

## ALLERGIC CONTACT DERMATITIS FROM A DISH-WASHING LIQUID CONTAINING LAURYL ETHER SULPHATE

Bertil Magnusson and Oscar Gilje <sup>†</sup>1

*From the Department of Dermatology in Malmö, University of Lund, Sweden, and the Department of Dermatology, University of Oslo, Norway*

**Abstract.** In Norway there occurred in 1966 an outbreak of severe allergic contact dermatitis in women who had used a new dish-washing agent. In connection with the dermatitis some of the patients also had systemic symptoms in the form of headache, nausea, fever and a certain degree of depression. The results of testing of patients and of sensitization tests in guinea pigs clearly showed that the cause of the dermatitis was in the lauryl ether sulphate component of the product. The results of testing of a sensitized factory worker and of guinea pigs with the unsulphated matter of LES 13-2035 and with extract of synthetic lauryl alcohol may suggest that the allergen is neither chemically bound to the lauryl ether sulphate molecule nor present in the actual raw product, fatty alcohol.

Two outbreaks of allergic contact dermatitis from products containing lauryl ether sulphate have since occurred elsewhere in Scandinavia. Work is in progress at various laboratories to identify the allergen and to trace its source and how to prevent its formation.

Alkyl ether sulphates (=alkyl ethoxy sulphates, AES) are important anionic surfactants that have been widely used for nearly 20 years in dish-washing liquids, shampoo mixtures, foam-bath agents, cosmetics and car cleaners. In Sweden the consumption of alkyl ether sulphates (containing various amounts of active matter) in commercially available products is at present about 3 000 tons a year (2).

In alkyl ether sulphates the alkyl group may vary in chain length, but the group with predominantly 12 carbon atoms is generally preferred for AES in shampoo mixtures and detergents. This alkyl group is usually referred to as the lauryl group, for which reason the abbreviation LES is used here for the corresponding ether sulphate.

LES is produced from technical fatty alcohol. The fatty alcohol may be synthetic or "natural", derived from, for example, coconut fat. The principal components of both are *n*-dodecyl and *n*-tetradecyl alcohol. The manufacture of ether sulphate from fatty alcohol is a three-stage procedure, namely first ethoxylation with ethylene oxide, then sulphation with e.g. sulphur trioxide, followed by neutralisation, usually with a solution of caustic soda (5). Some manufacturers finally bleach the product with a small amount of sodium hypochlorite or hydrogen peroxide. Due mainly to an incomplete sulphation reaction the technical product always contains a small percentage, counted on active matter, that is not LES. This matter is generally referred to as "unsulphated matter" and can be extracted from the LES by means of petroleum ether. The composition of technical LES thus does not exactly correspond to chemically pure lauryl ether sulphate and may differ slightly between different brands and even between different batches of the same brand. In complete detergent formulae the ether sulphate may be the only surfactant, or one of several. Other common ingredients are inorganic salts, solvents, perfume and pigments.

Hitherto, LES has generally been believed to have only a slight effect on the skin. Smeenk (12) and Valér (13) found LES to irritate the skin less than other detergents. Apart from these studies, little appears to have been published on the dermatological effects of LES. Extensive investigations have, however, been carried out by manufacturers of LES. Exaggerated exposure of large numbers of housewives to products containing LES has produced no evidence of sensitization (14).

<sup>†</sup> Oscar Gilje, M.D., was Docent and Assistant Chief Physician at the Department of Dermatology, Rikshospitalet, Oslo. He died in November 1966.

This opinion of the lack of any undesirable effect of LES on the skin must be revised in view of outbreaks of severe allergic contact dermatitis in Scandinavia caused by exposure to products containing LES from different manufacturers. The first outbreak, which occurred in Norway in 1966, was caused by a dish-washing liquid; the second in Sweden in 1968, by LES in a liquid soap; and the third, which recently occurred in Denmark, to LES in a dish-washing product.

