

Conflicts of interest

None to declared.

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References

- 1 Carr DF, Wang CW, Bellón T et al. Serum and blister-fluid elevation and decreased epidermal content of high-mobility group box 1 protein in drug-induced Stevens-Johnson syndrome/toxic epidermal necrolysis. *Br J Dermatol* 2019; **181**:166–74.
- 2 Olteanu C, Shear NH, Chew HF et al. Severe Physical complications among survivors of Stevens-Johnson syndrome and toxic epidermal necrolysis. *Drug Saf* 2018; **41**:277–84.
- 3 Dodiuk-Gad RP, Olteanu C, Feinstein A et al. Major psychological complications and decreased health-related quality of life among survivors of Stevens-Johnson syndrome and toxic epidermal necrolysis. *Br J Dermatol* 2016; **175**:422–4.
- 4 Sekula P, Dunant A, Mockenhaupt M et al. Comprehensive survival analysis of a cohort of patients with Stevens-Johnson syndrome and toxic epidermal necrolysis. *J Invest Dermatol* 2013; **133**:1197–204.
- 5 Chen CB, Abe R, Pan RY et al. An updated review of the molecular mechanisms in drug hypersensitivity. *J Immunol Res* 2018; **2018**:6431694.
- 6 Chung WH, Hung SI, Yang JY et al. Granulysin is a key mediator for disseminated keratinocyte death in Stevens-Johnson syndrome and toxic epidermal necrolysis. *Nat Med* 2008; **14**:1343–50.
- 7 Fujita Y, Yoshioka N, Abe R et al. Rapid immunochromatographic test for serum granulysin is useful for the prediction of Stevens-Johnson syndrome and toxic epidermal necrolysis. *J Am Acad Dermatol* 2011; **65**:65–8.
- 8 Nakajima S, Watanabe H, Tohyama M et al. High-mobility group box 1 protein (HMGB1) as a novel diagnostic tool for toxic epidermal necrolysis and Stevens-Johnson syndrome. *Arch Dermatol* 2011; **147**:1110–2.
- 9 Scaffidi P, Misteli T, Bianchi ME. Release of chromatin protein HMGB1 by necrotic cells triggers inflammation. *Nature* 2002; **418**:191–5.
- 10 White KD, Abe R, Arderm-Jones M et al. SJS/TEN 2017: building multidisciplinary networks to drive science and translation. *J Allergy Clin Immunol Pract* 2018; **6**:38–69.

Supporting Information

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Anatomical location differences in sodium lauryl sulfate-induced irritation

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Linked Article: Leskur et al. *Br J Dermatol* 2019; **181**:175–185.

Sodium lauryl sulfate [SLS; synonym: sodium dodecyl sulfate (SDS) or C₁₂H₂₅NaO₄S] is a surfactant that is used in many household and hygiene products. It has an irritating effect on skin and is therefore used extensively in models for testing the response of skin to irritants. Already in 1997 the European guideline on SLS exposure testing stated that 'skin penetration of SLS is expected to show a significant inter-individual and anatomical site variation'. Furthermore, the flexor side forearm skin (with cubital fossa and the wrist excluded) was recommended as a preferred study site.¹ Hereafter, several studies that involved SLS testing have nonetheless used the back as the anatomical test location, probably mostly because of its larger area.^{2–4} This prompted studies that aimed to prospectively assess whether there indeed was a difference in response to irritation between anatomical locations. These studies showed conflicting results,^{5–8} although the study by Lavrijsen et al., which showed no difference, probably had an insufficient sample size.⁶

In this issue of the *BJD*, Leskur et al. present a randomized controlled trial in which they aimed to investigate the response of two anatomical locations, the volar forearm and the upper back (subscapular area), to SLS-induced irritation *in vivo* using a one-time occlusive test.⁹ They set the number of participants at 25 to increase statistical power compared with earlier studies. The irritation was induced to provoke an acute reaction in healthy individuals and was compared with sham irritation using distilled water.¹ Concomitantly, the effect of an emollient cream on recovery of the irritation was tested.

The study shows that the upper back is more susceptible than the volar forearm to irritation by SLS, as measured by transepidermal water loss (TEWL), erythema and dryness. Furthermore, recovery from irritation also seems dependent on anatomical location, with the upper back recovering faster than the volar forearm (adjusted for the initial difference in irritation), confirming what was most often found in previous studies.^{5,7,8} Baseline pre-irritation TEWL values were comparable between the forearm and upper back. These values were clearly not suitable predictors for the varying skin response, which implies that there must be factors other than the barrier function of the stratum corneum that contribute to the difference in response to irritation between anatomical locations. This leads the authors to speculate that response to treatment may also be anatomical site-specific, owing to structural skin differences at various body locations.

