

## Darier's sign: A model for studying dermographism

Sir,

We read with interest, the article by Surjushe *et al.*<sup>[1]</sup> reviewing the clinical conditions that are associated with Darier's sign, *i.e.*, a type of dermographism confined to

lesional skin in the absence of generalized dermatographism. Taking advantage of this occasion 100 years after Darier's initial description, it is interesting to highlight the possibility that some common pathophysiological mechanisms must underlie the elicitation of dermatographism and this relatively common clinical sign. Due to the urtication of previously "normal" skin upon mechanical friction characterizing dermatographism, the potential of Darier's sign as a model for better understanding of the clinically more significant dermatographism can be advocated.

Physical (mechanical) mast cell activation seems to be the crucial event in the pathophysiological cascade leading to both conditions, *i.e.*, positive Darier's sign and dermatographism. However, increased histamine release in susceptible skin does not always rely on increased numbers of mast cells.<sup>[2]</sup> The exact mechanism of mechanical degranulation of tissue mast cells is still obscure. Possible mechanisms that can explain how friction forces (such as those used to elicit Darier's sign) may lead to mast cell degranulation include:

- (a) Minor tissue traumatization, probably mediated by local complement or plasminogen activation.
- (b) Irritation of neuronal structures of the skin resulting in degranulation of adjacent/connected/dependent mast cells. Mechanical nerve stimulation may result either "specifically" via 'professional mechanoreceptor' activation or "nonspecifically," *e.g.*, via local activation of nociceptive nerve endings. It can be further speculated that abnormal neuronal stimulation may result from pathological function of mechanoreceptors directly on nerve endings or indirectly on other interconnected cells, including epidermal keratinocytes. Alternatively, local pathologic neuronal-mast cell connections may mediate mast cell degranulation and confined urtication.
- (c) Finally, mechanical forces via tissue deformation may directly induce mast cells degranulation, probably via mechanoreceptors located on the mast cells themselves. In different species, mechano-sensitive ion channels seem to play a central role in the physiology of a wide spectrum of mammalian cell types, including mast cells.<sup>[3-5]</sup> According to this assumption, Darier's sign might reflect abnormal mechanosensitivity of mast cells within certain skin lesions. In analogy, constitutional generalized vulnerability of skin mast cells could underlie dermatographism in some individuals.

In conclusion, we propose that comparative studies of skin

lesions characterized by either positive or negative Darier's sign with respect to the physiology of the contained mast cells, could not only contribute to the delineation of the pathomechanism of this peculiar clinical sign, but they may also serve as a vehicle to better understand dermatographism.

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## REFERENCES

1. Surjushe A, Jindal S, Gote P, Saple DG. Darier's sign. *Indian J Dermatol Venereol Leprol* 2007;73:363-4.
2. Smith CH, Kepley C, Schwartz LB, Lee TH. Mast cell number and phenotype in chronic idiopathic urticaria. *J Allergy Clin Immunol* 1995;96:360-4.
3. Kung C. A possible unifying principle for mechanosensation. *Nature* 2005;436:647-54.
4. Stokes AJ, Shimoda L, Koblan-Huberson M, Adra C, Turner H. A TRPV2-PKA signalling module for transduction of physical stimuli in mast cells. *J Exp Med* 2007;6:137-47.
5. Bradding P, Okayama Y, Kambe N, Saito H. Ion channel gene expression in human lung, skin, and cord blood-derived mast cells. *J Leukoc Biol* 2003;73:614-20.