

ORIGINAL PAPER

Number of allergens to be tested to assess allergenic sensitization in epidemiologic studies: results of the European Community Respiratory Health Survey I

P.-J. Bousquet*, R. Hooper*, M. Kogevinas[†], D. Jarvis* and P. Burney*

*Imperial College, Emmanuel Kaye Building, London, UK and [†]Department of Social Medicine, Faculty of Medicine, Heraklion, Crete, Greece

Clinical and Experimental Allergy

Summary

Background Many clinical and epidemiological studies have measured the prevalence of IgE sensitization using skin tests and/or serum-specific IgE. Most of them have been done in only one country using a battery of selected allergens relevant to that country. In multi-centre studies, the number of tested allergens is often limited by the cost. It is therefore difficult to compare prevalence of sensitized subjects between studies.

Objective To define the number and the type of allergen that should be tested in order to characterize a person as sensitized.

Method Subjects were selected from the European Community Respiratory Health Survey I. All subjects underwent skin prick tests to nine of the most common allergens. In addition, two local allergens were tested in some centres.

Result Using nine allergens, 35.6% of the 11 355 subjects were sensitized. The prevalence of sensitization increased with the number of tested allergens. Seven allergens enabled the identification of almost all sensitized subjects, adding another one inducing, in most countries, an increase of prevalence under 0.5%. Adding one local allergen to the battery of tests increased the overall estimated prevalence by only 1%. This increase was not seen in Ireland and was less marked in the United Kingdom (0.3%) but was greater in France (2.6%), Australia (2.5%) and Belgium (1.9%).

Conclusion Seven selected allergens (*Dermatophagoides pteronyssinus*, cat, grass, birch, olive pollen, *Alternaria* and *Cladosporium*) allow the identification of almost all sensitized subjects in epidemiologic studies. Inclusion of local allergen should be considered in a standard panel for international studies.

Keywords allergen, ECHRS, epidemiologic study, sensitization, skin prick test

Submitted 18 October 2006; revised 23 February 2007; accepted 5 March 2007

Correspondence:

Peter Burney, Imperial College,
Emmanuel Kaye Building, Manresa
Road, London SW3 6LR, UK.
E-mail: p.burney@imperial.ac.uk

Introduction

The synthesis of allergen-specific IgE is required for the development of allergic diseases including allergic rhinitis (AR) [1] and asthma [2, 3]. The assessment of allergic sensitization may be determined using allergen-specific IgE in serum or skin tests with the relevant allergen [4–8].

Many clinical or epidemiological studies [5, 9–11] aim to assess the prevalence of IgE sensitization to any allergen and therefore need to be able to characterize study participants as IgE sensitized or not IgE sensitized. As being sensitized to one allergen is associated with sensitization to another, and the prevalence of

IgE sensitization to some allergens is uncommon, testing for a limited number of allergens may be sufficient for such purposes. However, the number and species of allergen to measure the prevalence of IgE sensitization with sufficient precision in populations has not been well characterized, particularly for multi-centre studies conducted over a wide geographical area such as the European Community Respiratory Health Survey (ECRHS) or the International Study of Asthma and Allergies in Childhood [12–14]. These multi-centre studies pose a particular problem as sensitization to allergens that are relevant in one area may have little relevance for other geographical regions.

The ECRHS-I, a multi-centre international cross-sectional survey of the general population [12, 13], is a unique study which may answer these questions as a very large number of well-characterized subjects were studied, and skin tests (Phazet[®], Pharmacia, Uppsala, Sweden) were tested with nine different allergens [7, 15–17].

The aim of the present study is to define the number and the type of skin prick test (SPT) allergens required to identify a subject as sensitized using results of SPT from ECRHS, a large international multi-centre community-based study of adults.

Materials and methods

Population and inclusion criteria

The population of this study is based on the ECRHS I conducted in 37 centres in 17 countries. Representative samples of the adult population aged between 20 and 44 years were obtained by random sampling from population-based registers, the details of which are described elsewhere [12, 13]. Centres were included in this analysis if they complied with the skin testing protocol – measuring nine allergens common to all centres and in addition measured one or two local allergens.

Sensitization and skin prick tests

In the present study, the allergen-coated Phazet[®] was used [7, 15–17] including *Dermatophagoides pteronyssinus*, timothy grass pollen, cat, *Cladosporium herbarum*, *Alternaria alternata*, birch, *Olea europea* (olive), *Parietaria judaica* and ragweed pollen. A histamine positive control and a negative control were also tested.

