

Longitudinal changes in skin-prick test reactivity over 2 years in a population of schoolchildren with respiratory symptoms

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Summary

As part of a larger epidemiological study, 114 children with respiratory symptoms, born between 1978 and 1980, were skin-prick tested to *Dermatophagoides pteronyssinus* (DP), mixed grass pollens (G) and cat dander (C), and to histamine and saline controls (Bencard, U.K.) using 1 mm prick-lancets (Dome/Hollister-Stier), between July and September 1987 and again in October 1989. A weal ≥ 2 mm to one or more allergens was regarded as a positive result. Each child was tested by the same investigator on each occasion, using similar techniques. Three children were excluded from analysis as they had failed to respond to histamine testing on one of the two occasions. In 1987, of the 111 children analysed, 58 (52%) children were skin-test positive, and 53 (48%) skin-test negative, while in 1989 62 (56%) were positive and 49 (44%) negative. Twelve children (11%) changed status from negative to positive, while eight (7%) changed from positive to negative. For the group as a whole the percentage agreement between the results obtained 2 years apart was 82%. In comparison to previous studies a greater number of subjects in this population than expected changed atopic status. We therefore further examined the data from those who had changed status and classified as borderline those subjects with no difference in weal size of greater than 2 mm for any allergen between 1987 and 1989. Only five children then changed status from negative to positive, none from positive to negative and 15 demonstrated only borderline changes. The coefficients of repeatability for the 106 children who did not change status were 3.37 mm, 2.80 mm and 2.33 mm for *D. pteronyssinus*, mixed grass pollens and cat dander respectively. The good short-term repeatability of the testing method was demonstrated in a group of 29 similar children; the coefficients of repeatability were 0.38 mm for DP and G, and 0.72 mm for C. These data demonstrate that, in a population of children with respiratory symptoms, skin-prick testing within individuals is highly repeatable over the short term, but poorly repeatable over a 2 year period. However, the percentage agreement in skin-prick test status for the group as a whole was high (82%). While no child became unequivocally skin-test negative having been previously positive, a small number of children changed status from negative to unequivocally positive, suggesting a genuine but small (4%) increase in the prevalence of skin-test positivity in this population.

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Introduction

Skin-prick testing has been used for over 50 years in both the clinical assessment of, and in research studies of,

allergic disease, particularly asthma [1,2] and allergic rhinitis [1]. There is a positive association between the magnitude of the skin-prick test reaction and the frequency of symptoms in allergic rhinitis [1] and between the skin-prick test reaction and the risk of bronchial hyperresponsiveness [3,4]. The weal size produced by skin-prick testing to aero-allergens correlates with serum levels of specific IgE [5-8]. Cross-sectional studies in normal populations demonstrate point-prevalence of positive skin-prick testing of between 20% and 50% [9-13], with peak prevalence occurring in the third and fourth decades [14,15]. Many factors account for the variation in prevalence shown between studies, including the number of allergens used for testing, the geographical variations in allergen load and sensitivity, the potency of the allergen preparations used, the age and sex of the population sample, and the criteria used to define a positive reaction. In addition, different methods used in carrying out the testing could account for variation in results, as the degree of response is known to depend on the depth of allergen penetration [16,17].

Two studies have examined the longitudinal changes in allergen skin-prick test reactivity. The first studied a cohort of 1333 subjects aged from 3 to over 75 years, testing with five allergens on two occasions a mean of 8.1 years apart [18]. The overall prevalence of skin-test positivity was 39% at the initial assessment and 51% at the follow up. The greatest increase in prevalence occurred in children and adolescents, but there was a net increase in prevalence over the study period in all the age groups. There were 133 children in the age group 5-14 years, none of whom became non-reactive having previously been skin-test positive.

In the second study 380 schoolchildren aged 8-10 years at enrollment underwent skin-prick testing to 13 allergens on three occasions, each 2 years apart [19]. Twenty-four per cent of children were skin-test positive at the outset, while a further 15% became so during the study. Four children who had a single positive reaction at the first study, and were negative at the subsequent studies were classified as skin test negative.

Thus these two studies of normal children demonstrated increases in the prevalence of skin-test positivity over time, with few reversions to negativity in subjects previously found to be skin-test positive.

