

Acute irritant contact dermatitis: recovery time in man

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Our understanding of the details of the recovery time of acute irritant contact dermatitis (ICD) is limited. We examined skin reactivity to a model surfactant, sodium lauryl sulfate (SLS), on previous acute ICD and normal sites over time with visual grading and noninvasive instruments. Acute ICD was induced on the upper arms of 18 volunteers (aged 30 to 51 years) by occluded application of 1% SLS for 24 h. Previous ICD and normal sites were provoked by occluded application of 2% or 7.5% SLS 30 min daily 4 consecutive days. Skin reactivity was assessed daily by visual erythema scoring (VES), transepidermal water loss (TEWL), skin color reflectance (SCR) and electrical capacitance (EC). Skin function of previous ICD sites assessed by VES, TEWL, SCR, and EC did not normalize until 2 weeks later; all parameters of previous ICD returned to normal after 3 weeks. While skin reactivity to 2% and 7.5% SLS showed no differences between previous ICD and normal sites at 4 weeks, differences of irritant reactivity especially 7.5% SLS between previous ICD and normal sites were significant at 3 weeks post-provocation. Our results demonstrate that irritation evaluated with irritant provocation was long-lasting, even though skin functional parameters assessed by various bioengineering instruments returned to normal. Complete recovery of skin function including irritability after acute ICD induced by 1% SLS was achieved approximately 4 weeks later. The data were generated with a model surfactant; it remains to be determined whether similar responses will be noted with chemicals of different physicochemical properties.

Key words: recovery time; acute irritant contact dermatitis; sodium lauryl sulfate; surfactants; bioengineering methods; transepidermal water loss; colorimetry; capacitance. © Munksgaard, 1997.

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One difficult judgment in the management of irritant contact dermatitis (ICD) in clinical practice is determining the recovery time needed for complete healing, so as to set dates for return to work or other chemical exposure. Complete healing means functional normality including a loss of irritability, as well as clinically normal skin and normal quantitative parameters measured by bioengineering instruments. Augmented reaction to reapplication of irritant may occur on subclinically irritated skin (1) and previous ICD sites (2), even though the skin appears normal clinically and functionally as measured by bioengineering instruments. This study defines the recovery time of augmented reactivity to a model irritant with an irritant provocation method.

Materials and Methods

Subjects

18 healthy volunteers, 6 male and 12 female, between 30 and 51 years (mean $\pm$ SD; 43.2 ± 6.6), skin

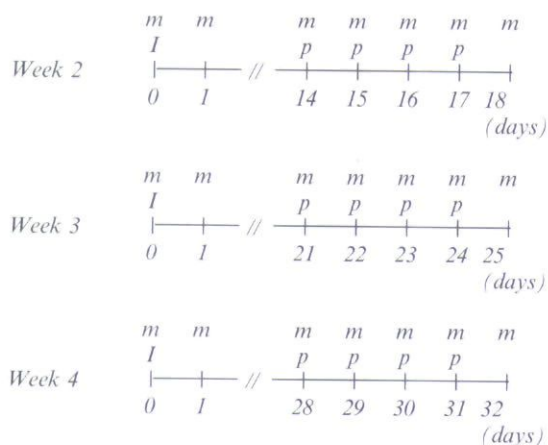
type II to IV, participated after giving written informed consent. We divided the 18 volunteers into 3 groups according to the provocation time schedule: 2, 3 and 4 weeks.

Materials

Sodium lauryl sulfate (99% purity, SLS; Sigma Chemical Co., St. Louis, MO, USA) was dissolved in deionized water at 1%, 2%, and 7.5% concentrations. Deionized water was used as the vehicle control. Polypropylene chambers with 20-mm diameter (Hill Top Lab., Cincinnati, OH, USA) were used. The chambers were fixed with nonocclusive paper tape (Scanpor; Norgeplaster A/S, Oslo, Norway).

Methods

Induction of acute ICD. Acute ICD was induced at 3 sites on the mid-volar surface of both upper arms



m: measurement of TEWL, VS, SCR and EC. I: induction with 1% SLS. p: provocation with 2% or 7.5% SLS or vehicle.

Fig. 1. Study protocol.

by occluded application of 200 μ l of 1% SLS for 24 h. The other 3 sites were non-treated control sites and another site was a normal control. All sites including 3 ICD induction sites were rotated to minimize anatomic variability.