According to a previous study [9], in the ECHRS I survey, a SPT was considered to be positive if the mean weal diameter was found to be over 0 mm. Subjects were excluded if they had a positive negative control (405 subjects, 2.2%) or had a mean weal diameter of over 30 mm for at least one allergen as this would lead to a practical difficulty in assessing the reaction to other allergens (two subjects, 0.01%).

Local allergens were tested if *a priori* considered to be important in the local area and when they were not included in the standard battery (*Aspergillus*, chestnut pollen, cockroach, *Dermatophagoides farinae*, dog, horse, *Leptidoglyphus destructor*, mugwort pollen, plantain pollen, and rye grass pollen).

Subjects with at least one positive SPT were considered to be sensitized.

Statistical analysis

The prevalence of sensitization was first assessed for each of the nine allergens tested in all centres using frequencies

and percentages. This allowed ordering of the allergens from the most to the least common, and the prevalence of sensitized subjects was then computed adding each allergen step by step. We defined a sufficient number of allergens as the point at which adding further allergens increased the estimated prevalence by no more than 0.5% for each allergen added. Information from testing to the local allergen was then used to determine the impact of these further tests on previous findings.

Results

Thirty-seven centres and 17 countries (18 794 participants) performed serum allergen-specific IgE measurement or SPT for the most common allergens (Fig. 1). Among them, five centres and 3528 subjects had to be excluded due to a variation in the protocol within the centre. In one centre, SPTs were not performed with the Phazet[®]. One centre did not perform ragweed pollen SPTs and two did not perform grass, olive, *Parietaria* and ragweed pollen SPTs. Another centre also had to be excluded due to technical failure (most of the subjects had a positive negative saline control). The analysis was therefore restricted to information from 32 centres in 13 countries (15 266 participants). Of these 2643 subjects were excluded 2370 because SPTs and serum allergen-specific measurement were not performed, 270 due to a lack of all nine SPTs, and three due to a lack of at least one SPT. As this study is part of a group of studies, and SPT cut-off was assessed in subjects with SPT and serum-specific-IgE measurement, 1268 subjects without serum-specific-IgE measurement were also excluded. These exclusions did not alter the sex ratio, age, symptoms frequencies (asthma, rhinitis, skin allergy), tobacco status (current, past, passive, and never smoker) or socioeconomic level of the population. The following results were similar with and without the later group of subjects.

The median age of the 11 355 subjects [5669 (49.9%) men and 5686 (50.1%) women] studied was 34.0 (27.9–40.1) years. Overall, 5.0% of the subjects currently had asthma (attack of asthma within the last year and/or used medication for asthma), 0.9% without rhinitis and 4.1% associated with an AR. Finally, 38.1% reported 'hayfever or nasal allergies' (AR).

Overall the prevalence of sensitization to ragweed, *Parietaria*, *Cladosporium*, olive pollen, and *Alternaria* was relatively low (1.3%, 1.5%, 2.3%, 3.7% and 4.4%, respectively). The prevalence of sensitization to birch was 8.2%. On the other hand, over 10% of the subjects were sensitized to cat, timothy grass, and *D. pteronyssinus* (10.2%, 16.6% and 20.9%, respectively). The prevalence of sensitized subjects increased from 20.9% (using one allergen: *D. pteronyssinus*) to 35.6% (using nine allergens) (Table 1). Six allergens (*D. pteronyssinus*, grass, cat, birch, *Alternaria* and olive pollen) gave a prevalence of 34.8%,

