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NEOMYCIN SENSITIVITY IN ATOPIC DERMATITIS AND OTHER ECZEMATOUS CONDITIONS

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Abstract. During the year 1965, 752 patients with different types of eczematous dermatitis and/or stasis leg ulcer were patch-tested with 50% neomycin sulphate in petrolatum. The incidence of positive reaction in the different categories of dermatitis has been compared. The figures do not support the view that the atopic state (as it occurs in atopic dermatitis patients) predisposes to neomycin sensitivity. Patients with stasis dermatitis of the lower leg had a significantly higher incidence of neomycin sensitivity than any of the other groups of eczematous dermatitis.

It has been suggested that contact allergy to neomycin is particularly frequent in atopic individuals (2, 6). Epstein (2) found evidence of atopy in more than 50% of 120 neomycin-sensitive patients and concluded that the atopic state predisposes to neomycin sensitivity. He also suggested that neomycin together with ragweed oil and nickel which have been observed to cause dermatitis particularly in atopics, might have a possible common denominator being responsible for the "dermal type" of contact sensitivity which they usually evoke.

If atopy predisposes to neomycin sensitivity, topical treatment of atopic dermatitis with neomycin-containing remedies should be expected to cause neomycin sensitivity more frequently than does this type of treatment in other dermatoses.

On the other hand, several authors have pointed out that patients with atopic dermatitis seem to have a lower tendency in general towards allergic contact sensitivity (8) as well as delayed type of sensitivity (dermal tests) to microbial antigens (3, 7) than in controls. This is in accordance with the present author's experience. Subjects suffering from long-lasting and wide-spread atopic dermatitis surprisingly seldom display signs of contact sensitivity to topical drugs when compared with other groups of eczematous patients. In our clinic, this appears to be valid for neomycin sensitivity also. This study was undertaken in order to elucidate whether patients with atopic dermatitis are more or less prone to develop neomycin sensitivity than other eczematous subjects.

MATERIAL AND METHODS

All eczematous patients referred to this department are tested with the same standard battery of patch tests, if contraindications are not present. The results are plotted on manual punch-cards. The incidence of positive reaction to neomycin during the year 1965 has been compared for different groups of eczematous dermatitis and stasis leg ulcer patients. The year 1965 was chosen because it was the first year of routine punch-card registration of patch tests. Neomycin-containing steroid ointments and creams were still in common use for eczema at that time in Norway, and had been so for several years. As from 1966, the prescription rate of such remedies has markedly decreased, as more general practitioners were subsequently informed that neomycin (used on eczematous skin) is a potent sensitizer. This is the reason why more recent material has not been included in the study.

Patch tests were carried out according to the Bloch-Jadassohn method, the test material being applied on the skin for 24 hours under cellophane discs of the Danish patch-testing tape Lysaplast Special. All tests were read 2 or 3 days after application, and when possible, the test sites were observed for up to a week. Neomycin sulphate 50% in petrolatum (w/w) was used as test substance. The full standard battery of patch tests employed (in 1965) is outlined in Table I.

The following were regarded as positive tests: skin reactions with papules or infiltrate and redness, vesicles or scaling occurring at 48 hours or later after application of the patch.

RESULTS

Out of the 752 eczematous patients tested, 37 responded with a positive neomycin reaction. The distribution among the different categories of ec-

Table I. *Standard series of patch tests employed in 1965*[a]

MEK = methyl ethyl ketone, w. = water, vas. = petrolatum.

1. Turpentine 25 % in olive oil
2. Colophony 40 % in MEK
3. Paraben esters (methyl-, ethyl-, propyl-, 5 % of each) in vas.
4. Nickel sulphate 5 % in w.
5. Formaldehyde 3.5 % in w.
6. Primula obcon. (leaf)
7. Potassium dichromate 0.5 % in w.
8. Quinine chloride 1 % in w.
9. Mercuric nitrate 0.03 % in w.
10. Iodine 0.5 % in alcohol
11. Phenyl mercuric acetate 0.03 % in alcohol
12. Balsam of Peru 25 % in MEK
13. Wood tars 20 % in MEK
14. Coal tar 20 % in MEK
15. Amino-azotoluene 2 % in MEK
16. *p*-Phenylene-diamine 2 % in MEK
17. *p*-Amino-phenol 5 % in vas.
18. 2-Mercaptobenzothiazole 1 % in vas.
19. Tetramethyldiuramdisulphide 1 % in vas.
20. Neomycin sulphate 50 % in vas.
21. Benzalkonium chloride 0.1 % in w.
22. Wool fat with 5 % salicyl. acid in vas.
23. Vaseline (petrolatum) with 5 % salicylic acid.
24. Eucerin with 5 % salicylic acid in vas.

