

Epidermal Rupture Is the Initiating Factor for the Koebner Response in Psoriasis

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The Koebner phenomenon was studied using low pressure suction and/or sellotape stripping. Each of 10 patients with psoriasis had 5 suction blisters induced and sellotape stripping. In each patient the roof of 4 of the 5 blisters was removed. In 6 of the 10 patients, psoriasis developed where the blister roof was removed, but not where the blister was left intact. However, only 3 of these 10 patients were also Koebner-positive at the tape-stripped site. Similarly, in a group of 37 psoriasis patients who were sellotape-stripped alone, only 8 (21.6%) were Koebner-positive at the tape-stripped site. In another experiment, 5 suction blisters were produced in each of 4 patients. The roof of 4 blisters was removed, one of which was occluded. Psoriasis developed in 3 of the 4 patients, but only where the blister roof had been removed and left unoccluded. These findings suggest that rupture of the epidermis can initiate the Koebner response, but that secondary dermal events are necessary for a psoriatic lesion to form.

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The Koebner phenomenon, in which injury can lead to the development of psoriatic lesions in susceptible individuals, is a useful experimental model for the study of the pathogenesis of psoriasis. However, only about 25% of patients give a positive response at any given point in time, and the numerous methods used to induce skin damage are difficult to standardize. Sellotape stripping, which has often been employed in studies on the Koebner response, had been assumed to produce only epidermal injury via removal of the stratum corneum. However, it is well known that sellotape stripping can cause surrounding erythema and the development of purpuric spots, i.e. dermal injury, but the number of strips needed to produce this effect varies from patient to patient. It has been

argued therefore that injury to both epidermis and dermis is necessary to produce a positive response (1, 2).

Sellotape-stripped sites on normal controls were therefore examined histologically for evidence of both epidermal and dermal damage.

Slow continuous suction is a method not previously used to investigate the Koebner response. However, it was used in this study because it is easy to standardize, and because preliminary experiments suggested that this method gave a greater frequency of positive Koebner responses (when the blister roofs were removed) than sellotape stripping did. Separation of the epidermis from the dermis by suction occurs between the basal cells and the basal lamina, with rupture of the hemi-desmosomes; no ultrastructural change in the epidermal cells, basal lamina and dermal components including blood vessels is observed (3). In addition, there is no evidence of inflammation or autolysis, suggesting that the injury is confined to the epidermal compartment of the skin (3). By removing the roof of some of the blisters (with or without occlusion) and leaving others intact, rupture of the epidermal layer as a possible initiating factor for the Koebner response could be studied.

METHODS AND PATIENTS

Subjects

Five normal volunteer subjects and 51 patients with psoriasis were studied. The controls comprised 1 female and 4 males, age range 27-55 years. Of the psoriatic patients, there were 28 females and 23 males, age range 20-80 yrs.

Methods

Sellotape stripping. This was carried out on an area of 3 cm² of the abdomen (when suction blisters were induced on the same occasion) or back, using standard sellotape. Stripping was continued until erythema and glistening had been produced; the number of strips needed to produce the same end point varied between 30 and 80.

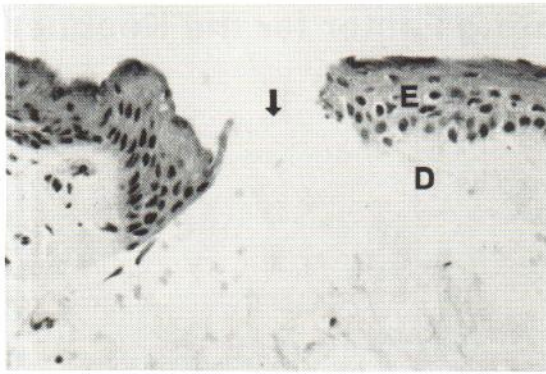


Fig. 1. Histology of normal skin after sellotape stripping. Arrow denotes epidermal cleft extending to dermis. E, epidermis; D, dermis.

Suction. This was performed on the abdomen, using a plastic cup with five holes, each with a diameter of 8 mm. The pressure applied was 200 mm of mercury and was maintained until blisters became visible, which took from 1 1/2 to 2 1/2 h.

Experiment 1

Thirty-seven patients had sellotape stripping performed to determine the incidence of Koebner positivity and the nature of the psoriatic lesions produced. Patients were seen subsequently at 2-weekly intervals for up to 8 weeks.

Experiment 2

Five controls had sellotape stripping performed and 3 mm punch biopsies taken to determine the nature of the injury. The biopsies were fixed in formol-saline and stained with haematoxylin and eosin.

Experiment 3

Suction-induced blisters and sellotape stripping were performed simultaneously on 10 patients with psoriasis. The roofs of the blisters were removed from 4 and left intact on 1 of each set of 5 blisters.

Experiment 4

Suction blisters were produced in 4 patients. Of the five blisters produced in each patient, the roof was removed from 4 and left intact on 1. One of four blisters from which the roof had been removed was occluded for 2 weeks with a Finn chamber used for routine patch testing.

The patients in experiments 3 and 4 were assessed clinically for the appearance of psoriasis, as shown by increasing thickness, erythema and scaling at the sites of injury, at weekly intervals for a 4-week period.