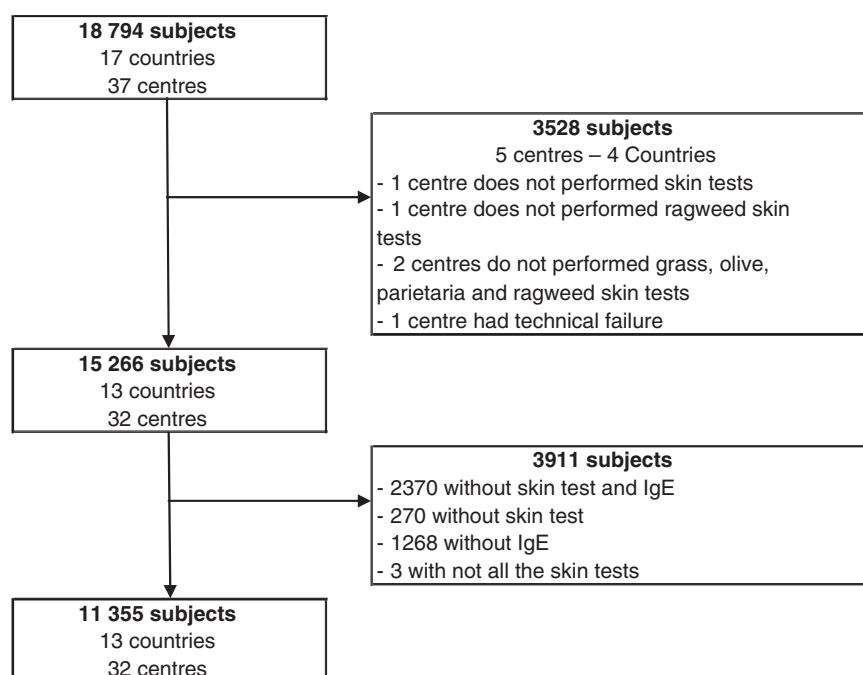


Fig. 1. Flow chart.

Table 1. Prevalence of sensitized subjects depending on the number of tested allergens

	Allergen prevalence alone (%)	Estimated sensitized prevalence	Increased in estimated of sensitization (%)
<i>Dermatophagoides pteronyssinus</i>	20.9	2373 (20.9%)	
+ Grass	16.6	3338 (29.4%)	8.5
+ Cat	10.2	3611 (31.8%)	2.4
+ Birch	8.2	3815 (33.6%)	1.8
+ <i>Alternaria</i>	4.4	3895 (34.3%)	0.7
+ Olive	3.7	3952 (34.8%)	0.5
+ <i>Cladosporium</i>	2.3	3997 (35.2%)	0.4
+ <i>Parietaria</i>	1.5	4031 (35.5%)	0.3
+ Ragweed	1.3	4042 (35.6%)	0.1

which was sufficient for the increase in prevalence with each subsequent allergen tested to be <0.5% (Table 1).

The number of allergens required in a given country to characterize an individual as sensitized was dependent on the choice (type) of the allergens. Using the same sequence of allergens in all the countries, the required number of allergens ranged from four in Belgium and Iceland (*D. pteronyssinus*, cat, grass and birch) to eight in Italy and Sweden (*D. pteronyssinus*, cat, grass, birch, olive pollen, *Alternaria*, *Cladosporium*, and *Parietaria*) (Table 2). In the United States, our criterion was not met with nine allergens: the ninth allergen (ragweed) increased prevalence by 0.9%. Thus, at a country-wide level, adding a seventh allergen (*Cladosporium*) to the six previously

selected meets the criterion for 10 out of 13 countries. Compared with nine allergens, the underestimated prevalence was under 1% for Sweden and the United States.

With allergens ordered according to their prevalence in a given country, the required number of allergens ranged from three in Spain to eight in Sweden (Table 3).

The overall prevalence of subjects sensitized to the most common local allergen tested in each centre was 12.8% (Table 4). However, two countries (Norway and the Netherlands) and three other centres (Barcelona – Spain, Pessac, and Grenoble – France) did not perform a local allergen SPT. Prevalence of SPT sensitization to the chosen local allergen was low for Belgium (mugwort – 3.9%) but was the most common positive skin test (rye grass – 37.6%) in Australia. SPT sensitization to the chosen local allergen was also high in New Zealand and Sweden (rye grass – 20.0 and dog – 16.2%, respectively). However, as most subjects who were sensitized to the local allergen were also sensitized to at least one of the other tested allergens, inclusion of the local allergen did not change markedly the classification of subjects as sensitized or not sensitized compared with the use of nine allergens. In France, cockroach induced an increase of 2.6% in the prevalence of allergy; in Belgium, mugwort a change of 1.9%; and in Australia rye grass a change of 2.5%. In the other centres, change in prevalence was <1% (Table 4). Overall, the estimated prevalence of sensitized subjects increased slightly from 35.3% (using nine allergens) to 36.3% (using nine allergens plus the local one). The results were similar when seven and seven plus the local one were tested. Except in Belgium, the

Table 2. Increase in estimate of prevalence of sensitization for each country on adding each successive allergen (%), with allergens in order of their prevalence in the whole population

