

Contact sensitivity to emulsifiers

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Common emulsifiers were tested in over 1,200 patients with eczema. Triethanolamine stearate tested at 5 % in petrolatum caused irritant reactions in 9.5 % of the patients. On the other hand, non-ionic emulsifying agents tested at 10-20 % produced irritation in only a few cases.

Allergic reactions were found in 2.1 % of those tested. Lanette, sorbitan sesquioleate, the Spans®, polyoxyethylene oxypropylene stearate, polyoxyethylene sorbitol lanolin derivative, and triethanolamine stearate each elicited allergic reactions in 0.3-0.7 % of the cases. The Tweens® caused an allergy in only two cases, but glycerol monostearate caused no reaction at all.

Five out of six patients sensitive to sorbitan sesquioleate reacted positively to the Spans® as well.

The patients allergic to one or more emulsifiers were also sensitive to several other substances included in our routine test series with the exception of four patients who reacted only to the emulsifying agents.

Key words: Dermatitis, contact (etiology) - emulsifiers - ointment bases - surface active agents.

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Several cases of emulsifier allergy were reported by us recently (Hannuksela et al. 1976). The number of patients examined was, however, so low that no definite conclusions could be made. Later, over 1200 patients with eczema were tested with eight common emulsifiers, and the results are presented here.

Patients and Methods

Between April 1, 1975, and January 31, 1976 a total of 1,206 patients (505 males and 701 females) were sent for routine epicutaneous test series to our allergy laboratory. The following emulsifiers were added to the series: Lanette N, sorbitan sesquioleate = Arlacel 83® (Atlas), sorbitan mono-

oleate = Span 80® (Atlas), sorbitan monostearate = Span 60® (Atlas), polyoxyethylene sorbitan monopalmitate = Tween 40® (Atlas), polyoxyethylene sorbitan mono-oleate = Tween 80® (Atlas), polyoxyethylene oxypropylene stearate = Atlas G 2162® (Atlas), polyoxyethylene sorbitol lanolin derivative = Atlas G 1441® (Atlas), glycerol monostearate = Aldo 33® (Glyco), and triethanolamine stearate. All these synthetic emulsifying agents were incorporated in petrolatum. Their concentrations are given in Table 1.

Wool alcohols (30 % in petrolatum) (Tro-lab) were included in the routine test series.

The epicutaneous tests were performed with the chamber method (Pirilä 1975) (Finn Chambers, Epitest Ltd. Oy, Frederikinkatu

Table 1. Reactions to synthetic emulsifiers and to wool alcohols

Substance	Concentration in pet.	No. tested	Allergic reactions		Toxic reactions	
			No.	%	No.	%
Lanette N®	20	1,206	8	0.7	4	0.3
Arlacel 83®	20	1,206	6	0.5	5	0.4
Span 60® + 80®	5 + 5	1,206	5	0.4	4	0.3
Atlas G 2162®	20	1,206	4	0.3	0	
Atlas G 1441®	20	1,132 ¹	5	0.4	1	0.1
Tween 40® + 80®	5 + 5	1,206	2	0.2	2	0.2
Aldo 33®	20	1,206	0		2	0.2
Triethanolamine stearate	5	1,132 ¹	5	0.4	108	9.5
All emulsifiers mentioned above		1,206	25	2.1		
Wool alcohols	30	1,206	22	1.8		

¹Triethanolamine stearate and Atlas G 1441® were tested in only 1,132 cases.

61, SF-00100 Helsinki 10). The occlusion time was 24 hours, and the readings were made about 20 minutes after removal of the tests, and after 2 and 4–5 days after the application of the tests.

All reactions were recorded. Irritant reactions were at their strongest on the first or second day, but disappeared or at least became markedly weaker within 4–5 days.

Results

Among the 1,206 cases tested with various synthetic emulsifiers, 146 (12%) showed a positive reaction to one or more of them. In the vast majority of the cases, the response was considered to be due to the irritant properties of these substances. Most of them, 108 cases, were caused by triethanolamine but only in 16 cases by other emulsifiers (Table 1).

In 25 cases (2.1%), the reactions were regarded as allergic (Table 1). Glycerol monostearate did not cause an allergic reaction in any patient, and the Tweens® in only two cases. Other emulsifiers elicited allergic reactions in 0.3–0.7% of the cases.

Topical preparations containing emulsi-

fiers responsible for sensitization were tested in 14 out of the 25 cases. The result was positive in all of them.

Two patients had suffered from a very severe eczema due to various ointments. The causative agent was Lanette in one of the cases, and sorbitan sesquioleate in the other. In three additional cases an allergic dermatitis of moderate degree was derived from emulsifiers (sorbitan sesquioleate in two cases and Lanette in one). Moreover, two patients with a positive epicutaneous test reaction to Lanette, and one patient with a positive reaction to the Tweens® but without any knowledge of clinical relevance of these findings were subjected to a challenge test. Two patients applied an ointment with Lanette and one patient an ointment with Tween 80® as the emulsifiers t.i.d. on the cubital area. An acute dermatitis with moderate or severe itching was elicited in one patient with a positive reaction to Lanette and in the particular patient with apparent Tween® allergy. Of the six patients sensitive to sorbitan sesquioleate (Arlacel 83®), five showed cross-sensitivity to the Spans® (Table 2). Various polyoxyethylene derivatives (Tweens®, Atlas G 2162®, and Atlas

