

The effect of population diversity on skin irritation

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The impact of many human variables on the response to skin irritating substances has been studied to varying degrees, including the impact of age, sex, and atopic status. However, the importance of ethnic origin has been more difficult to investigate, leading to a relative paucity of compelling data, either for or against the existence of differences. A primary reason for this lack is that studies on different ethnic groups often have to be undertaken in different locations thus introducing variables, e.g. time, environmental conditions that confound interpretations. In the present work, an attempt has been made to eliminate all variables except ethnicity by conducting a study on 2 distinct populations (Punjabis and Tamils) at the same location on the same day with a single assessor of the skin reactions, using sodium lauryl sulfate as the skin irritant. The skin reactions were assessed visually, and it was demonstrated that the modality of the reactions in these 2 populations had clear differences, but that the dose–response profiles were very similar. Thus, although the irritant response was expressed differently (e.g. erythema was much less evident in the darker Tamil population), the overall outcome was that the populations reacted in an equivalent manner.

Key words: ethnic differences; Indian; patch test; skin irritation; sodium lauryl sulfate; visual assessment. © Blackwell Munksgaard, 2006.

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It is well recognized that irritant contact dermatitis (ICD) responses to skin irritants commonly show interindividual variation (1, 2). When conducting human volunteer studies in order to generate risk assessment data on cosmetic products, a random population is commonly chosen in which to assess their skin irritation potential. Examples of such studies include the predictive human patch test and repeat open application use methods. Typically, effects of interindividual variation are controlled by inclusion of a suitable positive control and sufficient panel size to enable effective statistical analysis.

There are numerous published reports indicating that population diversity differences play a large part in the variation in irritant response to a known stimulus. For instance, Negroid skin is considered to be less sensitive than Caucasian skin, particularly when only visual assessment is used to compare differences in ICD according to different ethnicity (3). Consequently, organizations such as the European Cosmetic Trade Association (COLIPA) recommend that the testing of finished cosmetic products is conducted using

volunteers from the same population in which they are intended to be marketed in (e.g. in terms of sex, age, ethnic origin, and skin type) (4).

Historically, however, many of the reports suggesting a difference in ICD elicited in white and black skin have only compared erythematous reactions. It is well documented that this assessment parameter is notoriously difficult to assess in Negroid skin and hence could be deemed to give a false impression of skin irritation potential (5). Indeed, many dermatological disorders present differently in dark skin and hence assessment of skin reactions should take into account more than just an erythema assessment (6). To avoid potential misinterpretation due to only using visual assessment of erythema to assess ICD, other studies have incorporated bioengineering techniques (typically transepidermal water loss measurements and laser Doppler flowmetry) in order to compare different populations (7–9). However, use of other visual assessment parameters (such as assessing oedema, wrinkling, glazing, skin erosion/scabbing separately) to compare these differences has not been explored.

Although data are available that compare the skin irritation response to typical irritants in different Asian subgroups (Chinese, Malay, and Indian) (9), there are no published data that specifically look at the effect of population diversity within a single Indian population. Understanding interethnic population diversity differences would help in future evaluations of irritant profiles of products.

Hence, the purpose of this study was primarily to evaluate the role of interethnic population diversity in irritant responses to sodium lauryl sulfate (SLS) by comparing northern and southern Indian populations (Punjabi and Tamil populations, respectively). Skin tone in the 2 populations is clearly different, the Punjabi skin being pale brown (northern Indian skin has previously been described as Caucasoid) (10) and the Tamil skin (which is typical colouring of southern Indians) being more akin to the Negroid skin tone (Figs 1 and 2).

To avoid difficulties in interpretation of data resulting from only assessing erythema, several different visual assessment parameters were recorded and analysed separately in order to determine whether erythema is the most appropriate endpoint to assess Indian skin.