There are no reported studies assessing the short-term repeatability or the longitudinal changes of allergen skin-prick test reactivity in populations with respiratory symptoms, despite the fact that this test is frequently used in clinical practice and in epidemiological studies of such populations.

In this study we report the repeatability of duplicate skin-prick tests in a group of 29 schoolchildren with

respiratory symptoms, and the longitudinal changes over 2 years in skin-test reactivity in a cohort of 114 schoolchildren selected using the same criteria. We also examine the influence of the criteria used to define skin-test positivity on the interpretation of the longitudinal changes.

Materials and methods

Subjects

Longitudinal cohort The children reported in this study were taking part in a longitudinal study of bronchial responsiveness, peak expiratory flow changes and respiratory symptoms, the details of which are reported in full elsewhere [20].

These children, aged between 7 and 9 years, were recruited from the lists of 72 local General Practitioners by means of a postal questionnaire enquiring into the presence of respiratory symptoms (troublesome cough and/or wheeze). Children reporting respiratory symptoms were invited to attend for skin-prick testing. Between July and September 1987, 392 children underwent skin-prick testing: 192 of these were selected using a quota filling system to provide four groups of equal size—the groups comprised atopics with wheeze with or without cough, atopics with cough alone, non-atopics with wheeze with or without cough and non-atopics with cough alone. These 192 children then took part in a 12 month longitudinal study of bronchial responsiveness [20]. In October 1989, 187 of the 192 children who had finished the first study were invited to take part in a further longitudinal study examining the role of viral infections in respiratory symptoms. This was an even more arduous study than the first, involving invasive testing. One-hundred-and-fourteen children consented to undertake the second study, and underwent repeat skin-prick testing in October 1989.

Short term repeatability group In September 1991 a new cohort of children of the same age was selected from the lists of the same GP practices using a similar questionnaire. Children who responded positively to the question enquiring into the presence of wheeze and/or cough were invited for skin-prick testing. Twenty-nine children, taken in the order in which they returned their questionnaire responses, were tested in duplicate to assess the short-term repeatability of the testing method.

Skin-prick test methods

Skin-prick testing on all three occasions was carried out on the volar aspect of the forearm, using *D. pteronyssinus* (DP), cat dander (C) and mixed grass pollens (G) (Bencard, U.K.), and positive (histamine 1:1000) and

Table 1. The mean of the differences, 95% confidence intervals and coefficients of repeatability (mm) for each allergen and histamine control for the short-term repeatability group

	Histamine	<i>Dermatophagoides pteronyssinus</i>	Mixed grass pollens	Cat dander
Mean of differences	-0.07	-0.03	0.03	-0.07
95% confidence interval	-0.17-0.03	-0.11-0.04	-0.04-0.11	-0.21-0.07
Coefficient of repeatability	0.52	0.38	0.38	0.72

negative (0.9% saline) controls. Sterile skin-prick lancets (1 mm) (Dome/Hollister-Stier) were used as directed by the manufacturer. The 29 children in the short-term repeatability group were tested in duplicate on the same arm, with the duplicate allergen solutions separated by a distance of at least 3 cm.

The test was read after 10 min, the maximum diameter of the weal being measured in millimetres. A weal size of ≥ 2 mm to one or more allergens was regarded as a positive result. No child was taking any medication that might interfere with skin test reactivity, in particular no anti-histamine preparations. Each child was tested by the same investigator at the same time of day on the two occasions. The above methods (and in particular the 2 mm cut-off for a positive result) were used to allow comparison between the results of the first longitudinal study on bronchial responsiveness [20] and the related study of Josephs *et al.* [21].

Only the data on the 114 children who underwent testing on both occasions are presented; this subgroup is representative of the original cohort of 192 children, in that the proportions of children with cough alone and wheeze with or without cough, and the proportions of children skin-test positive and negative in the 192 children tested in 1987 (both initially 50:50), remained virtually unchanged at 52% cough and 48% wheeze and 51% skin-test positive and 49% skin-test negative in the 114 children who consented to be tested again in 1989.

Data analysis

Longitudinal cohort The percentages of children testing positively and negatively were calculated for the tests carried out in 1987 and in 1989, and the percentage agreement (the number of children with the same result on both occasions) was calculated.

For each allergen and the histamine control solution, the differences between the results of the tests in 1987 and 1989 were calculated for each child. The data for those children who had changed skin-prick test status was examined and those children who demonstrated no change in weal size greater than ± 2 mm to any of the

allergen extracts were considered to have undergone borderline changes only.