Though LES has been widely used for many years it has not previously been recognized as a contact allergen. One might well imagine that it is the conditions under which LES are manufactured that are decisive as to whether the product will be allergenic or not. It is also possible that LES is contaminated in such a way during the manufacturing process that it assumes allergenic properties. The allergenic factor in the sensitizing batches of LES has not been identified, but at several laboratories work is in progress to isolate and to prevent the production of the allergenic factor (6, 14). Reports on the outbreaks in Sweden, and in Denmark (to be published) have emphasized the urgency of pertinent research in this field. In this connection there is reason to mention that in Sweden in 1953-54 there was an outbreak of contact dermatitis caused by the washing powder "Surf", rather soon after its introduction on the market (3, 8, 11). The dermatitis was attributed to contact allergy to the brand of lauryl sulphate used in the washing agent (11). Since the composition of the product was changed the complaints have ceased.

This paper concerns a report of the Norwegian outbreak. It is based on a compilation of cases and patch test results by the late Oscar Gilje (4). Testing soon revealed that it was the LES component of the dish-washing liquid that was the cause of the eczema. One of us (B. M.) was approached by the Swedish manufacturer of the LES used in the product with the request to undertake animal experiments to confirm the sensitizing capacity of LES 13-2035 and to test sensitized animals with different fractions of the detergent to determine where in the manufacturing process the allergenic factor should be sought. In addition to the Norwegian outbreak the paper reports a case of allergic contact dermatitis from LES in a factory worker exposed to this material and sensitization experiments in quinea pigs with LES.



Fig. 1. Acute allergic contact dermatitis of hands and forearms from a dish-washing agent containing lauryl ether sulphate. (One of the patients of Dr O. Gilje.)

#### *Outbreak of dermatitis in Norway (1966)*

In February 1966 alarming reports of acute dermatitis in housewives who had used a new dish-washing liquid began to appear, mainly from the north of Norway. In some districts the spread assumed the nature of an epidemic. The sale of the product was immediately stopped and the public appropriately advised by radio and television.

The total number of cases was estimated at 500-1 000. In one doctor's district there were 65 cases. Most of the cases occurred in the north of Norway, where the product was first placed on the market in January 1966. Some cases were also observed in other parts of the country, particularly in the district of Stavanger and Oslo. It is estimated that 200 000-500 000 persons had been exposed.

#### *Symptoms*

As a rule, the dermatitis appeared about 2 weeks after the patient had begun to use the product. Only women were affected. Most were housewives or women who were working outside the home but who did their own housework. Most were young. Two girls, aged 12 years, who helped their mothers, also contracted dermatitis. Most of the affected persons had never had dermatitis before.

The onset was always acute. The earliest and most severe changes occurred on the hands, especially on the fingers and dorsum of the hand. The dermatitis often spread to the forearms and face (Figs. 1-2). Sometimes patchy dermatitis also occurred on the trunk. The skin reaction was severe with intense redness and oedema. Vesicles and papules were prominent; purpura was also present.

The tendency to oedema was marked with swelling of the neck, face and particularly around the eyes. Severe itching was the rule. Some complained of general malaise and moderate fever. Systemic symptoms included headache for a day or two, nausea, and a peculiar weakness and apathy. The dermatitis healed slowly within 3-4



Fig. 2. The same patient as in Fig. 1. Spreading of dermatitis to the face.

weeks. Some cases required hospitalization and systemic treatment with corticosteroids.

#### Patch testing

Patch tests were performed on 24 persons who had developed dermatitis after the use of the detergent. The testing was done in the north of Norway (Narvik) by Dr S. Weideborg; in the west (Stavanger) by Dr A. Jensen; and in Oslo by Dr O. Gilje. 29 patients, 21 women and 8 men receiving treatment for various skin diseases or for venereal diseases at the Department of Dermatology in Oslo, served as controls. None of the latter had used the detergent in question. The patients were tested with the product itself and with its components. The detergent contained 18.7% active material LES 13-2035 and 3.0% active material LES from a Norwegian supplier. The first 10 000 bottles of the dish-washing agent delivered contained LES 13-2035 only, thereafter the Norwegian LES was also included. Most of the patients were also tested with a standard series of 20 common contact allergens.

