

ALLERGY TO WOOL FAT

The Addition of Salicylic Acid for Patch Test Purposes

PER THUNE

Considering the enormous use of cosmetic and dermatologic preparations in which lanolin finds almost universal application, allergy to wool fat (*adepts lanae*, wool wax, lanolin) must be extremely rare and reports of sensitivity to lanolin are scarce until recent years. Ramirez (16) first published a report of allergy to lanolin in 1929. Sulzberger and Morse (21) observed two cases in 1931. Sézary (18) mentioned sensitivity to lanolin in 1936 and Bonnevie (3) in 1939.

During the last 15 years some investigations indicate that allergy to wool fat is more frequent than previously believed to be the case. However the incidence varies considerably in published reports, i.e. from 0.25 per cent to 18.6 per cent (Table 1) in various patient groups. This presumably is due both to differences in patient selection and in test methods. Thus one material consists of contact dermatitis (1) and another of various dermatologic conditions (25). Wereide (27) added salicylic acid to anhydrous lanolin and eucerin; a high proportion of the patients had lower leg eczema. All the patients investigated by Reichenberger (17) had leg ulcer. The frequently observed allergy to topically applied medicaments in patients with venous leg eczema (10, 12) may explain why Wereide (27, 28) and Reichenberger (17) observed a higher incidence of allergy to wool fat. The results of the various investigations can therefore hardly be compared.

Allergic contact dermatitis due to topically applied medicaments is very common (1, 4, 11, 13, 19, 24, 27) and sensitivity to lanolin seems to be among the most important causes (4, 5, 11, 12, 22, 23, 28).

The alcohol fraction of wool fat probably contains the responsible allergens (20, 22). This is however not universally accepted (8). In 1953 Sulzberger (22) discovered the allergenic agent in the mixed lanolin alcohols. Everall and Truter (6) demonstrated in 1954 that the causative agent was a glassy solid. Subsequently, another weakly allergenic compound was isolated in pure crystalline form (23). Because of the low concentration of allergens in wool fat, the addition of 5 per cent salicylic acid has been advocated in order to enhance the penetration of allergens through the epidermal barrier (10, 12, 28) and in order to detect a low level of sensitivity. As a control, tests with 5 per cent salicylic acid in vaseline has been employed. The procedure of adding salicylic acid to wool fat for patch test purposes introduces a factor which is likely to produce false reactions. It is criticised by Fisher (7) who points out "that lanolin itself is added to ointments because it is more miscible with sebum and is more penetrating than petrolatum". Cronin (5) also suggests that the addition of salicylic acid to lanolin may cause false positive reactions. Bonnevie (3) introduced in 1939 patch tests with 5 per cent salicylic acid in lanolin as a routine

Table 1. *Reported incidence of sensitivity to lanolin and eucerin*

Author	Selection of patients	Substance tested	Number examined	Positive
Warshaw (25) (1953) N.Y.	Various dermatologic conditions	Lanolin	1430	15 (1.04 %)
Baer <i>et al.</i> (1) (1955) N.Y.	Contact dermatitis	Lanolin	637	11 (2.5 %) (4.4 % reacting)
Bandmann <i>et al.</i> (2) (1957) Munich	Eczema	Eucerin	4000	10 (0.25 %)
Hjorth (9) (1959) Copenhagen	Cosmetic allergy	Lanolin	550	21 (3.8 %)
Hjorth (12) (1961)	Eczema	Eucerin	1878	39 (1.8 %)
(1962)	Eczema	Wool alcohols	1664	27 (1.6 %)
(1962)	Eczema	Lanolin and deriv.	1664	38 (2.28 %)
Wereide (1965) Oslo	Eczema	Lanolin 5 % Eucerin sal. acid	512	55 (10.7 %)
Reichenberger (1965) Munster	Leg ulcer	Eucerin	150	28 (18.6 %)

procedure in order to reveal sensitivity to salicylic acid. Hjorth *et al.* (12) realised that most positive reactions to tests with salicylic acid in lanolin were due to the latter.

