

## SUPPRESSED CELL-MEDIATED IMMUNITY ASSOCIATED WITH ECZEMATOUS INFLAMMATION

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**Abstract.** In order to determine if an eczematous inflammation could have any influence upon already established cell-mediated immune reactivity, a widespread allergic as well as primary irritant, eczematous dermatitis was produced in tuberculin-sensitive guinea pigs. Their tuberculin reactivity was significantly suppressed both by allergic contact dermatitis due to dinitrochlorobenzene and by primary irritant dermatitis due to croton oil. After the dermatitis had subsided, tuberculin reactivity was restored to approximately the same level as before the induction of the dermatitis, which suggests that the suppression is temporary.

**Key words:** Suppressed cell-mediated immunity; Tuberculin reactivity; Allergic contact dermatitis; Primary irritant dermatitis

It is well known that patients with atopic dermatitis display diminished delayed intradermal skin responses to bacterial, fungal and viral antigens (4, 9). They are also less susceptible to natural and experimental sensitization with potent antigens such as rhus or dinitrochlorobenzene (7, 8). However, it is not clear whether the suppressed cell-mediated immunity has any connection with the pathogenesis of the dermatitis, or whether the hyporeactivity is secondary to whatever is causing the dermatitis (8).

Recently, several studies have indicated that transient impairment of already established cell-mediated immune reactivity occurs in patients with various infectious as well as non-infectious, inflammatory processes (5, 6). One must therefore consider the possibility that the eczematous inflammation of atopic dermatitis per se might be involved in the diminished cell-mediated immunity in patients with this condition. In this connection, the present study was undertaken to determine if an eczematous inflammation could have any influence upon already established delayed skin reactivity in experimental animals.

### MATERIALS AND METHODS

**Animals.** The experimental animals were female guinea pigs weighing 250 to 300 grams at the start of the experiments.

**Immunization.** Forty guinea pigs were immunized by injecting 0.5 ml of Freund's complete adjuvant into each of the hind footpads. Four days later, they were also sensitized in the nape with three drops of an acetone solution of 30% dinitrochlorobenzene (DNCB).

**Induction of dermatitis.** Two weeks later, the skin of the left flank (8 by 10 cm in size, approximately 20% of the body surface) was shaved. In a group of 20 guinea pigs, an acetone solution of DNCB in a concentration of 0.1% was applied on the shaved skin (1.5 ml/80 cm<sup>2</sup>). In another group of 20 animals, the shaved skin was liberally painted with an acetone solution of croton oil in a concentration of 20%. After 24 hours, a florid dermatitis was produced in 17 animals of the first group and in all of the second group. The remaining 3 animals of the first group developed only a weak dermatitis and were excluded from the study.

**Intradermal skin tests.** All animals were skin tested three times by the intradermal injection of 0.1 ml of a tuberculin solution (1 µg PPD/ml) on the skin of the right back. The first test was performed 2 days before the induction of the dermatitis. The second test was done 2 days after the induction of the dermatitis, at which time the inflammation was still active. The third test was performed 2 weeks after the induction of the dermatitis, at which time the visible evidence of dermatitis had subsided. The reactions were graded 24 hours after skin testing by measuring the diameter of induration.

### RESULTS

#### *Influence of allergic contact dermatitis on delayed skin reaction*

Fig. 1 shows the tuberculin reactions before, during, and after the allergic contact dermatitis provoked by DNCB. In the presence of the dermatitis, the tuberculin reactions were clearly suppressed in all animals. Both the size of the skin test and the intensity of the reaction were reduced. The difference between tuberculin reactions before the der-

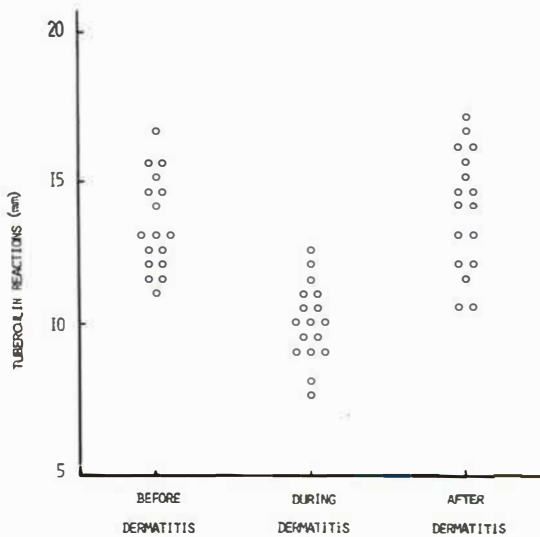


Fig. 1. Influence of allergic contact dermatitis on tuberculin reactivity.

matitis ( $13.6 \pm 1.9$  mm) and during the dermatitis ( $10.2 \pm 1.7$  mm) was significant ( $P < 0.01$ ). However, after the dermatitis had subsided, the tuberculin reactions in all animals returned approximately to the level before the induction of the dermatitis. There was no significant difference between tuberculin reactions before the dermatitis ( $13.6 \pm 1.9$  mm) and after the dermatitis ( $13.4 \pm 2.1$  mm).

