Topical Immunotherapy of Alopecia areata. A Follow-up Study
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Ninety-six patients suffering from alopecia areata have been treated with topical immunotherapy. Fifty-one have been treated with dinitrochlorobenzene and 45 with squaric acid dibutylerster. Analysis of our group showed that 55 patients out of those 96, who entered the study, experienced hair regrowth during a period of 6-17 weeks of treatment. Of these 55 patients, 25 (45.4%) had a recurrence of AA and 30 (53.6%) had a persistent regrowth during a follow-up of 16 months-6 years. The severity and early development of flare-up and induced allergic contact dermatitis have been the principal factors that have influenced the clinical results. Key words: Squaric acid dibutylerster; Hair regrowth. (Received August 6 1985.)
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The treatment of alopecia areata (AA) by immunotherapy was initiated by Rosenberg (1) with local applications of dinitrochlorobenzene (DNCB). Subsequently other authors have reported their results about DNBC treatment of AA. Some publications have reported good results in 60-80% of the cases (2-6) and others have reported less encouraging conclusions with positive results only in 20-25% (7-9). In the last few years the squaric acid dibutylerster (SADBE), another potent contact sensitizer, has been employed in the AA treatment with conflicting results (10-14). The purpose of this paper is to report our experience on DNBC and SADBE treatment of AA in a follow-up study and to identify the factors affecting treatment prognosis.

MATERIALS AND METHODS
The study comprised 96 patients with a persistent refractory AA. The group included 52 males and 44 females ranging in age from 5 to 61 years. There were 3 patients with alopecia universalis (AU), defined as loss of all scalp and body hair; 23 with alopecia totalis (AT), defined as loss of all scalp hair, and 50 with localized AA, 30 of whom had more than 30% of the scalp involved. All patients had been resistant to previous therapy included topical, intramaskal and systemic steroids, anthralin ointment and ultraviolet therapy in someone. No patients had received topical or systemic therapy for AA within 8 weeks from the beginning of the treatment. Patients were informed of the investigative nature of the treatment and informed consent was obtained in each case. Before topical therapy routine standard series examinations were made in each patient.

DNCB and SADBE solutions at different concentrations were prepared using acetone as solvent. Sensitizations was obtained with a 0.1 ml of the 2% solution applied to the forearm. After the sensitization the applications were made weekly and the DNBC and SADBE concentration was adjusted to the patient’s reactivity against the allergens, in order to maintain a contact dermatitis without blistering, oozing and crusting.

RESULTS
The values of laboratory tests were in the normal range before and after 15 weeks of treatment. Ten of the 96 patients, who entered the study, gave up the treatment after 3-5 weeks. Fifty-one patients have been treated with DNBC and 45 patients with SADBE.
Table I. Alopecia universalis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>DNCB = 13 → hair regrowth = 2</th>
<th>1 recurrence after 1 year</th>
<th>1 persistent hair after 4 years</th>
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<tr>
<td></td>
<td>SADBE = 10 → hair regrowth = 4</td>
<td>2 recurrences</td>
<td>2 persistent hair after 2 years</td>
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**Alopecia universalis**

In this group 13 patients have been treated with DNCB and 10 with SADBE. Of the 13 patients treated with DNCB the compliance has been obtained in 12 cases; in these patients we have observed hair regrowth in 2 during a period of 10.0±2.83 weeks of treatment. One of these 2 patients had AA recurrence after 1 year from the end of treatment, the other showed diffuse and persistent hair growth in a period of 4 follow-up years. Of the 10 patients treated with SADBE the compliance has been obtained in 9 subjects. The hair regrowth has been observed in 4 cases after 10.2±2.06 weeks of therapy, and the relapse occurred in 2 patients during the treatment, after a partial regrowth. In the other 2 cases the hair growth was present 2 years after the end of the treatment (Table I).

**Alopecia totalis**

Ten patients of this group have been treated with DNCB and 13 with SADBE. Among the 10 patients treated with DNCB, the compliance has been obtained in 7 cases. We have observed the hair regrowth in 5 patients during a period of 13.4±7.27 weeks of treatment and in 2 patients we have observed a relapse 1 year after the end of therapy. The other 3 patients showed persistent hair growth after 4–6 years of follow-up. Out of the 13 patients treated with SADBE, we had the compliance in 12 subjects and the hair regrowth in 4 cases during a period of 17.0±8.25 weeks of therapy. The AA recurrence occurred in 3 patients (Table II).