Provocation. 200 μ l of 2%, 7.5% SLS and vehicle were applied to 3 previous SLS-treated sites and 3 non-treated control sites 30 min daily of 4 consecutive days, so as to permit comparison of 3 pairs of provocation sites: previously treated+2% SLS (A1) versus non-treated +2% SLS (β 1), previously treated +7.5% SLS (A2) versus non-treated +7.5% SLS (B2), and previously treated+vehicle (A3) versus non-treated+vehicle (B3). The other 1 site was a normal control (non-treated+non-provocation (C)).

Measurements

Visual erythema scoring (VES). Visual erythema scoring utilized the following scale: 0, no erythema; 0.5, equivocal; 1, slight redness, either spotty or diffuse; 2, moderate uniform redness; 3, intense erythema; 4, fiery red with edema.

Transepidermal water loss (TEWL). TEWL was measured with an evaporimeter (Evaporimeter EP1; Servomed, Vallingby, Sweden). TEWL measurement followed the recommendations of Pinnagoda et al. (3). The values are expressed as $\text{g/m}^2/\text{h}$.

Capacitance. Capacitance was measured in duplicate with a capacitance meter (Corneometer CM 820 PC, Courage & Khazaka, Cologne, Germany) and expressed digitally in arbitrary units (au). Details are provided by Blichman and Serup (4).

Skin color reflectance. Erythema was quantified by skin color reflectance measurements with a tri-

stimulus colorimeter (CR 200, Minolta, Osaka, Japan). The measuring principle has been described in detail elsewhere (5). Basically, in the $L^*a^*b^*$ mode, a^* represents the color spectrum from total green (-100) to pure red ($+100$). Factor a^* correlated with erythema values. All parameters were measured 7 $\times$, before induction, 24 $\frac{1}{2}$ h after induction, and every week day of the provocation week, from Monday to Friday (Fig. 1). We measured all parameters at room temperature (18°C – 23°C) and 50–60% relative humidity. Volunteers rested at least 20 min before measurements.

Statistical evaluation

Differences in each parameter between pre-treated sites (A1, A2, A3), un-treated sites (B1, B2, B3) and control site (NC) were tested for their statistical significance using the Duncan multiple range test (significance level; 5%).

Results

TEWL

TEWL of pre-treated sites (A1, A2, A3), highly abnormal for 2 weeks, returned to normal 3 to 4 weeks later (Fig. 2). Daily 30-min application of 2% SLS increased values of TEWL gradually in both pre-treated sites (A1) and non-treated sites (B1) during provocation. There were no increases in TEWL values in vehicle application sites (A3, B3) and control sites (NC). Application of 7.5% SLS routinely increased TEWL values more than the TEWL values of application sites with 2% SLS in all 3 groups (Fig. 2).

TEWL of pre-treated sites (A2) in the 3-week group was statistically higher than TEWL of non-treated sites (B2) at days 2, 3, and 5 after provocation with 7.5% SLS (Fig. 2b). No differences were noted between TEWL values of pre-treated (A1, A2) and non-treated sites (B1, B2) even after provocation in the 4-week group (Fig. 2c).

Capacitance

Capacitance value (CV) of pre-treated sites (A1) was lower than CV of non-treated sites (B1) at 2 weeks (Fig. 3a). Following daily application of 2% and 7.5% SLS, CV of pre-treated (A1, A2) and non-treated sites (B1, B2) tended to decrease first and normalize later in all 3 groups (Fig. 3); there was a statistical difference at day 4 after provocation between pre-treated (A2) and non-treated sites (B2) in the 3-week group (Fig. 3b), otherwise no difference between sites of each group.

