

# Chronic irritant contact dermatitis: recovery time in man

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Chronic irritant contact dermatitis (ICD) is a common skin disease, especially in the workplace, but determining the recovery time of chronic ICD is not easy. To measure the recovery time of chronic ICD, we examined the skin reactivity to a model surfactant, sodium lauryl sulfate (SLS), on previous chronic ICD and normal sites by visual grade and non-invasive instruments. Chronic ICD was induced on the forearms of 10 volunteers (aged 23 to 43 years) by occluded application of 1% SLS for 30 min on 5 consecutive days each week for 3 weeks. Previous ICD and normal sites were provoked by the occluded application of 7.5% SLS for 30 min daily on 4 consecutive days, 2, 5 and 10 weeks after induction. Skin reactivity was assessed daily by awarding visual erythema scores, visual scale scores and measuring transepidermal water loss, skin color reflectance, and electrical capacitance. Skin reactivity of previous chronic ICD sites to SLS showed hyperreactivity compared to normal sites even after the 10th week post-induction.

**Key words:** chronic irritant contact dermatitis; recovery time; sodium lauryl sulfate; transepidermal water loss; colorimetry; capacitance; bioengineering methods; surfactants; repeated closed application. © Munksgaard, 2000.

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Chronic irritant contact dermatitis (ICD) is a common disease, and a major part of occupational skin diseases. Although it is not necessarily very serious and may be managed well by routine treatments, it may cause lost work time or a forced job change in some cases. Recovery time from chronic ICD is not clear and probably variable. Complete healing means functional normality, including a loss of susceptibility, as well as clinically normal skin and normal quantitative parameters as measured by bioengineering instruments (1). Several reports have been published on ICD skin response to SLS at various concentrations applied in different ways (2, 3).

This study was undertaken to define the recovery time of hyper- or hyporeactivity to a model surfactant using an irritant provocation method.

## Materials and Methods

### Subjects

10 healthy volunteers, 6 male and 4 female, between 23 and 43 years (mean  $\pm$  SD;  $29.9 \pm 7.6$ ), skin type III to IV, participated after giving written informed consent.

### Materials

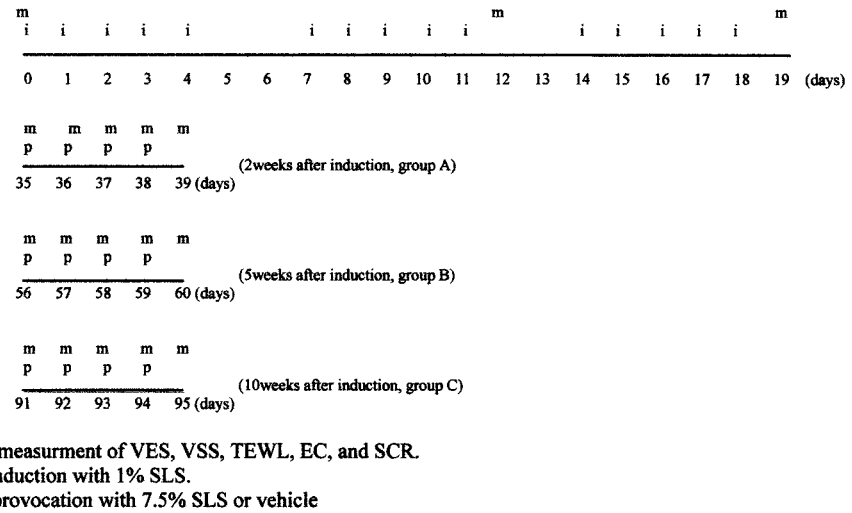
Sodium lauryl sulfate (99% purity, SLS; Sigma Chemical Co., St. Louis, MO, USA) was dissolved in deionized water at 1% and 7.5% concentrations. Polypropylene chambers of 19 mm diameter (Hill Top Lab., Cincinnati, OH, USA) were fixed with non-occlusive paper tape (Scanpor; Norgesplaster A/S, Oslo, Norway).