Materials and Method

Study population

103 healthy adults were recruited into the study from 2 diverse population groups, Tamils (51 panellists: 25 men and 26 women) and Punjabis (52 panellists: 27 men and 25 women). Tamils are typically very dark skinned and come from the far south of the Indian subcontinent. Punjabis in contrast come from the north of India and typically have skin that is much less dark. All panellists

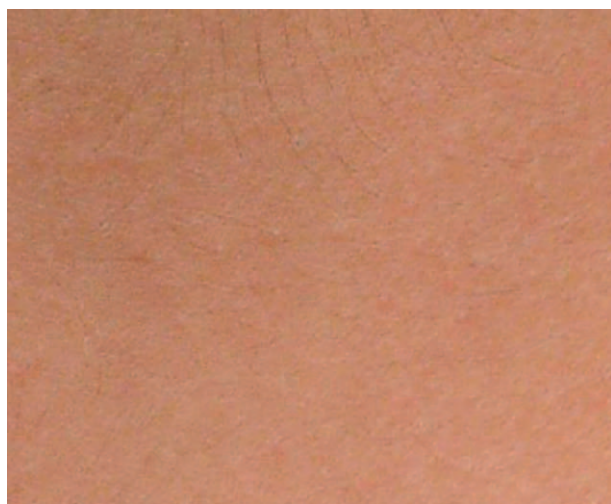


Fig. 1. Punjabi skin tone.



Fig. 2. Tamil skin tone.

were aged between 19 and 50 years (mean age for the Tamil group was 27 years, and mean age for the Punjabi group was 25 years). The volunteers were recruited in Mumbai, India, and all provided written informed consent prior to participating in the study. All volunteers selected had healthy skin, with no current skin condition or signs of local skin irritation on the upper arms. All study procedures were reviewed and approved prior to study initiation by a local independent research ethics committee.

Panellists were asked to confirm that they were of either Tamil or Punjabi descent and that both their parents were also of the same population group.

The study was conducted at the Environmental Safety Laboratory, Unilever, Andheri, Mumbai, India.

Test materials

1.0%, 2.0%, and 3.0% (w/v) SLS (commercially available 99% pure sample from Sigma Chemicals, Poole, Dorset, UK) were prepared in distilled water. Distilled water was also tested as a negative control.

Method

40 μ l of the test materials were applied to fully occlusive patches constructed of 4- $\times$ 12-mm Finn Chambers[®] (Epitest Limited, Oy, Finland) on Fixomull tape (BDF Beiersdorf AG, Hamburg, Germany). Each panellist was allocated a randomized treatment order, which was used to prepare patches for the study. Thus, when treatment sites were assessed they were assessed blind.

The patch was applied for 24 hr to the outer upper arm of volunteers. After 24 hr, patches were

removed, and the treatment sites were marked and wiped with moistened cotton wool. The skin condition of the treated sites was assessed 1, 24, 48, and 72 hr after removal of the patch. Erythema, dryness, and other visual parameters were assessed by a trained skin assessor using an open-ended grading scheme as previously published (11, 12).

Analysis of data

The Friedman test was used to compare the maximum score elicited, regardless of the parameter recorded, by each concentration of SLS and water at both the 1- and 24-hr assessments for the Tamil and Punjabi groups. This was preferred to a parametric alternative such as analysis of variance (ANOVA) because the responses, whilst 'ordinal' in describing severity, cannot be considered a continuous response. Assumptions of (ANOVA) would therefore not have been satisfied, and conclusions could have been misleading.

The Wilcoxon rank sum test was used to compare the 2 ethnic groups in terms of the 6 most frequently used assessment parameters (erythema, wrinkling, glazing, oedema, scabbing, and dryness) elicited by the 4 different treatments [water, 1%, 2%, and 3% (w/v) SLS] at each assessment time (1, 24, 48 and 72 hr).

The Friedman test was also used in order to compare the actual assessment grades to the 4 different treatments within each ethnic group, at the 4 time intervals.

Because these procedures involved many comparisons (at multiple time-points, comparing pairs of treatments), the default approach of performing many independent statistical tests each with a nominal 5% risk of yielding a 'significant' result in the absence of a genuine effect would consequently result in a vastly inflated type I error rate. In other words, reliable conclusions would be rendered impossible due to the high likelihood of inaccurate significant conclusions. Hence, Sidak's adjustment was applied to both the Wilcoxon rank sum and Friedman test *P* values in order to guard against the effect of these multiple comparisons.

Results

The grades of reaction elicited by each test material for each parameter are summarized in Tables 1 and 2. Dryness is not included as only very low levels of dryness were elicited during the study.