In our department patch tests with anhydrous lanolin and anhydrous eucerin—both with the addition of 5 per cent salicylic acid—have been included in our patch test series. Like other investigators (10, 12, 17, 28) we have found a considerable percentage of positive reactors to wool fat. The purpose of the present work has been to investigate:

1. The incidence of sensitivity to lanolin and eucerin.
2. The influence of the addition of salicylic acid to wool fat for patch test purposes.

3. The relationship between the patch test results and provocative testing.
4. The relation between lanolin and eucerin allergy.

Material and Method

A group of 230 patients with venous leg eczema (158 females and 72 males) were submitted to patch testing with anhydrous lanolin¹ and anhydrous eucerin² both with the addition of 5 per cent salicylic acid. As control test 5 per cent salicylic acid in vaseline was employed. The tests were left in place for 24 hours and read daily for at least four days. Criteria for a positive reaction were: erythema and infiltration lasting for more than 24 hours after removal of the patch.

¹ Pharmacopoea Nord. 1963.

² Supplied by Alf Nölke A/S, Oslo, composition: refined wool fat alcohols, 7 per cent in mineral soft paraffin; trade marke: Superhartolan (Croda Ltd., York, England).

Table 2. *Positive reactions to anhydrous lanolin and anhydrous eucerin with the addition of 5% salicylic acid in 230 patients*

Patch test results	Number of cases		
	Females	Males	Total
Adeps lanae positive Eucerin anhydr. pos.	7	3	10
Adeps lanae negative Eucerin anhydr. pos.	26	4	30
Adeps lanae positive Eucerin anhydr. neg.	1	2	3
Sum	34	9	43

The test site was the back or the anterior aspect of the thigh. The provocative test was performed by applying anhydrous lanolin and anhydrous eucerin without the addition of salicylic acid on eczematous skin for three days. Patch tests with anhydrous eucerin proper and with the addition of 2 per cent salicylic acid were performed on the outer aspect of upper arm.

Results

Out of 230 subjects there were 40 positive reactors to anhydrous eucerin with 5 per cent salicylic acid while 10 patients also reacted to anhydrous lanolin with 5 per cent salicylic acid and 3 patients only to lanolin with 5 per cent salicylic acid (Table 2). The sex distribution was: women 34/158 (21.5%), men 9/72 (12.5%).

Out of the 43 positive reactors to eucerin and lanolin—both with the addition of 5 per cent salicylic acid—only 16 subjects reacted to provocative tests with eucerin. Five of these 16 subjects showed positive provocative test also to lanolin. In other words, among 40 positive reactors to eucerin with 5 per cent salicylic acid only 5 reacted to provocative test with lanolin (Table 3). All the 16 patients with positive provocative tests reacted to patch tests with eucerin with 2 per cent salicylic acid. Three of them showed negative patch test with eucerin proper (Table 4). Unfortunately patch tests with 2 per cent salicylic acid in eucerin could only be performed in 33 out of the mentioned 40 positive reactors.

Among these 33 positive reactors to patch tests with eucerin with 5 per cent salicylic acid, only 26 showed positive reaction when 2 per cent salicylic acid was added to eucerin. Only 13 subjects reacted to patch tests with eucerin proper (Table 5).

There was a tendency of all the positive reaction to appear late. In 5 subjects delayed reactions appeared (after 5 days). Two patients showed infiltrate with hemorrhagic spots in reaction to eucerin with 5 per cent salicylic acid, but negative provocative test. One subject responded with bullae to patch test with lanolin proper. 3 patients showed positive reactions to 5 per cent salicylic acid in vaseline and are not included in the study.

Discussion

The patch test procedure varies from one clinic to another. Factors of importance when testing with wool fat are: the allergen concentration in the test substance (5, 12, 15, 28), the age of the sample (4), the test site and eventually the vehicle and the patient material. Eucerin has a higher content of allergens than lanolin.

Provocative patch tests to demonstrate sensitivity to weak allergens like lanolin etc. have been described by Kligman (14). He performed the provocative patch test by pre-treating the test site for one hour with an occlusive patch of 10% aqueous sodium lauryl sulfate. This technic is described as the "SLS provocative test".