### Methods

**Induction of chronic ICD.** Chronic ICD was induced at 6 sites (A1, A2, B1, B2, C1, C2) on the volar surface of both forearms by occluded application of 200  $\mu$ l of 1% SLS for 30 min daily on 5 consecutive days per week for 3 weeks. The other 2 sites (D1 and D2) were non-treated controls. All sites including the 6 ICD sites were rotated to minimize anatomic variability.

**Provocation.** A1 and A2 were challenged with 200  $\mu$ l of 7.5% SLS (A1) and vehicle (A2), 30 min daily on 4 consecutive days, 2 weeks after induction. B1 and B2 were challenged with 200  $\mu$ l of 7.5% SLS (B1) and vehicle (B2), 30 min daily on 4 consecutive days, 5 weeks after induction. C1 and

Fig. 1. Study protocol.



C2 were challenged with 200  $\mu$ l of 7.5% SLS (C1) and vehicle (C2), 30 min daily on 4 consecutive days, 10 weeks after induction. D1 and D2 were challenged with 200  $\mu$ l of 7.5% SLS (D1), and vehicle (D2), 30 min daily on 4 consecutive days, 2 weeks after induction.

### Measurements

**Visual erythema score (VES).** We awarded the visual erythema score using the following scales: 0, no erythema; 1, slight redness either spotty or diffuse; 2, moderate uniform redness; 3, intense erythema; 4, fiery red with edema.

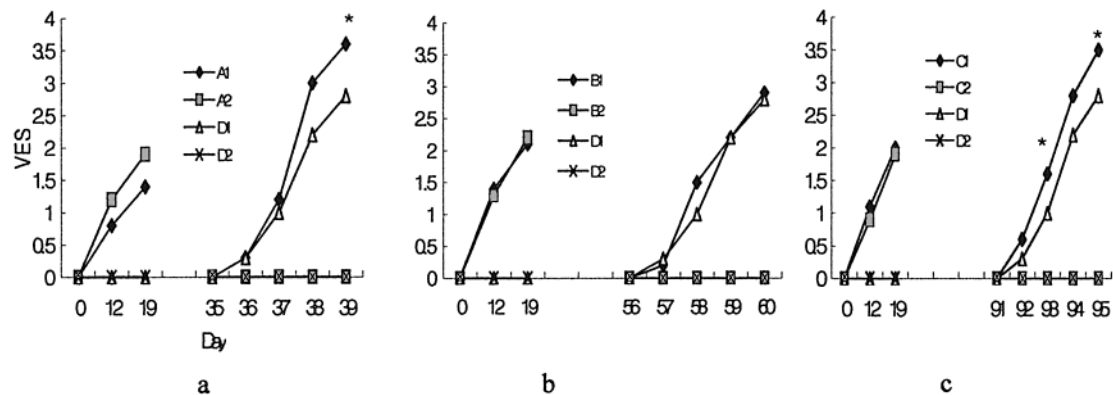
**Visual scale score (VSS).** To assess the visual scale score, the following scale was used: 0, none; 1, fine; 2, moderate; 3, severe flakes with scale.

**Transepidermal water loss (TEWL).** TEWL was

measured with a Tewameter (Tewameter EM 210, Courage & Khazaka, Cologne, Germany). Details of the measurement of TEWL were provided by Pinnagoda et al. (4). The values are expressed as  $\text{g/m}^2/\text{h}$ .