For both the Punjabi and Tamil groups, the maximum level of reaction elicited, regardless of the parameter recorded, by water and each concentration of SLS were compared using the Friedman test. For both the Punjabi and Tamil groups, there were significant differences between each of the substances at both the 1- and 24-hr assessments. The overall rank order of irritation at both the 1- and 24-hr assessments was as follows:

Punjabi: 3% SLS > 2% SLS > 1% SLS > water.
Tamil: 2% SLS = 3% SLS > 1% SLS > water.

Table 1. Number of Tamil subjects exhibiting each grade of reaction

Time (hr)	Grade	Erythema				Oedema				Scabbing				Glazing				Wrinkling			
		w	1%	2%	3%	w	1%	2%	3%	w	1%	2%	3%	w	1%	2%	3%	w	1%	2%	3%
1	N	48	17	12	8	50	38	32	24	51	51	50	40	51	22	19	22	50	33	32	35
	S	3	30	24	27	1	11	12	14	0	0	1	7	0	24	24	22	1	15	16	15
	D	0	4	13	14	0	2	6	11	0	0	0	4	0	5	6	5	0	2	3	1
	WD	0	0	2	2	0	0	1	2	0	0	0	0	0	0	1	2	0	1	0	0
	St	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
24	N	51	24	14	10	50	45	46	47	51	50	36	30	51	26	13	11	51	39	33	25
	S	0	25	24	26	1	6	5	3	0	0	13	12	0	19	35	34	0	10	17	23
	D	0	2	13	12	0	0	0	1	0	1	2	8	0	6	1	5	0	2	1	3
	WD	0	0	0	3	0	0	0	0	0	0	0	1	0	0	2	1	0	0	0	0
	St	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
48	N	51	31	18	11	51	51	50	48	51	47	37	32	51	22	16	10	51	31	23	16
	S	0	20	26	31	0	0	1	3	0	2	12	9	0	25	28	28	0	17	19	24
	D	0	0	7	9	0	0	0	0	0	1	2	9	0	4	4	11	0	3	8	8
	WD	0	0	0	0	0	0	0	0	0	1	0	1	0	0	2	2	0	0	1	3
	St	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
72	N	51	36	25	18	51	51	51	51	51	47	34	29	50	36	24	18	51	35	30	20
	S	0	15	22	29	0	0	0	0	0	2	14	10	1	14	22	26	0	15	16	23
	D	0	0	4	4	0	0	0	0	0	1	3	10	0	1	2	6	0	0	5	8
	WD	0	0	0	0	0	0	0	0	0	1	0	2	0	0	2	0	0	1	0	0
	St	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0

Time, time of assessment after patch removal; w, water; 1%, 1% (w/v) SLS; 2%, 2% (w/v) SLS; 3%, 3% (w/v) SLS; N, no reaction; S, slight reaction; D, distinct reaction; WD, well developed reaction; St, strong reaction; SLS, sodium lauryl sulfate.

Table 2. Number of Punjabi subjects exhibiting each grade of reaction

Time (hr)	Grade	Erythema				Oedema				Scabbing				Glazing				Wrinkling			
		w	1%	2%	3%	w	1%	2%	3%	w	1%	2%	3%	w	1%	2%	3%	w	1%	2%	3%
1	N	45	23	8	3	50	37	19	13	52	51	44	37	51	33	33	24	52	42	46	47
	S	6	20	29	24	2	13	21	16	0	1	7	11	1	18	18	25	0	10	6	5
	D	1	7	12	17	0	2	10	19	0	0	0	3	0	1	1	3	0	0	0	0
	WD	0	2	2	8	0	0	2	4	0	0	1	1	0	0	0	0	0	0	0	0
	St	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
24	N	52	13	1	1	52	41	36	33	52	48	30	15	52	37	32	32	52	43	35	35
	S	0	20	26	16	0	11	15	17	0	3	13	21	0	15	18	19	0	9	15	17
	D	0	19	15	24	0	0	1	2	0	1	8	13	0	0	1	1	0	0	2	0
	WD	0	0	10	10	0	0	0	0	0	0	1	2	0	0	1	0	0	0	0	0
	St	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
48	N	51	17	7	3	52	50	47	43	51	40	21	13	49	37	27	21	51	35	28	20
	S	1	26	23	24	0	2	4	7	0	11	19	13	2	15	24	30	1	15	18	25
	D	0	7	17	17	0	0	1	2	1	1	10	22	1	0	1	1	0	2	5	5
	WD	0	2	5	7	0	0	0	0	0	0	2	3	0	0	0	0	0	0	1	2
	St	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
72	N	51	25	10	8	52	51	51	50	52	42	18	12	52	37	27	27	52	38	22	22
	S	1	25	33	26	0	1	0	2	0	10	18	9	0	14	21	21	0	11	18	15
	D	0	2	7	16	0	0	0	0	0	0	13	23	0	1	4	4	0	3	9	13
	WD	0	0	2	2	0	0	0	0	0	0	3	7	0	0	0	0	0	0	3	2
	St	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0