	Prevalence with nine allergens (%)	Allergens*								
		1	2	3	4	5	6	7	8	9
Australia	49.1	36.4	9.1	0.7	0.4	1.6	0.5	0.4	0	0
Belgium	33.0	24.6	3.8	1.7	2.3	0.5	0.1	0	0	0
France	22.6	21.9	9.3	1.9	0.7	1.1	1	0.1	0.2	0.2
Iceland	51.9	8.6	7.6	3	1.4	0.2	0	0.4	0	0.2
Ireland	36.4	32.8	5.7	1.7	0	0	0	0.8	0	0.4
Italy	41.4	11.8	10.5	1.2	1.9	0.7	0.6	0	1.8	0.3
New Zealand	21.4	30.7	9	1.7	2.3	1.3	0.1	0.3	0	0
Norway	28.8	13	9	3.3	2.9	0.6	0	0.9	0	0
Spain	29.7	14.2	5.3	0.5	0.3	0.5	1.5	0.2	0.1	0
Sweden	45.4	12.7	13.2	6.2	3.2	0.3	0.2	0.4	0.6	0.4
The Netherlands	39.6	27.6	4.4	1.6	4.1	0.7	0.3	0.7	0.2	0
United Kingdom	41.2	27.7	8.4	2.3	0.8	1.5	0.1	0.3	0.1	0
USA	37.2	30.9	11.8	5.1	1.2	1.1	0.6	0.3	0	0.9
Whole population	35.6	20.9	8.5	2.4	1.8	0.7	0.5	0.4	0.3	0.1

The figure in bold in each row marks the point beyond which the increase is 0.5% or less for each additional allergen tested.

*Key to allergens: 1, *Dermatophagoides pteronyssinus*; 2, grass; 3, cat; 4, birch; 5, *Alternaria*; 6, olive pollen; 7, *Cladosporium*; 8, *Parietaria*; 9, ragweed.

United Kingdom, Iceland and New Zealand, the number of allergens needed to be tested in order to assess sensitization was reduced.

Finally, using 3 mm as an SPT cut-off did not change patterns of the results. Seven allergens remained sufficient to identify IgE-sensitized subjects (Table 5).

Discussion

Based on a multi-centre international study involving more than 11 000 subjects, we have shown that a common standardized battery of seven SPT allergens (*D. pteronyssinus*, cat, grass, birch, olive pollen, *Alternaria*, and *Cladosporium*) enabled the identification of IgE-sensitized subjects with sufficient precision for most purposes. If allergens were selected depending on the country, then only six allergens would need to be tested. Slight variations in prevalence were observed in some countries when local allergen was used. Finally, as this study is part of a group of studies and in order to be more relevant between studies, subjects without serum-specific IgE were excluded from the analysis. Results were still consistent after including these subjects.

The study was initially conducted on 37 centres. However, five centres were excluded as SPT data were not available. There is no obvious reason why inclusion of these centres would alter our results. A further 3911 (25.6%) of the 15 266 remaining subjects were excluded for a variety of reasons. The remaining population was representative of the whole population in terms of sex, age, symptoms (asthma, rhinitis, and skin allergy), tobacco status (current, past, passive, and never smokers)

and socio-economic level. There was no evidence that limitation of the sample to those who also had specific-IgE measures changed the results.

The usual definition of sensitization is based upon the presence of serum allergen-specific IgE [3, 9, 18]. While it is easy to achieve the standardization of criteria for positive and negative results with serum-specific IgE measures, the costs for the tests limit their use to a few allergens in epidemiologic or clinical studies. This limit increases the proportion of false-negative subjects (i.e. non-sensitized) in such studies. SPT are cheaper to perform but may be more difficult to standardize than serum-specific IgE [19, 20]. To decrease the variability of the SPT by different investigators, devices like the Phazet[®] have been proposed [15, 16]. This was found to be the most reproducible device [21], and has the advantage of bearing coated lyophilized allergens with a long shelf life. In the ECRHS study, identically standardized allergens originating from the same manufacturer (Pharmacia Diagnostics, Uppsala, Sweden) were used. Trained fieldworkers performed SPTs using the Phazet[®].

It has been reported that in a cohort of preschool children, 94% of atopic children could be detected by the four most common allergens (house dust mite, grass pollen, cat, and *A. alternata*) [22]. However, it is not possible to extrapolate results from childhood to adults as sensitization changes from childhood to adulthood [23].

In most centres, the addition of a local allergen made little difference to the overall prevalence as it was also previously found when using a more limited range of measurement for serum-specific IgE [18]. However, when cockroach was tested in France the prevalence of

Table 3. Increase in estimate of prevalence of sensitization for each country on adding each successive allergen (%), with allergens in order of their prevalence in each country

