

# Preliminary criteria for the definition of allergic rhinitis: a systematic evaluation of clinical parameters in a disease cohort (I)

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## Abstract

**Background** The aim of this study is to formulate criteria for the definition of allergic rhinitis. Other studies have sought to develop scoring systems to categorize the severity of allergic rhinitis symptoms but it was never used for the formulation of diagnostic criteria. These other scoring systems were arbitrarily chosen and were not derived by any statistical analysis. To date, a study of this kind has not been performed.

**Objective** The hypothesis of this study is that it is possible to formulate criteria for the definition of allergic rhinitis. This is the first study to systematically examine and evaluate the relative importance of symptoms, signs and investigative tests in allergic rhinitis. We sought to statistically rank, from the most to the least important, the multiplicity of symptoms, signs and test results.

**Methods** Forty-seven allergic rhinitis and 23 normal subjects were evaluated with a detailed questionnaire and history, physical examination, serum total immunoglobulin E, skin prick tests and serum enzyme allergosorbent tests (EAST).

**Results** Statistical ranking of variables indicated rhinitis symptoms (nasal, ocular and oronasal) were the most commonly occurring, followed by a history of allergen provocation, then serum total IgE, positive skin prick tests and positive EAST's to house dust mite, perennial rye and bermuda/couch grass. Throat symptoms ranked even lower whilst EAST's to cat epithelia, plantain and cockroach were the least important. Not all symptoms, signs and tests evaluated proved to be statistically significant when compared to a control group; this included symptoms and signs which had been considered historically to be traditionally associated with allergic rhinitis, e.g. sore throat and bleeding nose.

**Conclusion** In performing statistical analyses, we were able to rank from most to least important, the multiplicity of symptoms signs and test results. The most important symptoms and signs were identified for the first time, even though some of these were not included in our original selection criteria for defining the disease cohort i.e. sniffing, postnasal drip, oedematous nasal mucosa, impaired sense of smell, mouth breathing, itchy nose and many of the specific provocation factors.

**Keywords:** allergic rhinitis, parameters, preliminary diagnostic criteria, statistical analyses, definition of disease

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## Introduction

Allergic rhinitis has been recognized as a distinct clinical entity for a long time based upon careful history taking of a variety of symptoms and provoking factors, supported by skin testing and in some cases other investigations such as provocation tests, nasal cytology, radioallergosorbent tests (RASTs) or enzyme allergosorbent tests (EASTs) and immunoglobulin (Ig) E, but until now, no specific criteria to define allergic rhinitis have been developed. From the outset the aim of the study was to perform a systematic backcross check coupled to statistical evaluation. Not all symptoms, signs and tests evaluated proved to be statistically significant when compared to a control group; this included symptoms and signs that had been considered historically to be traditionally associated with allergic rhinitis, e.g. sore throat and bleeding nose. We also sought to statistically rank, from the most to the least important, the multiplicity of symptoms, signs and test results.

The lack of standardized defining criteria may contribute to the variation in reported prevalence figures: a World Health Organization (WHO) study estimated that at least 10% of Caucasoid populations suffer from allergic rhinitis [1], a prevalence of 15% was estimated in Danish medical students [2] whereas about 40 million Americans are thought to be affected (18% of the population) [3]. A study of American college students showed a prevalence of hay fever to be 21.1% [4].

We assembled a cohort of allergic rhinitis patients with unequivocal histories that satisfied the cumulative consensus (based on a literature review) for a diagnosis, and compared them with a group of normal unaffected subjects by subjecting their symptoms, signs, total IgE, skin prick tests and EAST results to a detailed statistical analysis. The data so obtained was used to formulate defining criteria, as will be reported in a subsequent publication.

## Materials and methods

A cohort of 47 allergic rhinitis and 23 normal subjects was assembled from the local Concord, Sydney, New South Wales, Australia area (staff members from Concord Hospital and local residents). Allergic rhinitis patients were selected on the basis that they had either perennial or seasonal nasal and/or eye symptoms such as nasal discharge, sneezing, blocked nose, watery or red eyes, for several hours a day, for several days of the week, for several weeks, and in the case of seasonal, for at least several weeks of a year, for 2 years. These symptoms were not noted to be of the infectious nature or 'flu-like'. The majority of these patients nominated allergen provocation and/or a particular season when symptoms abounded. These arbitrary selection criteria constituted a consensus, based on a historical review of the

literature [5–8] and their mode of derivation is detailed in [9]. No arbitrary selection of perennial or seasonal groups was attempted, as many of these randomly selected subjects had features of both and the pathological process for perennial and seasonal rhinitis is the same. (Both perennial and seasonal rhinitis have inflammation of the nasal and ocular mucosa, both have the same symptoms and signs apart from a seasonal or perennial presentation and both have the same results to the investigation [positive skin prick tests, positive RAST's and elevated total serum IgE] and the treatment is the same). Seasonal rhinitis occurs when pollen and other plant allergens are released into the atmosphere during specific seasons, e.g. Spring, whereas perennial allergens are present in a patient's local environment virtually all year round, e.g. house dust mite.

None of the patients had nasal polyps. The absence of nasal poliposis was evaluated by visual examination using an auroscope to inspect the anterior nasal passages. A posterior rhinoscopic examination was not carried out. Oedematous nasal mucosa was associated with observable swelling of the middle turbinates.

Normal subjects had to be without the prolonged symptoms encountered in the disease group or any allergic diseases such as asthma, urticaria and eczema. A totally unrelated nondisease group was chosen rather than a non-allergic rhinitis control group because we aimed to derive a scoring system that would unequivocally define the allergic rhinitis entirely without the possibility of missing relevant criteria.

Subjects were questioned on medical history, family history, symptoms, provoking agents, living environment and given a brief physical examination 2 weeks after cessation of rhinitis medication such as antihistamines, steroids and other nasal sprays. Rhinitis patients were questioned specifically on exacerbating and precipitating factors such as allergen provocation, environmental factors, food and emotional factors. Specifically, house dust mite provocation was indicated by a history of early morning and night symptoms of rhinitis and symptoms indoors and particularly after exposure to house dust during domestic cleaning of rooms and bedding. Pollen provocation was determined by symptoms precipitated when the patient was exposed to pollen dust and fresh flowers. Other specific questions regarding precipitation of nasal/ocular symptoms following exposure to allergens were asked, notably to cut grass, animal hair, sprays (aerosols), smoke, fumes, mouldy environment and medications. Patients on immunotherapy were excluded from the study.

An extensive questionnaire involving multiple symptoms and signs and known to be relevant to allergic rhinitis was utilized for all subjects to accrue data. The parameters assessed (see Tables 1,2) were selected on the basis of their citation in allergic rhinitis literature [5–8], ease of

**Table 1** Demographic data for an allergic rhinitis and normal subject cohort

|                       | Allergic rhinitis | Normal subjects |
|-----------------------|-------------------|-----------------|
| Age (median)          | 38                | 36              |
| Sex                   |                   |                 |
| Female                | 28/47 (60%)       | 15/23 (65%)     |
| Male                  | 19/47 (40%)       | 8/23 (35%)      |
| Ethnic background     |                   |                 |
| Caucasian             | 44/47 (94%)       | 23/23 (100%)    |
| Asian                 | 3/47 (6%)         |                 |
| Age of onset (median) | 15                | N/A             |
| Family history        |                   |                 |
| Maternal affected     | 15/47 (32%)       | 2/23 (9%)       |
| Paternal affected     | 8/47 (17%)        | 0/23 (0%)       |
| Sibbling affected     | 20/47 (43%)       | 5/23 (22%)      |
| Associated allergies  |                   |                 |
| Asthma                | 14/47 (30%)       | 0/23 (0%)       |
| Eczema                | 9/47 (19%)        | 1/23 (4%)       |
| Urticaria             | 8/47 (17%)        | 1/23 (4%)       |
| Smoking history       | 34/47 (72%)       | 8/23 (35%)      |

performance, controllable objective assessment and reproducibility characteristics. Consequently, rhinometry and nasal provocation with allergens were not included in this study (see Fig. 1).

