

Plantago lanceolata (English plantain) pollinosis in Japan

Yuji Nakamaru^{a,*}, Shiroh Maguchi^b, Nobuhiko Oridate^a, Dai Takagi^a,
Yasushi Furuta^a, Satoshi Fukuda^a

^aDepartment of Otolaryngology and Head and Neck Surgery, Hokkaido University Graduate School of Medicine,
West 7 North 15, Sapporo 060-8638, Japan

^bIshikariwan ENT Hospital, Sapporo, Japan

Received 8 December 2004; received in revised form 26 January 2005; accepted 25 March 2005

Available online 10 May 2005

Abstract

Objective: The objective was to ascertain the prevalence of *Plantago lanceolata* (English plantain) pollinosis in Japan.

Methods: A total of 160 patients with allergic rhinitis were examined at the Hokkaido University Hospital Otolaryngology Clinic between January 2002 and December 2003. We investigated the frequency of *P. lanceolata* antigen-specific immunoglobulin E (IgE) antibody-positive serum using the radioallergosorbent test (RAST), the *P. lanceolata* pollen counts in the Sapporo area and the clinical symptoms of patients with allergic rhinitis caused by this pollen.

Results: *P. lanceolata* pollen was dispersed throughout the Sapporo area from mid-May to early September, peaking in the latter half of May. The airborne pollen count showed little variation between years. The *P. lanceolata* RAST-positive rate was 12.8%, which was close to those for ragweed and sagebrush. All subjects showed overlapping antigen sensitization, that is, none displayed sensitization (by RAST) exclusively to *P. lanceolata*. The onset of subjective symptoms peaked in June and the symptoms worsened from April to October.

Conclusion: *P. lanceolata* was dispersed over a long period, from mid-May to early September. The *P. lanceolata* RAST-positive rate (12.8%) was similar to those for sagebrush and ragweed, which are dispersed during the fall. These results suggest that *P. lanceolata* is an important causative agent of pollinosis in Japan.

© 2005 Elsevier Ireland Ltd. All rights reserved.

Keywords: Allergic rhinitis; English plantain; *Plantago lanceolata*; Pollinosis; RAST

1. Introduction

Plantago lanceolata (English plantain) is widely distributed throughout Japan, from Hokkaido to Okinawa. As this weed grows naturally along roadsides and in similar habitats, there are many opportunities for human exposure to its pollen. *P. lanceolata* pollen causes approximately 20–30% of all seasonal allergic rhinitis in the West. This plant is, therefore, considered to be one of the most important agents of pollinosis.

The flowers of members of the family Plantaginaceae bloom for an extended period and disperse their pollen over a similarly long period. The pollen does not disperse at heights, as evidenced by the low detection rate reported by Usami [1] in his survey of airborne pollen dispersal measured on the tops

of buildings. For this reason, the pollen is not commonly recognized as a substantial cause of pollenosis; to date, the paper mentioned above is the only published abstract to discuss *P. lanceolata* pollinosis in Japan [1].

In the present study, we investigated the significance of *P. lanceolata* pollinosis by examining the frequency of *P. lanceolata* antigen-specific immunoglobulin E (IgE) antibody-positive serum using the radioallergosorbent test (RAST), the *P. lanceolata* pollen-dispersal patterns in Hokkaido (Sapporo), and the clinical symptoms of RAST-positive subjects.

2. Materials and methods

2.1. Subjects

We studied 160 individuals who were diagnosed with allergic rhinitis at the Hokkaido University Hospital

* Corresponding author. Tel.: +81 11 707 3387; fax: +81 11 717 7566.
E-mail address: nmaru@med.hokudai.ac.jp (Y. Nakamaru).

Otolaryngology Clinic, Japan, during a 2-year period from January 2002 to December 2003. This group comprised 83 males and 77 females, who ranged in age from 3 to 79 years; the median age was 35 years. Allergic rhinitis was diagnosed based on the Japanese Guidelines for Allergic Rhinitis (2002) [2].

2.2. Methods

2.2.1. Measurement of antigen-specific IgE antibody using RAST

The antigen-specific IgE antibody was measured using an antigen-specific IgE kit (Uni-Cap; Pharmacia Upjohn). The following 12 species are analyzed at our clinic: *P. lanceolata*, house dust, mites, birch, orchard grass, timothy, ragweed, sagebrush, dandelion, dog, cat and *Aspergillus*. The level of each fluctuates depending on the case. A RAST score of class II or above was considered to be positive.