The emollient tested by Leskur et al. was given post-irritation to assess its effect on recovery.⁹ No effect on skin irritation was seen when compared with sham-irritated skin. Possibly, the reaction that was invoked using the one-time occlusive test was too strong for treatment with an emollient only.¹⁰ Also, the possible beneficial effect of pretreatment (application of treatment before initiating the irritation) or application using a repeated exposure model (mimicking normal use of an emollient) was not assessed. In previous years, multiple topical formulations have been tested with SLS models, but anatomical location, method of SLS exposure (one-time occlusion, repeated occlusion, open test, immersion test) and/or SLS concentration often differ. The study by Leskur et al. reinforces the notion that different anatomical locations respond differently to irritation using SLS. To improve comparability between studies, it is essential that researchers report anatomical test-site location and carefully consider existing guidelines for standardization in studies that involve SLS testing.

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None to declare.

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References

- 1 Tupker RA, Willis C, Berardesca E et al. Guidelines on sodium lauryl sulfate (SLS) exposure tests. A report from the Standardization Group of the European Society of Contact Dermatitis. *Contact Dermatitis* 1997; **37**:53–69.
- 2 Fluhr JW, Kuss O, Diepgen T et al. Testing for irritation with a multifactorial approach: comparison of eight non-invasive measuring techniques on five different irritation types. *Br J Dermatol* 2001; **145**:696–703.
- 3 Slotosch CM, Kampf G, Löffler H. Effects of disinfectants and detergents on skin irritation. *Contact Dermatitis* 2007; **57**:235–41.
- 4 Mehling A, Chkarnat C, Degwert J et al. Interlaboratory studies with a proposed patch test design to evaluate the irritation potential of surfactants. *Contact Dermatitis* 2010; **62**:157–64.
- 5 Cua AB, Wilhelm KP, Maibach HI. Cutaneous sodium lauryl sulphate irritation potential: age and regional variability. *Br J Dermatol* 1990; **123**:607–13.
- 6 Lavrijsen AP, Geelen FA, Oestmann E et al. Comparison of human back versus arm skin region for its suitability to test weak irritants. *Skin Res Technol* 1996; **2**:70–7.

- 7 Fartasch M, Schnetz E, Diepgen TL. Characterization of detergent-induced barrier alterations – effect of barrier cream on irritation. *J Invest Dermatol Symp Proc* 1998; **3**:121–7.
- 8 Zhai H, Fautz R, Fuchs A et al. Human scalp irritation compared to that of the arm and back. *Contact Dermatitis* 2004; **51**:196–200.
- 9 Leskur D, Bukić J, Petrić A et al. Anatomical site differences of sodium lauryl sulphate-induced irritation: randomized controlled trial. *Br J Dermatol* 2019; **181**:175–85.
- 10 Jungersted J, Høgh J, Hellegren L et al. Effects of topical corticosteroid and tacrolimus on ceramides and irritancy to sodium lauryl sulphate in healthy skin. *Acta Derm Venereol* 2011; **91**:290–4.

Supporting Information

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Talimogene laherparepvec monotherapy, an elegant alternative to systemic immunotherapy for the treatment of early metastatic melanoma

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In-transit metastases in stage III melanoma are usually treated with (repeated) surgery and other locoregional treatments. Talimogene laherparepvec (T-VEC) is a modified herpes simplex virus type 1 and is given to patients with stage IIIb–IVM1a melanoma with injectable cutaneous, subcutaneous or lymph node metastases.¹ This oncolytic virus stimulates viral pathogenicity, enhances tumour-selective replication, and reduces virally mediated suppression of antigen presentation and thus induces tumour-specific T-cell responses.^{2–4} The first real-world data of T-VEC monotherapy is promising, with reported response rates varying from 56.5% up to 82.6%.^{5,6}

A very elegant characteristic of T-VEC monotherapy is its relatively mild side-effects. Patients often experience only self-limiting flu-like symptoms such as fever, decreased appetite, fatigue and local inconveniences such as itch, injection site pain or erythema. This makes T-VEC monotherapy a considerably less toxic alternative to systemic immunotherapies. For this reason, it can be considered also for frail and elderly patients. Currently, the potential synergetic effect of T-VEC in combination with immunotherapy is being investigated, studying pembrolizumab with T-VEC vs. pembrolizumab with placebo.⁷

This issue of the *BJD* includes an important case report describing an 58-year-old organ transplant recipient who was diagnosed with stage III melanoma with local progression of his metastases after topical treatment with imiquimod and cryotherapy.⁸ Organ transplant recipients are often not considered