

Clinical morphology of sodium lauryl sulfate (SLS) and nonanoic acid (NAA) irritant patch test reactions at 48 h and 96 h in 152 subjects

LOUISE REICHE¹, CAROLYN WILLIS¹, JOHN WILKINSON¹, STEPHANIE SHAW¹ AND O. DE LACHARRIÈRE²

¹Dermatology Department, Amersham General Hospital, Amersham, Bucks HP7 0JD, UK

²L'Oreal Applied Research Laboratories, Centre Eugene Schueller, Clichy, France

In this study of 152 women, comparison of patch test responses between 2 irritants over 96 h at 2 symmetrical anatomical sites is studied. 2 irritants, each at 4 different concentrations (nonanoic acid (NAA) 80%, 40%, 20%, 10%; sodium lauryl sulfate (SLS) 3%, 2%, 1% and 0.5%) and using propan-1-ol and 'water for injection' as the respective controls, were placed as 15 µl aliquots, soaked onto filter paper discs in Finn Chambers, on the volunteer's left and right lower back. The patches were removed at 47, and read at 48 and 96 h. Irritant reactions were evaluated for erythema and surface changes by degree and area affected. Statistical analysis of the results showed that erythema decreased with time for all concentrations of NAA, and at higher concentrations for SLS. Surface changes increased with time for SLS and at higher concentrations of NAA. There was no statistically significant difference comparing left and right sides. Traditionally in patch testing, reactions which fade after 48 h have been regarded as irritant rather than allergic. This study refutes that assumption. Data from our left to right comparisons, made in the same individuals at the same time, show that irritant reactions may be more reproducible than previously appreciated.

Key words: anatomical symmetry; erythema; hand dominance; irritant reproducibility; surface changes; sodium lauryl sulfate; nonanoic acid; patch test. © Munksgaard, 1998.

Accepted for publication 10 June 1998

Irritant responses are known to vary with different irritants (1), dose and concentration (2), exposure frequency (3), season (4), phase of the menstrual cycle (5), anatomical site (6) and atopic status (7, 8). To minimise environmental, disease and individual variability, in this study, each volunteer acted as their own control, by duplicating the test

irritants at symmetrical anatomical sites. Treffel et al. (9) found increased (baseline) transepidermal water loss on the dominant compared with the non-dominant forearm. We wondered if there would be a difference in clinical response to irritants over a 96 h period, when comparing left and right lower back.

Table 1. Scoring of irritant reaction erythema and surface changes

Erythema		Surface change	
nil	0	nil	0
doubtful	0.5	dry	1
very mild erythema	1	dryness and wrinkling	2
mild erythema	2	dryness and fissuring	3
moderate erythema	3	fissuring with cracks, splits, sores	4
severe erythema	4	bullous reactions	5
erythema with oedema	5	severe bullous/necrotic reactions	6
erythema with necrosis/bullae	6		
Size of reaction			
less than size of patch	1		
same as size of patch	2		
greater than size of patch	3		

Materials and Methods

152 female volunteers, all over 18 years of age, were assessed between January and April 1994. Exclusion criteria included pregnant women and those taking vasodilatory medication, i.e., calcium channel blockers, β blockers, nitrates; systemic corticosteroids, systemic retinoids or were using topical anti-inflammatory, anti-acne or retinoic acid preparations. Local ethical committee approval was granted for the study, and each volunteer provided fully informed, written consent.

2 irritants, sodium lauryl sulfate (SLS) and nonanoic acid (NAA), each at 4 concentrations, were placed in 8-mm Finn Chambers on the volunteer's lower back. 15 μ l of each solution were soaked onto filter paper discs. 4 concentrations of NAA: 80%, 40%, 20% and 10%, and using propan-1-ol as vehicle control, were placed in descending

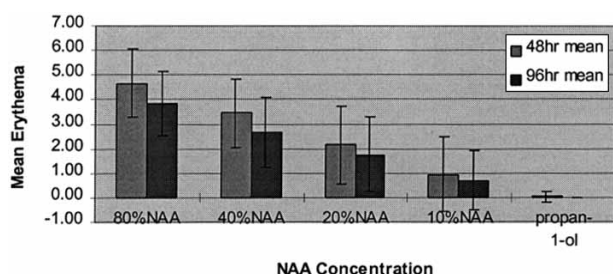


Fig. 1. Nonanoic acid (NAA) mean erythema at 48 h and 96 h, left back.