**Localized AA**

In this group 28 patients have been treated with DNCB and 22 with SADBE. Of the 28 patients treated with DNCB we had the compliance in 25 cases and hair regrowth in 23 patients during a period of 9.78±6.11 weeks of treatment. The relapse occurred in 10 patients; the other 13 subjects of this group showed persistent hair growth in a period of 4.3±1.76 years of follow-up. Of the 22 patients treated with SADBE, the compliance has been obtained in 21 cases and hair regrowth in 17 subjects during 10.1±4.20 weeks of treatment.

Table II. Alopecia totalis

<table>
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<th>Treatment</th>
<th>DNCB = 10 → hair regrowth = 5</th>
<th>2 recurrences after 1 year</th>
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<tr>
<td></td>
<td>SADBE = 13 → hair regrowth = 4</td>
<td>3 persistent hair after 4–6 years</td>
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treatment; we have observed a relapse in 7 patients. In 10 patients the hair growth was persistent after 14 months from the end of the therapy (Table III). In our patients no predictive value for hair regrowth has been assigned to a family or personal history of atopy, to family history of AA and to other aspects of the personal pathology history.

DISCUSSION

In our long-term follow-up study the therapeutic results obtained with DNCB are essentially the same as those obtained with SADBE: this is probably due to the fact that mechanism of action is a contact allergy rather than a systemic pharmacologic effect. Analysis of our group showed that 55 patients out of those 96, who entered the study, experienced hair regrowth during a period of 6–17 weeks of topical immunotherapy. Of these 55 patients, 25 (45.4%) had a recurrence of AA, and 30 (53.6%) had a persistent regrowth during a follow-up of 16 months–6 years. In previous studies some authors (8, 9, 10) had attempted to determine the criteria that might influence the clinical results of AA treatment with contact sensitizers. In their experience the duration of AA appears to play a certain role.

De Prost (8) and Temmerman (9), using DNCB, reported that good results were obtained in patients who had AA for less than 2 years. Happle (10), using SADBE, suggested that AA duration has some influence on the rate of response, but this point should be clarified in a larger series. In our experience the severity and early development of flare-up and induced allergic contact dermatitis have been the principal factors that have influenced the clinical results.

We have noticed better results in patients whom we have classified as high responders; in such patients the mean time of the appearance of flare-up was 2 weeks. It is remarkable that in this group 3 patients with AU showed complete hair regrowth even in untreated pubic, axillary and superciliary areas. Other important factors for the success of topical immunotherapy of AA are the duration of disease and the age of first manifest onset (mean 20.3 years). In general we have obtained less good results in patients who displayed the AA during the first 10–15 years of life (mean 11.9).

In our follow-up the familial or personal history of atopy and AA in close relatives have not influenced the clinical results. In the light of our findings we can say that topical immunotherapy is useful in some selected cases of AA.

REFERENCES


Erythema elevatum diutinum and Pre-AIDS

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Erythema elevatum diutinum (EED) is a chronic disease with symmetrical persistent erythematous nodules and plaques primarily in an acral distribution. EED is often associated with infections, especially of streptococci. An immunological reaction has been proposed as pathogenetic mechanism. We describe a patient, who developed EED secondary to a LAIV/HTLV III positive lymphadenopathy syndrome. Immunological investigation of a skin lesion and a lymph node biopsy is described. Key words: Monoclonal antibodies; Immunological investigation; Skin biopsy; Lymph node biopsy. (Received December 12, 1985.)

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Erythema elevatum diutinum (EED) is a rare chronic inflammatory dermatosis. Clinically it is characterized by symmetrically localized erythematous or purple nodules and plaques typically present on the extremities across the shins and buttocks. The nodules are often painful or burn, but frequently nonpruritic. The etiology is unknown. Histologically, the lesions are characterized by vasculitis with endothelial swelling, eosinophilic fibrinoid deposits, and a perivascular predominantly inflammatory infiltrate.