#### *Influence of primary irritant dermatitis on delayed skin reaction*

Fig. 2 shows the tuberculin reactions before, during, and after the primary irritant dermatitis provoked by croton oil. In the presence of the croton oil dermatitis, all animals showed diminished tuberculin reactivities. The difference between tuberculin reactions before the croton oil dermatitis ( $14.0 \pm 1.9$  mm) and during the dermatitis ( $10.6 \pm 1.2$  mm) was significant ( $P < 0.01$ ). But, when the dermatitis had subsided, all animals restored their tuberculin reactivities approximately to the same level as before the induction of the dermatitis. There was no significant difference between tuberculin reactions before the dermatitis ( $14.0 \pm 1.9$  mm) and after the dermatitis ( $14.1 \pm 1.2$  mm).

## DISCUSSION

This study demonstrated that a widespread allergic as well as primary irritant eczematous dermatitis

suppressed already established tuberculin reactivity in guinea pigs. But, when the dermatitis had subsided, the tuberculin reactivity returned to the level before the induction of the dermatitis. This indicates that the suppression is temporary.

The mechanism by which eczematous inflammation might lead to impaired cell-mediated immune reactivity is speculative. It has been reported that sensitization of experimental animals by topical application of DNCB is accompanied by increases in alpha globulins and that, during the sensitization, tuberculin-sensitive animals respond poorly to purified protein derivative in vitro and in vivo (3). Thus, the alpha globulin associated immunosuppression may play a role in the diminished tuberculin response of guinea pigs suffering from allergic contact dermatitis due to DNCB. Yet this type of immunosuppression would not explain the impaired tuberculin response of guinea pigs with primary irritant dermatitis due to croton oil, since chemically induced, toxic tissue damage does not lead to raised alpha globulin levels (3). Other investigators have shown that a subpopulation of immune lymphocytes (T blasts and their descendants) move non-specifically to sites of eczematous inflammation (1, 2). It is therefore likely that a widespread, allergic as well as primary irritant eczematous lesion produced in tuberculin-sensitive animals attracts a large number of immune cells in the circulating blood, so that the animals fail to respond normally to skin tests with PPD.

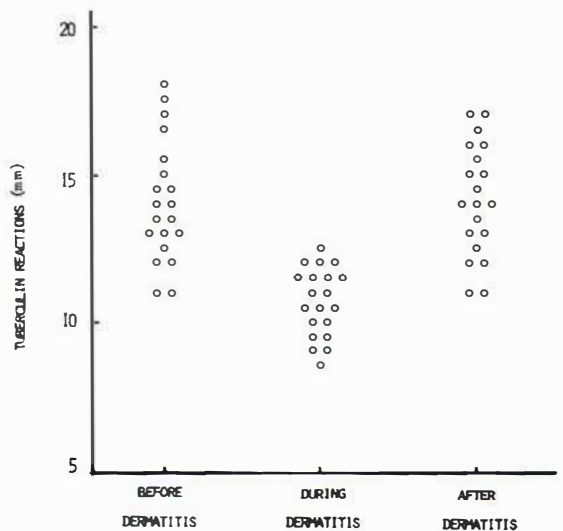


Fig. 2. Influence of primary irritant dermatitis on tuberculin reactivity.

Although the explanation for the association of eczematous inflammation with suppressed cell-mediated immunity is unclear, this association between eczematous inflammation and anergy seems to have an extensive clinical significance. Thus, in patients with eczematous inflammation such as atopic dermatitis, cellular immunity may be temporarily impaired by the presence of the dermatitis. This then suggests that, in the evaluation of cell-mediated immunity of patients with atopic dermatitis, it is necessary to investigate them not only when the dermatitis is active but also while they are in remission.

#### REFERENCES

1. Allwood, G. G.: The migratory behaviour of T blasts to contact sensitivity reactions in actively and passively sensitized mice. *Immunology* 28: 681, 1975.
2. Asherson, G. L., Allwood, G. G. & Mayhew, B.: Contact sensitivity in the mouse. XI. Movement of T blasts in the draining lymph nodes to sites of inflammation. *Immunology* 25: 485, 1973.
3. Burger, D. R., Lilley, D. P. & Vetto, R. M.: Lymphocyte suppression associated with alpha globulin. Changes in cellular immunity. *Cell Immunol* 10: 432, 1974.
4. Gudjónsson, H., Lodin, A. & Modée, J.: Besnier's prurigo in children. *Acta Dermatovener (Stockholm)* 46: 159, 1966.
5. Heiss, L. I. & Palmer, D. L.: Anergy in patients with leukocytosis. *Am J Med* 56: 323, 1974.
6. Howard, W. L., Klopfenstein, M. D., Steininger, W. J. & Woodruff, C. E.: The loss of tuberculin sensitivity in certain patients with active pulmonary tuberculosis. *Chest* 57: 530, 1970.
7. Jones, H. E., Lewis, C. W. & McMarlin, S. L.: Allergic contact sensitivity in atopic dermatitis. *Arch Dermatol* 107: 217, 1973.
8. Lobitz, W. C., Honeyman, J. F. & Winkler, N. W.: Suppressed cell-mediated immunity in two adults with atopic dermatitis. *Br J Dermatol* 86: 317, 1972.
9. Rajka, G.: Delayed dermal and epidermal reactivity in atopic dermatitis (Prurigo Besnier). III. Further studies with bacterial and viral allergens. *Acta Dermatovener (Stockholm)* 48: 186, 1968.

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