

LETTER TO THE EDITOR

DRESS syndrome reactivation due to ranitidine patch testing: The flare-up phenomenon

To the Editor,

We read with great interest the article by Teo and Arden-Jones,¹ entitled "Reactivation of drug reaction with eosinophilia and systemic symptoms [DRESS] with ranitidine patch testing" presenting a continuation of our own case study previously published in 2018 on ranitidine induced DRESS syndrome.² In the paper, the authors not only highlight the importance of considering multiple drug hypersensitivity in DRESS syndrome, but also, crucially, highlight the risk of DRESS syndrome reactivation with drug patch testing. They noted that repeat patch testing with ranitidine 30% pet. (in duplicate with adhesive tape stripping) led to eventual mild DRESS syndrome reactivation. Tape stripping modifies the skin barrier to facilitate drug penetration; however, it is not clear whether this was the causative factor in the observed reactivation. We agree with the authors that the intradermal testing previously performed would have delivered the drug even more efficiently through the epidermis (yet no reactivation was observed). The role of tape stripping in this reactivation event is, therefore, uncertain. In our own prospective study on drug patch testing in cutaneous adverse drug reactions,³ none of the 45 patients patch tested developed a flare reaction; however, there were two cases of mild reactivation from intradermal testing. It is, therefore, important to be aware that both intradermal testing and patch testing can induce systemic reactions and, therefore, patients should be counselled appropriately regarding this risk.

Additionally, the authors noted "separate lesions" at a "non-tested site" on the upper left back, distant to their patch test application site, which developed at around 24 hours post patch testing to ranitidine. Following careful examination of Figures 1A and 1B in the article and comparing these to the patch test result shown in Figure 3 of our report,² we can confirm that this unequivocally represents a flare-up of the original positive drug patch test reactions, which were elicited more than 3 years ago. From top to bottom, the old patch test sites reactivated correspond to ranitidine 30% pet., ranitidine undiluted solution, and cimetidine 30% pet. This is a very rare occurrence, one that in the context of drug patch testing has not been highlighted nor demonstrated in the literature previously, to our knowledge. This "flare-up phenomenon" of old patch test sites has been previously observed in cases of nickel allergy, the notable difference being that contact or systemic nickel exposure was the elicitor and not repeat patch testing.^{4,5} The pathogenesis of these flare-up reactions has been proposed to be due to reactivation of specific resident cutaneous memory T cells,⁶ in a similar mechanism that is noted in fixed drug eruptions.⁷ We hope this novel observation contributes further our understanding of Type IV drug hypersensitivity pathomechanisms and the utility of drug patch testing.

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AUTHOR CONTRIBUTIONS

Timothy Watts: Conceptualization; writing-original draft; writing-review & editing. **Rubaiyat Haque:** Writing-review & editing.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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