Skin prick tests were performed to ascertain IgE-mediated skin reactivity (as determined by weal responses via histamine release) to ubiquitous allergens. Skin prick tests were performed according to Pepys' method on the volar aspects of both forearms [10]. Skin prick tests included *Alternaria*, *Cladosporium*, *Aspergillus fumigatus*, *Helminthosporium*, *Dermatophagoides pteronyssinus*, *D. farinae*, Baker's yeast, Brewer's yeast, cockroach, cat epithelia, dog epithelia, privet, Acacia, flower mix, casuarina, hazelnut, perennial rye, bermuda (Couch), 7-grass mix, Bahia and Phalaris (Canary grass) Hollister-Stier, USA. The allergen extracts were prepared 1 : 20 (w/v) concentration in 50% glycerine. Control prick tests consisted of histamine (1 mg/mL in 50% glycerine) and glycerine (50%) alone. At 15 min, positive readings were read at  $\geq 2$  mm in two directions at 90 degrees to each other. Those readings  $< 2$  mm were recorded as a negative response.

EAST's included privet, cat epithelia, cockroach, *D. pteronyssinus*, *D. farinae*, bermuda (Couch), perennial rye and plantain. EAST's were performed according to the manufacturer's recommendations (Kallestad Specific IgE Allercoat East, Texas, USA) using discs pre-absorbed with allergenic protein. IgE antibodies bound to the antigen-coated solid support, enzyme-labelled antiserum was added, alkaline phosphatase substrate (PNPP) was

subsequently added following washes to produce an enzymatic reaction which was reflected by a colour change (yellow). The yellow colour was measured using an ELISA reader. What we called the RAST was actually an EAST or enzyme allergosorbent test which incorporates an ELISA test in its reading to detect specific IgE.

Serum total IgE was performed by a liquid phase radioimmunoassay where a mixture of  $^{125}$ I-labelled monoclonal and polyclonal antibodies were incubated with patients' serum. The reacted complexes were precipitated and the IgE level determined by comparison of the radioactivity in the precipitate to the standard radioactivity. The method was from Kallestad, Texas, USA.

#### Statistical tests

The statistical tests of Chi-squared and strength of association ( $\partial$  value) were performed and symptoms/abnormalities were ranked according to prevalence, chi-squared and  $\partial$  value. The strength of association, also known as the aetiological fraction ( $\partial$ ) is calculated with the formula

$$\partial = \frac{\text{FAD} - \text{FAP}}{1 - \text{FAP}}$$

where FAD is the frequency of the abnormality in the disease population and FAP is the frequency of the abnormality in the general population [11]. Mann-Whitney tests were performed using the Abacus Concepts, Statview Student (Abacus Concepts, Inc., Berkeley, CA, USA).

## Results

#### Demographic data of the allergic rhinitis and normal subjects

The age ranges and median ages of the allergic rhinitis group and normal subjects were similar, the range for allergic rhinitis subjects being 25–61 and the range for the normal subjects being 24–58 (Table 1). The ratio of male to female allergic rhinitis patients was 40 : 60 and similarly the ratio of male to female normal subjects was 35 : 65. All subjects tested were Caucasian except that 6% of allergic rhinitis patients were Asian.

The median age of onset of allergic rhinitis was 15 years of age. There were obvious differences in the family and medical histories of allergic rhinitis and normal subjects. Allergic rhinitis patients had 32%, 17% and 43% of mothers, fathers and siblings affected with allergic rhinitis, respectively, whereas normal subjects had only 9%, 0% and 22% affected. Chi-squared values were insignificant for maternal (3.35,  $P < 0.10$ ), paternal (2.90,  $P < 0.10$ ) and siblings affected (2.08,  $P < 0.20$ ). The allergological family history for asthma, urticaria and eczema was

**Table 2** Ranking of clinical and laboratory abnormalities in allergic rhinitis according to prevalence, Chi-squared and strength of association ( $\partial$ )

| Symptoms                     | Allergic rhinitis prevalence (%) | Symptoms                     | Chi-squared | P-value | Symptoms                     | $\partial$ |
|------------------------------|----------------------------------|------------------------------|-------------|---------|------------------------------|------------|
| Runny nose                   | 96                               | Runny nose                   | 49.17       | <0.001  | Runny nose                   | 0.96       |
| Sneezing                     | 93                               | Sniffing                     | 41.10       | <0.001  | Sneezing                     | 0.92       |
| Sniffing                     | 87                               | Sneezing                     | 40.04       | <0.001  | Sniffing                     | 0.86       |
| Impaired sense of smell      | 87                               | Mouth breath                 | 35.31       | <0.001  | Impaired sense of smell      | 0.83       |
| Blocked nose                 | 84                               | Watery eyes                  | 30.78       | <0.001  | Blocked nose                 | 0.82       |
| Oedematous nasal mucosa      | 80                               | Blocked nose                 | 29.50       | <0.001  | Oedematous nasal mucosa      | 0.79       |
| Pollen provocation           | 80                               | Pollen provocation           | 29.26       | <0.001  | Pollen provocation           | 0.78       |
| Red eyes                     | 79                               | Oedematous nasal mucosa      | 27.54       | <0.001  | Watery eyes                  | 0.77       |
| Mouth breathing              | 79                               | Postnasal drip               | 27.24       | <0.001  | Red eyes                     | 0.77       |
| Watery eyes                  | 78                               | Itchy nose                   | 27.24       | <0.001  | Mouth breathing              | 0.77       |
| Postnasal drip               | 78                               | Red eyes                     | 27.16       | <0.001  | Postnasal drip               | 0.76       |
| Itchy nose                   | 78                               | Impaired sense of smell      | 25.95       | <0.001  | Itchy nose                   | 0.76       |
| Itchy eyes                   | 76                               | Itchy eyes                   | 25.36       | <0.001  | Itchy eyes                   | 0.74       |
| HDM provocation              | 72                               | HDM provocation              | 21.92       | <0.001  | HDM provocation              | 0.69       |
| Smoke provocation            | 59                               | Smoke provocation            | 19.78       | <0.001  | Smoke provocation            | 0.59       |
| Serum IgE > 100 kU/L         | 57                               | Weather change provocation   | 17.32       | <0.001  | Weather change provocation   | 0.54       |
| Weather change provocation   | 54                               | Animal hair provocation      | 13.18       | <0.001  | Animal hair provocation      | 0.50       |
| Animal hair provocation      | 52                               | Mould provocation            | 13.01       | <0.001  | Spray provocation            | 0.48       |
| Spray provocation            | 48                               | Spray provocation            | 12.79       | <0.001  | Mould provocation            | 0.46       |
| Mould provocation            | 46                               | Flower provocation           | 10.23       | <0.01   | Flower provocation           | 0.39       |
| Itchy throat                 | 39                               | Serum IgE > 100 kU/L         | 7.82        | <0.01   | Itchy throat                 | 0.36       |
| Flower provocation           | 39                               | Itchy palate                 | 7.76        | <0.01   | Serum IgE > 100 kU/L         | 0.35       |
| Itchy palate                 | 32                               | Itchy throat                 | 7.63        | <0.01   | Itchy palate                 | 0.32       |
| Sore throat                  | 30                               | Fume provocation             | 7.00        | <0.01   | Fume provocation             | 0.30       |
| Fume provocation             | 30                               | Continual clearing of throat | 5.56        | <0.02   | Continual clearing of throat | 0.26       |
| Continual clearing of throat | 26                               | Chronic cough                | 4.22        | <0.05   | Chronic cough                | 0.22       |
| Chronic cough                | 22                               | Sore throat                  | 1.53        | <0.3    | Sore throat                  | 0.20       |
| Bleeding nose                | 13                               | Bleeding nose                | 0.14        | <0.8    | Bleeding nose                | 0.00       |

recorded for most of the subjects studied. For mothers, 8% had asthma, 2% had eczema and 2% had urticaria in the allergic rhinitis group, compared with 0%, 5% and 9% in the normal control group ( $P > 0.05$ ). For fathers, 6% had asthma, 2% had eczema and 0% had urticaria in the allergic rhinitis group, compared with 5%, 0% and 0% in the control group ( $P > 0.05$ ). Allergic rhinitis patients had a history of associated asthma (30%), eczema (19%) and urticaria (17%), respectively, compared with 0%, 4% and 4% of normal subjects. The chi-squared value for asthma was significant (6.80,  $P < 0.01$ ) but was insignificant for eczema (1.69,  $P < 0.20$ ) and urticaria (1.28,  $P < 0.30$ ). A higher but insignificant percentage of allergic rhinitis subjects (72%) had smoking histories compared with 35% of normal subjects. All but one of the disease subjects had at least one positive skin prick test or EAST.