2.2.2. Measurement of *P. lanceolata* airborne pollen counts

A Durham pollen collector was set up on a second-floor verandah of the Ishikariwan Otolaryngology Clinic in Ishikari City (on the outskirts of Sapporo) and the slide glass, which was covered with paraffin jelly, was replaced every 24 h. The collected pollen was stained with Carberla

solution and the pollen count (per cm²) was measured under a microscope. The *P. lanceolata* pollen was multiporate, approximately 26 µm in size and had around 10 palatal apertures (Fig. 1).

3. Results

3.1. *P. lanceolata* pollen-dispersal patterns in Sapporo

Fig. 2 shows the *P. lanceolata* pollen-dispersal pattern in Sapporo from 2002 to 2004. In 2002, the first day of observation and the first day of dispersal were both May 12, and the final dispersal day was September 16 (Fig. 2A). In 2003, the first observation day was May 20, the first dispersal day was May 26 and the final dispersal day was September 17 (Fig. 2B). In 2004, the first observation day was April 24, the first dispersal day was May 17 and the final dispersal day was September 16 (Fig. 2C). The total number of dispersals was 219 in 2002, 198 in 2003 and 245 in 2004; thus, there was little variation between years. In 2002 and 2004, pollen dispersal peaked in the latter half of May. In 2003, although pollen dispersal was prevalent during the latter half of May, there were also marked dispersal periods in June, July and September. Pollen was thus airborne for a relatively long period of time, from mid-May to early September.

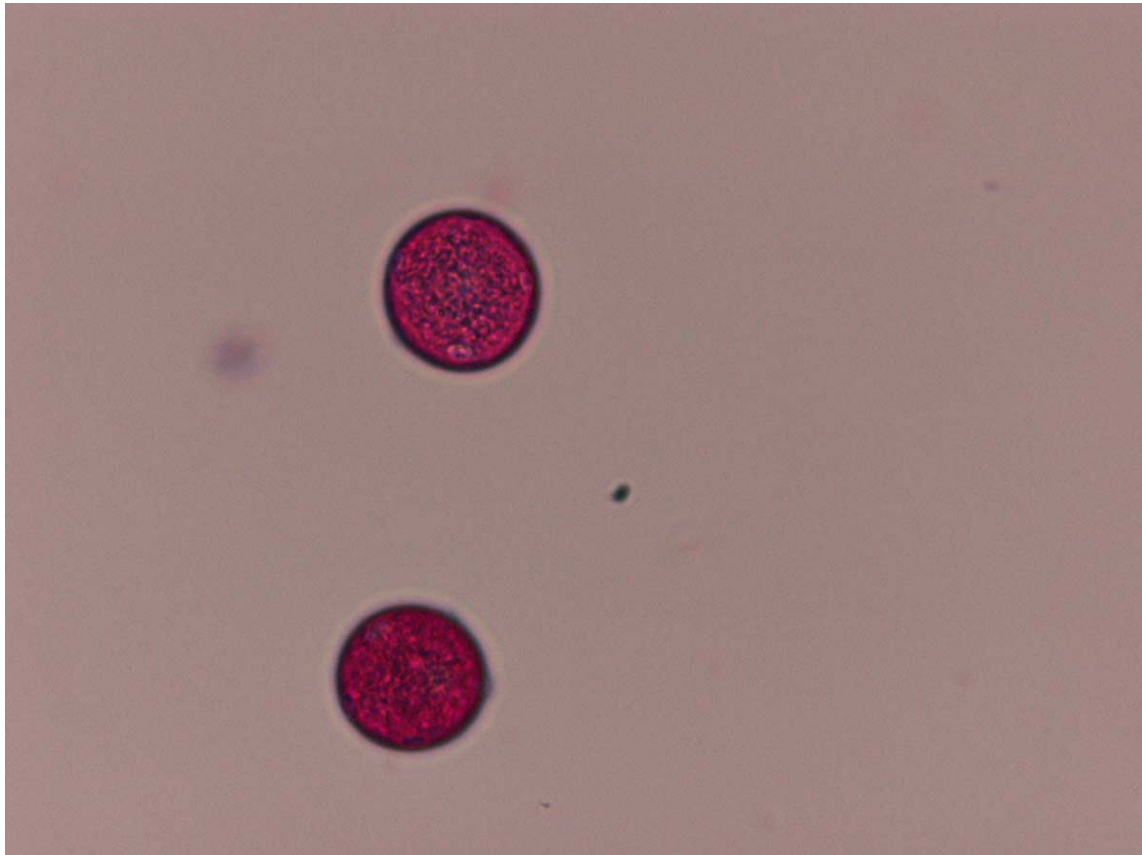


Fig. 1. *P. lanceolata* pollen. The pollen grains are multiporate and medium sized (about 26 µm).