	Prevalence with nine allergens (%)	Allergens*								
		1	2	3	4	5	6	7	8	9
Australia	49.1	36.4	9.1	0.8	1.6	0.4	0.6	0.4	0	0
Belgium	33.0	24.6	3.8	1.7	2.3	0.5	0.2	0	0	0
France	22.6	21.9	9.3	1.9	1.5	0.9	0.4	0.3	0.1	0.2
Iceland	51.9	10.2	6.0	3.0	1.4	0.2	0.4	0.2	0	0
Ireland	36.4	32.8	5.7	1.6	0	0	0	0.8	0	0.4
Italy	41.4	13.6	8.7	1.9	1.8	1.2	0.7	0.7	0.3	0
New Zealand	21.4	30.7	8.9	2.4	1.6	1.3	0.3	0.1	0	0
Norway	28.8	14.3	7.6	3.5	2.8	1.1	0.4	0	0	0
Spain	29.7	14.2	5.3	1.8	0.4	0.3	0.4	0.1	0.1	0
Sweden	45.4	17.7	8.5	3.7	5.5	0.3	0.2	0.4	0.6	0.3
The Netherlands	39.6	27.6	4.5	4.4	1.3	0.7	0.7	0.3	0.2	0
United Kingdom	41.2	27.7	8.3	2.4	1.5	0.8	0.2	0.2	0	0.1
United States	37.2	30.9	11.9	5.0	1.2	1.2	1.2	0.3	0.3	0
Allergens [†]	d1	e1	g6	m2	m6	t9	t3	w21	w1	
Australia	1	3	2	7	4	6	5	8	9	
Belgium	1	3	2	7	5	6	4	8	9	
France	1	3	2	8	5	4	6	7	9	
Iceland	2	3	1	6	5	8	4	9	7	
Ireland	1	3	2	7	4	5	6	8	9	
Italy	2	5	1	9	7	6	3	4	8	
New Zealand	1	4	2	6	5	7	3	8	9	
Norway	2	4	1	5	6	7	3	8	9	
Spain	1	4	2	8	6	3	5	7	9	
Sweden	4	2	1	7	5	6	3	8	9	
The Netherlands	1	4	2	6	5	7	3	8	9	
United Kingdom	1	3	2	6	4	7	5	9	8	
USA	1	3	2	7	5	8	4	9	6	

The figure in bold in each row marks the point beyond which the increase is 0.5% or less for each additional allergen tested.

*Allergen order for each country.

[†]Key to allergens: d1, *Dermatophagoides pteronyssinus*; g6, grass; e1, cat; t3, birch; m6, *Alternaria*; t9, olive pollen; m2, *Cladosporium*; w21, *Parietaria*; w1, ragweed.

sensitization increased by 2.6%. Cockroach allergy is most likely to be relevant in some countries with hot and humid climate, and particularly in deprived populations [24–27]. It is possible that the prevalence of allergy would have been slightly higher in some Southern centres and Australia if cockroach has been included in the battery of allergens. However, there is some evidence that mono-sensitization to cockroach is not common in Italy or in the United States [25, 27].

In conclusion, a standardized battery of seven selected allergens allowed the identification of most sensitized subjects in an epidemiologic study. Use of additional local allergens raised the estimated prevalence relatively slightly, but by more than the 0.5% criterion that we set. Inclusion of potential local allergens in the standard skin tests should be considered at the beginning of a study. The

cost implication would be small and subsequent analysis more straightforward than adding them to a limited number of centres.

Acknowledgements

P.-J. Bousquet is a recipient of a GA²LEN and APARD travel grant.

GA2LEN centre no. 26, supported by EU Framework programme for research, contract no. FOOD-CT-2004-506378.

The authors have no conflict of interest.

Financial support for ECRHS I

The following grants helped to fund the local studies: Australia: Allen and Hanbury's, Australia.; Belgium: Belgian Science Policy Office, National Fund for Scientific

Table 4. Prevalence of the most common local allergen for each country

	N	Allergen tested	Missing value	Positive*	Change in prevalence	
					9	7
Belgium	578	Mugwort	13 (2.2%)	22 (3.9%)	1.9	1.9
Spain	1362	†	169 (12.4%)	68 (5.7%)	0.6	0.6
France‡	1821	Cockroach	940 (51.6%)	80 (9.1%)	2.6	2.8
Ireland	244	Dog	–	23 (9.4%)	0	0
Italy	744	Rye grass	–	77 (10.3%)	0.8	0.9
United Kingdom	1212	Dog	–	137 (11.3%)	0.3	0.3
Iceland	499	Dog	–	44 (8.8%)	0.6	0.6
Sweden	1502	Dog	–	244 (16.2%)	0.8	1.1
New-Zealand	696	Rye grass	–	139 (20.0%)	0.6	0.6
Australia	517	Rye grass	1 (0.2)	194 (37.6%)	2.5	2.5
Whole population	9175		1123 (12.2%)	1029 (12.8%)	1.0	

*Negative and positive: percentages based on non-missing value.

Change in prevalence: difference between tested nine allergens and nine + local one; and seven allergens and seven + local one.

†Spain: Barcelona: no local allergen; Galdakao: knaume grass; Sevilla: cocksfoot; Albacete, Huelva: dog.