[a] More recently, the following substances have been included: Hexachlorophene, Trichlorocarbanilide and Bisthionol. Benzocaine, Procaine, Percaine and Lidocaine. Cobalt chloride. Diglycidyl ethers (epoxy). Wool fat alcohols.

zematous dermatitis and stasis leg ulcer cases is presented in Table II.

With the exception of group F (primary irritant dermatitis, nummular eczema etc.), the incidence of neomycin sensitivity (judged by positive patch tests) was lower in the atopic dermatitis group than in any of the others. However, the difference between the groups of atopic and seborrheic dermatitis is not statistically significant. Neither is the difference significant when the atopic dermatitis cases are compared with the cases of allergic contact dermatitis and group F together. This combined group (B + F) is supposed to be a more satisfactory control group than B alone, since group F are in a way the remainder when positive patch test cases have been classified as belonging to the group B. The incidence of positive neomycin patch test in the group B + F is 12 out of 468 cases, i.e. 2.6 %.

Thus, the risk of neomycin sensitivity appears to have been almost equal among the present series of eczematous patients, when the cases of lower leg stasis dermatitis are excepted. The latter (C + D) showed a greatly increased incidence of neomycin sensitivity when compared with the others, and this difference is highly significant ($p < 0.01$).

The atopic dermatitis group had a lower incidence of positive neomycin patch test (2/88 = 2.3 %) than the remainder of the material as a whole (35/664 = 5.3 %). This difference, however, is not statistically significant ($\chi^2 = 0.92$, $p > 0.1$).

DISCUSSION

Conceivably, the present group of atopic dermatitis patients have been treated with topical neomycin approximately to the same extent as the other eczematous cases, when those with leg ulcer and stasis dermatitis are excluded. A comparison of the incidence of positive neomycin patch test in the groups A, B + F and E (Table II) should therefore reflect any significant difference in predisposition for neomycin sensitivity between the groups. However, no such difference was found.

Table II. *Neomycin sensitivity in consecutive patients patch-tested through 1965*

Case category	Patients tested			Neomycin positive		
	F	M	F + M	F	M	F + M
A. Atopic dermatitis	48	40	88	1	1	2 (2.3 %)
B. Allergic contact dermatitis	147	142	289	8	4	12 (4.2 %)
C. Stasis dermatitis (leg) without ulcer	21	27	48	3	6	9 (18.8 %)
D. Stasis dermatitis (leg) combined with ulcer	22	18	40	4	4	8 (20.8 %)
E. Seborrheic dermatitis	40	43	83	1	2	3 (3.0 %)
F. Primary irritant dermatitis, nummular eczema etc.	94	85	179	0	0	0
G. Stasis ulcer (leg) without present dermatitis	16	9	25	3	0	3 (12.0 %)
Total	388	364	752	20	17	37 (4.9 %)

Several authors have underlined the pronounced tendency of lower leg stasis dermatitis to develop contact allergy to the topical drugs used on it (5, 9). That this also applies to neomycin is clearly supported by the figures of the present study.

Neomycin is poorly resorbed through a normal epidermal barrier, but penetrates more easily through the disturbed barrier of eczematous skin. Hjorth et al. (4) have demonstrated that the risk of sensitization to neomycin is greater with a greasy ointment than with a vanishing cream. This might be due mainly to the more occlusive effect of an ointment, enhancing penetration. In patch tests on symptom-free skin, neomycin must be applied in a rather high concentration, if false negative reactions are to be omitted. We have not encountered false positive reactions with 50% neomycin in petrolatum. By testing with dermal injections, the test concentration might be as low as 1/1000. When neomycin is applied epicutaneously on healthy skin, the transfollicular way of penetration will dominate. Thus, in a positive patch test, the tissue response might consequently be more dermal than epidermal. Contact allergy to neomycin is unlikely to be immunologically different from other delayed type allergies maintained by committed lymphocytes. That the inflammatory reaction in patch tests is often more dermal with neomycin than with many other allergens, might well be explained by a different localization of the optimal concentration of conjugated hapten within the tissue, dependent on physico-chemical properties of the allergen, included its route of penetration. Even when primarily a neomycin patch test reaction is purely dermal, it will later become more epidermal with scaling or crusts, if the sensitivity, as well as the test concentration, is of sufficient magnitude. Thus the concept of "dermal type" contact allergy to neomycin (1) is probably more confusing than helpful.

Provided that the diagnosis of atopic dermatitis in the present series of patients can be accepted as a valid criterion for the atopic state, this study does not support the view that atopy per se predisposes specifically to contact allergy to neomycin.

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