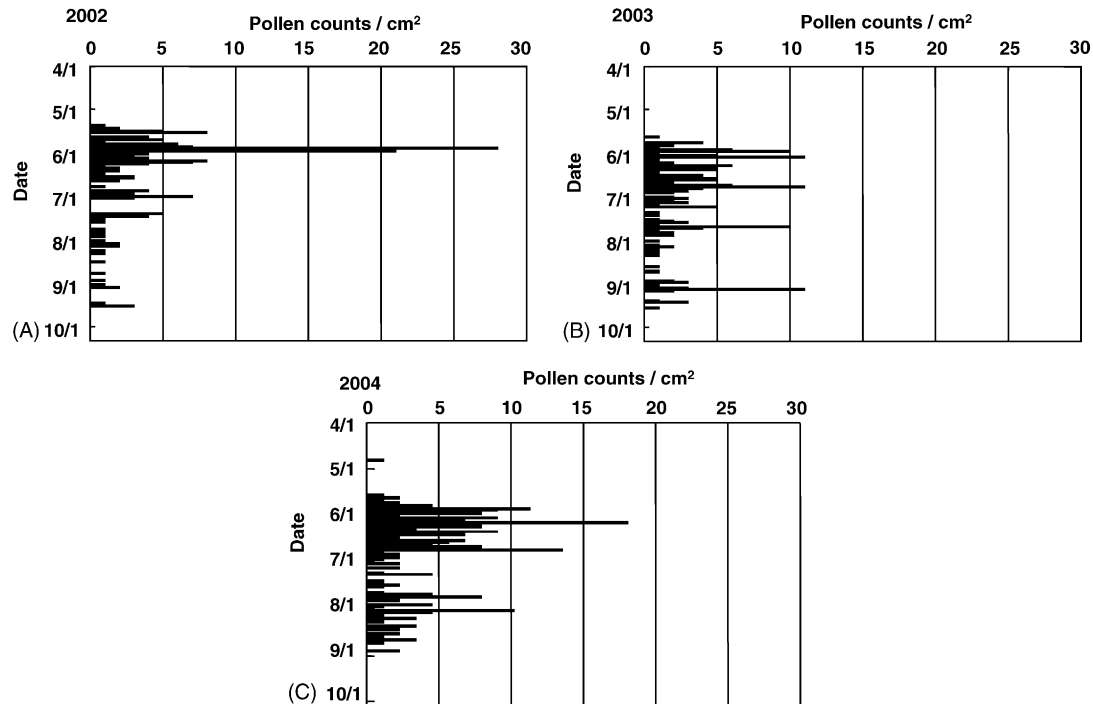


Fig. 2. *P. lanceolata* pollen-dispersal pattern in Sapporo from 2002 to 2004. (A) Pollen-dispersal pattern in 2002, (B) pollen-dispersal pattern in 2003 and (C) pollen-dispersal pattern in 2004. The total number of dispersals was 219 in 2002, 198 in 2003 and 245 in 2004; thus, there was little variation between years.

3.2. *P. lanceolata* RAST-positive rates

Of the 160 patients who were diagnosed with allergic rhinitis at our clinic during 2002 and 2003, 141 underwent RAST for *P. lanceolata*. A total of 18 of these patients tested positive to *P. lanceolata*, giving a RAST-positive rate of 12.8%. Among the *P. lanceolata*-RAST positive patients, 14 were scored as class II, three were scored as class III and one was scored as class IV. The RAST-positive rates for the other antigens tested were as follows (the figures in parentheses indicate the number of RAST-positive cases/the total number of measured cases): 38.2% (55/152) for birch; 28.4% (44/154) for orchard grass; 27% (39/143) for timothy; 16% (23/144) for ragweed; 15.9% (24/151) for sagebrush; 16.7% (25/150) for dandelion; 14% (20/143) for dog; 15.2% (22/145) for cat; and 4.7% (7/150) for *Aspergillus*. These results showed that the *P. lanceolata* pollen RAST-positive rate was similar to those for ragweed and sagebrush, among others (Fig. 3).