Transepidermal Water Loss

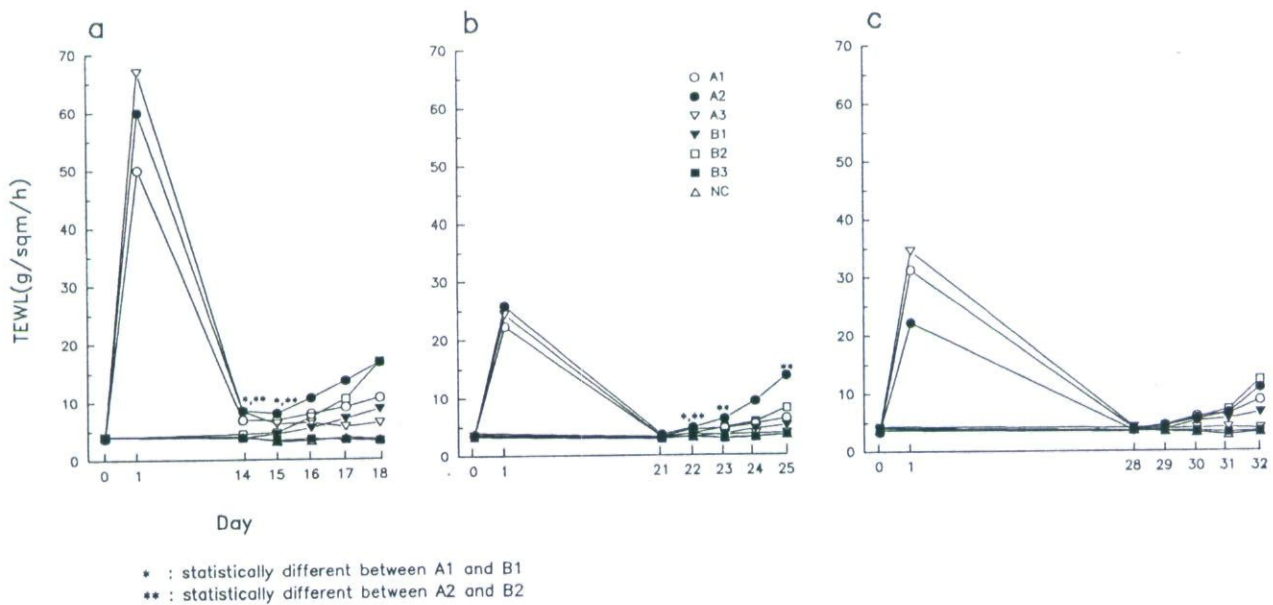


Fig. 2. Mean transepidermal water loss (TEWL) of pre-treated (A1, A2, A3), non-treated (B1, B2, B3) and control site (NC) before and after application of 2% (A1, B1) or 7.5% (A2, B2) sodium lauryl sulfate (SLS) or vehicle (A3, B3) for 4 consecutive days 2 weeks (a), 3 weeks (b) and 4 weeks (c) post-induction (A1: treated +2% SLS, A2: treated +7.5% SLS, A3: treated +vehicle, B1: non-treated +2% SLS, B2: non-treated +7.5% SLS, B3: non-treated +vehicle, NC: non-treated+non-treated).

