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COMPARISON OF PATCH TEST RESULTS IN TWO ADJACENT AREAS OF ENGLAND. II. MEDICAMENTS

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Abstract. A 3-year study of patch test reactions to the Standard European Battery (S. E. B.) has been carried out in two adjacent areas of South-east England with the same climatic and cultural background. The source of materials and method of testing were identical; all observers have worked together in the same Contact Dermatitis Clinic and the interpretation of reactions can therefore be considered to be consistent. The main differences between the two areas lay in the pattern of employment and in local prescribing habits. Only the second aspect is considered here. Seven allergens—lanolin, neomycin, parabens, iodochlorhydroxyquinoline, ethylene diamine, caine 'mix' and chlorocresol—accounted for approximately 30% of all positive patch test reactions. 'Medicament sensitivity' correlated well with the known prescribing haibts of both regions. Certain sites were shown to be especially important in the pathogenesis of medicament contact sensitivity.

Key words: Patch test results; Regional differences; Medicaments; Prescribing habits; Site differences

In a previous paper (1), we compared patch test results with respect to industrial allergens in two adjacent areas of South-east England. In this paper, we shall discuss those allergens included in our Standard Patch Test Battery that are concerned with medicament sensitivity. We have already mentioned the difficulty of making valid comparisons unless the racial, climatic and cultural background of the sample is known and unless the sample is 'matched' with respect to selection of material. We have attempted to do this by means of our 'MOHL' index (Table I). This specifies the percentage of *M*ales, the number of *O*ccupational cases and the percentage of patients with either *H*and eczema or *L*eg ulcers/stasis eczema included in our series.

Medicament sensitivity has been the subject of many reports (2, 3, 6, 10, 14, 15, 20, 24, 29); several have drawn attention to the importance of allergic contact dermatitis in patients with leg ulcers or stasis eczema (1, 4, 5, 9, 13, 19, 21, 25). Others have studied the incidence of allergic contact dermatitis among patients with pressure sores (27) or in those with atopic dermatitis (8, 12, 26). Although the overall level and pattern of medicament sensitivity varies from country to country (12, 24), probably as the result of differences in prescribing habits and usage, certain compounds are common universal sensitizers. Sensitivity to ethylenediamine is closely related to the prescribing of Mycolog/Triadcortyl cream (10, 22, 29) and this close relationship between prescribing habits and sensitivity has also been demonstrated for several other medicaments.

Dermatological prescribing in Great Britain tends to follow the pattern set by the local consultant dermatologist and consequently varies from area to area. Oxford has always used more neomycin, Aureomycin and Triadcortyl cream than High Wycombe where iodochlorhydroxyquinoline preparations were preferred. We were interested to see, therefore, how such differences might be reflected in our patch test results.

MATERIALS AND METHODS

The study embraced the three years 1975 to 1977, during which 1 680 patients were patch-tested with a standard patch test battery. Materials and technique were similar in both areas and interpretation was made rather easier by the fact that all three authors had worked together. The allergens (Trolab) were applied in strips of five or six, on the back, using Al-strip which was secured with occlusive non-allergenic tape. They were removed at 2 D and subsequently read again at 4 D.

The type and selection of material was, broadly speaking, similar in both areas—the patients being referred from general practitioners or other hospital clinics. The main differences in our patient selection are shown in Table I. Both centres have a specialized leg ulcer clinic and routinely patch-test these patients. There was a small but significant group of patients with anogenital pruritus who were patch-tested at High Wycombe, accounting for just over 4% of all patients tested. This group was not significantly represented at Oxford.

Table I. *'MOHL' index*

An analysis of 1680 patients patch tested at Oxford and High Wycombe, 1975–1977

	Oxford	High Wycombe
Total number of patients tested	651	1 029
Positive reactors (%)	38.4	42.5
Males (%)	40.6	36.2
Occupational (%)	26[a]	18
Hand eczema (%)	32[a]	28
Stasis eczema/leg ulcers (%)	20[a]	13[a]

[a] Mid-term assessment 1976/77.

RESULTS AND COMMENTS

Patch test results for seven medicament allergens are shown in Table II. Balsam of Peru, wood tar and PPD have not been included in view of the difficulty in knowing whether they relate to medicament or cosmetic exposure.