Because of its long duration venous leg eczema is susceptible to allergic contact dermatitis. In the present material there is a preponderance of females. But even when this is taken into account it appears that females are more readily sensitized by wool fat than men are. This may be ascribed to a longer history of leg eczema and a more extensive use of lanolin containing cosmetics. It appears that only one of the 16 positive reactors to provocative test had a duration of eczema less than one year (Table 3). The low incidence of positive reactions to the provocative test procedure is noticeable. This test procedure is very sensitive and it is likely that it indicates

Table 3. Duration of eczema, sex distribution and results of provocative tests in 43 patients with positive reactions to anhydrous eucerin or anhydrous lanolin with 5 per cent salicylic acid

Duration of eczema in years	Females	Males	Eucerin with 5% salicyl. ac.		Eucerin provoc. test		Lanolin with 5% salicyl. ac		Lanolin provoc. test	
			Pos.	Neg.	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.
0-1	3	1	4	0	1	3	0	4	0	4
2-5	8	3	9	2	5	6	3	8	1	10
6-10	11	2	13	0	6	7	5	8	2	11
11-20	11	2	13	0	4	9	4	9	1	12
Above	1	1	1	1	0	2	1	1	1	2
Total	34	9	40	3*	16	27	13	30	5	39

* These patients had positive reaction to adeps lanæ with 5 per cent salicylic acid but negative provocative test. Adeps lanæ with 2 per cent salicylic acid was negative.

Table 4. Results of patch tests with anhydrous eucerin without and with the addition of 2 per cent salicylic acid in 16 patients who showed positive provocative tests

Number of patients	Patch tests	
	Anhydrous eucerin with 2% salicyl. ac.	Anhydrous eucerin as is
13	Positive	Positive
3	Positive	Negative

Table 5. Results of patch testing with anhydrous eucerin without and with the addition of 2 per cent salicylic acid and of provocative tests in positive reactors to anhydrous eucerin with 5 per cent salicylic acid

Test substance	Positive	Negative	Total
Anhydrous eucerin with 2% salicyl. ac.	26	7	33
Anhydrous eucerin as is	13	20	33
Provocative test with anhydr. eucerin as is	16	28	43

the real incidence of sensitivity. Presumably only 16 patients in this material were sensitive to wool fat; the remaining reactions probably were false positive ones.

There was an increasing number of positive reactors when testing with eucerin by itself, with provocative tests and with the addition of 2 per cent and 5 per cent sali-

cyclic acid (ratio being 13:16:26:33) as appears from Fig. 1. This supports the view that too many false positive reactions may occur when salicylic acid is added to wool fat. Eucerin provocative test show 16 positive reactors and lanolin provocative test only 5. This must be due to the higher content of allergens in eucerin. The dotted line in Fig. 1 indicates the real incidence of sensitivity.

Three patients reacted only to lanolin with 5 per cent salicylic acid, all other tests being negative. The reactions are probably false positive since the provocative test and the patch test with addition of 2 per cent salicylic acid were negative. In total 13 patients reacted to lanolin with 5 per cent salicylic acid and only 5 to provocative tests (Fig. 1). It must be presumed that 8 of the positive reactors to lanolin with 5 per cent salicylic acid are false positive reactors. It is probable that the patch test with eucerin by itself is the only patch test which shows the real incidence of sensitivity to wool fat alcohols although a few false negative reactions may occur. The few positive reactors to lanolin provocative tests indicate that eucerin is a stronger sensitizer than lanolin.

