Induction of Allergic Contact Dermatitis in Patients with Sarcoidosis. (23608)

WILLIAM L. EPSTEIN AND ROBERT L. MAYOCK (Introduced by Colin M. MacLeod)
Dep'ts. of Dermatology and of Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pa.

A diminished incidence of delayed allergic reactions to the intradermal injection of bacterial, viral and fungal antigens is characteristic of sarcoidosis(1,2,3). Since allergic contact dermatitis is also a form of delayed (tuberculin-type) hypersensitivity, similar diminished responses might be expected with contact allergens. The object of the present study was to test this hypothesis using contact sensitizers to which the patient had never been exposed, as well as a commonly encountered contact allergen. By the use of chemical compounds with varying ability to sensitize, some quantitation of the response of patients with sarcoidosis was obtained.

Materials and methods. The sensitizers used in the study were: (1) pentadecyl catechol; (2) 2,4-dinitrochlorobenzene; and (3) paranitrosodimethyl aniline. Hereafter, these compounds will be referred to as PDC, DNCB and NDMA, respectively. PDC is one of the catechols in dermatitis producing plants of the genus Rhus. These catechols are among the most potent sensitizers known, and the incidence of pre-existing sensitization in adults ranges between 75 and 85% when a 1:100 concentration of PDC is used for testing(4). Sensitization to PDC was not attempted, but to test for pre-existing poison ivy sensitivity, 0.25 ml of a 1:100 concentration of PDC in acetone was applied to the forearm of each subject by the open patch method within the area of a cup 2.9 cm in diameter. The test sites were observed after 4 to 6 days. DNCB and NDMA are also potent sensitizers, but it has been found that within a certain range of concentrations, including that used in this study, DNCB is a moderately strong sensitizer and NDMA a weaker one(5,6). In contrast to the observations with PDC in which previous exposure had to be assumed, the subjects were *actively* sensitized with DNCB and NDMA, under controlled conditions of exposure. 0.25 ml of 0.005 molar DNCB and 0.25 ml of 0.005 molar NDMA in acetone were applied to the skin at separate sites by the same open patch method as was used with PDC. Thirty days later the subjects were retested by a similar application at new sites with a 1:1000 dilution of each sensitizer in acetone, and the reactions observed in 4-6 days.

Twenty-three ambulatory out-patients with sarcoidosis, 18 of whom were Negro, were tested with the 3 contact allergens. There were 14 females and 9 males in the group. Although their state of health varied from asymptomatic to chronically ill, none was moribund and all had stigmata of sarcoidosis at the time of the study. One had received 50 mg of cortisone daily for 3 months, an amount not likely to affect sensitization(7).

One hundred thirty-five healthy males of comparable ages, 108 of whom were negro, were used as controls. They were sensitized to DNCB and NDMA and tested to the three compounds in the manner described above. Because Negroes appear to be less easily sensitized to contact allergens as compared to whites (Table I)(4,8), the ratio of Negro to white in the sarcoidosis and control groups was made the same in order to keep the composition of the groups statistically comparable (Table II). No significant sex difference has been observed in the response of normals(9) or patients with sarcoidosis(1) to delayed skin test antigens. Statistical analysis was performed by the chi square method.

Results are summarized in Table II.

1. With PDC, the most potent sensitizer, there was no significant difference in the inci-

TABLE I. Control Group. Comparison of incidence of sensitization to contact allergens between Negro and White.

	DNCB	NDMA
Negro	70/114 = 61%	49/108 = 45%
White	26/ 27 = 93%	17/ 27 = 63%

TABLE II. Incidence of Positive Reactors to Contact Allergens; Combined Negro and White Groups.

	Naturally acquired contact sensitivity	Experimentally produced contact sensitivity	
	PDC	DNCB	NDMA
Controls	101/135 = 75%	96/141 = 68%	66/135 = 49%
Patients with sarcoidosis	18/ 22 = 81%	8/ 23 = 35% (P = <.01)	3/ 23 = 13% (P = <.01)

dence of sensitization in patients with sarcoidosis and in control subjects.

2. With DNCB and NDMA, a highly significant decrease in frequency of sensitization was observed in patients with sarcoidosis as compared to controls. DNCB was about ½ as effective in sensitizing the patients with sarcoidosis as the control subjects, while NDMA, the least potent allergen used, was about ¼ as effective.

Comment. These findings demonstrate that the lowered incidence of reactivity in sarcoidosis is not apparent when a very strong sensitizer, PDC, is used. It is only with weaker allergens that the difference becomes apparent. Actually DNCB and NDMA are considerably more potent than commonly encountered contact allergens such as formalin, vioform and heavy metals(10), so that one might expect a greatly depressed incidence of contact sensitization in patients with sarcoidosis if these latter compounds were to be tested.

Patients with sarcoidosis *are capable* of reacting to these and other skin test antigens although the incidence of sensitization is decreased. For this reason the use of batteries of such tests probably has little diagnostic value in sarcoidosis as has been suggested (11).

Summary. 1) The incidence of naturally occurring skin sensitization to a poison ivy allergen, PDC, and of experimentally induced skin sensitization to 2 chemical sensitizers, DNCB and NDMA, was determined in 23 patients with sarcoidosis and 135 control subjects. 2) The incidence of sensitization to the strongest sensitizer, PDC, was the same in the control group and in the patients with sarcoidosis. 3) With the less effective sensitizers, DNCB and NDMA, a significantly decreased frequency of sensitization was observed in the patients with sarcoidosis. 4) This finding with the latter compounds is consonant with the decreased incidence of delayed type hypersensitivity reactions observed by others using antigens injected intradermally.

1. Friou, G. J., *Yale J. Biol. and Med.,* 1952, v24, 533.

2. Sones, M., and Israel, H. L., *Ann. Int. Med.,* 1954, v40, 260.

3. Quinn, E. L., Bunch, D. G., and Yagle, E. M., *J. Invest. Derm.,* 1955, v24, 595.

4. Kligman, A. M., *Arch. Dermat.*

5. Epstein, W. L., and Kligman, A. M., *Jour. Invest. Dermat.,*

6. Rostenberg, A., and Kanof, N., *ibid.,* 1941, v4, 505.

7. Dougherty, T. F., *Prog. All.,* 1954, v4, 319; S. Karger, Basel-N.Y.

8. Sulzberger, M. B., and Rostenberg, A., *J. Immun.,* 1939, v36, 17.

9. Schwartz, M., *J. All.,* 1953, v24, 143.

10. Sulzberger, M. B., *Dermatologic Allergy,* C. C. Thomas, Springfield, 1940, Appendix II.

11. James, D. G., and Thomson, A. D., *Arch. Middlesex Hosp.,* 1954, v4, 263.

Received September 5, 1957. P.S.E.B.M., 1957, v96.