**Electrical capacitance (EC).** 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 & Serup (5).

**Skin color reflectance (SCR).** Erythema was quantified by skin color reflectance measurements with a tristimulus colorimeter (CR 300, Minolta, Osaka, Japan). Of the possible  $L^*$ ,  $a^*$  and  $b^*$  modes,  $a^*$  represents the color spectrum from total green ( $-100$ ) to pure red ( $+100$ ). Because the  $a^*$  mode is correlated with erythema values, it was



\*: statistically different between treated +7.5% SLS-challenged site and non-treated +7.5% SLS-challenged site

Fig. 2. Mean VES of pre-treated (A1, A2, B1, B2, C1, C2) and non-treated (D1, D2) before and after application of 7.5% (A1, B1, C1) SLS or vehicle (A2, B2, C2) for 5 consecutive days 2 weeks (a), 5 weeks (b), 10 weeks (c) post-induction (A1: treated+7.5% SLS, A2: treated+vehicle, B1: treated+7.5% SLS, B2: treated+vehicle, C1: treated+7.5% SLS, C2: treated+vehicle, D1: non-treated+7.5% SLS, D2: non-treated+vehicle).

used as the value for SCR. Details about measuring SCR are described by Wilhelm & Maibach (6).

All parameters were measured 8×, 3× during the induction period (days 0, 12 and 19), and every weekday during the provocation week, from Monday to Friday (Fig. 1). All parameters were measured at room temperature (18–22°C) and 40–60% relative humidity. Volunteers rested at least 20 min before measurements.

#### Statistical evaluation

Differences in each parameter between all sites were tested for their statistical significance using the Duncan multiple range test ( $p < 0.05$ ).

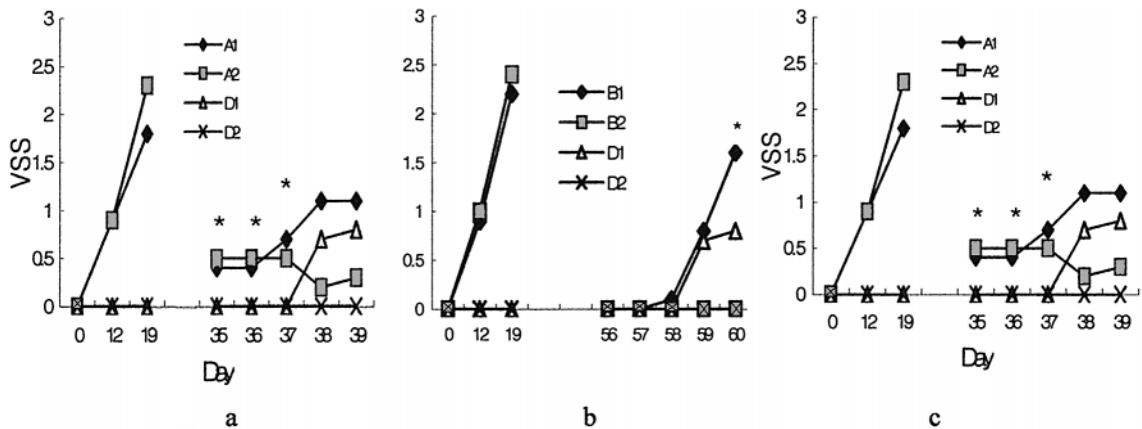
### Results

#### Visual erythema score (VES)

Mean VES of 1% SLS-applied sites increased during the induction period (A, B, C group), and returned to normal 2 weeks after induction. VES of vehicle application sites (A2, B2, C2) during the provocation period were unchanged. VES of A1 (day 39), C1 (days 93, 95) were significantly higher than that of D1 on the corresponding day (Fig. 2).