Table 2. Reaction patterns of 22 patients with allergic reactions to various emulsifiers

Patient No.	Allergic reactions to
1	Lanette N, vioform
2	Lanette N, Atlas G 2162®, neomycin, bacitracin, dequaline, balsam of Peru, paraphenylenediamine, formalin, wool alcohols
3	Lanette N, Arlcel 83, the Spans, Atlas G 1441®, wool alcohols, dequaline, propylene glycol (2% in water)
4	Lanette N, neomycin, bacitracin, dequaline, balsam of Peru
5	Lanette N, balsam of Peru
6	Lanette N, dequaline
7	Lanette N, balsam of Peru
8	Lanette N, neomycin, bacitracin, balsam of Peru
9	Lanette N, benzocaine
10	Arlcel 83®, nickel
11	Arlcel 83®, the Spans®, dequaline, vioform, neomycin, bacitracin
12	Arlcel 83®, the Spans®, neomycin, bacitracin, dequaline
13	Arlcel 83®, the Spans®
14	Arlcel 83®, the Spans®, Hg, balsam of Peru, thiomersal, wood tars
15	Atlas G 2162®, balsam of Peru, colophony, wood tars, neomycin, bacitracin, dequaline
16	Atlas G 2162®, Atlas G 1441®, the Tweens®
17	Atlas G 2162®, Atlas G 1441®, neomycin, bacitracin, vioform, potassium dichromate, TMTD
18	Atlas G 1441®, neomycin, bacitracin, wool alcohols
19	Atlas G 1441®, balsam of Peru
20	the Tweens®, neomycin, bacitracin, TMTD
21	triethanolamine, nickel, formalin
22	triethanolamine, propylene glycol (2% in water), formalin
23	triethanolamine, benzocaine
24	triethanolamine
25	triethanolamine

G 1441®) gave positive results in one case (Patient No. 16 in Table 2) who failed to react to other emulsifying agents. Simultane-

ous sensitivity to Lanette and wool alcohols was found in two cases.

Of the 22 cases allergic to one or more emulsifiers, nine were hypersensitive to neomycin and bacitracin, eight to balsam of Peru, seven to dequaline chloride, and 12 to various other substances. Only four patients did not react positively to any other of the 25 substances of our routine test series.

Discussion

Emulsifying agents, especially the non-ionic ones, are usually considered to be harmless in the concentrations commonly used in topical preparations. This may be the reason why they are not routinely tested and why the manufacturers do not give information about the emulsifiers.

Recently, we reported several cases of emulsifier allergy (Hannuksela et al. 1976). The results of the present study confirm the previous ones suggesting that allergy to various synthetic emulsifying agents is more common than has been realized thus far. Triethanolamine is the only one which has previously been tested in a large number of cases. Hypersensitivity to it has been noted in 0.9–2% of patients (Fisher et al. 1971, Meneghini et al. 1971, Angelini et al. 1975). The corresponding figure in the present study was only 0.4%. Lanette 0 and Lanette N (Bandmann & Dohn 1967), Tween 80®, and sorbitan monolaurate (Finn & Forsyth 1975) have been found to cause allergy in only occasional cases.

Cross-reactions between various emulsifiers are of considerable importance. Sorbitan sesquileate and the Spans®, especially Span 80® (sorbitan mono-oleate), are structurally closely related, making cross-reactions understandable. On the other hand, however, the corresponding polyoxyethylene derivatives did not cause reactions in patients allergic to the Spans®. The finding that two patients showed allergic reactions

to both wool alcohols and Lanette can be considered to be a coincidence rather than a true cross allergy. Moreover, the vast majority of the patients with emulsifier allergy were hypersensitive to many other agents, too.

Emulsifiers as surface active agents can be expected to cause irritant reactions in epicutaneous tests. By removing the tests after 24 hours and by reading the results three times during 4–5 days we were able to follow up the reactions at the test sites. Irritant reactions were at their strongest usually on the first day and as a rule faded away in 4–5 days. In fact, irritant reactions were found to be very few with the exception of triethanolamine.

In seven cases the clinical relevance of the reactions regarded as allergic was confirmed by producing an acute eczema using an ointment containing the particular emulsifier.

The concentrations used in this study were chosen according to the concentrations commonly used in o/w and w/o emulsions. Tested with an ordinary patch test method, triethanolamine is non-irritant up to 15 % (Bandmann & Dohn 1967). However, triethanolamine stearate tested at 5 % in petrolatum with the chamber method produced an irritation in 9.5 % of our cases.

Lanette can be tested undiluted (Bandmann & Dohn 1967). However, 20 % in petrolatum seems to be high enough to detect hypersensitivity.

One can only guess at the incidence of emulsifier allergy in other countries. Since the frequency of sensitivity to parabens and wool alcohols is higher in central and wes-

tern European countries and in the U.S.A. than in Finland (Hannuksela et al. 1976), reactions to emulsifying agents might also be more frequent outside Finland.

This study concerned only a few of the dozens of common emulsifiers. It seems worth examining the incidence of sensitivity to other emulsifiers, too, and the possible cross-reactions between them.

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