We have attempted to relate our patch test findings to the gross consumption of neomycin-containing, vioform-containing and ethylenediamine-containing medicaments prescribed by the central hospitals of both areas (Table III). Leg ulcers have been analysed separately (Table IV) and, at High Wycombe, it was also possible to separate off those patients with pruritus ani/pruritus vulvae. A comparative site/sensitivity analysis is shown in Fig. 1.

Medicament sensitivity is now the most important cause of allergic contact dermatitis in our region, accounting for 36% of all positive patch test results (to S. E. B.) in the Oxford area and 27% of all positive patch test results at High Wycombe. Certain sites have been shown to exhibit a significantly higher level of medicament contact sensitivity and even weak potential allergens should probably be avoided in these body regions.

Lanolin was an important sensitizer in both areas and was especially common in women. This female predominance persisted even when leg ulcers were analysed separately. The reason for this is not known but it may reflect past or concomitant lanolin exposure (17). Jordan & King (16) have suggested, on the basis of repeated insult tests, that for some allergens women may be more easily sensitized than men.

Neomycin was also an important sensitizer, especially in the Oxford area where more neomycin-containing preparations were used.

Sensitivity to parabens is now quite common in our region and appears to be higher than elsewhere. This may relate to the large number of patients with leg ulcers included in our series or to the traditional use of paste bandages for this group of patients. Aureomycin cream (containing a high percentage of parabens) was also widely used in the Leg Ulcer Clinic at Oxford at this time.

Sensitivity to ethylenediamine was, as expected, higher at Oxford; it was also more common among men. We can confirm that ethylenediamine sensitivity is almost always associated with the use of Triadcortyl/(Mycolog) cream. Twelve out of 13 patients that we investigated had used this product. We have not found any cross reactivity with EDTA (23) and in this respect we are in agreement with other authors (11, 22, 28); nor have we found it to be a significant industrial allergen in our area.

Iodochlorhydroxyquinoline preparations are widely used in both areas for the treatment of leg ulcers (Quinaband) and in combinations with steroids. Considering the amount used, it appears to have a relatively low sensitizing potential.

Table II. *Results of patch testing (Standard European Battery) medicaments—Oxford and High Wycombe, 1975–1977*

	Oxford, %			High Wycombe, %		
Allergen	M (267)	F (384)	Total (651)	M (373)	F (656)	Total (1 029)
Wool alcohol	6	7.3	6.8	4.6	7	6.1
Neomycin	4.5	6	5.4	4.3	2.3	3.0
Parabens	3	5.5	4.5	2.1	3.0	2.7
Ethylene diamine	4.7	1.4	2.7	1.9	0.9	1.3
Caine mix	1.9	2.6	2.3	4.3	1.8	2.7
Quinoline	1.5	2.3	2	2.7	1.1	1.6
Chlorocresol	0.5	1.1	0.8	1.3	0.3	0.7

Table III. *Comparison of topical prescribing habits in Oxford and High Wycombe districts 1976–1977*

Annual consumption (central hospital pharmacies) in kg

	Oxford	High Wycombe
Neomycin and related topicals	12.8 (3.6[a])	8 (7.9[a])
Iodochlorhydroxyquinoline (Vioform, Chinoform) containing topicals	6.1	12.3
Ethylene diamine containing topicals	1.8	Nil

[a] Gentamycin-containing topicals.

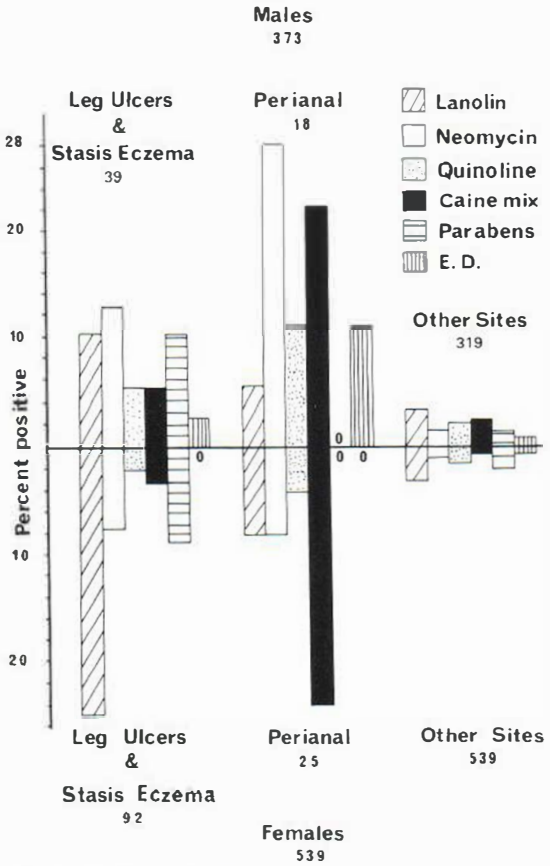

Fig. 1. Medicament sensitivity according to site in 1 029 patients.