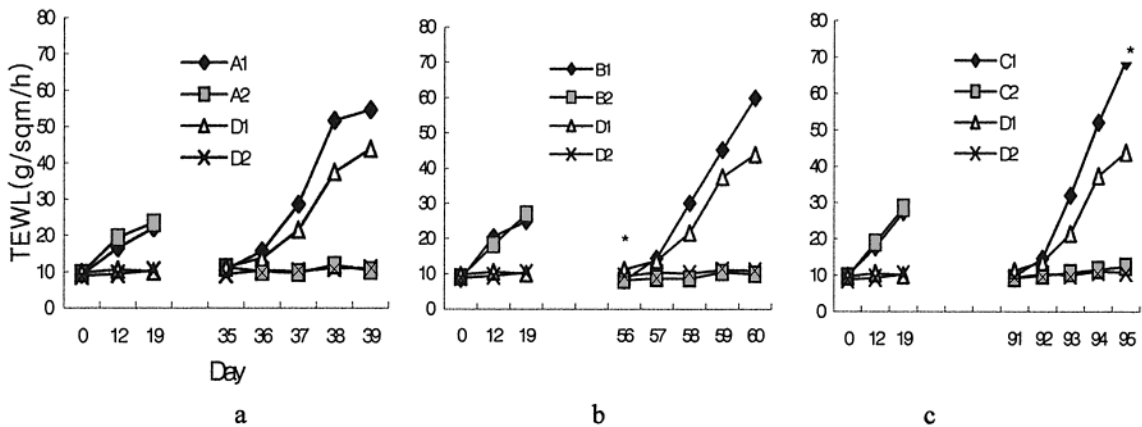
#### Visual scale score (VSS)

Mean VSS of 1% SLS-applied sites increased during the induction period (A, B, C group), and returned to normal 5 weeks after induction. VSS of



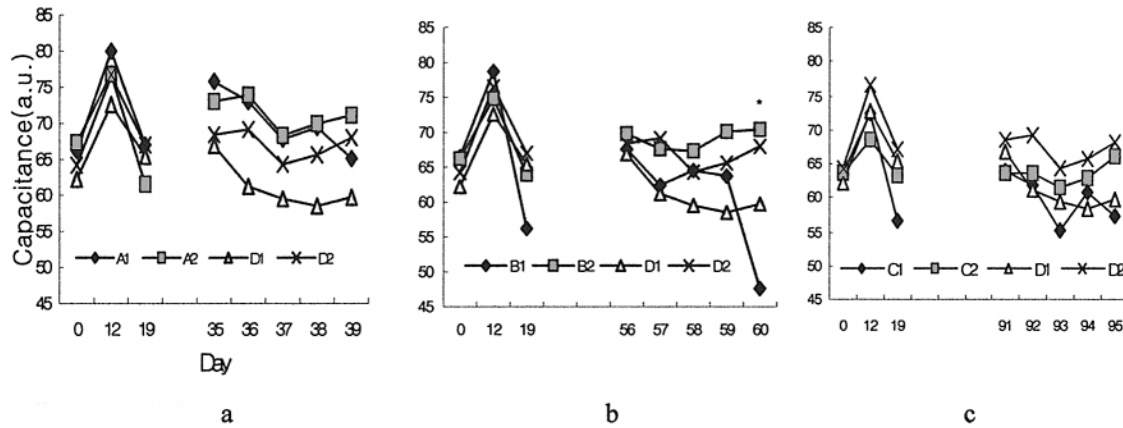
\*: statistically different between treated +7.5% SLS-challenged site and non-treated +7.5% SLS-challenged site

Fig. 3. Mean VSS of pre-treated (A1, A2, B1, B2, C1, C2) and non-treated (D1, D2) before and after application of 7.5% (A1, B1, C1) SLS or vehicle (A2, B2, C2) for 5 consecutive days 2 weeks (a), 5 weeks (b), 10 weeks (c) post-induction (A1: treated+7.5% SLS, A2: treated+vehicle, B1: treated+7.5% SLS, B2: treated+vehicle, C1: treated+7.5% SLS, C2: treated+vehicle, D1: non-treated+7.5% SLS, D2: non-treated+vehicle).



