THE EFFECT OF TRANQUILIZERS ON THE IMMEDIATE SKIN WHEAL REACTION

A Preliminary Report

Harvey I. Wolfe, M.D., and Vincent J. Fontana, M.D., New York, N. Y.

THE biochemical reactions associated with the immediate skin reaction are not fully understood although liberation of free histamine has been implicated as the most important substance involved in these phenomena.[1] Suppression of the immediate skin test has been observed while the known reactor has been under hypnosis.[2] Antihistamines,[3, 4, 6] aminophylline,[5, 6] and the sympathicomimetic drugs [5, 6] such as epinephrine, ephedrine, and isoproterenol in therapeutic doses have been shown to suppress the immediate skin reaction to various allergens. ACTH and cortisone, in therapeutic doses, do not significantly alter this reaction.[7, 8]

This preliminary study was designed to observe the effects of the more commonly used tranquilizers—chlordiazepoxide hydrochloride,* meprobamate,† and hydroxyzine‡—on the diagnostic intradermal testing procedure, with ragweed employed as the test antigen.

GENERAL METHOD

This is a study of 17 children between the ages of 6 and 16 years with a clinical history of ragweed pollinosis and exhibiting a positive skin test to 0.02 ml. of ragweed antigen, 100 protein nitrogen units per cubic centimeter. The intradermal tests were placed on the lateral aspect of the upper arm over the insertion of the deltoid, and the reactions were observed at the end of 15 minutes. The size of the wheal was recorded by tracing the original bleb and subsequent wheal on transparent wax paper. A control, i.e., a skin test without drug administration, was performed at the beginning and the end of this study in most cases. Each week one of the previously mentioned drugs was begun 48 hours

From the Department of Pediatrics, New York University Medical Center, Pediatric Allergy Section.

*Librium, supplied by Hoffmann-La Roche, Inc.

†Equanil, supplied by Wyeth Laboratories.

‡Atarax, supplied by J. B. Roerig & Co.

prior to testing, as scheduled in Table I. In all instances, the last dose was given approximately 2 hours prior to skin testing. The drugs did not produce any observable effects on the central nervous system function. No other medication was taken within 72 hours prior to the experimental procedure.

TABLE I. SCHEDULE OF DOSAGE OF EACH DRUG BEFORE TESTING

DRUG	DOSE USED	RECOMMENDED DOSE (FOR THIS AGE GROUP)
Chlordiazepoxide hydrochloride (Librium)	10 mg. every 12 hours	5-10 mg. every 8-12 hours
Meprobamate (Equanil)	200 mg. every 8 hours	100-200 mg. in divided doses/day
Hydroxyzine (Atarax)	25 mg. every 8 hours	50-100 mg. in divided doses/day

RESULTS

The results are presented in Table II. Determination of wheal area was made according to the method described by Kagan and Pellegrino.[9] It appears that the wheal reaction was not significantly suppressed in 8 out of 9 subjects in whom chlordiazepoxide hydrochloride was employed. In 8 out of 10 instances, meprobamate did not significantly affect the wheal reaction. In 6 out of 8 cases, hydroxyzine suppressed the intradermal wheal. In 11 out of 13 subjects, the size of the control wheal appeared reproducible. Under the conditions of this study, it is suggested that hydroxyzine in 75 per cent of the cases reduced the skin test response 50 to 75 per cent, whereas chlordiazepoxide hydrochloride and meprobamate in 84 per cent of the cases reduced the response less than 10 per cent. While previous investigators have studied the suppression of the wheal and erythema reaction, we have limited our observations to the wheal response. It is our impression that the wheal reaction is more specific than the erythema response in the evaluation of the immediate skin reaction.

TABLE II. TRANQUILIZERS AND THEIR EFFECT ON THE WHEAL AREA (IN SQUARE CENTIMETERS)

PATIENT	CONTROL (BEGINNING)	CONTROL (END)	CHLORDIAZEPOXIDE HYDROCHLORIDE	MEPROBAMATE	HYDROXYZINE
R. R.	3.90	5.70	3.50		
F. T.	4.70	3.75	4.00		
A. A.	11.20		10.25		
C. L.	12.75	3.85	2.00		
J. M.	4.65	7.90	5.50		
A. R.	8.90	6.75	14.10		
L. W.	12.85	28.0	9.20		
I. S.	7.45			5.25	1.85
S. C.	17.65		15.05	12.05	8.25
R. B.	6.65	4.85	3.50	4.80	1.40
J. C.	6.40	10.50		11.30	1.45
M. C.	5.85	5.05		5.00	
E. S.	15.00	14.30		12.20	
G. R.	3.45	3.80		4.05	0.80
L. B.	7.20	7.70		9.35	14.30
A. W.	10.95	11.45		10.00	3.95
I. L.	2.45			4.25	1.60

CONCLUSION

Meprobamate and chlordiazepoxide hydrochloride did not appreciably affect the wheal reaction. Hydroxyzine, which possesses antihistaminic and tranquilizing properties, markedly suppressed the wheal reaction.

These preliminary findings should suggest to the physician engaged in allergy testing that some tranquilizers may be administered to overly anxious patients prior to testing without adversely affecting the wheal reaction. However, one must be alerted to the possibility that certain other tranquilizers possess antihistaminic properties which may alter the result of the skin testing procedure.

REFERENCES

1. Stuttgen, G.: Mechanismen der allergischen Hautreaktionen, Acta allergol. **16**: 428, 1961.
2. Black, S.: Inhibition of Immediate-Type Hypersensitivity Response by Direct Suggestion Under Hypnosis, Brit. M. J. **5335**: 925, 1963.
3. Serafini, U.: Studies on Histamine and Histamine Antagonists, J. ALLERGY **19**: 256, 1948.
4. Arbesman, C. E., Koepf, G. F., and Miller, G. E.: Some Antianaphylactic and Antihistaminic Properties of N Pyridyl, N Benzl, Dimethylenediamine Monohydrochloride (Pyribenzamine), J. ALLERGY **17**: 203, 1946.
5. Tuft, L., and Brodsky, M. L.: The Influence of Various Drugs Upon Allergic Reaction, J. ALLERGY **7**: 238, 1936.
6. Mosko, M., and Marshall, R. B.: A Study on the Effect of Various Drugs on the Whealing Reaction, J. ALLERGY **21**: 242, 1950.
7. Feinberg, S. M., Dannenberg, T. B., and Malkiel, S.: ACTH and Cortisone in Allergic Manifestations, J. ALLERGY **22**: 195, 1951.
8. Cooke, R. A. et al.: ACTH and Cortisone in Allergic Diseases, J. ALLERGY **22**: 211, 1951.
9. Kagan, I. G., and Pellegrino, J.: Critical Review of Immunolologic Methods for Diagnosis of Bilharziasis, Bull. World Health Organ. **25**: 611, 1961.