

EDITORIAL

Skin tests in clinical practice and epidemiology

The technical aspects of skin testing are often regarded as a dry subject, but in fact they are central to clinical and epidemiological studies of atopy and deserve to be better understood. In the UK, interest in skin testing has diminished now that immunotherapy has lost popularity. Indeed, some manufacturers have withdrawn their skin test products from the UK market, while the introduction of topical corticosteroids and non-sedating anti-histamines has made the treatment of allergic and non-allergic forms of asthma and rhinitis almost identical [1,2]. Consequently, many UK clinicians have questioned the relevance of skin testing to their clinical practice. It is therefore pertinent to ask whether there is still a case for skin testing, and if so, how positive tests should be interpreted. To answer these questions it is first necessary to understand something of the epidemiology of atopy and the precision of skin testing methods.

Most population studies have found that skin test reactivity is acquired progressively during childhood, peaking between 15 and 25 years and declining gradually thereafter [3–5]. Approximately half of those with positive skin tests will have some atopic symptoms (rhinitis, conjunctivitis, asthma or eczema), although the proportion with disease varies depending on the definition of disease and the definition of a positive skin test. It is worth noting that positive skin tests in asymptomatic individuals can not simply be dismissed as false positives: a careful prospective study has shown that asymptomatic children with positive skin tests have a 50% risk of developing rhinitis and a 5% risk of developing asthma over a 5 year follow-up period [6].

Ideally, a skin test result should reflect only the degree of sensitization of the test subject. In fact, many other factors can affect the accuracy and precision of skin tests: these include the composition and potency of the allergen extract, the test technique, the cut-off point chosen, the age, sex and race of the subject, and concomitant drug treatment [7]. Among these, the choice of cut-off point is a critical issue. Careful epidemiological work has shown that a true reaction diameter of 3 mm represents a tenfold greater concentration of specific IgE than a true reaction of 2 mm [8]. Moreover, the reproducibility of individual skin prick tests is quite poor, even in the hands of experienced investigators [9], so a true reaction of 5 mm diameter has a 95% confidence interval of 3.1 to 6.9 mm, while a true reaction of 4 mm diameter has a 95% confidence interval of 2.3 to 5.7 mm [10]. The minimum cut-off which predicts a positive RAST or bronchoprovocation test is 5 mm [11,12], which clearly represents a

much higher specific IgE concentration than a 3 mm cut-off.

In this issue of *Clinical and Experimental Allergy*, Johnston and colleagues have attempted to address rates of skin test conversion in children with respiratory symptoms, using skin test data from an epidemiological study of bronchial hyperresponsiveness in children [13]. At face value, this study shows a 4% per annum increase in the prevalence of skin test positivity in children with respiratory symptoms. This conversion rate is greater than has been reported in the general population at this age [6]. It is interesting that these children had symptoms before they acquired positive skin tests: in other studies skin test positivity often precedes and predicts the development of respiratory symptoms [6]. The main question posed, but left unanswered by the study of Johnston *et al.* is whether the 4% annual conversion rate among symptomatic children represents a true excess over the increase that would be expected for the general population of children. Because their study was a spin-off from another piece of work, there are some problems with the study design. In particular, the sequential selection process is a source of potential bias and there was no asymptomatic group for comparison. Moreover, the fact that only single skin tests were performed make the confidence limits on their data quite wide. Johnston *et al.* comment on the surprising number of children whose skin tests reverted to negative, but it seems likely that this is a methodological artefact due to using single tests and a 2 mm cut-off. In fact, their data could be used to support the view that a 2 mm cut-off is too low for epidemiological use, in that their net conversion rate was identical whether a 2 mm or 3 mm cut-off point was used, while reversion to negativity was much reduced with the 3 mm cut-off.

What then can we conclude about the utility of skin tests in clinical practice? As with any diagnostic test, doctors need to look carefully at the use that they make of skin test results. Performing a test but not acting on the results is a waste of everyone's time. On the other hand, before acting on the results clinicians need to understand how the test performs and what a positive result really means. To make skin tests worthwhile in clinical practice, physicians also need to have available some form of intervention which influences the results of allergic sensitization and whose use is predicated on the skin test results. In seasonal allergic rhinitis and conjunctivitis, the diagnosis will usually be evident from the history, and skin tests provide confirmation that a particular allergen is involved. Sensitivity to indoor allergens (dust mites and

animal danders) is an important causative factor in many cases of perennial rhinitis. In contrast to seasonal allergies, patients with perennial symptoms are often unaware of the allergic basis of their disease: demonstrating positive skin tests are useful in persuading patients to take measures to contain house dust exposure or to part with their pets. Immunotherapy is the treatment of choice for patients with hymenoptera sensitivity and it remains an option for patients with seasonal rhinitis whose symptoms are poorly controlled with conventional medication [14]. In both cases, the history should be confirmed by skin tests and RAST tests prior to starting injection immunotherapy.

Thus, properly performed skin tests do have a place in the diagnosis of allergic rhinitis and asthma, and can be helpful in advising patients on specific measures that they can take to minimize their symptoms. The important caveats are that allergy skin tests should only be interpreted in the context of the clinical history, and doubtful results should be checked, preferably in duplicate, before any action is taken. Positive skin tests in asymptomatic individuals do appear to have some predictive value for future development of allergic disease [6], but in the absence of any intervention which can arrest progression to the symptomatic allergy, no specific action can be recommended.

In epidemiological work, skin testing can be used in cross-sectional and longitudinal studies to determine rates of allergic sensitization. General population studies have shown wide variation in the prevalence of atopy with reported rates between 19% and 70% [10]. Most of this variability is probably due not to true population differences, but rather to variation in technique and in extract potency. Consequently it has been difficult to test claims that the prevalence of atopy is increasing [15]. It is now clear that the variability of single skin tests is unacceptable for epidemiological surveys. Duplicate testing should be regarded as the minimum acceptable standard [10] and some authorities have suggested quadruplicate testing in scientific work [7]. To facilitate comparison between studies, future epidemiological studies should use biologically standardized extracts and published reports should include data on the precision and reproducibility of the skin testing technique. A revised version of the EAACI position paper on skin testing for type I hypersensitivity will be published in 1992 and I would warmly commend this (and the original version [16]) to anyone with a clinical or scientific interest in skin tests.

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