Time, time of assessment after patch removal; w, water; 1%, 1% (w/v) SLS; 2%, 2% (w/v) SLS; 3%, 3% (w/v) SLS; N, no reaction; S, slight reaction; D, distinct reaction; WD, well developed reaction; St, strong reaction; SLS, sodium lauryl sulfate.

The Friedman test was also used to compare the level of reaction elicited by the test materials for each different parameter assessed for both the Tamil and Punjabi groups at each assessment occasion. At the 1- and 24-hr assessments, there were significant differences detected between the level of erythema, oedema, and scabbing elicited by the different concentrations of SLS, and the rank order of irritation as assessed by those 2 parameters was as follows:

Erythema (1- and 24-hr assessments)

Punjabi: 3% SLS > 2% SLS > 1% SLS > water.

Tamil: 3% SLS = 2% SLS > 1% SLS > water.

Oedema (1-hr assessment)

Punjabi: 3% SLS > 2% SLS > 1% SLS > water.

Tamil: 3% SLS > 2% SLS > 1% SLS > water.

Oedema (24-hr assessment)

Punjabi: 3% SLS = 2% SLS > 1% SLS > water.

Tamil: 3% SLS = 2% SLS = 1% SLS = water.

Scabbing [24-hr assessment (48- and 72-hr assessments also)]

Punjabi: 3% SLS > 2% SLS > 1% SLS > water.

Tamil: 3% SLS > 2% SLS > 1% SLS = water.

3% and 2% SLS elicited significantly higher levels of scabbing than 1% SLS in the Punjabi group at the 1-hr assessment. There were no significant differences in the levels of scabbing

elicited in the Tamil group at the 1-hr assessment. There were no significant differences between the level of glazing, wrinkling, or dryness elicited by the 3 concentrations of SLS for either the Punjabi or Tamil groups at the 1-hr assessment. At the 24-hr assessment, 3% SLS elicited a higher level of wrinkling than 2% and 1% SLS in the Tamil group and 3% SLS elicited a higher level of glazing than 1% SLS also in the Tamil group. Low levels of dryness were elicited during the study, and there were no significant differences between the level of dryness elicited by the 3 concentrations of SLS for either the Punjabi or the Tamil groups.

The Wilcoxon test was used to compare the ethnic groups in terms of each of the different assessment parameters recorded for each test material at each assessment time. The erythematous reactions elicited by SLS at each concentration were significantly greater in the Punjabi group than in the Tamil group at the 24-, 48-, and 72-hr assessments (Wilcoxon rank sum test).

A significantly higher level of oedema was elicited by 2% and 3% SLS in the Punjabi group compared with the Tamil group at the 24-, 48-, and 72-hr assessments (Wilcoxon rank sum test). In the Punjabi group, there was also a single occasion when there was a significantly higher level of scabbing elicited by 3% SLS than in the Tamil subjects; this was recorded at the 48-hr assessment.

In the Tamil group, glazing, wrinkling, and dryness reactions were greater than in the Punjabi

group. For glazing, the differences were significant at 24-, 48-, and 72-hr assessments for both 2% and 3% SLS, and also at the 1-hr assessment for 2% SLS. Wrinkling and dryness were significantly greater in the Tamil group than in the Punjabi group at the 1-hr assessment for 3% SLS (Wilcoxon rank sum test). Examples of typical reactions in the 2 groups are shown in Figs 3 and 4. Figure 3 shows distinct wrinkling with no perceptible erythema in a Tamil volunteer, which was a common reaction in this group. Figure 4 shows a well-developed erythema and scabbing in a Punjabi volunteer; erythema was a typical response in this group, and the degree of scabbing elicited was also high in this group.

