

Intradermal Antigen Tests in Psoriasis

J. P. McFADDEN¹, A. V. POWLES¹, B. S. BAKER¹, H. VALDIMARSSON² and LIONEL FRY¹

¹Department of Dermatology, St. Mary's Hospital, London, England and ²Landspítallin, Reykjavik, Iceland

To assess whether elicitation of delayed hypersensitivity may be superior to trauma in inducing the Koebner reaction in psoriasis, 12 affected patients and 9 control subjects were tested with 0.1 ml intradermal injections of streptokinase/streptodornase (20 μ /5 μ per 0.1 ml), PPD (1 in 1000) and saline control solutions in a double-blind study; Koebner status was also established in the psoriatic patients. Injected sites were examined at 48 h and 7, 14, 21 and 28 days for local development of psoriasis, erythema and induration (diameter). One patient was Koebner-positive and developed psoriasis at all three injection sites. The other, Koebner-negative psoriatic subjects did not develop psoriasis locally. However, compared with non-psoriatic controls they showed a marked delay in resolution of the delayed hypersensitivity reaction to the PPD antigen and a similar but less marked phenomenon was observed for streptokinase/streptodornase. These findings indicate that intradermal antigen, of the nature and amount used in this study, is no more effective in inducing the Koebner phenomenon than injury alone. However, the ability of psoriasis patients to switch off cell-mediated immune reaction appears to be impaired. **Key words:** Koebner; Delayed hypersensitivity; Erythema.

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J. P. McFadden, Department of Dermatology, St. Mary's Hospital, London W2 1NY, England.

A recent hypothesis on the pathogenesis of psoriasis proposes a disease of abnormal keratinocyte proliferation, induced by cytokines released from activated lymphocytes within the epidermis (1). This further postulates that the disease is antigen induced. Trauma to the epidermis with subsequent development of psoriasis ('Koebner-positive' response) is well documented but only occurs in approximately 25% of patients (2). Although there have been several studies on the 48-hour reaction to intradermal antigen in psoriasis (3, 4, 5), observations of these sites for longer periods of time have not been performed, in particular as to whether localised psoriasis develops as a direct response to antigenic stimulation. Development of localised psoriasis has been claimed to occur with patch tests of killed sonicated microflora (6). This study looked at whether

Koebner-negative subjects develop localized psoriasis in response to intradermal antigen injections.

MATERIALS AND METHODS

Twelve patients with psoriasis (9 males and 3 females, mean age 50.8 yrs, range 19-80 yrs) and 9 normal control subjects (6 male, 3 female, mean age 40 yrs, range 26-65 yrs) were included in the study. The clinical pattern of psoriasis was 10 plaque and 2 guttate-type, with 4 of the 'plaque' group having a history of guttate psoriasis attacks in the past. To determine the Koebner status, a 0.5 cm forearm scratch was made with a venesection needle so as to cause small pinpoint bleeding sites. This was observed for local development of psoriasis over a 28-day period ('Koebner-positive' reaction). For each patient, forearm intradermal tests were performed in a double-blind manner with the following 0.1 ml injections: streptokinase/streptodornase ('Varidase' solution) 20 μ /5 μ per 0.1 ml; PPD 1/1000 solution; saline control solution with thiomersal preservative in the same concentration as the 'Varidase' solution used (0.0004%).

Assessment of intradermal injection site was made at 48 hours, and then 7, 14, 21 and 28 days after the local development of psoriasis and the cutaneous inflammatory reaction as regards both erythema and induration (mm diameter and severity, graded 0-4). Statistical analysis of results, comparing the two groups at the observed times, was performed using the Mann-Whitney U-test.

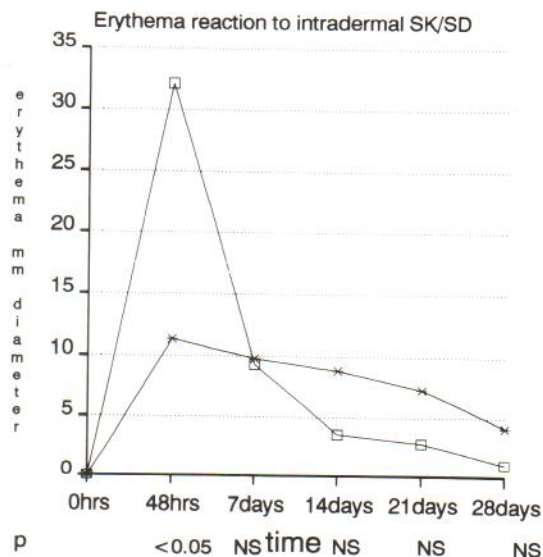


Fig. 1. Mean erythema diameter in response to intradermal streptokinase/streptodornase. *, psoriasis; □, controls.