#### *Statistical ranking of clinical abnormalities in allergic rhinitis*

A cluster of symptoms is a collection of symptoms grouped together according to the similarity of the nature of the symptoms (e.g. provocation symptoms, nasal symptoms) and also the similarity of the strength of association ( $\partial$  value), i.e. the  $\partial$  values of the symptoms are similar. Table 2 represents a ranking of abnormalities in allergic rhinitis as determined by several statistics: prevalence, Chi-squared (and its associated  $P$ -value) and strength of association ( $\partial$  value). The most prevalent abnormality was rhinorrhea, and this also had the highest  $\partial$  value, as well as being highly significant ( $P < 0.001$ ;  $\partial = 0.96$ ). This was followed (according to  $\partial$  values) by nasal symptoms which grouped together as a cluster, i.e. sneezing, sniffing, impaired sense of smell, blocked nose, oedematous nasal mucosa and itchy nose ( $\partial = 0.76$ – $0.92$ ). Of this group, blocked nose and impaired sense of smell had the lowest  $\partial$  values of this cluster, although all were highly significant on Chi-squared testing ( $P < 0.001$ ).

Pollen provocation ranked seventh according to prevalence, Chi-squared and strength of association ( $\partial = 0.78$ ). The next most important cluster of symptoms according to prevalence and strength of association ( $\partial$  value) included ocular symptoms, i.e. watery eye, red eyes and itchy eyes and oronasal symptoms (mouth breathing and postnasal drip) and all of these had equivalent  $\partial$  values ( $\partial = 0.74$ – $0.77$ ). Of this group, all were highly significant on Chi-squared testing ( $P < 0.001$ ).

The next cluster of symptoms, with a prevalence of 39–72% and  $\partial$  values of 0.39–0.69 were the provoking and precipitating factors, i.e. house dust, smoke, weather change, animal hair, spray, mould and flower provocation in decreasing order of prevalence, Chi-squared ( $P < 0.01$ ) and  $\partial$  values. The least prevalent cluster included the throat symptoms (itchy throat, itchy palate, sore throat, continual

clearing of the throat, chronic cough, fume provocation and bleeding nose) ( $\partial = 0$ – $0.36$ ). All were statistically significant ( $P < 0.05$ ) except for sore throat and bleeding nose. None of the allergic rhinitis subjects had polyps on clinical examination at the time of the study.

#### *Prevalence of exacerbating/precipitating factors in allergic rhinitis*

Rhinitis patients had a symptoms prevalence in the indoor environment of 83% and in the outdoors of 80%. Pollen provocation prevalence was 80% and house dust mite provocation was 72%. Windy weather had a prevalence of 74%. The next most important cluster of exacerbating and precipitating factors included smoke, weather change, animal hair, spray, mould, flower and fume provocation with a prevalence range of 30–59%.

Symptom exacerbation in the morning had a higher prevalence (65%) compared to evening symptoms (41%). Symptom exacerbation in Spring was more common (43%) compared with Summer and Autumn (24% each). Environmental symptom exacerbation in the cold had a prevalence of 39% compared with 20% for warm environment. Wet weather exacerbation was more common (33%) compared with dry weather (13%).

Emotional factors as a cluster ranked low on the list of precipitating/exacerbating factors, stress and anxiety having a prevalence of only 20%, followed by depression (10%) and hyperactivity (2%). The least important cluster of precipitating factors was food with a prevalence of only 28%. Individual food items were also low ranking with alcohol having a prevalence of 20%, and milk having a prevalence of 10%. The rest of the foods all had prevalences of less than 10% (which included spicy foods, yeast, mushrooms, strawberries, potatoes, flour, cereal and chocolate).

#### *Prevalence of positive allergen skin prick tests in allergic rhinitis and normal subjects*

The most important and prevalent cluster of positive skin prick tests to individual allergens in allergic rhinitis patients included grasses (perennial rye, Phalaris, 7-grass, Bahia grass and Bermuda (Couch) and both *D. pteronyssinus* and *farinae* house dust mite preparations, all with prevalences ranging from 70 to 87% (Table 3). All were statistically significant according to Chi-squared ( $P < 0.01$ ) and Mann–Whitney tests ( $P \leq 0.0006$ ). There was a high range of  $\partial$  values for this group of allergens (0.54–0.82).

The other skin prick test results which were statistically significant according to the Chi-squared and Mann–Whitney tests were cat epithelia, plantain, flower mix and Brewer's yeast ( $P < 0.05$ ) whereas the  $\partial$  values for

**Table 3** Prevalence of positive skin prick tests to specific allergens in allergic rhinitis and normal subjects

| Skin prick tests             | Allergic rhinitis (n = 47) | Normal subjects (n = 23) | Allergic rhinitis prevalence (%) | Control subjects prevalence (%) | Chi-square | P-value | $\partial$ | Mann-Whitney P-value |
|------------------------------|----------------------------|--------------------------|----------------------------------|---------------------------------|------------|---------|------------|----------------------|
| Perennial rye                | 41                         | 7                        | 87                               | 30                              | 20.56      | <0.001  | 0.82       | 0.0001               |
| <i>D. pteronyssinus</i>      | 38                         | 9                        | 83                               | 39                              | 10.37      | <0.01   | 0.69       | 0.0003               |
| Phalaris                     | 35                         | 8                        | 76                               | 35                              | 8.66       | <0.01   | 0.61       | 0.0003               |
| 7-grass                      | 35                         | 7                        | 76                               | 30                              | 10.71      | <0.01   | 0.63       | 0.0004               |
| <i>D. farinae</i>            | 35                         | 6                        | 74                               | 26                              | 12.97      | <0.001  | 0.65       | 0.0001               |
| Bahia grass                  | 33                         | 8                        | 71                               | 25                              | 6.6        | <0.02   | 0.54       | 0.0006               |
| Bermuda/couch                | 33                         | 6                        | 70                               | 26                              | 10.46      | <0.01   | 0.60       | 0.0004               |
| Cockroach                    | 30                         | 11                       | 64                               | 57                              | 1.04       | <0.50   | 0.31       | 0.1131               |
| Cat epithelia                | 29                         | 11                       | 62                               | 48                              | 6.48       | <0.02   | 0.27       | 0.0003               |
| Plantain                     | 29                         | 7                        | 62                               | 30                              | 4.86       | <0.05   | 0.45       | 0.0095               |
| Privet                       | 28                         | 8                        | 60                               | 35                              | 2.87       | <0.10   | 0.38       | 0.0884               |
| Alternaria                   | 27                         | 9                        | 57                               | 39                              | 1.41       | <0.30   | 0.30       | 0.1184               |
| Flower mix                   | 27                         | 6                        | 57                               | 26                              | 4.9        | <0.05   | 0.42       | 0.0166               |
| Don                          | 26                         | 6                        | 55                               | 30                              | 2.9        | <0.10   | 0.36       | 0.0684               |
| Acacia                       | 23                         | 6                        | 49                               | 26                              | 2.45       | <0.20   | 0.31       | 0.0755               |
| Casuarina                    | 20                         | 4                        | 43                               | 17                              | 3.29       | <0.10   | 0.30       | 0.0783               |
| Baker's yeast                | 19                         | 5                        | 40                               | 22                              | 1.64       | <0.20   | 0.24       | 0.1021               |
| Brewer's yeast               | 18                         | 2                        | 38                               | 9.0                             | 5.26       | <0.05   | 0.32       | 0.0169               |
| Heiminthosporium             | 17                         | 4                        | 36                               | 17                              | 1.78       | <0.20   | 0.20       | 0.1453               |
| Cladosporium                 | 16                         | 4                        | 34                               | 17                              | 1.36       | <0.30   | 0.23       | 0.1061               |
| Hazelnut                     | 14                         | 9                        | 30                               | 39                              | 0.26       | <0.70   | 0.15       | 0.6531               |
| <i>Aspergillus fumigatus</i> | 14                         | 6                        | 30                               | 26                              | 0.0016     | <0.98   | 0.05       | 0.301                |

plantain and flower mix were 0.45 and 0.42, respectively, and 0.27 and 0.32 for cat epithelia and Brewer's yeast, respectively. None of the other skin prick test results were statistically significant by Chi-squared and Mann-Whitney tests.

Within our allergic rhinitis cohort, two of 47 (4%) were monosensitized patients who had positive skin prick test or

EAST to only one allergen. Of the 47, 45 (96%) were polysensitized patients; these had positive skin prick test or EAST to two or more allergens.

All but one allergic rhinitis subject was found to have a positive skin prick test or EAST during the poststudy period. Perhaps this one subject had an allergen sensitivity which had not been tested for.