In this study of sensitivity to wool fat the number of subjects with positive provocative test amounted to 16 (6.9%) among 230 individuals with venous leg eczema. A much lower incidence can be expected in a total in-patient material and among the general population. Because of its wide-spread use an increasing incidence

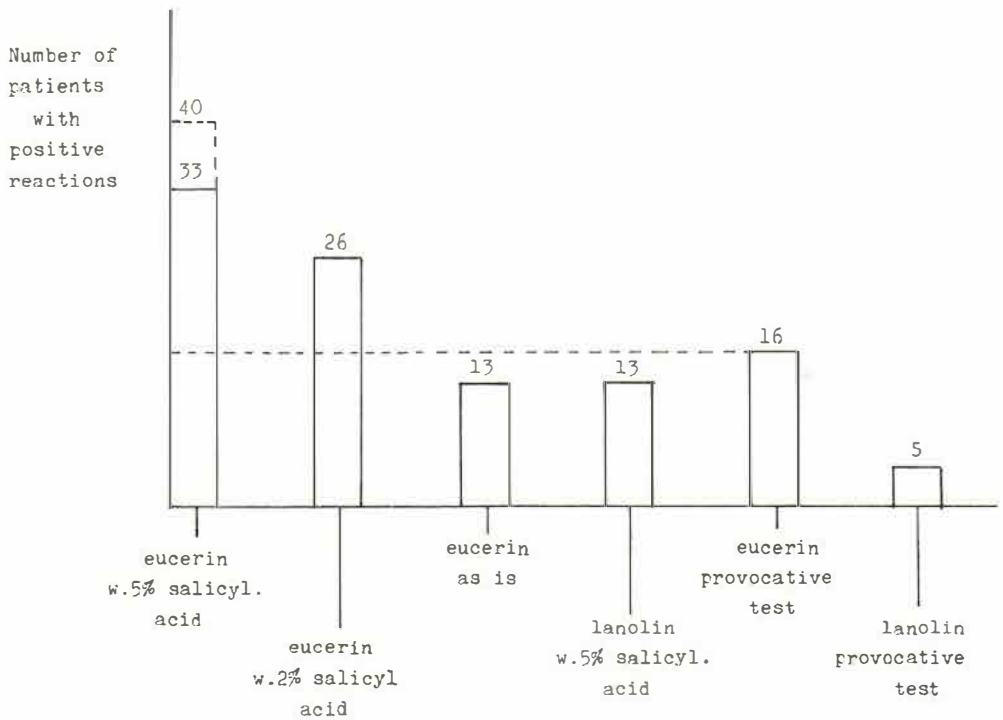


Fig. 1. Positive reactors to eucerin as is, eucerin provocative test and eucerin with the addition of 2 per cent and 5 per cent salicylic acid, and positive reactors to lanolin provocative test and to lanolin with 5 per cent salicylic acid.

of sensitivity to wool fat presents great problems to both physician and patient. Accordingly certain chemical modifications of lanolin with less allergenic properties are produced (12, 25, 26). However, the results of this investigation (see also table 1) indicate that there is reason to believe that the incidence is not increasing. The result differences are due to different test methods and the selection of the patient materials.

This study indicates that the addition of salicylic acid to wool fat yields false positive results. Even an addition of 2 per cent salicylic acid may produce false positive reactions. The control test has been performed with salicylic acid in vaseline which probably is less penetrating than lanolin. The control test should be performed with salicylic acid in a more penetrating vehicle as some of the patients may have false negative reactions to salicylic acid in vase-

line. Kligman (14) mentions that as a practical rule, petrolatum would seem to be the vehicle of choice for routine use. But he continues: "This will certainly not always be true."

Sensitivity to allergens which are present in lanolin and not in eucerin is very unusual. Due to the higher content of allergens in eucerin one might suggest that the patch test for wool fat sensitivity should be performed with eucerin as is with forty-eight hours exposure. In doubtful cases and when lanolin sensitivity is suspected provocative test should be performed.

SUMMARY

Out of 230 patients with venous leg eczema 40 reacted to anhydrous eucerin with 5 per cent salicylic acid and 13 to anhydrous lanolin with 5 per cent salicylic acid. Sixteen of the positive reactors showed posi-

tive provocative tests with eucerin applied on eczematous skin. Only 5 showed positive provocative tests with lanolin. Among the positive reactors 33 were patch tested with eucerin proper and with the addition of 2 per cent salicylic acid. The number of positive reactions were 13/33 and 26/33, respectively. The investigation indicates that the addition of salicylic acid to lanolin or eucerin may cause false positive reactions. Patch tests for wool fat sensitivity should be performed with eucerin as such.

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