The following three groups were identified: Group 1 representing those children with no change in skin-prick test status, Group 2 those with only borderline change and Group 3 those with unequivocal change in skin-prick test status.

The data was also analysed using a 3 mm cut-off for skin-test positivity to examine the influence of our choice of a 2 mm cut-off on the results of the study.

The means and 95% confidence intervals (CI) of the differences between the weal sizes measured in 1987 and 1989 were calculated for each allergen and for histamine control for each of the three groups, and the coefficients of repeatability were calculated for each allergen and for histamine control, for each of the three groups, as recommended by Chinn [22]: by taking the differences, calculating the mean of the differences, and deriving the coefficient of repeatability ($2 \times$ the standard deviation of the differences) according to the method of Bland and Altman [23].

To test the hypothesis that children in Group 3 had significantly changed their skin-prick test status, while those children in Group 2 had not, the differences in weal size for each allergen and for histamine control for each of the three groups were compared using one-way analysis of variance (SPSS), and the Newman-Keuls test (SPSS) was used for multiple comparisons between groups. The frequency distributions of the number of children who had initially reported wheeze or cough, in Groups 2 and 3 were compared using Fisher's exact test.

Short-term repeatability group The repeatability of the skin-prick testing method for each allergen and the histamine control solution was assessed by comparing the coefficients of repeatability, derived as above.

Results

Short-term repeatability group The means of the differences and 95% confidence intervals for the duplicate skin-prick tests, and the coefficients of repeatability for each

Table 2. Skin-prick test weal size (mm) in 1987 and 1989, and the overall change, for children in groups 2 and 3

Child's initials	<i>Dermatophagoides pteronyssinus</i>		Mixed grass pollens		Cat dander		Overall change
	1987	1989	1987	1989	1987	1989	
CAB*	0	5	0	10	0	4	+19
MWG*	0	4	0	6	0	2	+12
STS*	0	6	0	3	0	3	+12
NIL*	1	6	0	6	0	0	+11
STW*	1	0	0	6	0	4	+9
PAR†	0	2	0	0	0	1	+3
CAA†	0	0	0	2	0	0	+2
ANA†	0	2	0	0	0	0	+2
SYB†	0	0	0	0	0	2	+2
LAP†	0	0	0	2	0	0	+2
PAT†	0	0	0	2	0	0	+2
EDR†	0	2	0	0	1	0	+1
PEW†	2	1	1	1	0	1	0
DOW†	0	0	2	1	0	0	-1
EMH†	3	1	0	0	0	0	-2
CAD†	0	0	2	0	0	0	-2
EMK†	2	0	0	0	0	0	-2
JRL†	1	0	2	0	0	0	-3
JEL†	2	0	2	0	0	0	-4
GIC†	2	0	2	0	2	0	-6

*, children with unequivocal change in skin-prick test status (Group 3)

†, children with borderline change in skin-prick test status (Group 2)

Table 3. The mean of the differences, standard error of the means and coefficients of repeatability (mm) for the allergen and histamine control induced weal sizes in 1987 and 1989 for Groups 1, 2, 1 and 2 combined and Group 3

Group	Histamine	<i>Dermatophagoides pteronyssinus</i>	Mixed grass pollens	Cat dander
1 (<i>n</i> =91) Mean of differences	0.25	0.29	0.12	0.26
95% confidence interval	0.0-0.6	-0.1-0.6	-0.2-0.4	0.0-0.5
Coefficient of repeatability	2.88	3.43	2.79	2.42
2 (<i>n</i> =15) Mean of differences	0.47	-0.27	-0.20	0.07
95% confidence interval	-0.4-1.3	-1.1-0.5	-1.0-0.6	-0.4-0.6
Coefficient of repeatability	3.10	2.88	2.84	1.76
1 and 2 (<i>n</i> =109) Mean of differences	0.28	0.21	0.07	0.24
95% confidence interval	0.0-0.6	-0.1-0.5	-0.2-0.3	0.0-0.5
Coefficient of repeatability	2.9	3.37	2.8	2.33
3 (<i>n</i> =5) Mean of differences	1.6	3.80	6.20	2.60
95% confidence interval	0.5-2.7	0.4-7.3	3.1-9.3	0.5-4.7
Coefficient of repeatability	1.79	5.54	4.98	3.34