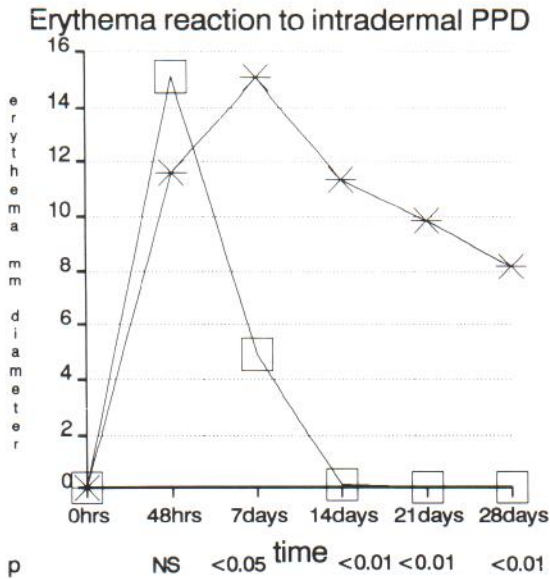


Fig. 2. Mean erythema diameter in response to intradermal PPD *, psoriasis; □, controls.

RESULTS

Development of psoriasis

Psoriasis developed in the one patient who was Koebner-positive, in all three injection sites by 21 days. Psoriasis did not develop in the 'Koebner-negative' psoriasis subjects. Saline injection sites did not develop inflammation in the 'Koebner-negative' subjects.

Reaction to intradermal streptococcal antigen (Fig. 1)

Psoriatic subjects had a reduced inflammatory response at 48 h as adjudged by mean erythema diameter (mean 11 mm, range 0–30 mm) compared with normal control subjects (mean 32 mm, range 0–70 mm), $p < 0.05$. A similar significant difference as regards induration was also found, $p < 0.05$. However, the decrease in erythema diameter from 48 h to 7 days was greater in normal subjects ($p < 0.05$), the psoriatic group tending to have a more persistent inflammation. There was no significant difference in inflammation as adjudged by graded intensity of erythema or induration over the 28-day period.

Reaction to intradermal PPD (Fig. 2)

At 48 h the mean erythema diameter was 11.5 mm in the psoriatic group, compared with 15 mm in the control group (N.S.). However, the erythema diam-

eter in the psoriatic group was more persistent, as measured at 7 days, compared with the control subjects ($p < 0.05$) and this difference persisted to 28 days. The intensity of erythema was also greater in the psoriasis group from 7–28 days. Likewise there was no significant difference in induration between the two groups at 48 h but the psoriasis group had a greater erythema diameter (7–28 days $p < 0.05$) and intensity (7–21 days $p < 0.05$) on prolonged follow-up.

DISCUSSION

In this study, stimulation with intradermal antigens did not induce localized psoriasis reactions in Koebner-negative subjects. This does not exclude the possibility of such reactions with larger or repeated doses, or with a different antigen. The lack of psoriasis reaction indicates that the local antigenic stimulus was unable to overcome a systemic inhibiting factor, thought to be operative in 'Koebner-negative' subjects (7). There were, however, differences in the development of cell-mediated immune response between psoriatic and normal subjects, with a decreased 48-h response, but a more persistent inflammation.

The differential response did not correlate with disease activity, as measured by percentage body surface area inflammation. As noted by Krueger et al. (3), there is considerable overlap between normal and psoriatic individuals, but taken as a group there is a detectable difference in delayed-type hypersensitivity reactions to intradermal antigen.

The cause of the differences observed must await better understanding of the mechanisms that regulate delayed hypersensitivity and psoriasis reactions. Speculation regarding inherent factors which may be altered in psoriasis include failure in the antigen-clearing mechanisms, defective T suppressor cell function, abnormal cytokine production, or an altered response of psoriatic epidermal keratinocytes to cytokines. Psoriatic keratinocytes have already been shown to respond differently to gamma-interferon, compared with normal keratinocytes (8).

REFERENCES

1. Valdimarsson H, Baker BS, Jonsdottir I, Fry L. Psoriasis: a disease of abnormal keratinocyte proliferation induced by T lymphocytes. *Immunol Today* 1986; 7: 256–259.
2. Eyre RW, Krueger GG. Response to injury of skin

- involved and uninvolved with psoriasis, and its relation to disease activity: Koebner and 'reverse' Koebner reactions. *Br J Dermatol* 1982; 106: 153-159.
3. Krueger GG, Hill HR, Jederberg WW. Inflammatory and immune cell function in psoriasis - a subtle disorder. *J Invest Dermatol* 1978; 71: 189-194.
 4. Obalek S, Haftek M, Glinski W. Immunological studies in psoriasis. *Dermatologica* 1977; 155: 13-23.
 5. Rimbaud P, Meynadier J, Guilhou JJ, Clot J, Barthelme J. A study of immunity to cellular mediation in psoriasis. *Bull Soc Fr Dermatol Syphiligr* 1973; 1: 477-78.
 6. Lober CW, Belew PW, Rosenberg EW. Patch tests with killed sonicated microflora in patients with psoriasis. *Arch Dermatol* 1982; 118: 322-325.
 7. Stankler L. Blood and tissue factors influencing the Koebner reaction in psoriasis. *Br J Dermatol* 1969; 81: 207-212.
 8. Baker BS, Powles AV, Valdimarsson H, Fry L. An altered response by psoriatic keratinocytes to gamma interferon. *Scand J Immunol* 1988; 28: 735-740.