Stratum Corneum Hydration

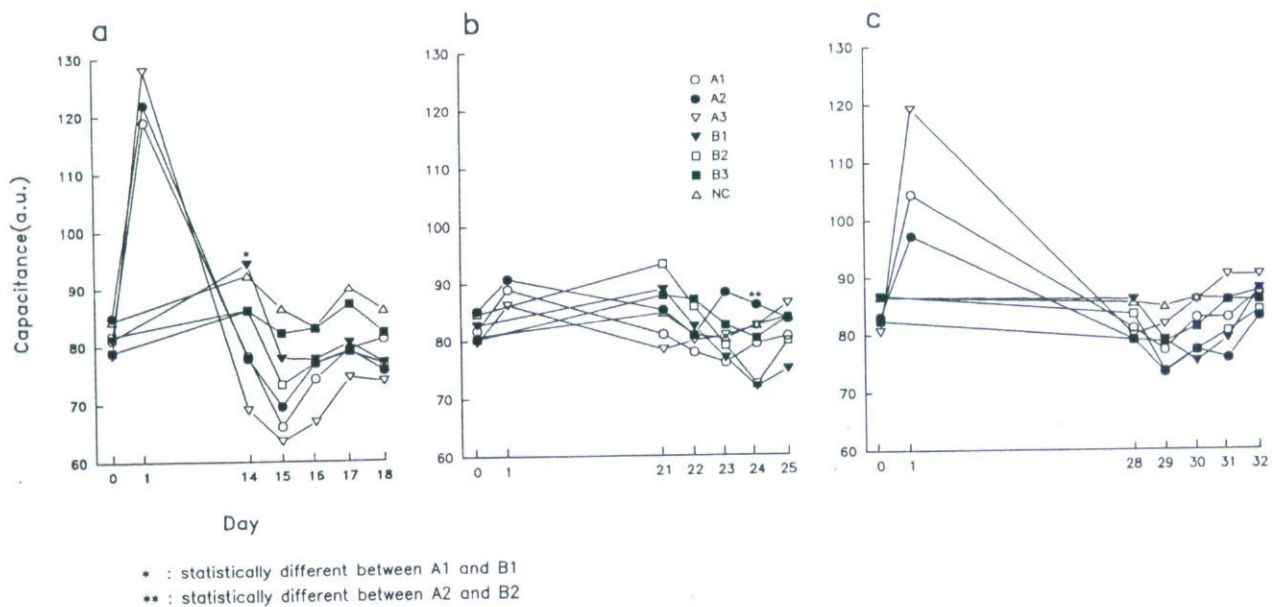


Fig. 3. Mean electrical capacitance of pre-treated (A1, A2, A3), non-treated (B1, B2, B3) and control site (NC) before and after application of 2% (A1, B1) or 7.5% (A2, B2) sodium lauryl sulfate (SLS) or vehicle (A3, B3) for 4 consecutive days 2 weeks (a), 3 weeks (b) and 4 weeks (c) post-induction (A1: treated +2% SLS, A2: treated +7.5% SLS, A3: treated +vehicle, B1: non-treated +2% SLS, B2: non-treated +7.5% SLS, B3: non-treated +vehicle, NC: non-treated+non-treated).

Skin color reflectance

Erythema increased nearly twice, 1 day after the 24-h patch of 1% SLS in all 3 groups. Although erythema did not resolve 2 weeks after ICD, erythema was fully resolved 3 and 4 weeks later (Fig. 4). Erythema tended to increase gradually after 2% and 7.5% SLS provocation, but erythema at vehicle application and normal control sites was not changed. Provocation of 7.5% SLS made a difference between erythema values of pre-treated and non-treated sites on days 4 and 5 in the 3 week group, statistically (Fig. 4b). Otherwise no difference in erythema between pre-treated and non-treated sites was shown with 2% SLS provocation at 3 weeks post-induction. There were no differences in erythema between pre-treated and non-treated sites after 2% and 7.5% SLS provocation at 4 weeks post-induction (Fig. 4c).

Visual erythema scoring

Mean visual erythema scores (VES) of induction sites increased to 1.5–3.0 1 day after application of 1% SLS in all 3 groups. VES were normalized 3 and 4 weeks after induction but were still higher than normal at 2 weeks after induction (Fig. 5). VES of normal control and vehicle provo-

cation sites (A3, B3) was not changed. VES findings were similar to findings measured with the chromameter: VES of pre-treated sites (A1, A2) were significantly higher than that of non-treated sites (B1, B2) before and after provocation of both 2% and 7.5% SLS in the 2-week group (Fig. 5a). Although there were different VES between pre-treated (A2) and non-treated sites (B2) after 7.5% SLS provocation, no differences were noted between pre-treated (A1) and non-treated sites (B1) after 2% SLS provocation statistically at 3 weeks (Fig. 5b). No significant VES changes were induced by both of 2% and 7.5% SLS provocation in pre-treated and non-treated sites at 4 weeks (Fig. 5c).

Discussion

Our study shows that acute irritant contact dermatitis induced by 24-h occlusion of 1% sodium lauryl sulfate did not return toward normal clinically and functionally as evaluated by TEWL, capacitance and chromameter until 2 weeks after induction, but normalized 3 and 4 weeks later. These findings agree with studies by Wilhelm et al. (6) which showed TEWL and capacitance returned to baseline 14 days and 17 days after induction, respectively, erythema not being completely resolved