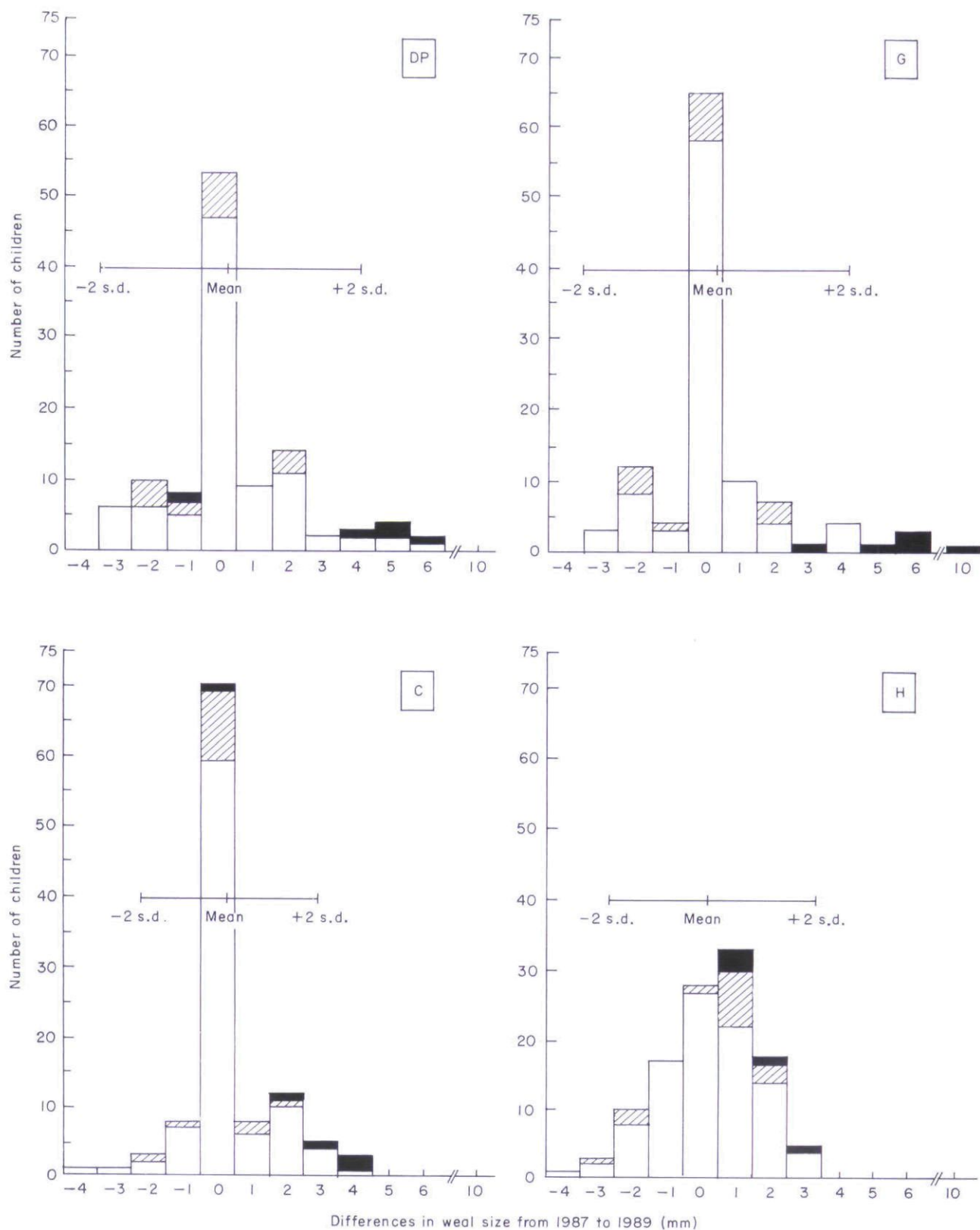


Fig. 1.

allergen and histamine control are presented in Table 1. The testing method is repeatable in the short term with the coefficients of repeatability being 0.38 mm or 0.72 mm depending on the allergen used.