‡France: Pessac, Grenoble: no local allergen.

Table 5. Increase in estimate of prevalence of sensitization for each country on adding each successive allergen (%), with allergens in order of their prevalence in the whole population

Allergen*	1	2	3	4	5	6	7	8	9
Australia	34.43	9.3	0.4	0.4	1.5	0.6	0.2	0	0
Belgium	20.76	2.9	1.6	2.6	0.3	0.2	0.2	0	0
France	19.55	8.6	1.2	0.7	1	0.8	0.1	0.2	0.2
Iceland	5.01	6.4	3.8	1.6	0.2	0	0	0	0
Ireland	28.28	4.9	1.6	0.4	0	0	0.8	0	0
Italy	9.41	9.4	0.9	1.9	0.7	0.8	0	1.9	0.3
New	25.29	9.2	0.9	2.6	1	0	0.3	0	0
Norway	12.32	8.2	2.8	3.1	0.4	0	0.9	0	0
Spain	13.14	5.1	0.5	0.3	0.5	1.5	0.1	0.2	0
Sweden	9.79	12.8	5.9	3.9	0.3	0.2	0.3	0.6	0.2
The Netherlands	21.62	3.9	0.9	3.8	0.5	0.1	0.3	0	0
United Kingdom	22.44	8.1	1.5	0.8	1	0.1	0.1	0	0
United States	21.96	13.7	3	0.9	1.5	0.6	0.6	0	0.6
Whole population	17.6	8	1.9	1.9	0.7	0.4	0.2	0.3	0.1

Skin prick tests cut-off 3 mm.

The figure in bold in each row marks the point beyond which the increase is 0.5% or less for each additional allergen tested.

*Key to allergens: 1, *Dermaphagoides pteronyssinus*; 2, grass; 3, cat; 4, birch; 5, *Alternaria*; 6, olive pollen; 7, *Cladosporium*; 8, *Parietaria*; 9, ragweed.

Research; France: Ministère de la Santé, Glaxo France, Institut Pneumologique d'Aquitaine, Contrat de Plan Etat-Région Languedoc-Rousillon, CNMATS, CNMRT (90MR/10, 91AF/6), Ministre délégué de la santé, RNSP; Germany: GSF, and the Bundesminister für Forschung und Technologie, Bonn; Italy: Ministero del Università e della Ricerca Scientifica e Tecnologica, CNR, Regione Veneto grant RSF n. 381/05.93; New Zealand: Asthma Foundation of New Zealand, Lotteries Grant Board, Health Research Council of New Zealand; Norway: Norwegian Research Council project no. 101422/310; the Nether-

lands: Dutch Ministry of Wellbeing, Public Health and Culture; Spain: Ministerio Sanidad y Consumo FIS (grants #91/0016060/00E-05E and #93/0393), and grants from Hospital General de Albacete, Hospital General Juan Ramón Jiménez, Consejería de Sanidad Principado de Asturias; Sweden: The Swedish Medical Research Council, the Swedish Heart Lung Foundation, the Swedish Association against Asthma and Allergy; Switzerland: Swiss National Science Foundation grant 4026-28099; UK: National Asthma Campaign, British Lung Foundation, Department of Health, South Thames Regional Health

Authority; and USA: United States Department of Health, Education and Welfare Public Health Service (grant #2 S07 RR05521-28).

List of principal participants

Co-ordinating Centre (London)

Peter Burney, MD, Susan Chinn, DSc, Christina Luczynska, PhD, Deborah Jarvis, MFPHM, Eric Lai, BSc.

Project Management Group

Peter Burney, MD (project leader), Susan Chinn, DSc, Christina Luczynska, PhD, Deborah Jarvis, MFPHM, (London); Paul Vermeire, MD, (Antwerp); Hugo Kesteloot, MD, PhD, (Leuven); Jean Bousquet, MD, (Montpellier); Dennis Nowak, MD, (Hamburg); the late John Prichard, PhD, FRCPI, (Dublin); Roberto de Marco, MD, (Verona); Bert Rijcken, MD, PhD, (Groningen) Josep M. Anto, MD, (Barcelona); Jose Alves, MD, (Oporto); Gunnar Boman, MD, (Uppsala)