**Table 4** Prevalence of serum IgE to specific allergens (EAST) in allergic rhinitis and normal subjects

| EAST                    | Allergic rhinitis (n = 44) | Normal subjects (n = 22) | Allergic rhinitis Prevalence (%) | Control subjects Prevalence (%) | Chi-square | P-value | $\partial$ | Mann-Whitney P-value |
|-------------------------|----------------------------|--------------------------|----------------------------------|---------------------------------|------------|---------|------------|----------------------|
| <i>D. pteronyssinus</i> | 28                         | 3                        | 0.64                             | 0.14                            | 12.28      | <0.001  | 0.58       | 0.0001               |
| <i>D. farinae</i>       | 26                         | 3                        | 0.59                             | 0.14                            | 10.53      | <0.01   | 0.52       | 0.0002               |
| Perennial rye           | 25                         | 5                        | 0.57                             | 0.23                            | 5.57       | <0.02   | 0.44       | 0.0047               |
| Bermuda/couch           | 14                         | 2                        | 0.32                             | 0.09                            | 2.98       | <0.10   | 0.25       | 0.0225               |
| Cat epithelia           | 13                         | 1                        | 0.3                              | 0.05                            | 4.09       | <0.05   | 0.26       | 0.0605               |
| Plantain                | 12                         | 1                        | 0.27                             | 0.05                            | 3.46       | <0.10   | 0.24       | 0.0132               |
| Cockroach               | 10                         | 0                        | 0.23                             | 0                               | 4.28       | <0.05   | 0.23       | 0.0143               |
| Privet                  | 7                          | 0                        | 0.16                             | 0                               | 2.4        | <0.20   | 0.16       | 0.0555               |

**Table 5.** Correlation between allergen provocation symptomatology and specific skin and EASTs

|                 | Chi-square | P-value | Sensitivity | Specificity |
|-----------------|------------|---------|-------------|-------------|
| Dust mite SPT   | 3.009      | <0.10   | 0.97        | 0.29        |
| Dust mite EAST  | 3.335      | <0.10   | 1.00        | 0.19        |
| Pollen SPT      | 0.0392     | <0.90   | 0.80        | 0.33        |
| Pollen EAST     | 101.84     | <0.001  | 0.85        | 0.26        |
| Animal hair SPT | 0.1374     | <0.80   | 0.62        | 0.50        |
| Animal EAST     | 2.2319     | <0.20   | 0.83        | 0.50        |
| Mould SPT       | 0.0049     | <0.95   | 0.47        | 0.57        |

*Prevalence of serum IgE to specific allergens (EAST) in allergic rhinitis and normal subjects*

The most prevalent cluster of positive EASTs included *D. pteronyssinus*, *D. farinae* and perennial rye which had a prevalence range of 57–64% (Table 4). Perennial rye, *D. farinae* and *D. pteronyssinus*, were all statistically significant according to Chi-squared ( $P < 0.02$ ) and Mann–Whitney testing ( $P \leq 0.005$ ) with  $\phi$  values ranging from 0.44 to 0.58. Bermuda/couch grass was not statistically significant according to Chi-squared testing ( $P > 0.05$ ) but was significant according to Mann–Whitney testing ( $P = 0.02$ ). The  $\phi$  value for Bermuda/couch was 0.25. A less prevalent cluster of positive EAST results included cat epithelia, plantain and cockroach which were all statistically significant according to Chi-squared ( $P < 0.05$ ), but they had low strength of association  $\phi$  values (0.23–0.26). Plantain and cockroach were statistically significant according to Mann–Whitney ( $P = 0.01$ ) but cat epithelia was not ( $P = 0.06$ ). Privet was not found to be statistically significant according to Chi-squared and Mann–Whitney tests, and had the lowest  $\phi$  value (0.16).

*Correlation of specific IgE (skin prick test and EAST) with allergen provocation*

Correlations between specific IgE (skin prick test and EAST) and specific allergen provocation symptomatology in allergic rhinitis subjects were examined by Chi-squared testing, and specificity/sensitivity calculations. Only the EAST for pollen/grasses was found to be significantly correlated with grass-induced symptoms by Chi-squared testing. Nevertheless, the sensitivities for dust mite SPT and EAST, pollen/grasses SPT and EAST and animal hair EAST were high (sensitivity = 0.80–0.97) and specificities were all low (see Table 5). This weak correlation between positive specific IgE tests and clinical history of allergen provocation may result from the subjectivity in patient history, i.e. the patient is unaware of the provoking factors(s) responsible for symptom production.

## Discussion

Although there are many reports in the literature concerning allergic rhinitis, a systematic evaluation of the symptoms and signs that can be used to diagnose this disorder has yet to appear. Therefore we sought to determine the relative importance of clinical symptoms, signs, serum total IgE, skin prick testing and serum EASTs as a preliminary step to enable the devisement of diagnostic criteria. Although there are no formal criteria in the literature for the definition of allergic rhinitis, review of the original reports documenting its existence, and subsequent reviews reveal that there is a consensus as to the most common symptoms and signs [5–8] and these constitute our selection criteria, this being cited in [9].

Two patient populations (disease and nondisease) were assembled from the local Concord, NSW, Sydney, Australia area (staff members from Concord Hospital and local residents) and the allergic rhinitis patients' constituent data revealed that although a family history of allergic rhinitis was higher in allergic rhinitis subjects, in particular the maternal history of allergic rhinitis patients was 32% compared with paternal history of 17% and 43% of siblings, none of these were significant. A study by Kuehr *et al.* [11] in Germany tested sensitization to four common inhalant allergens in 302 nuclear families and found that maternal but not paternal sensitization increased the child's relative risk to be sensitized ( $P = 0.001$ ). These results may point to the importance of maternal history in allergic rhinitis. Although the allergic rhinitis patient cohort had associated histories of asthma (30%,  $P < 0.01$ ), eczema (19%,  $P < 0.20$ ) and urticaria (17%,  $P < 0.30$ ), respectively, only the asthma association was significant. Comparison of our demographic data with that of others revealed that in previously reported questionnaire studies, a positive family history was present in 50% of 'allergic' children sampled from a presumed Danish population [13]. The familial occurrence of both 'atopy' and allergic disorders per se is well known, but when there are no 'atopic' family members, 5–15% of the children are likely to be 'atopic'. This figure rises to 20–40% when one parent is atopic and 40–75% when both

parents are atopic [14]. 'Atopy' in these reports was defined as the presence of specific IgE antibodies to one or more of the inhalant allergens usually demonstrated by a positive skin test. Nasal symptoms have been reported in up to 78% of asthma patients and occur more often in those who have an allergic basis for their asthma [15]. The prevalence of asthma in patients with allergic rhinitis has been reported to be less than 20% of patients in some other countries. For the above citations, no statistical significances were calculated. Considering the above, we therefore feel that the cohort of allergic rhinitis patients reported here is representative as it is similar in its allergic association prevalences to those previously surveyed.

#### *Key factors important in defining allergic rhinitis*

Examination of the ranking of symptoms, signs, skin prick tests, total serum IgE and serum EASTs was performed according to prevalence, Chi-squared and strength of association ( $\partial$  value) [11].  $\partial$  values, which are essentially weighted prevalence values for disease cohorts, are considered to be comparable between different classes of factors [11]. As seen in Table 2 there was an anatomically related stratification of factors such that nasal symptoms (rhinorrhea, sneezing, sniffing, impaired sense of smell, blocked nose, oedematous nasal mucosa and itchy nose) ranked the highest ( $\partial$  value = 0.96–0.76); ocular symptoms (watery eyes, red eyes and itchy eyes,  $\partial$  = 0.77–0.74) and oronasal symptoms (mouth breathing, postnasal drip and itchy nose,  $\partial$  = 0.77–0.76) followed next; allergen provocation and also precipitating factors (house dust mite, smoke, weather change, animal hair, spray, mould and flower provocation) were of moderate rank ( $\partial$  = 0.69–0.39); serum IgE ranked equally with allergen provocation ( $\partial$  = 0.40); and throat symptoms (itchy throat, itchy palate, continual clearing of the throat, chronic cough and sore throat) had the lowest rank ( $\partial$  = 0.36–0.20). The relative importance of allergen provocation, and the relationship of the above symptoms to each other has not been previously reported.