Longitudinal cohort When tested in 1987, no child responded to saline, or failed to respond to histamine; when the tests were repeated 2 years later, one child reacted to skin-testing with saline in producing a 1 mm weal (in this child the response to each allergen was a weal ≥ 2 mm), while three children failed to respond to histamine (these children were skin-prick test negative to all allergens on both occasions). However, only data on the 111 children completing satisfactory testing on both occasions is presented. When first tested in 1987, 58 (52%) children were skin-prick test positive, while 53 (48%) were skin-prick test negative. Two years later 62 (56%) children were skin-prick test positive and 49 (44%) were skin-prick test negative. Twelve children (11%) changed status from skin-prick test negative to skin-prick test positive during the 2 year span, while eight (7%) children reverted from positive to negative testing. The percentage agreement (percentage of all the children with the same positive or negative test result on the two occasions) was 82%.

Ninety-one children did not change skin-prick test status (Group 1), 15 children demonstrated borderline changes only (Group 2), and five children demonstrated unequivocal changes (Group 3). The individual skin-prick test weal sizes in millimetres for the children with borderline (Group 2), and unequivocal (Group 3) changes are presented in Table 2. The mean of the differences in weal size, 95% confidence intervals and the coefficients of repeatability for each allergen and histamine control, for each Group, and for Groups 1 and 2 combined are presented in Table 3. In contrast to the short term repeatability the repeatability of skin-prick testing over a 2 year interval was poor, with coefficients of repeatability for Group 1 (no change in status) ranging from 2.42 mm for cat dander to 3.43 mm for *D. pteronyssinus*.

The frequency distribution of the differences in weal sizes for each allergen and for histamine control for the entire cohort, are depicted in Fig. 1. For *D. pteronyssinus*, mixed grass pollens and cat dander respectively, 53, 65 and 70 of the 111 children had the same measured weal responses to allergen testing on the two occasions, while 6, 5 and 10 children respectively, demonstrated differences in weal size of more than 2 s.d. (all but two of these demonstrating an increase rather than a decrease in weal size).

The data presented in Table 3, demonstrate that the means of the differences in weal size and the coefficients of repeatability for the three allergens and for histamine control are virtually identical for Groups 1 and 2, while for Group 3 the means of the differences for the allergens are at least tenfold greater, and coefficients of repeatability approximately two times greater than Group 1 or Group 2, yet the coefficient of repeatability for histamine control for Group 3 is smaller than that for Groups 1 and 2. This suggests that there are no significant differences in the skin-prick test status between Groups 1 and 2 (no change in status and borderline change respectively), while the changes in skin-prick testing observed in Group 3 may represent significant changes. Statistical analysis supports this interpretation, in that there were significant differences between the three groups in allergen-induced weal size for each allergen ($P < 0.0001$, one way analysis of variance). Multiple comparison testing revealed that the differences between Groups 1 and 2 were not significant ($P = \text{n.s.}$ for each allergen, Newman-Keuls test), while the differences both between Group 3 and Group 2 and between Group 3 and Group 1 were significant ($P < 0.05$ for each allergen, Newman-Keuls test). The differences between Groups 1, 2 and 3 in histamine induced weal size were, however, not significant ($P = \text{n.s.}$, one way analysis of variance).

When the data were analysed using a 3 mm cut-off 12 children changed status from skin-test negative to skin-test positive (11%), and four children changed from skin-test positive to skin-test negative (3.5%). There was a similar pattern of degrees of change in that employing a difference in allergen induced weal size of greater than 3 mm to represent unequivocal change, resulted in six (5%) children having changed status unequivocally, all six becoming skin test positive having previously been negative, while 10 (9%) children demonstrated only borderline changes (Table 4).

Discussion

This study demonstrates that skin-prick testing to common allergens using 1 mm prick lancets in a population of

Fig. 1. Histograms showing the numbers of children and the differences in weal size in millimetres from 1987 to 1989 for each allergen and for histamine control. Graphs clockwise from top left are for *Dermatophagoides pteronyssinus* (DP), mixed grass pollens (G), histamine (H) and cat dander (C). The horizontal axes represent the differences in weal size in millimetres for each child between 1987 and 1989. The vertical axes represent the number of children in each category. The horizontal bars represent the mean ± 2 s.d.'s of the differences. □, Group 1 (no change in skin-prick test status). ▤, Group 2 (borderline change). ■, Group 3 (unequivocal change).