For patch testing, Lysaplast (Nordisk Plaster Industri A/S, Copenhagen, Denmark) was used. The patches were applied for 24 hours to the thigh or the back. The results were read 24 and 48 hours after removal. In two of the patients the tests produced severe flare-ups of their dermatitis. One also got general symptoms of shiver-

ing, apathy and weakness. The shock-like symptoms started half an hour after the test patches had been applied and lasted for about 30 min; the shivering lasted for about 3 hours.

#### Results

The results are summarized in Table I. The tests with the detergent and its two LES components produced strong allergic reactions in affected individuals. All of 23 persons tested reacted to a 30% concentration of the actual product, i.e. 6.5% concentration of LES. Also, 3 of 29 controls reacted to this concentration. All 18 patients tested with LES 13-2035 in a concentration of 18.7% reacted positively, and 16 of them to the Norwegian LES in a concentration of 3%. Positive reactions were seen in 5 and 2, respectively, of the 29 controls. Eight of 24 patients reacted positively to LES 13-2035 in a low concentration (0.02%) and 6 of 24 to the Norwegian LES in a concentration of 0.003%. None of the controls reacted to LES in these low concentrations.

Of the patients with dermatitis from the detergent, 3 reacted positively not only to the LES, but also to other components of the detergent, namely 2 to naphthol green and 1 to the bactericide (formaldehyde). Testing with the standard series revealed that 2 of these patients gave positive reactions to nickel and formaldehyde. In addition, 4 other patients reacted to formaldehyde.

#### Factory worker with allergic contact dermatitis from LES

The patient was a 45-year-old man with no previous history of eczema, except for dryness and fissures of the palms for which he consulted a dermatologist in 1962.

In March 1967, while working at the Swedish factory which manufactured LES 13-2035 he developed dermatitis of the hands and also of other parts of the body. The dermatitis occurred some weeks after he had been

Table I. Results of patch testing of patients with contact dermatitis from the dish-washing liquid and in unexposed controls

Test substance	Conc. (%)	Patients Pos./Total	Controls Pos./Total
Dish-washing liquid	30.0	23/23	3/29
LES 13-2035 (Swedish)	18.7	18/18	5/29
LES 13-2035 (Swedish)	0.02	8/24	0/29
LES (Norwegian)	3.0	16/18	2/29
LES (Norwegian)	0.003	6/24	0/29

emptying LES from barrels into a mixer. Several of the barrels contained LES of the batch which had been included in the above-mentioned Norwegian dish-washing agent and which had now been returned to the manufacturer. During this work the man had occasionally got LES on his hands, and on one occasion he spilled LES on his ankles and lower legs.

The dermatitis started on the backs of the hands and spread to the forearms and eyelids. He also got dermatitis of the ankles and lower legs where he had spilled the LES. By the time of examination at the Out-patient Department of Dermatology, Sahlgrenska sjukhuset, Gothenburg, 3 weeks after the onset of his skin symptoms, the dermatitis had nearly healed. In the areas mentioned the skin was red, dry and here and there it was desquamating.

#### Patch testing

The patient was tested with LES 13-2035 and with LES from a batch that had been produced later. He was also tested with the extracted unsulphated matter of LES 13-2035 and with material obtained by extractive distillation with propylene glycol of synthetic lauryl alcohol, the raw material used. This distillate consisted mainly of hydrocarbon contaminants and was obtained as described by Bore & Gataud (1). (The fractions were prepared by J. Törnquist, MoDoKemi AB, Stenungsund, Sweden). The two LES samples and the two extracts were all used in 1.0% concentration in water for patch testing. By testing 10 controls with these materials the concentrations chosen were checked and found to be non-irritant. In addition, the patient was tested with a standard series comprising 20 of the most common contact allergens (9). The test patches were applied to the back for 48 hours. The results were read 24 hours after removal of the patches.

#### Results

The patient showed clear-cut positive patch test responses to both LES samples and to the extracted unsulphated matter of LES 13-2035. Biopsies from the test reaction sites showed a histological picture in good agreement with that of an allergic reaction (H. Gisslén). The patient did not react to the extract of lauryl alcohol or to any of the substances in the standard series.