The relative importance of skin prick tests in defining allergic rhinitis can be assessed by comparing the  $\partial$  values in Table 2 and Table 3, and this indicates that performing skin prick tests is just as important as obtaining a history of allergen provocation since  $\partial$  values for allergen provocation (0.30–0.69) are similar to the range of  $\partial$  values for positive skin prick tests ( $\partial$  = 0.32–0.69) with the exception of perennial rye ( $\partial$  = 0.82). A positive history of nasal, ocular and oronasal symptoms is more important however ( $\partial$  = 0.76–0.96). This is a clear indication that a history of allergen provocation should be supported by positive skin prick test results for the reliable diagnosis of allergic rhinitis.

Mygind *et al.* [16] in studies performed in Denmark

reported that the average frequency of positive immediate-type skin test reactions to different allergens in patients with perennial rhinitis varied from 30 to 60%, the predominant allergen being house dust mite. Allergy to moulds was found in 17% of cases [17]. Brown *et al.* [18] reported that in Arizona, USA, Bermuda grass produced positive skin prick tests in 62% of the allergics and 30% of the non-allergics, Careless weed in approximately 55% of the allergics and 34% of the nonallergics, cat dander in 28% of the allergics and 15% of the nonallergics and Olive in 50% allergics and 30% nonallergics. In spite of the geographical differences, our prevalences are remarkably similar to these figures (see Table 3).

An interrelational evaluation of the relevance of serum EAST's to the above variables by comparison of the  $\partial$  values seen in Table 4 with those in Tables 2 and 3 indicates that the EASTs for *D. pteronyssinus*, *D. farinae* and perennial rye ( $\partial$  = 0.44–0.58) are just as informative as the corresponding skin prick tests ( $\partial$  = 0.32–0.69). The other EASTs, Bermuda (couch), cat epithelia, plantain and cockroach ( $\partial$  = 0.23–0.26) were less important than some of the throat symptoms ( $\partial$  = 0.22–0.36) and a history of allergen provocation ( $\partial$  = 0.30–0.69) or their corresponding skin prick tests ( $\partial$  = 0.27–0.45). An interesting point is that the cockroach skin prick test was not statistically significant but the cockroach EAST was. Privet EAST was not statistically significant at all and probably is only required for confirmation of specific provocation history to privet, when skin prick testing is not appropriate.

A comprehensive literature search for stringent statistical comparisons of the above variables, particularly in relation to serum RAST and EAST results, as we have performed here, has only yielded studies which show that RAST's and EAST's have a good correlation with *in vivo* skin tests [19–25]. In particular, Krilis *et al.* found correlations between skin prick test results and RAST scores which ranged from 64% to 80% for the following extracts: house dust, house dust mites (*T. putrescentia*, *D. farinae* and *D. pteronyssinus*), cat, dog, horse epitheliae, feather mix, Timothy grass, rye grass, *Aspergillus* and *A. alternata* [25]. This latter research was performed in Sydney, Australia, and the results are very similar to those in this paper. The mild variation between percentage correlations reported by different groups may be attributed to differences in patient populations, the allergens in the area investigated and the diversity of allergen preparations. No ranking or cluster analyses of these tests in relation to one another or to specific clinical features have been reported to date, but we will do this in another publication, which will also show that our correlative percentages between positive SPT's and EAST's are similar to the above cited figures (as can be inferred from the  $\partial$  values shown here), again indicating that our disease cohort is representative.

According to the literature, there is a highly significant correlation between high serum total IgE and an increased number of positive skin tests and positive RAST results [26]. Stuckey *et al.* [27] showed that a higher proportion of subjects with high serum IgE reacted to at least six allergens as compared to subjects with low IgE ( $P < 0.001$ ). Mogi *et al.* [28] showed that mean IgE increased with increasing numbers of positive skin prick tests.

There have been a considerable number of studies done showing that positive allergen skin prick tests and RASTs occur in completely asymptomatic subjects just as we have shown here (see Table 3) [29–32]. In Copenhagen, although almost 10% of a student population were found to have positive skin prick tests to grass pollen extracts they had no allergic rhinitis symptoms; it is predicted that a proportion of the skin test positive subjects (percentage not stated) will develop symptoms in subsequent years. A proportion of these subjects may eventually go on to develop allergic rhinitis [29–33]. It seems that not all skin prick tests are worthwhile for diagnosis since asymptomatic subjects can have positive skin prick tests and as reported here, positive responses to certain allergens are not statistically significant even in allergic rhinitis patients. For example, in the western area of Sydney, skin prick tests to privet, *Alternaria*, dog, acacia, casuarina, Baker's yeast, helminthosporium, *Cladosporium*, hazelnut and *Aspergillus fumigatus* may be omitted unless required to confirm a very specific history of provocation to these allergens. A serum RAST for cockroach allergy is a more valuable test to perform than a skin prick test.

The statistical analyses performed in this study indicate that it is essential to obtain a history of the rhinoconjunctival symptoms (rhinorrhea, sneezing, sniffing, impaired sense of smell, blocked nose, watery eyes, red eyes, mouth breathing, postnasal drip, itchy nose and itchy eyes) ( $\partial = 0.74$ – $0.96$ ) as well as allergen provocation and precipitating factors ( $\partial = 0.30$ – $0.69$ ), to perform physical examination and rhinoscopy for a glairy clear fluid and pale bluish pink, moist, enlarged and oedematous nasal turbinates ( $\partial = 0.79$ ). Performing total serum IgE ( $\partial = 0.40$ ) is of similar value to a positive history of allergen provocation ( $\partial = 0.30$ – $0.69$ ) or positive skin prick tests ( $\partial = 0.32$ – $0.69$ ) and because each complements the other according to their  $\partial$  values, this suggests that all three parameters should be evaluated in each presenting patient. Raised IgE levels are found in 50% of adults with hay fever or perennial rhinitis [30–35]. Throat symptoms (itchy throat, itchy palate, continual clearing of the throat and chronic cough) ( $\partial = 0.22$ – $0.36$ ) are less important but are statistically significant.

Investigation with serum EASTs to *D. pteronyssinus*, *D. farinae* and perennial rye ( $\partial = 0.44$ – $0.58$ ) is just as effective as performing skin prick tests to these allergens ( $\partial = 0.32$ – $0.69$ ) and therefore would be indicated in circumstances

where there is dermographism, widespread atopic dermatitis, where interpretation of skin prick tests is difficult or when treatment which interferes with interpretation of skin prick tests cannot be ceased (such as antihistamines, adrenaline, ephedrine, aminophylline and some  $\beta$ -adrenergic agents) [36]. The RAST/EAST is objective, semiquantitative, it is valuable in standardizing allergen extracts and evaluating crossed reactivities among allergens, stored sera can be used for longitudinal studies and serum may be shipped to other laboratories to test for unusual, locally unavailable allergens [13]. Other EASTs such as Bermuda (couch), cat epithelia and plantain ( $\partial = 0.24$ – $0.26$ ) are not as effective as skin prick tests ( $\partial = 0.32$ – $0.69$ ) but may be performed in cases where the performance of skin prick tests is inappropriate. The cockroach EAST ( $\partial = 0.23$ ) can be performed instead of the cockroach skin prick test, and may be done if clinically indicated to confirm a positive history.

For ubiquitous allergens, although there was a high clinical sensitivity between specific allergen provocation and a corresponding positive prick test or EAST result, this was only statistically significant for pollen EAST (Table 5). This weak correlation between positive specific IgE tests and clinical history of allergen provocation may result from the subjectivity in patient history, i.e. the patient is unaware of the provoking factor(s) responsible for symptom production. This clearly indicates the need to assemble several criteria in order to diagnose allergic rhinitis.

The practical implications of this study are presented in [9], wherein the  $\partial$  values derived for all the statistically significant symptoms, signs and investigations were used to devise a scoring system which can be used to diagnose allergic rhinitis. The allergic rhinitis defining criteria utilized for the scoring system were the statistically significant symptoms, signs and investigations with the  $P$ -value  $< 0.05$  as determined from the data reported in this study.

## Summary

The most important factors to be considered in the diagnosis of allergic rhinitis are those related to nasal and ocular symptoms, i.e. the symptoms of rhinorrhea ( $\partial = 0.96$ ), sneezing ( $\partial = 0.92$ ), sniffing ( $\partial = 0.86$ ), impaired sense of smell ( $\partial = 0.83$ ), blocked nose ( $\partial = 0.82$ ), oedematous nasal mucosa ( $\partial = 0.79$ ), watery eyes ( $\partial = 0.77$ ), red eyes ( $\partial = 0.77$ ), mouth breathing ( $\partial = 0.77$ ), postnasal drip ( $\partial = 0.76$ ) and itchy nose ( $\partial = 0.76$ ). That is, the 'allergic' element, either a history of allergen provocation ( $\partial = 0.30$ – $0.69$ ), positive skin prick tests ( $\partial = 0.32$ – $0.69$ ) or serum EASTs ( $\partial = 0.23$ – $0.58$ ) and total serum IgE ( $\partial = 0.40$ ) is not the predominant element, but of these factors, a history of allergen provocation, specific skin prick tests, total serum IgE and certain EAST's (dust mite and perennial rye) are of

similar importance, with the lowest yield residing with other EAST's (Bermuda/couch, cat epithelia, plantain and cockroach).