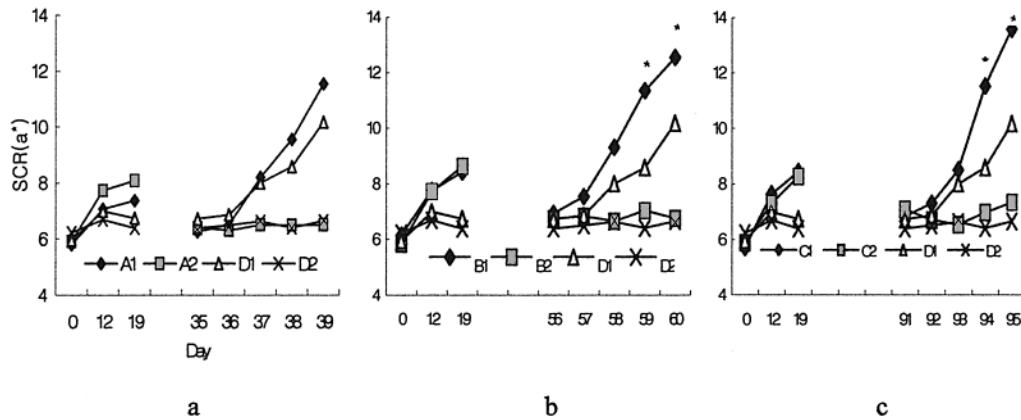
\*: statistically different between treated +7.5% SLS-challenged site and non-treated +7.5% SLS-challenged site

Fig. 4. Mean TEWL of pre-treated (A1, A2, B1, B2, C1, C2) and non-treated (D1, D2) before and after application of 7.5% (A1, B1, C1) SLS or vehicle (A2, B2, C2) for 5 consecutive days 2 weeks (a), 5 weeks (b), 10 weeks (c) post-induction (A1: treated+7.5% SLS, A2: treated+vehicle, B1: treated+7.5% SLS, B2: treated+vehicle, C1: treated+7.5% SLS, C2: treated+vehicle, D1: non-treated+7.5% SLS, D2: non-treated+vehicle).



\*: statistically different between treated +7.5% SLS-challenged site and non-treated +7.5% SLS-challenged site

Fig. 5. Mean EC of pre-treated (A1, A2, B1, B2, C1, C2) and non-treated (D1, D2) before and after application of 7.5% (A1, B1, C1) SLS or vehicle (A2, B2, C2) for 5 consecutive days 2 weeks (a), 5 weeks (b), 10 weeks (c) post-induction (A1: treated+7.5% SLS, A2: treated+vehicle, B1: treated+7.5% SLS, B2: treated+vehicle, C1: treated+7.5% SLS, C2: treated+vehicle, D1: non-treated+7.5% SLS, D2: non-treated+vehicle).



\*: statistically different between treated +7.5% SLS-challenged site and non-treated +7.5% SLS-challenged site

Fig. 6. Mean SCR of pre-treated (A1, A2, B1, B2, C1, C2) and non-treated (D1, D2) before and after application of 7.5% (A1, B1, C1) SLS or vehicle (A2, B2, C2) for 5 consecutive days 2 weeks (a), 5 weeks (b), 10 weeks (c) post-induction (A1: treated+7.5% SLS, A2: treated+vehicle, B1: treated+7.5% SLS, B2: treated+vehicle, C1: treated+7.5% SLS, C2: treated+vehicle, D1: non-treated+7.5% SLS, D2: non-treated+vehicle).

vehicle application sites (A2, B2, C2) during the provocation period were unchanged. VSS of A1 (days 35, 36, 37), B1 (day 60), and C1 (days 94, 95) were significantly higher than that of D1 on the corresponding day (Fig. 3).

#### Transepidermal water loss (TEWL)

TEWL of 1% SLS-applied sites increased during the induction period (A, B, C group), and returned to normal 2 weeks after induction. TEWL of the vehicle application sites (A2, B2, C2) during the provocation period were unchanged. TEWL of B1 (day 56) and C1 (day 95) were significantly higher than that of D1 on the corresponding day (Fig. 4).

#### Electrical capacitance (EC)

The electrical capacitance values (EC) of 1% SLS pretreated sites (A, B, C group) were not statistically different from the EC of non-treated sites (D group) during the induction and provocation period except B1 (day 60). The changes in patterns of EC of the pre-treated sites were not different from the non-treated sites during either the induction or provocation period (Fig. 5).