Results from investigating which of the 4 time-points showed the peak response was dependant on the assessment parameter and the concentration of SLS. For erythema, both the Tamil and Punjabi groups showed a similar response curve, with reactions peaking at 24 hr and showing clear signs of recovery by the 72-hr assessment. Dryness was only seen to any degree at the 1-hr assessment and only in the Tamil group. The frequency of oedema and scabbing reactions differed between the 2 groups (with more observed in the Punjabi group); however, the speed of response between the 2 groups was similar, with the highest number of oedematous reactions recorded at the 1-hr assessment, but with scabbing predictably developing later (the majority of scabbing reactions had developed by 48 hr). Similarly, when considering glazing and wrinkling, the frequency and severity of reactions were different between the 2 groups (with more observed in the Tamil group), as seen with oedema; however, the speed of response



Fig. 3. Scabbing and erythema in a Punjabi subject.



Fig. 4. Wrinkling reaction in a Tamil subject.

between the 2 groups was similar. Both glazing and wrinkling reactions were evident as early as the 1-hr assessment and were recorded at a fairly high frequency throughout the study, including the 72-hr assessment.

Discussion

There have been extensive reviews conducted that investigate the impact of ethnicity on ICD (3, 4, 13). These reviews highlight how conflicting the data on this subject area can be. The data suggest that differences in skin physiology may well exist (e.g. stratum corneum thickness, melanosome distribution, ceramide levels in the skin) (3, 4, 13), but the extent to which these influence differences in ICD in different population groups requires further investigation. Some suggest that Negroid skin is less sensitive than Caucasian skin, particularly when only visual assessment is used to compare an irritant response in the 2 populations (13). Based on this type of evidence, it is suggested that it would be more suitable to test cosmetic products using volunteers from the same population in which they are intended to be marketed in, rather than a random population sample.

In the present study, 2 different ethnic groups recruited from Mumbai (Punjabi and Tamil) were tested during a single week in June 2005 at the same location, using a multiparameter visual skin assessment scheme (11, 12) and a single skin assessor. The 2 Indian subpopulations were similar in terms of ranking and general trends, with both populations demonstrating a clear dose-response relationship for the different concentrations of SLS tested; however, some subtle differences were apparent. In particular, erythema was difficult to assess in the Tamil group, which may explain why people with Negroid skin are often considered less

sensitive than Caucasian skin types (3, 14). Indeed, in this study, if the erythematous reactions were considered alone, the Punjabi subjects appeared to be more sensitive than the Tamil subjects, whereas when glazing and wrinkling were looked at alone, the Tamil group appeared more sensitive. Only when all the assessment parameters were considered together, were the differences far less apparent.

Stronger oedematous and scabbing reactions were elicited in the Punjabi group; however, at the 1-hr assessment, both the Tamil and Punjabi groups exhibited the same, clear dose–response in terms of the level of oedema elicited by the test materials, and at the 24-, 48-, and 72-hr assessments, the same dose–response relationship was reported in terms of the scabbing reactions elicited in each population.

The fact that statistical differences exist between different populations is supported here, but the data also highlight how, in terms of dose–response ranking, the 2 populations are in fact similar. The evidence supports the view that data obtained from 1 population are broadly applicable (15, 16), as the irritant response in the 2 populations is sufficiently similar in terms of general trends, to support the continued use of mixed population panels to gain data supporting claims and risk assessment. However, the data highlight the importance of not overemphasizing the erythema score, which may not necessarily be the predominant manifestation of damage to the skin; instead, when assessing irritation visually, all parameters should be considered, particularly when looking at darker skin tones, which make erythema difficult to see.

More recent investigations into ethnic differences have used bioengineering tools to assess differences in the skin properties of different populations (14, 17, 18), and the evidence suggests that there may be differences in the skin of different racial groups. However, this evidence is conflicting, and there is limited investigation into the effect of topical irritants on the properties of the skin, in different populations, using bioengineering tools. Furthermore, there is nothing that can be derived from this work concerning the intrinsic properties of skin that could serve to indicate what the impact of these differences might be on the nature and degree of the response to irritant challenge.