3.3. Overlapping antigen-positive rates

None of the patients were exclusively sensitized to *P. lanceolata*; rather, all patients showed some type of overlapping antigen sensitization. We examined the RAST-positive rates for other antigens among the *P. lanceolata* RAST-positive cases and found overlapping sensitization to other pollen antigens, including birch and orchard grass, as well as to house dust and mites (Fig. 4).

3.4. Timing of the onset of subjective symptoms

We examined the timing of the onset of nasal symptoms among *P. lanceolata* RAST-positive cases. This was achieved by patients completing a questionnaire at their initial examination, in which they recorded the time at which their subjective symptoms worsened. This revealed that although many patients were simultaneously sensitized to different antigens and developed nasal symptoms at different

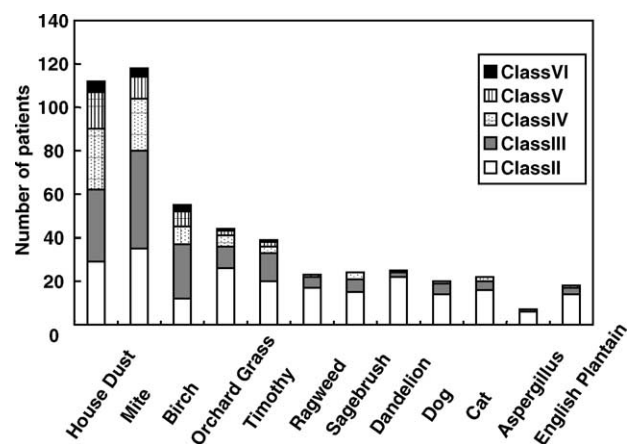


Fig. 3. The number of RAST-positive patients for each antigen. Of the 160 patients who were diagnosed with allergic rhinitis, 141 underwent RAST for *P. lanceolata*. A total of 18 of these patients tested positive to *P. lanceolata*, giving a RAST-positive rate of 12.8%. The *P. lanceolata* pollen RAST-positive rate was similar to those for ragweed and sagebrush, among others.

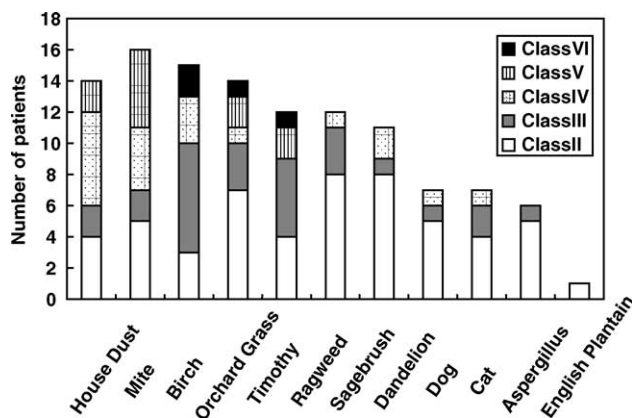


Fig. 4. The number of RAST-positive patients showing sensitization to other antigens. Overlapping sensitization was found to other pollen antigens, including birch and orchard grass, as well as to house dust and mites.

times throughout the year, the symptoms were generally aggravated from April to October, and tended to peak in June (Fig. 5). There is a significant difference between pollen scattering periods and non-scattering periods ($p = 0.0149$ by Mann–Whitney U -test). However, there is no significant relation between *P. lanceolata* RAST score and nasal symptoms.