Participating centres providing samples for assays of immunoglobulin E

Australia: Michael Abramson, MB, BS, PhD, Jozica Kutin, BA, MPsych, (Melbourne); *Belgium:* Paul Vermeire, MD, Frank van Bastelaer, MD, (Antwerp South, Antwerp Central); *France:* Jean Bousquet, MD, (Montpellier); Françoise Neukirch, MD, Renata Liard, PhD, (Paris); Isabelle Pin, MD, Christophe Pison, MD, (Grenoble); André Teytard, MD, (Bordeaux); *Germany:* Helgo Magnussen, MD, Dennis Nowak, MD, (Hamburg); H-Erich Wichmann, MD, Joachim Heinrich, MD (Erfurt); *Iceland:* Thorarinn Gislason, MD, PhD, H. David Gislason, MD, (Reykjavik); *Ireland:* the late John Prichard, D Phil, FRCPI, Shane Allwright, PhD, Dominic MacLeod, MB, BSc, (Dublin); *Italy:* Massimiliano Bugiani, MD, Caterina Bucca, MD, Canzio Romano, MD, (Turin); Roberto de Marco, MD, Vincenzo Lo Cascio, MD, Cesare Campello, MD, (Verona); Alessandra Marinoni, MD, Isa Cerveri, MD, Lucio Casali, MD, (Pavia); *Netherlands:* Bert Rijcken, MD, PhD, Anja M. Kremer, MD, PhD, (Groningen, Bergen-op-Zoom, Geleen); *New Zealand:* Julian Crane, FRACP, Simon Lewis, BSc, (Wellington, Christchurch, Hawkes Bay); *Norway:* Around Gulsvik, MD, PhD, Ernst Omenaas, MD, PhD, (Bergen); *Spain:* Josep M. Anto, MD, Jordi Sunyer, MD, Felip Burgos, Resp Tech, Jordi Castellsague, MD, Josep Roca, MD, Joan Soriano, MD, Aureli Tobias, BSc, Dip Stat, (Barcelona); Nerea Muniozguen, MD, Jacinto Ramos-Gonzalez, MD, Alberto Capelastegui, MD, (Galdakao); Jose Castillo, MD, Jose Rodriguez-Portal, MD, (Seville); Jesus Martinez-Moratalla, MD, Enrique Almar-Marques, MD, (Albacete); Jose Maldonado-Pérez, MD, Antonio Pereira, MD, Jose Sfinchez-Ramos, MD (Huelva); Roman Quiros, MD, Ismael Huerta, MD, Felix Payo-Losa, MD (Oviedo); *Sweden:* Gunnar Boman, MD, PhD, Christer Janson, MD, PhD, Eythor Björnsson, MD, PhD, (Uppsala); Leif Rosenhall, MD, PhD, Eva Norrman, MD, Bo Lundbgck, MD, PhD (Umeå), Nalle Lindholm, MD, PhD, Peter Plaschke, MD (Goteborg); *Switzerland:* Ursula Ackermann-Lieblich,

MD, Nino Künzli, MD, André Perruchoud, MD (Basel); *United Kingdom:* Michael Burr, MD, Jane Layzell, MRCGP, (Caerphilly); B. Russell Hall, MD, (Ipswich); Brian Harrison, FRCP, (Norwich); John Stark, MD, (Cambridge); *United States:* A. Sonia Buist, MD, William M. Vollmer, PhD, Molly L. Osborne, MD, PhD, (Portland).

References

- 1 Bousquet J, Van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001 Nov; **108** (Part 2):S147-334.
- 2 Platts-Mills TA. The role of allergens in the induction of asthma. *Curr Allergy Asthma Rep* 2002; **2**:175-80.
- 3 Sunyer J, Jarvis D, Pekkanen J *et al*. Geographic variations in the effect of atopy on asthma in the European Community Respiratory Health Study. *J Allergy Clin Immunol* 2004; **114**:1033-9.
- 4 Demoly P, Michel F, Bousquet J. In vivo methods for study of allergy. Skin tests, techniques and interpretation. In: Middleton E, Reed C, Ellis E, Adkinson N, Yunginger J, Busse W, eds. *Allergy, principles and practice, fifth edition*. St Louis, Mo: Mosby Co, 1998; 530-9.
- 5 Paggiaro PL, Bacci E, Amram DL, Rossi O, Talini D. Skin reactivity and specific IgE levels in the evaluation of allergic sensitivity to common allergens for epidemiological purposes. *Clin Allergy* 1986; **16**:49-55.
- 6 Schafer T, Hoelscher B, Adam H, Ring J, Wichmann HE, Heinrich J. Hay fever and predictive value of prick test and specific IgE antibodies: a prospective study in children. *Pediatr Allergy Immunol* 2003; **14**:120-9.
- 7 Kerkhof M, Dubois AE, Postma DS, Schouten JP, de Monchy JG. Role and interpretation of total serum IgE measurements in the diagnosis of allergic airway disease in adults. *Allergy* 2003; **58**:905-11.
- 8 Oppenheimer J, Nelson HS. Skin testing. *Ann Allergy Asthma Immunol* 2006; **96** (Suppl. 1):S6-12.
- 9 Chinn S, Jarvis D, Luczynska CM, Lai E, Burney PG. Measuring atopy in a multi-centre epidemiological study. *Eur J Epidemiol* 1996; **12**:155-62.
- 10 Kerkhof M, Schouten JP, De Monchy JG. The association of sensitization to inhalant allergens with allergy symptoms: the influence of bronchial hyperresponsiveness and blood eosinophil count. *Clin Exp Allergy* 2000; **30**:1387-94.
- 11 Ronchetti R, Villa MP, Pagani J *et al*. Immediate skin reactivity to histamine and to allergens in cohorts of 9-year-old school-children studied 16 years apart. *Clin Exp Allergy* 2003; **33**:1232-7.
- 12 Burney PG, Luczynska C, Chinn S, Jarvis D. The European community respiratory health survey. *Eur Respir J* 1994; **7**:954-60.
- 13 Janson C, Anto J, Burney P *et al*. The European community respiratory health survey: what are the main results so far? European Community Respiratory Health Survey II. *Eur Respir J* 2001; **18**:598-611.
- 14 Weiland SK, Björkstén B, Brunekreef B, Cookson WO, von Mutius E, Strachan DP. Phase II of the international study of asthma and allergies in childhood (ISAAC II): rationale and methods. *Eur Respir J* 2004; **24**:406-12.