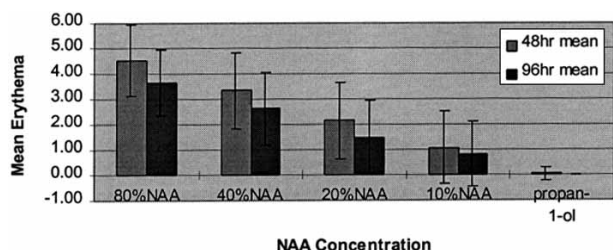


Fig. 2. Nonanoic acid (NAA) mean erythema at 48 h and 96 h, right back.

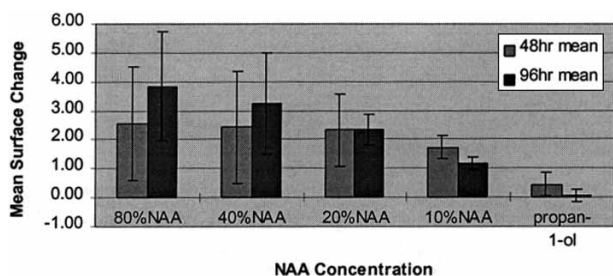


Fig. 3. Nonanoic acid (NAA) mean surface changes at 48 h and 96 h, left back.

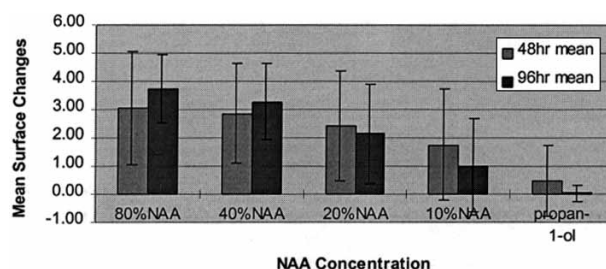


Fig. 4. Nonanoic acid (NAA) surface changes at 48 h and 96 h, right back.

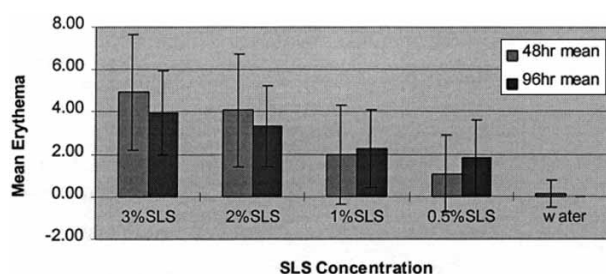


Fig. 5. Sodium lauryl sulfate (SLS) mean erythema at 48 h and 96 h, left back.

order just lateral to the spine inferiorly. 4 concentrations of SLS: 3%, 2%, 1% and 0.5%, and using 'water for injection' as a control, were placed laterally to NAA in descending order. The patches were removed at 47 h and read at 48 and 96 h. Irritant reactions were evaluated for erythema and surface changes as shown in Table 1.

The degree of erythema or surface change and the respective associated area involved were summated for each irritant reaction, thus the range for any value was 0–9. These were then averaged and a standard deviation calculated for each concentration, using Microsoft Excel 5.0. Nonparametric analysis was performed using the Mann Whitney U test (MW) on Minitab version 10.2.

