

CORRESPONDENCE

Wheal and flare skin reactions to aminophylline

To the Editor:

Recently we reported (J. ALLERGY CLIN. IMMUNOL. 48: 165, September, 1971) the case of a 12-year-old asthmatic boy with a generalized urticarial reaction following the intravenous administration of aminophylline on 2 different occasions. An immediate wheal and flare reaction (2+ erythema and 10 mm. wheal) to aminophylline (25 mg. per milliliter) was obtained that could be passively transferred using the classic Prausnitz-Küstner procedure. To confirm the immunologic nature of the reaction, the rat mast cell degranulation technique was applied, and a significant degranulation was obtained using the patient's serum and aminophylline or anti-IgE.

Two atopic control subjects with a prior history of repeated aminophylline administration were tested with the same aminophylline preparation and failed to exhibit a significant wheal and flare reaction. Upon further testing the skin-reactive properties of aminophylline in 15 Allergy Clinic patients, we obtained the following results. Out of 15 patients, 4 failed to show any wheal or flare beyond that obtained with a control diluent solution; 6 out of 15 patients showed a 1+ wheal and flare reaction (erythema and 5 mm. wheal); and 5 out of 15 patients exhibited a ++ wheal and flare reaction (erythema and 10 mm. wheal). These 5 patients had no history of an untoward reaction to aminophylline, as the reported patient did.

All 15 patients belonged to the pediatric age group, ranging in age from 12 to 17, and were tested intracutaneously with 0.02 ml. of a 25 mg. per milliliter commercially available aminophylline solution (Premo Pharmaceutical Labs., Inc., South Hackensack, N. J.).

Of these 15 control individuals, 10 were tested by the scratch skin test method using a Center Scarifier (Center Laboratories, Port Washington, N. Y.) and gave no wheal and flare reaction to the same aminophylline preparation at the same concentration (25 mg. per milliliter). Two attempts at passive transfer of the wheal and flare reaction using the serum of one control individual (with a 2+ wheal and flare reaction) were unsuccessful. This is in contrast with the reported patient's serum ability to transfer the wheal and flare reaction to a nonatopic control who showed no wheal and flare reaction to a 25 mg. per milliliter concentration of aminophylline.

While these findings do suggest that aminophylline in a concentration of 25 mg. per milliliter may have significant skin irritative properties and may give rise to nonspecific or clinically nonsignificant wheal and flare reactions, as in the 5 patients with a ++ wheal and flare skin reaction without a history of clinical hypersensitivity to aminophylline, it cannot be ruled out that these individuals did indeed have skin-sensitizing antibodies to aminophylline.

In any case, this points out the limitation of the skin testing method in general and the problem of evaluating allergy to low molecular weight therapeutic agents in particular, especially if the skin tests are not performed with adequate controls on a significant number of individuals with a potential "new" allergen. It also re-emphasizes the need for an adequate and practical in vitro test for detection of specific IgE antibodies to antigens or haptens as may occur in drug hypersensitivity.

*Zack H. Haddad, M.D.
Los Angeles, Calif.*