to be implicated in allergic contact dermatitis, such an allergy is known as 'mango dermatitis'.^{2,3} The allergens in mangoes, including heptadecadienylresorcinol, heptadecenylresorcinol and pentadecylresorcinol, are found mostly in the fruit skin, the sap, the bruised leaves and the stem.^{2,4} Thus, eating peeled mango does not theoretically induce an allergic reaction. In our case, the eruption had never appeared when the patient had eaten peeled mango. The diagnosis of 'mango dermatitis' is not difficult if clinicians take a detailed clinical history of unpeeled mango consumption and see itchy eruptions on the lips and face. It should be noted that the eruptions do not appear soon after antigen exposure; eruptions due to allergic contact dermatitis usually develop 24–96 h after exposure to the antigens.⁵ Patch testing using urushiol, which may cross-react with the antigens of mangoes, ginkgoes and toxicodendron, is useful for the diagnosis of mango dermatitis.⁴ In summary, the clinical history of how the mango was eaten is important for the diagnosis of mango dermatitis.

H. Miyazawa,¹ W. Nishie,^{1,*} H. Hata,¹ K. Matsumura,²
H. Shimizu¹

¹Department of Dermatology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, N15 W7, Kita-ku, Sapporo, 060-8638, Japan, ²Department of Dermatology, JCHO Sapporo Hokushin Hospital, 2-6-2-1, Atsubetu Chuo, Atsubetu-ku, Sapporo, Hokkaido, 004-8618, Japan

*Correspondence: W. Nishie. E-mail: nishie@med.hokudai.ac.jp

References

- 1 Pongpaiboj K, Ale I, Andersen KE *et al.* Proposed ICDRG classification of the clinical presentation of contact allergy. *Dermatitis* 2016; **27**: 248–258.
- 2 Calvert ML, Robertson I, Samarasinghe H. Mango dermatitis: allergic contact dermatitis to *Mangifera indica*. *Australas J Dermatol* 1996; **37**: 59–60.
- 3 Hershko K, Weinberg I, Ingber A. Exploring the mango-poison ivy connection: the riddle of discriminative plant dermatitis. *Contact Dermatitis* 2005; **52**: 3–5.
- 4 Oka K, Saito F, Yasuhara T, Sugimoto A. A study of cross-reactions between mango contact allergens and urushiol. *Contact Dermatitis* 2004; **51**: 292–296.
- 5 Saint-Mezard P, Rosieres A, Krasteva M *et al.* Allergic contact dermatitis. *Eur J Dermatol* 2004; **14**: 284–289.

DOI: 10.1111/jdv.14656

Oral manifestations as the main feature of late-onset recessive dystrophic epidermolysis bullosa

Editor

Dystrophic epidermolysis bullosa (EB) is a heterogeneous group of inherited blistering diseases with skin cleavage beneath the basement membrane caused by mutations in *COL7A1*, encoding collagen VII.¹ Clinical features include skin and mucosal blistering and scarring, and cover a broad range of degrees of severity. Clinical manifestations of severe generalized dystrophic EB due to loss-of-function mutations are typical, allowing a clinical diagnosis. In contrast, in cases with discrete skin fragility, the diagnosis may remain unrecognized, as presented here.

A 54-year-old female was referred for evaluation of lesions of the oral mucosa, progressive microstomia and jaw pain which she suffered from for at least 15 years. A dental restoration was planned but postponed due to gingival scarring and small mouth opening. Oral leukoplakia simplex and mandibular myoarthropathy were diagnosed in 2010. On clinical examination, she showed a mouth opening of 2.5 cm, whitish and scarring lesions of the oral mucosa (Fig. 1a), without any erosion or signs of infection. Noticeable was early dental replacement with several teeth being crowned since her late thirties. Otherwise, she was well, without any symptoms (i.e. dysphagia) or medications.

Initially, oral lichen planus was clinically suspected. Histopathology of a punch biopsy of the oral mucosa revealed subepidermal blistering without significant inflammatory infiltrate, while direct and indirect immunofluorescence were negative, as well as BP180 and BP230 ELISA. In the follow-up, detailed history and clinical examination revealed loss of toe nails and lacquered finger nails because of nail dystrophy (Fig. 1b). In addition, one eroded blister at her left forearm as well as scarring at her elbows, knees, shins and feet (Fig. 1c), but no milia were noted. Skin fragility was confirmed by the patient,