

Letter to the editor

The optimum concentration for skin prick testing

In the July issue of *Allergy*, Di Berardino & Angrisano (1) comment in a letter on the optimum concentration for skin prick testing. I would like to comment on the following points (in boldface) in their letter.

“Perhaps [the authors] were convinced that a higher extract concentration would not increase the wheal area proportionately or make the test more effective in its prediction of allergy . . .”

- 1) The dose response of allergen is flat (2), but the response continues to increase even at allergen concentrations corresponding to 1000 000 BU/ml in median-sensitive patients (3).
- 2) The sensitivity increases to 1 million BU/ml, but the specificity is optimal at 10 000 BU/ml (4).

“ . . . 10 000 BU/ml might be considered the best concentration [for diagnosis] because it produces a positivity equal to the reaction produced by the positive control.”

There is a million-fold difference in sensitivity between the most and the least sensitive patient in a population (2) (10 000 times in those selected for biologic standardization [3]), as measured by skin prick testing; i.e., an increase from 2 mm to (by 1.5-fold increases in wheal diameter for 10-fold increases in skin sensitivity) 23 mm in diameter with a very potent extract (1 million BU/ml) inducing positive skin tests in all patients sensitive to the allergen. With such an extract, most subjects would experience wheals about 6.8 mm in diameter; those attending specialist clinics would probably exhibit larger wheals.

The numbered “points” mentioned in the letter must also be discussed.

- 1) Yes, in most patients in Western Europe, “histamine 10 mg/ml induces wheals about 5.5 mm in diameter”.
- 2) Yes, it is true that “one person may require a histamine concentration 10 times stronger than another [person] to elicit wheal reactions of the same size [Frankland]”; however, not only the potency of the histamine solution, but also other

factors, most important the technique/pressure applied, must be considered (5).

- 3) By the log/log model of dose response, which is best fitted, the coefficient of variation (c.v.) is similar at different dose levels (by definition of a well-fitted model). With a lin-log model, the c.v. will vary with the size of the wheals.
- 4) The reactions to histamine are smaller in children than in adults. This is not true in those sensitized, but is true for the population. Menardo et al. (6) have reported on smaller histamine wheals in children, but we found sizes in sensitized infants and children to be similar to those in teenagers and young adults. The difference can be explained by the fact that infants are sensitized to a lower degree than young adults, since Stuckey et al. (7) convincingly showed that the histamine sensitivity of the skin is related to the degree of sensitization, e.g., to total IgE or the number of positive skin tests.

I propose that the response to histamine skin testing may serve as an indicator of skin hyper-reactivity, similar to that of the bronchi.

“[From] our clinical experience, we are convinced that an allergen extract containing 20 000 BU/ml is the optimum concentration [for skin prick testing].”

We should continue to study the properties of histamine and allergen when tested in the skin, since there are many problems unsolved. However, we must document our position as well as possible. Niemeijer et al. (8) reported 30 000 BU/ml as optimal. We question this and have reported (4) that 10 000 BU/ml has a high specificity, whereas 1000 000 BU/ml has a high sensitivity for diagnosing clinical allergy to dog dander. Perhaps different concentrations are needed to diagnose all clinical problems, since patients are exposed during longer periods of time to some allergens such as those of mite and animal dander (hypothesis for future research).

Key words: allergen; biologic units; dose response; histamine; skin hyperreactivity; skin prick test.

S. DREBORG

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