3.5. Example case study

A 44-year-old man reported experiencing aggravated seasonal sneezing, nasal discharge and nasal congestion from May to August for the last 10 years. He complained chiefly of snoring and apnea, and was therefore, examined initially at a local respiratory center where he underwent polysomnography. The results revealed a mild apnea index of 2.8/hour and severe nasal congestion, so he was referred to our clinic. At the initial examination, the severity of his allergic rhinitis was categorized as 1+ for paroxysmal

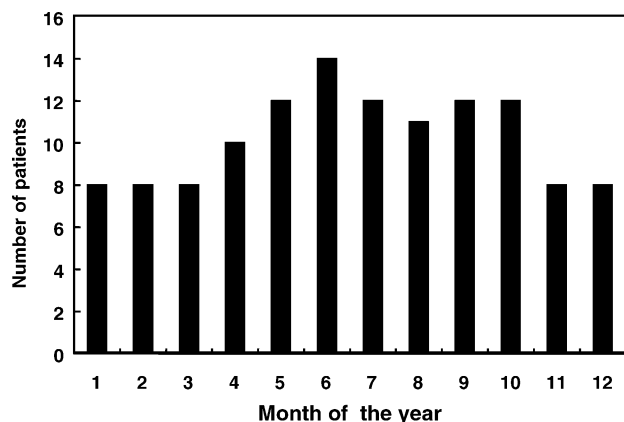


Fig. 5. Timing of the onset of subjective symptoms. Although many patients were simultaneously sensitized to different antigens and developed nasal symptoms at different times throughout the year, the symptoms were generally aggravated from April to October, and tended to peak in June.

sneezing, 3+ for nasal discharge and 3+ for nasal congestion. He had never kept a pet and presented with no other atopic disease comorbidities, such as asthma or atopic dermatitis. He worked as a massage therapist and had no history of antigen inhalation. A nasal cavity examination revealed a mildly deviated nasal septum, bilateral inferior turbinate paling and swelling and a transparent colorless nasal discharge in the common nasal meatus.

At the initial examination, the patient tested positive to eosinophils in the nasal mucus, and was RAST-positive to *P. lanceolata* (class III), house dust and mites (both class IV). However, he tested negative to the remaining potential allergens (orchard grass, timothy, *Aspergillus*, ragweed, sagebrush, birch, dandelion, dog and cat). Computed tomography (CT) revealed no pathological shadows in the nasosinuses, but did show constricted sites in the mesopharynx and larynx.

The patient was diagnosed with snoring caused by nasal congestion from allergic rhinitis, and was started on treatment with fluticasone nasal drops. The course of his condition was good; after about 2 months of treatment, the nasal congestion and snoring had improved to where the patient only required nasal drops when the symptoms were aggravated.

4. Discussion

4.1. Botanical characteristics of *P. lanceolata*

P. lanceolata is native to Europe and is an exotic species in Japan. However, it has excellent reproductive power and has proliferated more than the naturally growing *Plantago asiatica* in Japan. Although there are approximately 250 confirmed species of Plantaginaceae, *P. lanceolata* is the most common [3]. This species is distributed throughout the world, including Europe, North America and Australia [4].

P. lanceolata is a perennial herb, which forms a bundle of many leaves from a thick stem. It has long thin spatula-shaped leaves in contrast to the oval-shaped sharp-tipped leaves of *P. asiatica*. The stems grow to a height of 20–70 cm, and the tips have 3–5 cm long spikes. The *P. lanceolata* flowers blossom slowly from the base of the spikes, although the blossoming portion is so narrow that the flower appears as a band between the fruit and the bud (Fig. 6). The flowers are open for a relatively long period, from April to August [5].

4.2. Pollen dispersal

The present study revealed that *P. lanceolata* pollen is dispersed from mid-May to early September, and that the dispersal shows little variation between years.

Previous nationwide surveys of *P. lanceolata* pollen dispersal in Japan [6,7] detected airborne pollen at eight institutions in Asahikawa, Hakodate, Kanazawa, Sagami-



Fig. 6. The *P. lanceolata* flowers. These blossom slowly from the base of the spikes. The blossom is so narrow, such that the flowers appear as a band between the fruit and the bud.

hara, Fukuoka, Sapporo and Akita, although the airborne counts were relatively low. In addition, Usami reported relatively low pollen-detection rates in a survey of rooftops and other high places [1]. In the present study, we sampled pollen from a second-floor verandah and obtained similar pollen counts to those reported previously. Usami [1] found that *P. lanceolata* pollen dispersal was greater in late October than in September. However, in the present study, no airborne pollen was detected after late September. This discrepancy might be due to the fact that Usami carried out his investigation in Hamamatsu in Shizuoka Prefecture, where the blossoming and pollen dispersal periods might differ from those in Hokkaido.