It is therefore critical to evaluate a history of rhinitis, allergen provocation and skin prick tests or EAST's and perform physical examination and serum total IgE in order to make a diagnosis of allergic rhinitis, according to the population study reported here.

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**Appendix 1. DATA SHEET FOR RHINITIS**

|                                                    |        |                                                |
|----------------------------------------------------|--------|------------------------------------------------|
| <i>General Instructions</i>                        | 1 [ ]  | Card Number    Patient Sticker                 |
| Use the following code unless otherwise specified: | 2 [ ]  |                                                |
| 0 = Not known                                      |        |                                                |
| 1 = Yes/Positive                                   | 3 [ ]  |                                                |
| 2 = No/Negative                                    |        |                                                |
| 3 = Not done                                       | 4 [ ]  | Typing lab code.                               |
|                                                    | 5 [ ]  |                                                |
| <i>Ethnic group (12)</i>                           |        |                                                |
| 1 = Caucasian                                      | 6 [ ]  |                                                |
| 2 = Japanese                                       |        |                                                |
| 3 = Chinese                                        | 7 [ ]  |                                                |
| 4 = Indian                                         |        |                                                |
| 5 = Australian Aborigine                           | 8 [ ]  | Cell Identification                            |
| 6 = Other (Specify)                                | 9 [ ]  |                                                |
|                                                    | 10 [ ] | Sex 1 = Male 2 = Female                        |
| <i>Relationship to the patient (16)</i>            |        |                                                |
| 1 = Father                                         | 11 [ ] | Occupation                                     |
| 2 = Mother                                         |        |                                                |
| 3 = Grandfather                                    | 12 [ ] | Ethnic Group                                   |
| 4 = Grandmother                                    |        |                                                |
| 5 = Brothers                                       | 13 [ ] | Is subject a relative of patient studied?      |
| 6 = Sisters                                        | 14 [ ] | If yes give a number of the relatives studied. |
| 7 = 1st Cousins                                    |        |                                                |
| 8 = Uncles                                         | 15 [ ] |                                                |
| 9 = Aunts                                          | 16 [ ] | Relationship to the patient                    |
|                                                    | 17 [ ] |                                                |
| <i>Parental History (18)</i>                       |        |                                                |
| 0 = Father Not known                               |        |                                                |
| 1 = Father-Rhinitis                                | 18 [ ] | Parental History                               |
| 2 = Father-Eczema                                  |        |                                                |
| 3 = Father-Asthma                                  | 19 [ ] |                                                |
| 4 = Father-Urticaria                               |        |                                                |
| 5 = Father-Angioedema                              | 20 [ ] |                                                |
| 6 = Father-Drug allergy                            | 21 [ ] |                                                |
| 7 = Father-Insect allergy                          |        |                                                |
| 8 = Father-Food allergy                            | 22 [ ] |                                                |
| 9 = Mother-Hay fever                               | 23 [ ] | Sib History                                    |
| 10 = Mother-Eczema                                 |        |                                                |
| 11 = Mother-Asthma                                 | 24 [ ] |                                                |
| 12 = Mother-Urticaria                              |        |                                                |
| 13 = Mother-Angioedema                             | 25 [ ] |                                                |
| 14 = Mother-Drug allergy                           |        |                                                |
| 15 = Mother-Insect allergy                         | 26 [ ] |                                                |
| 16 = Mother-Food allergy                           | 27 [ ] | Medical History                                |
| 17 = Mother-Not known                              | 28 [ ] |                                                |
|                                                    | 29 [ ] |                                                |
| <i>Sib history (23)</i>                            |        |                                                |
| 0 = None                                           |        |                                                |
| 1 = Asthma                                         | 30 [ ] | Age of rhinitis diagnosis (yrs).               |
| 2 = Rhinitis                                       |        |                                                |
| 3 = Eczema                                         | 31 [ ] |                                                |
| 4 = Urticaria                                      |        |                                                |
| 5 = Angioedema                                     | 32 [ ] | Age of rhinitis onset (yrs).                   |
| 6 = Drug allergy                                   | 33 [ ] |                                                |
| 7 = Insect allergy                                 |        |                                                |
| 8 = Food allergy                                   | 34 [ ] | Xerophthalmia                                  |

|                                        |        |                                                             |
|----------------------------------------|--------|-------------------------------------------------------------|
| <i>Medical History</i> (27)            | 35 [ ] | Xerostomia                                                  |
| 0 = None                               | 36 [ ] | Itchy eye                                                   |
| 1 = Asthma                             | 37 [ ] | Watery eye                                                  |
| 2 = Eczema                             | 38 [ ] | Itchy nose                                                  |
| 3 = Urticaria                          | 39 [ ] | Blocked nose                                                |
| 4 = Angioedema                         | 40 [ ] | If yes unilateral 1. Bilateral 2.                           |
| 5 = Drug allergies                     | 41 [ ] | Runny nose.                                                 |
| 6 = Insect allergies                   | 42 [ ] | Bleeding nose                                               |
| 7 = Food allergies (Specify)           | 43 [ ] | Sniffing                                                    |
| <i>Runny Nose</i> (41)                 | 44 [ ] | Sneezing                                                    |
| 0 = No                                 | 45 [ ] | Itchy palate                                                |
| 1 = Watery                             | 46 [ ] | Itchy throat                                                |
| 2 = Murcoid                            | 47 [ ] | Mouth breathing                                             |
| 3 = Purulent                           | 48 [ ] | Post nasal drip                                             |
| 4 = Blood stained                      | 49 [ ] | Chronic cough                                               |
| <i>Phlegm</i> (52)                     | 50 [ ] | Continual clearing of throat                                |
| 0 = None                               | 51 [ ] | Sore throat                                                 |
| 1 = Clearn                             | 52 [ ] | Phlegm                                                      |
| 2 = Mucoid                             | 53 [ ] | Neurasthenia                                                |
| 3 = Yellow                             | 54 [ ] | Anorexia                                                    |
| 4 = Green                              | 55 [ ] | Impaired sense of smell                                     |
| <i>Impaired Smell</i> (55)             | 56 [ ] | Headache                                                    |
| 0 = No                                 | 57 [ ] | Character of headache                                       |
| 1 = Loss of smell                      | 58 [ ] | Frequency of headache                                       |
| 2 = Decreased sense of smell           | 59 [ ] | Symptoms of headache associated with exercise               |
| 3 = Altered perception of known aromas | 60 [ ] | Decreased taste sensation                                   |
| 4 = Unusual aroma constantly perceived | 61 [ ] | Earache                                                     |
| <i>Headache</i> (56)                   | 62 [ ] | What time of the day more symptomatic? (hay fever symptoms) |
| 0 = No                                 | 63 [ ] |                                                             |
| 1 = Global                             | 64 [ ] | Which season of the year more symptomatic?                  |
| 2 = Frontal                            | 65 [ ] |                                                             |
| 3 = Maxillary                          | 66 [ ] | More symptomatic Indoor/Outdoor.                            |
| 4 = Ethmoidal                          | 67 [ ] | Symptoms with geographic changes.                           |
| 5 = Occipital                          | 68 [ ] |                                                             |
| 6 = Migraneous                         | 69 [ ] | Symptoms associated with emotions?                          |
| 7 = Temporal                           |        |                                                             |
| <i>Character</i> (57)                  |        |                                                             |
| 0 = Not known                          |        |                                                             |
| 1 = Sharp                              |        |                                                             |
| 2 = Dull                               |        |                                                             |
| 3 = Throbbing                          |        |                                                             |
| <i>Frequency</i> (58)                  |        |                                                             |
| 1 = Once/hour                          |        |                                                             |
| 2 = Once/day                           |        |                                                             |
| 3 = Once/week                          |        |                                                             |
| 4 = Once/mth                           |        |                                                             |
| 5 = Once/6mth                          |        |                                                             |
| 6 = Once/yr.                           |        |                                                             |
| <i>Symptoms</i> (62)                   |        |                                                             |
| 0 = No correlation                     |        |                                                             |
| 1 = Morning                            |        |                                                             |