#### Skin color reflectance (SCR)

SCR of 1% SLS-applied sites (A, B, C group) increased during the induction period and returned to normal 2 weeks after induction. SCR of vehicle

application sites (A2, B2, C2) during the provocation period were unchanged. The pattern of change of SCR with time was similar to that of VES, VSS and TEWL.

SCR of B1 (days 59, 60), C1 (days 94, 95) were significantly higher than that of D1 on the corresponding day (Fig. 6).

### Discussion

Chronic irritant contact dermatitis is caused by repetitive exposure to 1 or more irritants. If the accumulation of invisible subclinical skin damage, caused by irritation, exceeds a threshold, clinical dermatitis can occur. Malten (7) described this clinical dermatitis as 'the tip of the iceberg'. Wilhelm et al. (8) reported TEWL and capacitance returned to baseline 14 days and 17 days after the induction of ICD. Freeman (3) showed augmented irritant response to repeated occlusion of 2% SLS on a pre-irritant contact dermatitis site, even though the skin appeared normal. Lee et al. (1) also reported upon the hyperreactivity of previous ICD sites, second and third weeks after induction, even though TEWL and capacitance returned to normal. This suggests that measurement of irritant response after provocation on previously induced ICD sites is a more practical method of evaluating skin healing after ICD.

In this study, the skin function of previous ICD sites assessed by VES, TEWL, SCR, and capacitance normalized by 2 weeks after induction, VSS returning to normal 5 weeks after induction. Hyper-responses of VSS (in the A, B and C groups), TEWL (in the B and C groups), VES (in the A and C groups), SCR (in the B and C groups), and capacitance (in the B group) were observed, and compared to those of the control group (D group).

Complete recovery of skin function after chronic ICD induced by 1% SLS needed longer than 10 weeks. The patterns of value changes of VES, TEWL, SCR, VSS were similar.

Widmer et al. (9) reported hyporeactivity of pre-irritated sites 6 and 9 weeks after provocation. The study protocol they adopted was 1-h application of 0.5% SLS for 3 weeks to induce chronic ICD and a 23-h application of 2% SLS 3, 6 and 9 weeks after induction, as a rechallenge phase to assess the chronic ICD recovery time. In contrast, we induced chronic irritant contact dermatitis with a 30-min application of 1% SLS for 3 weeks and challenged with a 30 min application of 7.5% SLS on 4 consecutive days, 2, 5 and 10 weeks after induction. The reason why a 30-min application of SLS for 4 consecutive days was chosen was to create a situation similar to

that of real life, and we used 7.5% SLS to ensure provocation of irritation in such a short time as 30 min daily for 4 consecutive days. These different induction and challenge methods may have caused the difference in the results, and additional study is needed to clarify the reasons for potential areas of difference.

The pathogenic mechanisms of hyporeactivity and hyperreactivity are not clear. Lee et al. (1) hypothesized that the 2 quite different reactions may be induced by the reapplication of irritant on ICD sites. Serup (10) suggested that the development of hypo or hyperreactivity after repeated exposures depends on individual defence and repair mechanisms which had a memory and change of threshold during and after induction phase of ICD. Possible explanations for hyporeactivity are changes in the composition of the stratum corneum lipids and/or reactive hyperkeratosis (9), while changes in skin lipids (11, 12), keratin protein (13, 14), viable epidermis (15, 16), and dermis (17, 18) have been offered as reasons for hyperreactivity.

The fact that the values of capacitance were not different from those of the control, except on 1 day (60 day), suggests that capacitance is less sensitive than the other parameters.

Although SLS is a model surfactant, it is not believed that the results of this study can be applied universally to chronic ICD, because it is known that irritant type, concentration level and variable periods of induction and challenge can also affect the results. This study suggested that chronic ICD required a longer recovery time than acute ICD. Further study with other widely used irritants and real-life schedules will be needed to clarify our results.

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