#### Sensitization of guinea pigs to LES

In May 1966 the allergenicity of LES 13-2035 was assessed on 25 guinea pigs according to the maximization technique (10) at the Department of Dermatology, Gothenburg. For the intracutaneous induction 5% of the LES in water was used and for topical induction 1 week later, 25% of the LES, also in water. The animals were challenged 2 weeks after the second induction exposure with 0.5% of LES in water applied as an occluded patch for 24 hours. The results were read 24 hours after removal of the patches.

In September 1966, when the above-mentioned two extracts of LES 13-2035 were available, a new series

of 23 guinea pigs were treated with LES 13-2035 in the same way as the first series in order to test sensitized animals also with these two materials (extracted unsulphated matter of LES 13-2035 and distillate of the alcohol raw material). At challenge, a 0.5% concentration of the materials in water was used.

#### Results

In the first series 22 out of the 25 animals showed definite positive reactions to LES 13-2035. No reactions were seen in 25 non-exposed control animals.

In the second series 9 out of the 23 animals became sensitized. Of the 9 LES-allergic animals 5 reacted also to the extracted unsulphated matter of LES 13-2035. None of the animals reacted to the distillate of the raw material, i.e. fatty alcohol. All 23 control animals proved negative at challenge with the three test substances used.

## DISCUSSION

The outbreak of allergic contact dermatitis from the dish-washing agent in Norway is remarkable in two respects: in some of the affected persons the dermatitis was associated with systemic symptoms and, second, the cause proved to be a type of surfactant that had been used for many years in various parts of the world without having previously been described as possessing allergenic properties.

In most cases sensitization had occurred rapidly—within 2 weeks of initial exposure to the dish-washing agent. The clinical picture was alarming not only because of the intensity of the dermatitis, but also because some patients had general symptoms in the form of headache, nausea, fever and a certain degree of depression. In one of the patients the relatively small amount of allergen applied at patch testing of the dish-washing agent was sufficient to produce such general symptoms. The symptoms appeared within 30 minutes, suggesting a simultaneous immediate type of allergy, which was followed by a flare-up of the dermatitis. That some of the patients were highly sensitive was also obvious from the fact that at patch testing of 24 of the patients, 6 reacted positively to LES (Norwegian) diluted to give such a low concentration as 0.003%, and 8 of the 24 to LES 13-2035 in a dilution of 0.02%. The positive reactions of some of the controls to tests with high concentrations of LES (3.6% and 18.7%) were

probably irritant reactions. This also applies to 3 controls who reacted positively to the dish-washing compound at a 30% concentration.

A literature search failed to reveal any reports of the above-mentioned types of systemic reactions in association with contact dermatitis following external exposure to contact allergens. However, the reactions resemble those apt to occur after intramuscular injection of Rhus extract in hypersensitization of highly sensitive persons in whom the injections may cause not only severe local symptoms but also fever, malaise and a grippelike syndrome (7).

The results of testing of patients and of sensitization tests in animals showed that the cause of the outbreak of dermatitis was in the LES component of the dish-washing agent. It is probable that LES 13-2035 was the primary sensitizer and that the reactions to the testing with the Norwegian LES were signs of cross-allergy. This assumption gains strength from the observation that the outbreak of eczema started even after use of the earliest batches of dish-washing compound before the Norwegian LES had been added, i.e. batches consisting of LES 13-2035 only.

It is not yet possible to explain why or how LES, which is otherwise allergologically inert, can act like a very strong contact allergen. The results of testing of the sensitized factory worker and of guinea pigs with the unsulphated matter of LES 13-2035 and with extract of synthetic lauryl alcohol may suggest that the allergen is neither chemically bound to the lauryl ether sulphate molecule nor present in the actual raw product, fatty alcohol. Later evidence confirms that purified lauryl ether sulphate does not contain the allergen (14) which thus seems to form in some stage of the manufacturing process.

The outbreak of contact dermatitis observed in Sweden in 1953-54 was also caused by an otherwise allergologically inert surfactant, sodium lauryl sulphate. As far as we know, it has never been explained how that particular brand of lauryl sulphate could act as a sensitizer. It is to be noted that LES always contains about 15% sodium lauryl sulphate (5, 15).

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B. Magnusson, M.D.  
Department of Dermatology  
Malmö General Hospital  
S-214 01 Malmö  
Sweden