|                                |         |                                               |
|--------------------------------|---------|-----------------------------------------------|
| 2 = Midday                     | 70 [ ]  |                                               |
| 3 = Evening                    | 71 [ ]  | Symptoms associated with temperature?         |
| 4 = Night                      | 72 [ ]  | Symptoms associated with humidity of the air. |
| <i>Seasons (64)</i>            |         |                                               |
| 0 = No correlation             | 73 [ ]  | Food(s) which precipitate the symptoms?       |
| 1 = Winter                     | 74 [ ]  |                                               |
| 2 = Spring                     | 75 [ ]  |                                               |
| 3 = Summer                     | 76 [ ]  |                                               |
| 4 = Autumn                     | 77 [ ]  |                                               |
| 5 = Perennial                  |         |                                               |
| <i>Symptoms (66)</i>           |         |                                               |
| 1 = Indoor                     | 78 [ ]  | Chemicals which precipitate the symptoms      |
| 2 = Outdoor                    | 79 [ ]  |                                               |
| 3 = Both                       | 80 [ ]  |                                               |
| <i>Geographic changes (67)</i> |         |                                               |
| 0 = No definite correlation.   | 81 [ ]  | Provoking agents                              |
| 1 = City                       | 82 [ ]  |                                               |
| 2 = Country                    | 83 [ ]  |                                               |
| 3 = N.S.W.                     | 84 [ ]  | Provoking drugs                               |
| 4 = QLD                        | 85 [ ]  |                                               |
| 5 = Vic.                       | 86 [ ]  | Treatment taken previously                    |
| 6 = S.A.                       | 87 [ ]  |                                               |
| 7 = Tas.                       | 88 [ ]  |                                               |
| 9 = N.T.                       | 89 [ ]  | Treatment taken currently                     |
| 10 = Overseas.                 | 90 [ ]  |                                               |
| <i>Emotions (69)</i>           |         |                                               |
| 0 = No correlation             | 91 [ ]  |                                               |
| 1 = Stress/anxiety             | 92 [ ]  | Routes of medication                          |
| 2 = Depression                 | 93 [ ]  |                                               |
| 3 = Hyperactivity              | 94 [ ]  | Drug allergy                                  |
| <i>Temperature (71)</i>        |         |                                               |
| 0 = No correlation             | 95 [ ]  | Symptoms associated with hormonal changes     |
| 1 = Warm                       | 96 [ ]  | Type of house                                 |
| 2 = Cold                       | 97 [ ]  | Age of the house                              |
| <i>Humidity (72)</i>           |         |                                               |
| 0 = No correlation             | 98 [ ]  | Recent renovation                             |
| 1 = Dry Weather                | 99 [ ]  | House dampness                                |
| 2 = Wet Weather                | 100 [ ] | Floor carpet                                  |
| 3 = Windy Weather              | 101 [ ] | Type of carpet                                |
| <i>Food (73)</i>               |         |                                               |
| 0 = unknown                    | 102 [ ] | Age of carpet                                 |
| 1 = Milk                       | 103 [ ] | Bed                                           |
| 2 = Egg                        | 104 [ ] | Bedding                                       |
| 3 = Apple                      |         |                                               |
| 4 = Banana                     |         |                                               |
| 5 = Nuts                       |         |                                               |
| 6 = Spinach                    |         |                                               |
| 7 = Soya                       |         |                                               |
| 8 = Tomatoes                   |         |                                               |
| 9 = Celery                     |         |                                               |
| 10 = Cocoa                     |         |                                               |

11 = Fish  
 12 = Grapes  
 13 = Shellfish  
 14 = Chicken  
 15 = Cereal  
 16 = Any other  
 17 = None

*Chemicals (78)*

0 = Unknown  
 1 = Salicylates  
 2 = Nitrate  
 3 = Benzoate  
 4 = Tartrazine  
 5 = Metabisulphite  
 6 = Others  
 7 = None

*Provoking Agents (81)*

0 = Not known  
 1 = House dust  
 2 = Cut grass  
 3 = Flowers  
 4 = Animal Hair  
 5 = Sprays  
 6 = Timothy grass  
 7 = Smoke  
 8 = Fumes  
 9 = Mouldy environment  
 10 = Temperature change

*Provoking drugs (84)*

0 = None  
 1 = NSAIDS  
 2 = anti Ht  
 3 = B-blockers  
 4 = VIX  
 5 = Other

*Treatment (86, 89, 94)*

0 = None  
 1 = Antihistamine  
 2 = Antihypertensive  
 3 = Steroids  
 4 = Antibiotic  
 5 = Intal  
 6 = Vasoconstrictor  
 7 = Garlic  
 8 = Horseradish peroxidase  
 9 = Laser  
 10 = Acupuncture  
 11 = Hypnotherapy  
 12 = Evening primrose  
 13 = Narcotics  
 14 = Unspecified  
 15 = Any Other

105 [ ] Age of Bedding  
 106 [ ] Pets — Location  
 107 [ ] Pets — Type  
 108 [ ]  
 109 [ ] Duration of association with these pets  
 110 [ ] Dust exposure  
 111 [ ]  
 112 [ ] Present smoking history  
 113 [ ] Past smoking history  
 114 [ ] Cessation of smoking  
 115 [ ] Exposure to aerosols  
 116 [ ]  
 117 [ ] Symptoms associated with aerosols  
 118 [ ]  
 119 [ ]  
 120 [ ]  
 121 [ ]  
 122 [ ] Injected conjunctiva  
 123 [ ] Skin about the nose reddened  
 124 [ ] Rhinoscopy appearance  
 125 [ ] Allergic crease  
 126 [ ] Allergic shiner  
 127 [ ] Deneys (Inf. orbital crease).  
 128 [ ] Nasal provocation  
 129 [ ] Hearing test  
 130 [ ] Drum appearance  
 131 [ ] Skin rashes  
 132 [ ] Eczema  
 133 [ ] Dermographism  
 134 [ ] Height (cm)  
 135 [ ]  
 136 [ ]  
 137 [ ] Weight (kg)  
 138 [ ]  
 139 [ ]

|                                        |         |                                       |
|----------------------------------------|---------|---------------------------------------|
| <i>Routes</i> (92)                     | 140 [ ] | Schirmer' Test                        |
| 0 = None                               |         |                                       |
| 1 = Nasal                              | 141 [ ] |                                       |
| 2 = Oral                               | 142 [ ] |                                       |
| 3 = Sublingual                         |         |                                       |
| 4 = Subcutaneous                       | 143 [ ] |                                       |
| 5 = Intramuscular                      |         |                                       |
| 6 = Intravenous                        | 144 [ ] | Nasal cytology                        |
|                                        | 145 [ ] | Nasal washing                         |
| <i>Hormonal Changes</i> (95)           |         |                                       |
| 0 = No correlation                     | 146 [ ] | Serum IgE                             |
| 1 = Pregnancy                          | 147 [ ] |                                       |
| 2 = Menstruation                       |         |                                       |
| 3 = Coitus                             | 148 [ ] |                                       |
| 4 = OCP                                | 149 [ ] |                                       |
| <i>Type of House</i> (96)              | 150 [ ] |                                       |
| 1 = Weatherboard                       |         |                                       |
| 2 = Fibro                              | 151 [ ] | RAST                                  |
| 3 = Brick veneer                       |         |                                       |
| 4 = Double brick                       | 152 [ ] | Pollen Mix                            |
|                                        | 153 [ ] | Animal/Epithelia                      |
| <i>Age of the house</i> (97)           |         |                                       |
| 1 = <5 years                           | 154 [ ] | E 1 Cat Epithelia                     |
| 2 = 5–10 years                         |         |                                       |
| 3 = 10–20 years                        | 155 [ ] | E 2 Dog Epithelia                     |
| 4 = >20 years                          | 156 [ ] | Cockroach                             |
|                                        | 157 [ ] | House Dust/Mite                       |
| <i>Carpet</i> (100)                    |         |                                       |
| 0 = None                               | 158 [ ] | <i>Dermatophagoides pteronyssinus</i> |
| 1 = Long                               |         |                                       |
| 2 = Short                              | 159 [ ] | <i>Dermatophagoides farinae</i>       |
|                                        | 160 [ ] | Grass mix                             |
| <i>Type of Carpet</i> (101)            |         |                                       |
| 0 = None                               | 161 [ ] | G 2 - couch/Bermuda grass             |
| 1 = Wool                               |         |                                       |
| 2 = Synthetic                          | 162 [ ] | G 5 - Perennial rye                   |
|                                        | 163 [ ] | G 10 Johnson grass                    |
| <i>Age of Carpet</i> (102)             |         |                                       |
| 1 = <5 years                           | 164 [ ] | G 13 Velvet grass                     |
| 2 = 5–10 years                         |         |                                       |
| 3 = 10–20 years                        | 165 [ ] | G 17 Bahia grass                      |
| 4 = >20 years                          | 166 [ ] | Mould mix                             |
|                                        | 167 [ ] | M 1 <i>Penicillin notatum</i>         |
| <i>Bed</i> (103)                       |         |                                       |
| 1 = Foam                               | 168 [ ] | M 2 <i>Cladosporium herbarum</i>      |
| 2 = Water bed soft sided               |         |                                       |
| 3 = Water bed wood sided               | 169 [ ] | M 3 <i>Aspergillus fumigatus</i>      |
| 4 = Feathers                           |         |                                       |
| 5 = Conventional mattress inner spring | 170 [ ] | M 6 <i>Alternaria feniis</i>          |
| 6 = Wool mattress                      | 171 [ ] | Weed mix                              |
| 7 = Futon (Japanese bed)               | 172 [ ] | W 1 Common Ragweed (short)            |
|                                        | 173 [ ] | W 7 Ox-eye Daisy                      |
| <i>Bedding</i> (104)                   |         |                                       |
| 1 = Blanket                            |         |                                       |
| 2 = Doona                              | 174 [ ] | W 9 English Plantain                  |
| 3 = Polyester                          |         |                                       |