Previous research has tended to compare different populations, such as Negroid skin with Caucasian, Asian, or Hispanic skin (3, 5, 7, 13–16), and there have been conflicting results with regard to the effect of ethnicity on ICD. In the present study, 2 groups within a single group were

investigated, and the data suggest that when assessing irritant reactions visually, there are differences in the presentation of ICD within a single population. While supporting the continued use of mixed population panels for risk assessment and for claiming support, it would be of interest to investigate the differences highlighted further, perhaps combining visual assessment with the use of bioengineering tools to enhance the sensitivity of a multiparameter assessment method. Investigation of a wider set of irritant chemicals/formulations would also be worth completing to further investigate potential differences between ethnic groups.

References

1. Basketter D A, Griffiths H A, Wang Z M, Wilhelm K-P, McFadden J. Individual, ethnic and seasonal variability in irritant susceptibility of skin: the implications for a predictive human patch test. *Contact Dermatitis* 1996; 35: 208–213.
2. Judge M R, Griffiths H A, Basketter D A, White I R, Rycroft R J G, McFadden J P. Variation in response of human skin to irritant challenge. *Contact Dermatitis* 1996; 34: 115–117.
3. Modjtahedi S P, Maibach H I. Ethnicity as a possible endogenous factor in irritant contact dermatitis: comparing the irritant response among Caucasians, blacks and Asians. *Contact Dermatitis* 2002; 47: 272–278.
4. Walker A P, Basketter D A, Baverel M et al. Test guidelines for assessment of skin compatibility of cosmetic finished products in man. *Food Chem Toxicol* 1996; 34: 651–660.
5. Berardesca E, Maibach H I. Sensitive and ethnic skin: a need for special care agents? *Dermatol Clin* 1991; 9: 89–92.
6. Manning J. The assessment of dark skin and dermatological disorders. *Nurs Times* 2004; 100: 48.
7. Kompaore F, Marty J-P, Dupont Ch. In vivo evaluation of the stratum corneum barrier function in Blacks, Caucasians and Asians with two noninvasive methods. *Skin Pharmacol* 1993; 6: 200–207.
8. Berardesca E, Maibach H I. Racial difference in sodium lauryl sulphate induced cutaneous irritation: black and white. *Contact Dermatitis* 1988; 18: 65–70.
9. Goh C L, Chia S E. Skin irritability to sodium lauryl sulphate – as measured by skin water vapour loss – by sex and race. *Clin Exp Dermatol* 1988; 13: 16–19.
10. Yosipovitch G, Theng C T S. Asian skin: its architecture, function and differences from Caucasian skin. *The Cosmetic Site.Com* September 2002 (retrieved from <http://www.thecosmeticsite.com/formulating/skincare/959721.html>).
11. Basketter D A, Reynolds F, Rowson M, Talbot C, Whittle E. Visual assessment of human skin irritation: a sensitive reproducible tool. *Contact Dermatitis* 1997; 37: 218–220.
12. Basketter D A, Gerberick F, Kimber I, Willis C. *Toxicology of Contact Dermatitis: Allergy, Irritancy and Urticaria*. Chichester: John Wiley and Sons Ltd, 1999.
13. Robinson M K. Population differences in skin structure and physiology and the susceptibility to irritant and allergic contact dermatitis: implications for skin safety testing and risk assessment. *Contact Dermatitis* 1999; 41: 65–79.
14. Wesley N, Maibach H I. Racial (ethnic) differences in skin properties. *Am J Clin Dermatol* 2003; 4: 843–860.
15. Foy V, Weinkauf R, Whittle E, Basketter D A. Ethnic variation in the skin irritation response. *Contact Dermatitis* 2001; 45: 346–349.

16. Robinson M. Population differences in acute skin irritation responses. *Contact Dermatitis* 2002; 2: 86–93.
17. Reed J T, Ghadially R, Elias P M. Skin type, but neither race nor gender, influence epidermal permeability barrier function. *Arch Dermatol* 1995; 131: 1134–1138.
18. Modjtahedi S P, Maibach H I. Ethnicity. In: *Irritant Dermatitis*, Chew A-L, Maibach H I (eds): Berlin, Springer, 2006: 177–183.

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