RESULTS

Tape stripping

Experiment 1. In 8 of the 37 patients (21.6%), psoriasis occurred at the site of sellotape stripping. In each

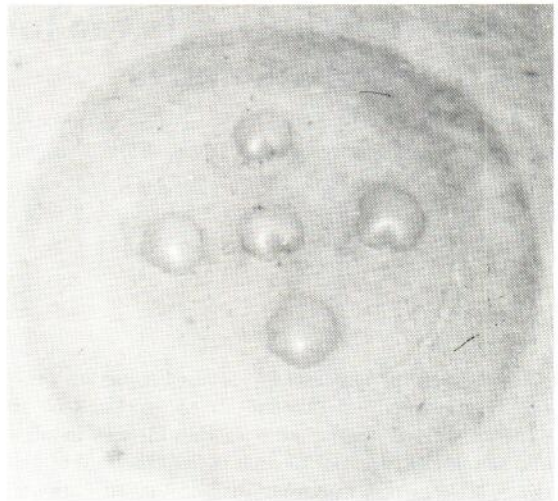


Fig. 2. Intact blisters immediately after induction by low pressure suction for 1 1/2 h.

case the psoriasis was punctate and did not involve the whole area which had been stripped. Psoriasis was clinically evident in all 8 patients by 4 weeks after stripping.

Experiment 2. Biopsies taken from 5 normal individuals immediately after stripping showed loss of the stratum corneum and epidermal clefts, extending to the dermis (Fig. 1).

Suction blisters

Experiment 3. In 6 of the 10 patients, psoriasis was evident by 4 weeks at the site of the blisters whose roofs were removed (Figs 2, 3). The psoriasis was distributed evenly over the blister site and did not extend beyond it. However, psoriatic lesions did not develop in any of these 6 patients where the blisters were left intact (Fig. 3).

Three of the 6 patients demonstrated to be Koebner-positive by suction blister induction also developed psoriasis at the sites of sellotape stripping. However, the other 3 patients did not (Table I). The lesions in the stripped sites were distributed in a punctate pattern.

Experiment 4. In 4 patients who each had 5 suction blisters, the roofs of 4 blisters were removed (one of which was subsequently occluded), and 1 blister was left intact.

Three patients developed psoriasis where the blister roof was removed and left uncovered. However,



Fig. 3. Suction blisters 3 weeks after induction. Psoriasis developed in the sites of the four outer blister whose roofs were removed (double arrow), but not in that of the central blister which was left intact (single arrow).

lesions were not observed in these same patients where the blister roof was removed and subsequently occluded, or where the blister was left intact (Table II).

DISCUSSION

This study has shown that the Koebner response can be initiated by rupture of the epidermal layer subse-

Table I. Incidence of Koebner response in sellotape stripping and suction-induced blisters

Patient no.	Suction blister		Sellotape stripping
	Roof removed	Roof intact	
1	+	-	+
2	+	-	+
3	+	-	+
4	+	-	-
5	+	-	-
6	+	-	-
7	-	-	-
8	-	-	-
9	-	-	-
10	-	-	-

Table II. Koebner response to intact roof, roof removed, and/or occluded suction blisters

Patient no.	Suction blister		
	Roof intact	Roof removed	Roof removed but occluded
11	-	+	-
12	-	+	-
13	-	+	-
14	-	-	-

quent to induction of a blister by slow suction, and that this type of injury is more effective than sellotape stripping. Second, and more importantly, it has been demonstrated that with the same initial injury, psoriasis will only develop if the roof of the blister is removed; intact blisters or those with the roof removed and subsequently occluded do not become psoriatic.

The less effective induction of the Koebner response by sellotape stripping compared with that of low-pressure suction (only half of the patients who were Koebner-positive after suction developed lesions at a tape-stripped site) may be related to variations in the degree of epidermal injury induced by this method. Thus psoriasis develops in a punctate rather than confluent pattern, possibly at the site of epidermal clefts; simple removal of the stratum corneum does not appear to be a sufficient stimulus for induction of psoriasis.

The observation that, when the blisters were left intact or the blister bed was occluded, the Koebner response was negative, whereas when the blister roofs were removed and left unoccluded, the Koebner response was positive in the same patient at the same time, may be explained by the results of a classic experiment by Kiistala et al. (4) who studied the influx of inflammatory cells into the fluid of suction blisters. These authors demonstrated that a small break in the epidermal roof will induce a significantly greater influx of neutrophils and mononuclear cells into the blister fluid than if the blister is left intact, and that this is further increased in the presence of antigen (4). This is probably due to the release of chemotactic factors such as Epidermal Thymocyte-activating Factor (ETAF), a process that may be inhibited by occlusion. Indeed, when wounds are occluded rather than left exposed, there is a considerable reduction in the influx of inflammatory cells into

the wound (5). In addition, Langerhans' cells within the ruptured epidermis may be stimulated by antigens in the environment to produce increased amounts of the T cell chemoattractant II-1; presentation of such antigens to T lymphocytes would result in the latter's activation (6). Stimulation of epidermal cell growth by products of these activated T cells, as proposed by Valdimarsson et al. (7), could then result in the initiation of a psoriatic lesion.

Thus the results of this study appear to show for the first time that rupture of the epidermis will provoke a Koebner response in those patients who are susceptible; the ensuing development of psoriasis is likely to be mediated by inflammatory cells that invade the site.

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