|                                   |         |                                     |
|-----------------------------------|---------|-------------------------------------|
| 4 = Wool                          | 175 [ ] | Artemesia                           |
| 5 = Wool underlay                 | 176 [ ] | Lambs quaters W 10                  |
| 6 = Electric blanket              | 177 [ ] | Food mix                            |
| 7 = Impervious covers             | 178 [ ] | F × 1 Egg white                     |
| <i>Age of Bedding</i> (105)       | 179 [ ] | F × 2 Milk                          |
| 0 = Unknown                       | 180 [ ] | F × 3 Codfish                       |
| 1 = less than 1 year              | 181 [ ] | F × 5 Rye                           |
| 2 = 1–2 years                     | 182 [ ] | <i>Alternaria</i> prick (m.m)       |
| 3 = 3–5 years                     | 183 [ ] |                                     |
| 4 = 5–10 years                    | 184 [ ] | <i>Cladosporium</i> prick (m.m)     |
| 5 = >10 years                     | 185 [ ] |                                     |
| <i>Pets</i> (106)                 | 186 [ ] | <i>Aspergillus</i> prick (m.m)      |
| 0 = None                          | 187 [ ] |                                     |
| 1 = Inside                        | 188 [ ] | <i>Helminthosporium</i> prick (m.m) |
| 2 = Outside                       | 189 [ ] |                                     |
| 3 = Inside and outside            | 190 [ ] | <i>D. pteronyssinus</i> prick (m.m) |
| <i>Pets</i> (107)                 | 191 [ ] |                                     |
| 0 = None                          | 192 [ ] | <i>D. farinae</i> prick (m.m)       |
| 1 = Cat                           | 193 [ ] |                                     |
| 2 = Dog                           | 194 [ ] | Control prick (m.m)                 |
| 3 = Horse                         | 195 [ ] |                                     |
| 4 = Birds                         | 196 [ ] | Yeast (Baker) prick (m.m)           |
| 5 = Mice                          | 197 [ ] |                                     |
| 6 = Guinea pig                    | 198 [ ] | Yeast Brewer prick (m.m)            |
| <i>Association</i> (109)          | 199 [ ] |                                     |
| 1 = <1 year                       | 200 [ ] | Cockroach prick (m.m)               |
| 2 = 1–3 years                     | 201 [ ] |                                     |
| 3 = 3–5 years                     | 202 [ ] | Cat prick (m.m)                     |
| 4 = 5–10 years                    | 203 [ ] |                                     |
| 5 = >10 years                     | 204 [ ] | Dog prick (m.m)                     |
| <i>Dust</i> (110)                 | 205 [ ] |                                     |
| 0 = None                          | 206 [ ] | Histamine prick (m.m)               |
| 1 = House dust                    | 207 [ ] |                                     |
| 2 = Flour                         | 208 [ ] | Privet prick (m.m)                  |
| 3 = Silicon                       | 209 [ ] |                                     |
| 4 = Asbestos                      |         |                                     |
| 5 = Timber                        |         |                                     |
| 6 = Organic dust eg. Pigeons      |         |                                     |
| 7 = Grain                         |         |                                     |
| 8 = Other — Specify               |         |                                     |
| <i>Smoking History</i> (112, 113) |         |                                     |
| 0 = Zero                          |         |                                     |
| 1 = 1–10/day                      |         |                                     |
| 2 = 11–20/day                     |         |                                     |
| 3 = 21–30/day                     |         |                                     |
| 4 = >30/day                       |         |                                     |
| <i>Cessation of smoking</i> (114) |         |                                     |
| 0 = No                            |         |                                     |
| 1 = Yes over last 1–2 years       |         |                                     |
| 2 = Yes over last 3–5 years       |         |                                     |

|                                               |         |                                     |
|-----------------------------------------------|---------|-------------------------------------|
| 3 = Yes over last 6–10 years                  | 210 [ ] | Acacia prick (m.m)                  |
| 4 = Yes over last >10 years                   | 211 [ ] |                                     |
| <i>Exposure to aerosols</i> (115)             | 212 [ ] | Flower mix prick (m.m)              |
| 0 = None                                      | 213 [ ] |                                     |
| 1 = Room freshner                             | 214 [ ] | Casuarina prick (m.m)               |
| 2 = Pesticides                                | 215 [ ] |                                     |
| 3 = Deoderants                                | 216 [ ] | Hazelnut prick (m.m)                |
| 4 = Perfumes                                  | 217 [ ] |                                     |
| 5 = Hairsprays                                | 218 [ ] | Rye perennial prick (m.m)           |
| <i>Examination Injected Conjunctiva</i> (122) | 219 [ ] |                                     |
| 0 = None                                      | 220 [ ] | Control prick (m.m)                 |
| 1 = Right                                     | 221 [ ] |                                     |
| 2 = Left                                      | 222 [ ] | Bermuda (Couch) prick (m.m)         |
| 3 = Both                                      | 223 [ ] |                                     |
| <i>Rhinoscopy appearance</i> (124)            | 224 [ ] | Plantain 4 prick (m.m)              |
| 0 = Not done                                  | 225 [ ] |                                     |
| 1 = Normal                                    | 226 [ ] | 7 grass prick (m.m)                 |
| 2 = Injected mucosa                           | 227 [ ] |                                     |
| 3 = Oedematous mucosa                         | 228 [ ] | Histamine prick (m.m)               |
| 4 = Polyps                                    | 229 [ ] |                                     |
| 5 = Pus                                       | 230 [ ] | Bahia prick (m.m)                   |
| 6 = Foreign bodies                            | 231 [ ] |                                     |
| <i>Nasal provocation</i> (128)                | 232 [ ] | Phalaris (Canary grass) prick (m.m) |
| 0 = Not done                                  | 233 [ ] |                                     |
| 1 = Positive                                  |         |                                     |
| 2 = Negative                                  |         |                                     |
| <i>Hearing Test</i> (122)                     |         |                                     |
| 0 = Not done                                  |         |                                     |
| 1 = Normal                                    |         |                                     |
| 2 = R side                                    |         |                                     |
| 3 = L side                                    |         |                                     |
| 4 = Both sides                                |         |                                     |
| <i>Drum Appearance</i> (123)                  |         |                                     |
| 0 = Normal                                    |         |                                     |
| 1 = Injected                                  |         |                                     |
| 2 = Canal obstruction                         |         |                                     |
| 3 = Pus                                       |         |                                     |
| 4 = Perforated Drum                           |         |                                     |
| <i>Nasal Cytology</i> (144)                   |         |                                     |
| 0 = Not done                                  |         |                                     |
| 1 = Eosinophils                               |         |                                     |
| 2 = Basophils                                 |         |                                     |
| 3 = Goblet cells                              |         |                                     |
| 4 = Malignant cells                           |         |                                     |