- 15 Chanal I, Horst M, Segalen C, Dreborg S, Michel FB, Bousquet J. Comparison between modified skin prick test with standardized allergen extracts and Phazet. *J Allergy Clin Immunol* 1988; **82** (Part 1):878–81.
- 16 Osterballe O, Nielsen JP. Allergen-coated lancets (Phazet) for skin prick testing in children. *Allergy* 1989; **44**:356–62.
- 17 Scordamaglia A, Passalacqua G, Pisati P *et al.* A multi-allergen ELISA screening method. Comparison with Pharmacia CAP system and Phazet skin prick test. *Allergol Immunopathol (Madrid)* 1992; **20**:179–83.
- 18 Burney P, Malmberg E, Chinn S, Jarvis D, Luczynska C, Lai E. The distribution of total and specific serum IgE in the European Community Respiratory Health Survey. *J Allergy Clin Immunol* 1997; **99**:314–22.
- 19 Droste JH, Kerhof M, de Monchy JG, Schouten JP, Rijcken B. Association of skin test reactivity, specific IgE, total IgE, and eosinophils with nasal symptoms in a community-based population study. The Dutch ECRHS group. *J Allergy Clin Immunol* 1996; **97**:922–32.
- 20 Witteman AM, Stapel SO, Perdok GJ *et al.* The relationship between RAST and skin test results in patients with asthma or rhinitis: a quantitative study with purified major allergens. *J Allergy Clin Immunol* 1996; **97** (Part 1):16–25.
- 21 Demoly P, Bousquet J, Manderscheid JC, Dreborg S, Dhivert H, Michel FB. Precision of skin prick and puncture tests with nine methods see comments. *J Allergy Clin Immunol* 1991; **88**:758–62.
- 22 Arshad SH, Tariq SM, Matthews S, Hakim E. Sensitization to common allergens and its association with allergic disorders at age 4 years: a whole population birth cohort study. *Pediatrics* 2001; **108**:E33.
- 23 Kurukulaaratchy RJ, Matthews S, Arshad SH. Defining childhood atopic phenotypes to investigate the association of atopic sensitization with allergic disease. *Allergy* 2005; **60**: 1280–6.
- 24 Akerman M, Valentine-Maher S, Rao M *et al.* Allergen sensitivity and asthma severity at an inner city asthma center. *J Asthma* 2003; **40**:55–62.
- 25 Arbes SJ Jr, Gergen PJ, Elliott L, Zeldin DC. Prevalences of positive skin test responses to 10 common allergens in the US population: results from the third National Health and Nutrition Examination Survey. *J Allergy Clin Immunol* 2005; **116**:377–83.
- 26 Arbes SJ, Sever M, Mehta J, Collette N, Thomas B, Zeldin DC. Exposure to indoor allergens in day-care facilities: results from 2 North Carolina counties. *J Allergy Clin Immunol* 2005; **116**:133–9.
- 27 Riario-Sforza GG, Della Torre F, Antonicelli L *et al.* Sensitization to cockroach in Italy: a multicentric study. *Allergy Asthma Proc* 1997; **18**:23–8.