7-9-year-old children with troublesome respiratory symptoms is highly repeatable when duplicate tests are performed simultaneously. However, the repeatability of individual skin-prick tests over 2 years in a similar population was poor. The percentage agreement between skin-prick test status in 1987 and 1989 for the group as a whole was good at 82%.

The overall conversion rate from skin-test negativity to positivity over 2 years was 11% while that from skin-test positivity to negativity was 7%. Two previously published studies in healthy children by Barbee *et al.* [18] and Peat *et al.* [19], found an increase in the prevalence of positive skin-prick test reactions of 19.5% (2.4% per year) and 15.3% (3.8% per year) respectively, and reversion from skin-prick test positive to negative in 0% and 3% (0.75% per year), when the subjects were tested over intervals of 8 years and 4 years respectively. The study reported here has demonstrated higher conversion rates from skin-prick test negative to positive status (5.5% per year), and from skin-prick test positive to negative status (3.5% per year). These differences may be accounted for by differences in the study populations, the children in this study having reported troublesome respiratory symptoms, while those in the two studies cited above were healthy children. However, the overall prevalence of skin test positivity in the two studies at the final testing (58.6% [18] and 39% [19]) were similar to the population reported here (54%).

A further possible explanation is the fact that the studies used different methods for the skin-prick tests and employed different definitions of a positive reaction. Both previous studies [18,19] used the method according to Pepys [24], while the study reported here employed 1 mm skin-prick lancets. In this study a weal ≥ 2 mm was regarded as a positive reaction. Peat *et al.* [19] regarded a weal ≥ 4 mm as a positive reaction, while Barbee *et al.* [18] used an index of skin reactivity, with all reactions graded 0-4, and a reaction greater than control being considered positive. We chose to use 1 mm skin-prick lancets as these have been shown to be more reproducible than a 25 gauge needle [25]. The choice of a weal size ≥ 2 mm as a definition for a positive reaction was made to allow comparison of the original cohort of 192 children with the study of Josephs [21]. The EAACI position paper on skin testing [25] recommends the use of a 3 mm cut-off for a positive reaction and the use of 1 mm lancets. The conversion rates observed when the data was analysed using a 3 mm cut-off were almost identical to those found with a 2 mm cut-off, the choice of the lower cut-off of 2 mm is therefore unlikely to be an important factor in interpreting these results.

The definitions used in the division of those children changing skin-prick test status into those with borderline

(Group 2) and unequivocal (Group 3) were arbitrary. However, the validity of this division is supported by statistical analysis which suggests that there was no significant change in the skin-prick test status of Groups 1 and 2, while that observed in Group 3 was significant. This interpretation is illustrated in Fig. 1 where the children in Group 3 occupy positions that are almost exclusively outside 2 s.d.'s of the mean value (95% confidence limit) for each allergen, but not for histamine control, suggesting that in Group 3 the reactivity to allergen had changed significantly, while that to histamine had not. The minor differences observed over 2 years in the skin-prick tests in children in Groups 1 and 2 might be a result of a combination of technical factors, such as variations in the depth of allergen penetration, which is known to be an important determinant of the test result [16,17], and the fact that the testing in 1987 was carried out during the 3 months at or soon after the end of the pollen season, while that in 1989 was carried out well after the end of the pollen season. This variation in timing would tend to underestimate the number of children changing from a negative test to a positive test, and to overestimate the number of children changing from a positive test to a negative test. The fact, however, that the increases in mean weal size for the whole cohort over the 2 years are virtually identical for grass pollen (0.37 mm, CI 0.01-0.72 mm), *D. pteronyssinus* (0.35 mm, CI -0.01-0.71 mm) and cat dander (0.34 mm, CI 0.10-0.58 mm) suggests that this effect, if present must be small.

In contrast the changes in skin responses observed in Group 3 (unequivocal change) are more likely to represent true changes in skin-prick test status, and to reflect a small increase (4%) in the prevalence of skin-prick test positivity in the cohort of schoolchildren with increasing age, as shown in other studies [18,19].