Skin Color Reflectance

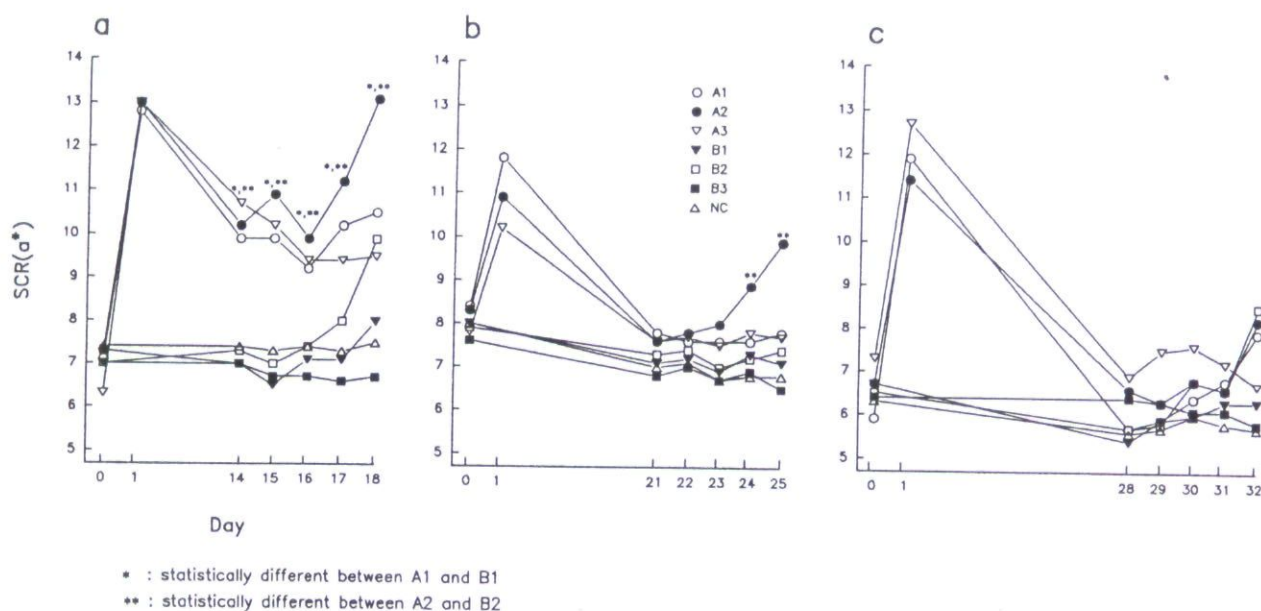


Fig. 4. Erythema measured by skin color reflectance of pre-treated (A1, A2, A3), non-treated (B1, B2, B3) and control site (NC) before and after application of 2% (A1, B1) or 7.5% (A2, B2) sodium lauryl sulfate (SLS) or vehicle (A3, B3) for 4 consecutive days 2 weeks (a), 3 weeks (b) and 4 weeks (c) post-induction (A1: treated +2% SLS, A2: treated +7.5% SLS, A3: treated +vehicle, B1: non-treated +2% SLS, B2: non-treated +7.5% SLS, B3: non-treated +vehicle, NC: non-treated+non-treated).

