

Letters to the editor

Histamine-positive skin prick testing

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The Northern (Scandinavian) Society of Allergology used histamine as a standard reference for skin prick testing (SPT) in 1974 (12). Aas, however, pointed out (1) that there may be many variables when performing an SPT in a standard manner. It may be found that one person requires a 10 times stronger histamine concentration than another to elicit wheal reactions of the same size. The same tester may show regular variations of more than $\pm 30\%$ from the mean. Standardized puncture lesions may also depend upon the use of different types of needles in SPT. The whole subject of SPT has been well reviewed by Nelson (10).

Coca introduced the concept of atopy into allergology (3). He founded the *Journal of Immunology* and served as its first editor for 25 years. Yet, what he called the strange diseases in man were restricted to hay fever and asthma. In contrast, Pepys (13), when writing on SPT in diagnosis, states that the word "atopy" should be used without clinical implications. It is that form of immunologic reactivity in which IgE antibodies are readily produced in response to ordinary exposure to common allergens of the subject's environment. SPT used in type 1 allergy was the basis of a position paper prepared by a subcommittee of the European Academy of Allergology and Clinical Immunology (EAACI) in 1989 (4). The size of the wheal and flare response obtained by the SPT has interested many workers. There is a circadian rhythm in the size of skin reactions to allergens and histamine, a maximal wheal

size appearing at night (6). The reaction to histamine is less pronounced in infants, increases in young adults, and then declines gradually (15).

Quantitative SPT using 1 or 10 mg/ml histamine dihydrochloride has a reproducibility which has a clinical application in the assessment of pharmacologically induced or immunotherapy-induced changes (9). The size of the skin response in individual patients varies considerably, and because of small wheal area and low reproducibility with histamine 1 mg/ml, it has been recommended that histamine 10 mg/ml be used as an international positive reference (8). Because it has been considered to be necessary for a quantitative approach for the size of the SPT procedures, precise area determination can be validated by the use of a scanning device and software for a personal computer. Such equipment is expensive, but it may be essential for some scientific studies (14).

History of skin prick testing

Skin testing as a form of clinical investigation had to be reinvented several times over 300 years before it became an established method of allergy investigation. In 1873, Blackley (2) confirmed his own grass-pollen allergy by scarifying the skin of his forearm, applying moist pollen, and noting the large wheal that was produced. When Noon, at St Mary's Hospital, London, UK, performed the first successful desensitizing treatment by injection of a pollen ex-

tract in grass-pollen-allergic patients (11), conjunctival tests, and not SPT, formed the basis of diagnosis and treatment. In 1911, Freeman (5) used the same method. Freeman's medical notes on his hay fever patients show that, in 1935, he was using SPT and carefully measuring the wheal size after 15 min – he did not use a histamine-positive SPT control. Yet, by 1950, David Harley, working with Freeman in the allergy department at St Mary's Hospital, London, routinely used a histamine-positive SPT on all patients attending the department. I believe he took the idea from Freeman, who knew Dale, the discoverer of histamine, well and who often discussed the importance of histamine in allergic reactions. Dale had a friend, Thomas Lewis, who was conducting research on vascular reactions of the skin to injury; this he later described as the triple response. Lewis decided that Dale's histamine would be a better means than trauma to the skin to perform his experiments. In their paper of 1924 (7), Lewis & Grant point out that Eppinger, in 1913, had noticed that whealing of the skin could be produced by scarifying the skin and subsequently applying a dilute solution of this tissue poison. Histamine wheals were further explored by Sollman and Pilcher in 1917, but scarification distributed histamine too irregularly in the skin. Many other methods were tried, including pricking the skin with fine glass capillary points. Finally, a successful method was found: "In practice we have found the most suitable method to be a more simple one; a small drop of the solution is placed on the skin and the skin is pricked through the centre of this drop with a fine needle" (7). It is also of some interest that the paper states that the histamine employed was the synthetic and crystalline diphosphate of β -iminazolyethylamine obtained from Messrs Burroughs & Wellcome, who supplied the substance under the trade name of Ergamine acid phosphate. The above description of 1924 seems to be the first description of the use of the histamine SPT, later used by the allergy department at St

Mary's Hospital, London, and which, as a positive control, is the most important SPT performed by any allergist.

References

1. AAS K. Some variables in skin prick testing. *Allergy* 1980; 35: 250–2.
2. BLACKLEY CH. Experimental researches on the causes and nature of catarrhus aestivus (hay-fever and hay-asthma). London: Baillière, Tindall & Cox, 1873.
3. COCA AF, COOKE RA. On the classification of the phenomena of hypersensitivity. *J Immunol* 1923; 8: 163–82.
4. EAACI. Skin tests used in type 1 allergy testing. Position Paper. *Allergy* 1989; 44: Suppl. 10.
5. FREEMAN J. Further observations on the treatment of hay fever by hypodermic inoculation of pollen vaccine. *Lancet* 1911; ii: 814.
6. LEE RE, SMOLENSKY MH, LEACH CS, MCGOVERN TP. Circadian rhythms in the cutaneous reactivity to histamine and selected antigens, including phase relationship to urinary cortisol excretion. *Ann Allergy* 1977; 38: 231–6.
7. LEWIS T, GRANT RT. Vascular reactions of the skin to injury. II. The liberation of a histamine-like substance in injured skin; the underlying cause of factitious urticaria and of wheals produced by burning; and observations upon the nervous control of certain skin reactions. *Heart* 1924; 11: 208–65.
8. MALLING HJ. Skin prick testing in the use of histamine references. *Allergy* 1984; 39: 596–601.
9. MALLING HJ. Reproducibility of skin sensitivity using a quantitative skin prick test. *Allergy* 1985; 40: 400–4.
10. NELSON S. Diagnostic procedures in allergy. I. Allergy skin testing. *Ann Allergy* 1983; 51: 411–17.
11. NOON L. Prophylactic inoculation against hay fever. *Lancet* 1911; i: 1572.
12. Northern (Scandinavian) Society for Allergology. Standardisation of diagnostic work in allergy. *Acta Allergol* 1974; 29: 239–40.
13. PEPYS J. Skin tests in diagnosis. In: GELL PGH, COOMBS RRA, LACHMANN PJ, eds. *Clinical aspects of immunology*. 3rd ed. Oxford: Blackwell Scientific, 1975: 55–80.
14. POULSEN LK, LIISBERG C, BINDSLEV-JENSEN C, MALLING HJ. Precise area determination of skin prick tests: validation of a scanning device and software for a personal computer. *Clin Exp Allergy* 1993; 23: 61–8.
15. SKASSA-BRODIEK W, MANDERSCHIED JC, MICHEL FB, BOUSQUET J. Skin test reactivity to histamine from infants to old age. *J Allergy Clin Immunol* 1987; 80: 711–16.

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