In 1987, 52% of the children reported cough alone while 48% reported wheeze with or without a cough. Interestingly 80% of the group with unequivocal change reported wheeze in 1987, compared with only 20% of the borderline change group ($P < 0.05$, Fisher's exact test). Clifford *et al.* carried out a cross-sectional study of atopy and respiratory symptoms in 7- and 11-year-old children [26]. Among children with cough alone, atopy was detected in 22% of 7-year-olds and 27% of 11-year-olds. The prevalence of atopy was also greater at 11 than 7 among children with wheeze (68% vs. 52%) and among children with wheeze and breathlessness (78% vs. 53%). Clifford *et al.* also found the prevalence of both cough, and wheeze when it was not associated with the combination of bronchial hyperresponsiveness and atopy, to be higher in 7- than 11-year-old children [27,28]. Clifford *et al.* suggested that the group with wheeze, bronchial hyperresponsiveness and atopy represented children with

Table 4. Allergen weal sizes (mm) in 1987 and 1989, for children changing skin-test status using 3 mm as the cut-off for positivity

Child's initials	<i>Dermatophagoides pteronyssinus</i>		Mixed grass pollens		Cat dander	
	1987	1989	1987	1989	1987	1989
CAB*	0	5	0	10	0	4
MWG*	0	4	0	6	0	2
STS*	0	6	0	3	0	3
NIL*	1	6	0	6	0	0
STW*	1	0	0	6	0	4
JOH*	0	5	0	4	2	4
ALT†	2	4	2	4	2	0
MAS†	2	4	0	0	0	3
ANB†	1	0	2	4	0	0
IAH†	2	4	0	0	0	0
SNW†	0	3	0	0	0	0
CLM†	0	2	2	3	0	0
CHP†	3	0	0	0	5	2
STF†	0	0	4	2	0	0
EMH†	3	1	0	0	0	0
ANI†	1	1	3	2	0	2

*, children with unequivocal changes in skin-test status

†, children with borderline changes in skin-test status

a separate disease entity than the groups with either cough alone or with wheeze in the absence of bronchial hyper-responsiveness and atopy. This suggestion is supported in part by the disparity in symptoms reported by Groups 2 and 3 in this study. It is tempting to speculate that at least for the children in Group 3, the symptom of wheeze may be an early manifestation of the atopic diathesis accompanied by the later development of positive skin-prick tests. It is more difficult to interpret the significance of the preponderance of children originally reporting cough in Group 2.

Despite the recommendations made in the EAACI position paper [25], no consensus has been reached as to which methods of skin-testing should be employed, and as to what the criteria for skin-test positivity should be, particularly as differing weal sizes will be produced by different methods [16, 17] and when testing different ages [18]. It would therefore seem wise when considering longitudinal changes in skin-test reactivity, to consider the weal sizes and the changes involved, and to relate the degrees of change to the intrinsic repeatability of the testing method, rather than considering changes from atopic to non-atopic or vice versa, as the definition of what weal size identifies an atopic individual is, by necessity, arbitrary. A possible criticism of this study is

the fact that the longitudinal testing was not performed in duplicate, and therefore that the differences in testing between 1987 and 1989 may have been due to inaccuracies in the testing methods rather than real changes in skin-test reactivity. Duplicate testing was not carried out at the initial testing in 1987, as a follow-up study in the same children was not planned at that stage. Having decided to perform the further study in 1989, skin-prick testing was repeated using the same methods as on the first occasion. We have attempted to answer this criticism by confirming the reproducibility of the skin-testing methods used, in a similar population of children, using identical methods, and have demonstrated good short-term reproducibility. Neither of the two previous longitudinal studies performed skin-testing in duplicate [18,19], and so the comparisons made between this study and the previous studies are likely to be valid.

In conclusion, this study confirms that skin-prick testing using 1 mm lancets in a paediatric population with respiratory symptoms is highly repeatable in tests carried out in duplicate, while over a period of 2 years the repeatability of individual tests is poor. However, for the group as a whole, the percentage agreement between the children's skin-prick test status over 2 years was good. The interpretation of population data in longitudinal

studies of skin-prick testing is therefore likely to be reliable, while interpretations based on changes in individual skin-prick test results, as used in immunotherapy studies where changes in skin-prick tests are used to direct therapy, may be less so.

Five (4%) children changed skin-prick status unequivocally from negative to positive, while unequivocal change from positive to negative status was not demonstrated.

This work highlights some of the difficulties involved in the interpretation of skin-prick tests, and the need for the introduction of standardized skin-prick testing techniques, using standardized allergen preparations and 1 mm prick lancets, possibly with a device to standardize the depth of allergen penetration. It is desirable that any future longitudinal studies on skin-prick testing employ such methods, preferably with testing being performed in duplicate.

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