Visual Erythema Score

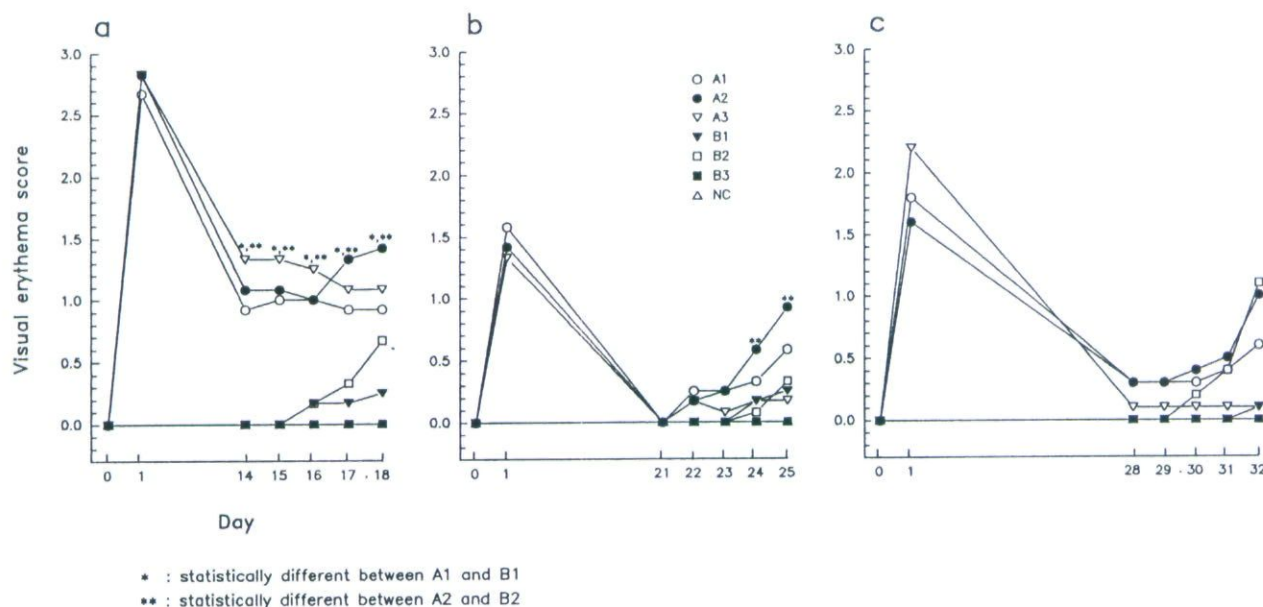


Fig. 5. Mean visual erythema scores of pretreated (A1, A2, A3), non-treated (B1, B2, B3) and control site (NC) before and after application of 2% (A1, B1) or 7.5% (A2, B2) sodium lauryl sulfate (SLS) or vehicle (A3, B3) for 4 consecutive days 2 weeks (a), 3 weeks (b) and 4 weeks (c) post-induction (A1: treated +2% SLS, A2: treated +7.5% SLS, A3: treated +vehicle, B1: non-treated +2% SLS, B2: non-treated +7.5% SLS, B3: non-treated +vehicle, NC: non-treated+non-treated).

until 18 days post-induction. Following repeated provocation of 2% and 7.5% SLS, augmented reaction was noted in the pre-treated site, but not in the non-treated, vehicle and normal control sites, at 2 and 3 weeks, returning to normal at 4-week post-induction. Although at provocation onset, both pre-treated and non-treated sites showed normal parameters, augmented reaction occurred only in pre-treated sites; this might suggest that pre-treated sites had subclinical irritation not detected by clinical inspection and currently used instruments until at least 3 weeks post-induction.

Freeman (2) described augmented irritant response to repeated occlusion of 2% SLS on the pre-irritant contact dermatitis site, even though the skin appeared normal, suggesting that although skin may appear to be morphologically normal, it may not be functionally healed. Lee (1) showed that subclinical irritation might augment the cumulative irritant contact dermatitis caused by repeated open exposure to surfactants. In contrast to these reports, Patil (7) reported that values of TEWL at new exposure sites are higher than values at repeatedly applied sites. They explained that repeated application of SLS may be associated with more dehydration in the repeatedly applied site, thus causing a rapid decline in TEWL as compared to a freshly exposed and relatively more hydrated

area. Widmer et al. (8) also reported hyporeactivity rather than hyperreactivity of pre-irritated sites 6 and 9 weeks after provocation by the same irritants. Their study differed from ours in the manner of induction and challenge. They induced chronic irritant dermatitis with a 1-h application of 0.5% SLS for 3 weeks and challenged with 23-h application of 2% SLS; in contrast, we induced acute irritant contact dermatitis with 24-h application of 1% SLS and challenged with 30 min application of 2% and 7.5% SLS for 4 consecutive days. Widmer et al. (8) explained the hyporeactivity as changes in the composition of stratum corneum lipids and/or reactive hyperkeratosis.

The pathogenic mechanism of this hyperreactivity is unclear. Surfactants including SLS can affect skin lipids (9, 10), keratin protein (11, 12), viable epidermis (13, 14) and dermis (15, 16), and eventually provoke inflammation. Although stratum corneum lipids recovered rapidly, repair of keratin protein, dermal damage and skin inflammation could be delayed even after normalization of TEWL and other parameters.

Taken together, we hypothesize that there are 2 contrasting responses of previously irritated skin; hyporeactivity may be noted if an epidermal response, including hyperkeratosis and dryness, was a major reaction to irritant; on the other hand, if

a dermal reaction, such as erythema and edema, were a major component, hyperreactivity may develop. Clearly, much remains to be understood before we will fully comprehend the complex biology. Clinically, our results suggest that previously irritated skin, even though appearing normal, should be protected from irritant stimuli for some weeks for complete healing.

We do not wish to overgeneralize the clinical significance of this information. This relatively facile and robust model might profitably be used with other physicochemical classes of irritants and additional irritant exposure schedules. Since treatment was not utilized here, it too requires elucidation.

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