Results

152 women were studied. The average age was 44 ± 15.7 years (range 18–83 years). 37 of these were atopic, as defined by ≥ 1 positive Type I allergy (prick) tests (using house dust mite, birch, beech, grass, cat, and dog allergens). On both left and right lower backs, NAA induced greater erythema at 48 h than 96 h ($p < 0.0001$ MW for every concentration except 20% NAA for the left back where $p = 0.0161$) as displayed in Fig. 1, 2. Surface changes from NAA were statistically significantly greater at 96 h than 48 h with 80% ($p < 0.0001$, MW) and 40% NAA ($p = 0.0015$, MW) for the left back and at 80% NAA ($p = 0.0043$, MW) for the

right back, and greater at 48 h than 96 h with 10% NAA ($p=0.008$ MW, left back and $p=0.0004$ MW, for the right back), as shown in Figs. 3 and 4. With 3% SLS, the erythema was greater at 48 h than at 96 h ($p<0.0001$, MW left and right backs), whereas at 0.5% SLS the converse was true, ($p=0.0001$ MW, left and right backs) as displayed in Fig. 5, 6. Surface changes induced by 3%, 2% and 1% SLS were greater at 96 than 48 hours ($p<0.05$ for left and right backs). Clinically, the irritant reactions showed reduced severity of reaction with decreasing concentration of irritant and symmetry of response (Figs. 7, 8).

Comparing the mean values on the left and right backs for SLS and NAA erythema and surface changes, there were no statistically significant differences, with the exception of the surface changes seen with 80% NAA at 48 h ($p=0.04$ MW). The data was re-analysed comparing the dominant (as

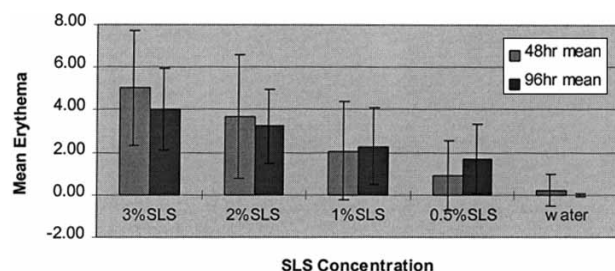


Fig. 6. Sodium lauryl sulfate (SLS) mean erythema at 48 h and 96 h, right back.

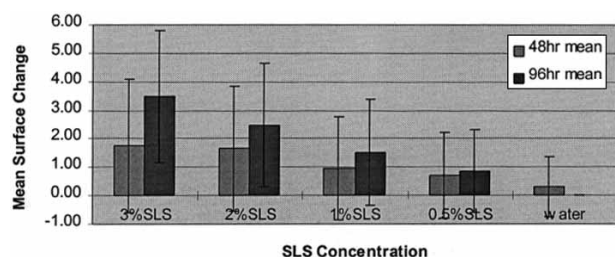


Fig. 7. Sodium lauryl sulfate (SLS) mean surface changes at 48 h and 96 h, left back.

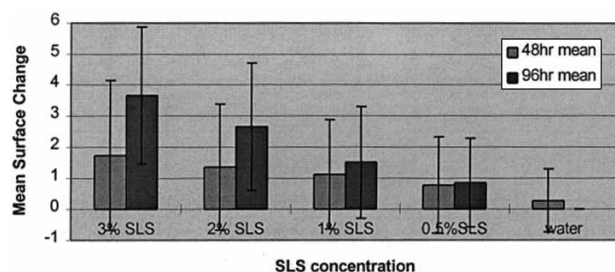


Fig. 8. Sodium lauryl sulfate (SLS) mean surface changes at 48 h and 96 h, right back.

Table 2. ICDRG scale of recording patch (allergic) test reactions (10)

?+	doubtful reaction; faint erythema only
+	weak positive reaction; erythema, infiltration, possibly papules
++	strong positive reaction; erythema, infiltration, papules, vesicles
+++	extreme positive reaction; intense erythema and infiltration and coalescing vesicles
IR	Irritant reaction of different types

determined by hand dominance) and non-dominant sides, and again there was no statistically significant difference for either irritant at any concentration.