Caine 'mix' sensitivity was a characteristic feature of patients with anogenital pruritus. Chlorocresol was not a significant sensitizer in either area and has shown no increase over successive years (30).

The reason why many medicament sensitivities were more common among men at High Wycombe remains obscure.

It can be seen from Fig. 1 that the legs and perineum were especially vulnerable as regards the development of allergic contact dermatitis to medicaments. Other sites, including the hands and face, were far less important.

The pattern of sensitivity in these sites has certain regional characteristics. Parabens and lanolin sensitivity was a feature of patients with leg ulcers and stasis eczema and sensitivity to these two substances was especially high during 1976 at Oxford when routine patch testing of all leg ulcer patients was first introduced. Sensitivity to neomycin and iodochlorhydroxyquinoline was as common in patients with perineal conditions as in those with stasis eczema. Sensitivity to local anaesthetica occurred chiefly in patients with anogenital dermatitis. Why parabens sensitivity was so uncommon in this latter group remains unclear.

CONCLUSION

Medicament sensitivity is now the single largest cause of allergic contact dermatitis in our two areas.

Table IV. *Patch test results in patients with leg ulcers and stasis eczema 1975–1977*

	Oxford, %			High Wycombe, %		
	M (11)	F (34)	Total (45)	M (36)	F (92)	Total (128)
Wool alcohol	9	32	26.7	11.1	26.1	21.9
Neomycin	27.3	26.5	26.7	16.6	7.6	10.2
Parabens	9	20.6	17.8	11.1	9.8	10.2
Quinoline	9	11.8	11.1	5.6	1.1	2.3
Ethylene diamine	18	5.9	8.9	2.2	0	1.6
Chlorocresol	9	2.9	4.4	0	1.1	0.8

Seven allergens—lanolin, neomycin, parabens, caine 'mix', ethylenediamine, iodochlorhydroxyquinoline and chlorocresol—account for approximately 30% of all positive reactions obtained.

Neomycin and ethylenediamine sensitivity correlated well with the known prescribing habits of both regions.

Site of application was important. Two sites—the lower legs in patients with leg ulcers or stasis eczema and the perineum in those with pruritus ani or pruritus vulvae were especially prone to develop allergic contact dermatitis to medicaments. The pattern of sensitivity was often characteristic, lanolin and parabens being the most common allergens in patients with leg ulcers and sensitivity to local anaesthetics occurring chiefly in those with anogenital dermatitis. Neomycin and iodochlorhydroxyquinoline sensitivity was seen in both groups.

The high level of neomycin sensitivity reflects its widespread usage as a topical antibiotic. Lanolin sensitivity may relate to both medicament and cosmetic usage. The fact that this sensitivity was more prevalent among women suggests that total lanolin exposure may be a factor. Considering their widespread usage, both iodochlorhydroxyquinoline (Vioform/Chinoform) and chlorocresol appear to be relatively safe antibacterial agents. 'Caine' sensitivity was predominantly seen in patients with perineal pruritus. Sensitivity to ethylenediamine was nearly always due to the use of Triadcortyl/(Mycolog) cream.

The risk of medicament contact sensitivity could be reduced if certain strong sensitizers were avoided and if other potential sensitizers were not used on especially vulnerable sites. The principle of 'allergen replacement' (7) is already well established in industry and should now, perhaps, be extended to the field of topical prescribing.

The value of this study is obviously limited by the number of patients whom we were able to patch test during the period under review. This could not have been lengthened without destroying some of the tenets on which the study was based. However, we think that an analysis of the type that we have attempted does at least confirm the importance of local prescribing habits in the pathogenesis of medicament contact dermatitis and re-emphasizes how the selection of material affects the results obtained (18).

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