4.3. *P. lanceolata* as a cause of pollinosis

In Europe, *P. lanceolata* has been recognized since the turn of the present century as a causative plant for pollinosis [4]. Recent research has shown that 34% of individuals with respiratory allergies test positive to *P. lanceolata* (by RAST), and intracutaneous studies have indicated that 28% of patients with seasonal respiratory allergies show a positive reaction to *P. lanceolata* [8]. These sensitivity rates were higher than those reported for members of the Betulaceae (23% positivity based on intracutaneous testing)

and *Artemisia* (16% positivity based on intracutaneous testing), so this plant is commonly associated with pollinosis in the West. However, patients who are exclusively sensitive to *P. lanceolata* are rare; individuals are usually simultaneously sensitized to other plants, such as members of the family Gramineae, which provoke symptoms during the same time period. It has, therefore, been unclear to what extent *P. lanceolata* contributes to the onset of the symptoms of pollinosis [4].

In the present study, the *P. lanceolata* RAST-positive rate was 12.8%, which was lower than that reported in the West. However, this was similar to the sensitivity to ragweed and sagebrush pollen, and thus cannot be ignored. Usami reported a *P. lanceolata*-sensitivity rate of about 18% using intracutaneous testing. According to this author, the negativity to *P. lanceolata* in the RAST was high; therefore, it is possible that our study might have produced a slightly higher sensitivity rate if we had used intracutaneous testing.

Mehta and Wheeler [8] identified the components that were responsible for much of the IgE-binding activity of the *P. lanceolata* extract. They also showed that there were no common IgE-binding epitopes in other grass pollen and plantain pollen extracts, indicating that *P. lanceolata* RAST should not necessarily be interpreted in terms of cross-reaction.

Previous reports from studies conducted in the West have also shown that overlapping sensitivity is prevalent—there has yet to be a single confirmed case of sensitivity to *P. lanceolata* alone. Further work will, therefore, be necessary to clarify the precise extent of the involvement of *P. lanceolata* pollen in pollinosis. However, reports of aggravated nasal symptoms during periods of *P. lanceolata* pollen dispersal without overlapping sensitivity to other pollens, such as the case presented here, and the fact that the onset of symptoms is common during the pollen dispersal period suggest that *P. lanceolata* both causes and aggravates allergic rhinitis.

It is possible that from May to September, *P. lanceolata* pollen becomes antigenic in symptomatic allergic rhinitis. This pollen must, therefore, be considered when investigating the causes of this condition.

5. Conclusion

P. lanceolata was airborne in Sapporo for a relatively long period, from mid-May to early September. The RAST-positive rate was 12.8%; this was similar to the values reported for sagebrush and ragweed, which are both dispersed in the fall. These results suggest that *P. lanceolata* pollen is an important causative antigen of pollinosis in Japan.

Acknowledgement

We are deeply indebted to Sai Shibuya of the Clinical Testing Department of Hokkaido University Hospital for his help with the investigation of specific IgE antibodies.

References

- [1] Usami A. Plantain pollinosis. *JIAO* 1999;17:222–3.
- [2] Members of the Japanese Guideline for Allergic Rhinitis. Examination and diagnosis. In: Okuda M, editor. Japanese guideline for allergic rhinitis 2002. Tokyo: Life Science Ltd.; 2002. p. 18–27.
- [3] Sahashi N. Polygonaceae, Typhaceae and Urticaceae. In: Sahashi N, Saito Y, editors. Plants for allergy. Tokyo: Iyakunomon Ltd.; 1994. p. 25–7.
- [4] Calabozo B, Barber D, Polo F. Purification and characterization of the main allergen of *Plantago lanceolata* pollen, Pla I 1. *Clin Exp Allergy* 2001;31:322–30.
- [5] Yamazaki K. Plantaginaceae. In: Satake Y, Ohwi J, Kitamura S, Watari S, Tominari T, editors. Wild flowers of Japan. Tokyo: Heibonsha Ltd.; 1981. p. 141–2.
- [6] Nagano J, editor. Airborne pollen in Japan. Tokyo: Hokuryukan Ltd.; 1978.
- [7] Nagano J, editor. Airborne pollen in Japan II. Tokyo: Hokuryukan Ltd.; 1992.
- [8] Mehta V, Wheeler AW. IgE-mediated sensitization to English plantain pollen in seasonal respiratory allergy: identification and partial characterisation of its allergenic components. *Int Arch Allergy Appl Immunol* 1991;96:211–7.