Discussion

The International Contact Dermatitis Research Group (ICDRG) (10) have defined a simple method of evaluating erythema (Table 2) but there is no such standard for the surface changes that we all observe in patch testing. Reaction sites with equivalent degrees of erythema but with different areas of involvement (i.e., part of the chamber size versus the whole chamber size), with or without concomitant surface change (wrinkling, scaling, fissures, etc.) cannot be considered equivalent. Determining a rank order of severity of surface changes is difficult, but may be easier in the future when we gain more comparative clinicohistopathological and electronmicroscopic data. In the meantime, the grading system employed in this study attempts to quantify some common surface changes. For both erythema and surface change, both the degree and area affected by these were graded.

There is a dogma that erythematous changes that persist in patch testing support an interpretation of an allergic reaction in preference to an irritant change, which is more likely to show erythema at 48 h and fading rapidly thereafter. This study showed that NAA and SLS provoke different irritant effects when compared at 48 and 96 h for both erythema and surface change, at the concentrations used herein, and that both induce *persistent erythema*. An apparent crossover phenomenon was demonstrated with these irritants, at the middle concentrations, of greater erythema or surface change at 48 h versus 96 h. NAA induces greater surface changes at 96 h with concentrations of 80% and 40% and greater surface change at 48 h at a concentration of 10%. SLS induces greater erythema at 48 h at concentrations of 3% and 2% but greater erythema at 96 h with 0.5%.

One could postulate that mild irritant damage induces a smaller quantity or different collection of

cytokine release, inducing delayed enhanced blood flow, altered epidermal lipid metabolism and accelerated cell turnover (accounting for altered surface change), whereas higher irritant concentration deals a more toxic insult, inducing greater and quicker changes. Irritant reactions suffer under a prejudice of been transient and non-reproducible, but this study shows that irritant-induced erythema and surface changes not only persist, but are symmetrically reproducible.

Acknowledgement

We thank the following other participating personnel: Maria Nicholson, Sally Barth, Alison Wylie and Denise Cockrean who provided technical and secretarial support. Funding for this study was provided by The Erasmus Wilson Dermatological Research Fund, and L'Oreal Laboratoires de Recherche Avancée, Paris.

References

1. Agner T, Serup J. Skin reactions to irritants assessed by non-invasive bioengineering methods. *Contact Dermatitis* 1989; 20: 352–359.
2. Bruynzeel D P, Van Ketel W G, Scheper R J, Von Blomberg-van der Flier B M E. Delayed time course of irritation by sodium lauryl sulphate: observations on threshold reactions. *Contact Dermatitis* 1982; 8: 236–239.
3. Widmer J, Elsner P, Burg G. Skin irritant reactivity following experimental cumulative irritant contact dermatitis. *Contact Dermatitis* 1994; 30: 35–39.
4. Agner T, Serup J. Seasonal variation of skin resistance to irritants. *Br J Dermatol* 1989; 121: 323–328.
5. Agner T, Damm P, Skouby S. Menstrual cycle and skin reactivity. *J Am Acad Dermatol* 1991; 24: 566–570.
6. Cua A, Wilhelm K, Maibach H. Cutaneous sodium lauryl sulphate irritation potential: age and regional variability. *Br J Dermatol* 1990; 123: 607–613.
7. Nassif A, Chan S, Storrs F, Hanifin J M. Abnormal skin irritancy in atopic dermatitis and in atopy without dermatitis. *Arch Derm* 1994; 130: 1402–1407.
8. Agner T. Susceptibility to atopic dermatitis patients to irritant dermatitis caused by sodium lauryl sulphate. *Acta Dermato-venereologica* 1991; 71: 296–300.
9. Treffel P, Panisset F, Faivre B, Agache P. Hydration, trans-epidermal water loss, pH and skin surface parameters: correlation and variations between dominant and non-dominant forearms. *Br J Dermatol* 1994; 130: 325–28.
10. Fregert S. *Manual of contact dermatitis* 2nd edition. Copenhagen: Munksgaard 1981.

Address:

L. Reiche
City Health Doctors
22 Victoria Ave.
Palmerston North
New Zealand