
Bee pollen sensitivity in airborne pollen allergic individuals

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Background: Physicians who practice alternative medicine often prescribe bee pollen as a food supplement and a treatment for various ailments.

Objectives: To determine the qualitative and quantitative composition of bee pollen and to investigate the cutaneous reactivity of atopic patients to bee pollen extracts.

Methods: The absolute number of pollen grains per gram of bee pollen was calculated, and morphologic identification of the botanical family was performed. Five extracts of bee pollen were prepared for skin prick testing, according to standard methods. Two hundred two volunteers participated in the study; 145 were atopic patients with respiratory allergy. The remaining 57 were healthy volunteers or nonatopic patients and served as a control group. All participants underwent skin prick testing with a standard battery of 6 aeroallergens (olive, grasses mix, *Parietaria*, mugwort, *Dermatophagoides pteronyssinus*, and *Dermatophagoides farinae*) and with all homemade bee pollen extracts.

Results: All samples of bee pollen contained Oleaceae pollen in high concentrations. Small amounts of anemophilous pollen (Compositae, Chenopodiaceae) were detected in various samples. A strong positive correlation was observed between cutaneous reactivity to bee pollen extracts and olive, grasses, and mugwort.

Conclusions: Bee pollen contains a large amount of pollen, which belongs to various allergenic families of plants. Bee pollen retains its allergenic potential as demonstrated by strong cutaneous responses to bee pollen extracts observed in atopic patients in contrast to nonatopic subjects. Regarding pollen allergic individuals, further studies are needed to evaluate the safety of ingesting large amounts of bee pollen.

Ann Allergy Asthma Immunol. 2006;97:703–706.

INTRODUCTION

Bee pollen is often referred to as nature's most complete food. It consists mainly of the male germ of plants (flowers or blossoms), but it also contains insect body parts, fungus, bacteria, and bee fecal material. Bee pollen became popular as a nutritional supplement after Finnish marathon runners claimed that it increased their stamina and improved their performance in the 1972 Olympics in Munich, Germany.

Bee pollen is used throughout the world in a surprising number of applications.^{1–5} Even though the beneficial health effects of bee pollen have not been rigorously evaluated in clinical trials, traditional health care practitioners prescribe it widely. Claims that it improves the oxygen-carrying capacity of the blood were not upheld in a study that involved swimmers, and another study in runners showed no difference in performance between the group ingesting bee pollen supplement and the placebo group.^{6,7}

Increasing consumption of bee pollen has been followed by reports of allergic reactions, such as acute urticaria or angioedema, anaphylaxis, gastrointestinal symptoms (nausea, abdominal pain, diarrhea),⁸ and eosinophilic gastroenteritis.⁹ Acute hepatitis due to bee pollen has also been reported,¹⁰ whereas photosensitivity reaction has been attributed to the combination of bee pollen ingestion with other herbal supplements.¹¹

Each bee pollen pellet contains more than 2 million pollen grains, and 1 tsp contains more than 2.5 billion grains.¹² Bee pollen is the food of the young bee and is composed of proteins (25%–35%), carbohydrates (30%–55%), lipids (1%–20%), minerals, vitamins, and trace amounts of other organic substances.¹² In Greece, bee pollen is collected mainly during April, May, and June, because in this period the bees need to feed the offspring; furthermore, this is the main pollen season in this area.

The aim of this study was to evaluate the composition of bee pollen by performing qualitative and quantitative analysis of different samples. Skin test sensitivity of atopic and nonatopic individuals to homemade extracts of bee pollen was also studied. Lastly, the obtained skin test reactions were compared with dermal responses to commercial extracts of 6 major airborne allergens common in Greece.

MATERIALS AND METHODS

Qualitative and Quantitative Analysis of Bee Pollen

Bee pollen was acquired from 5 different districts of Greece, representing inland (Kiato, Lamia, Preveza) and island (Crete

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This work was supported by a grant from the National Institutes of Health, National Institute of Allergy and Infectious Diseases (K23AI059318), to Dr A. Nowak-Wegrzyn.

Received for publication May 8, 2006.

Accepted for publication in revised form July 5, 2006.

and Skiros) flora. Bee pollen was analyzed as follows: 5 spherules of different tinge were chosen from each sample. Fifty micrograms of each spherule was mixed with 0.05 mL of safranin O aqueous solution. The suspension was placed on a slide, covered with a coverslip, and examined under oil immersion lenses ($\times 100$ magnification). Pollen grains were counted, and their absolute number per gram of pollen was calculated. Pollen grains were identified according to their morphologic features and were described as botanical families or plant gender. Pollen grain that represented more than 50% of the total identified pollen in an individual spherule was considered to be a major pollen.

Production of Allergenic Extracts

The bee pollen was prepared by removing its fatty components with ethyl acetate and drying it; subsequently, it was extracted with a buffer solution (phosphate-buffered saline), according to a standardized method.¹³ The concentration of the final extract was 0.02 g/mL (dilution in glycerine 1:2).

Patients

Adult volunteers were recruited among the personnel and the patients who had been referred to the Department of Allergology and Clinical Immunology, "Laikon" General Hospital, Athens, Greece, for investigation of respiratory symptoms, drug allergy, or urticaria during a 1-year period. Pregnant or lactating women and individuals who had received antihistamines or centrally active drugs during the last 10 days were excluded from the study, according to international guidelines.¹⁴ In addition, no patient who ever underwent immunotherapy was included in the study. The hospital scientific committee approved the study, and each patient gave informed consent.

Skin Prick Testing

Skin prick testing (SPT) was performed to the 5 homemade extracts of bee pollen and to a panel of commercial allergenic extracts (Alyostal Prick, Stallergenes, France), including 2 mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*) and 4 pollen extracts: olive (*Olea europea*), grasses mix (*Dactylis glomerata*, *Poa pratensis*, *Holcus lanatus*, *Lolium perenne*, and *Phleum pratense*), *Parietaria* mix

(*Parietaria officinalis* and *Parietaria judaica*), and mugwort (*Artemisia vulgaris*). Negative (glycerinated phosphate-buffered saline) and positive controls (histamine dihydrochloride, 10 mg/mL) were used. SPT was performed on the volar side of the forearm with a sterile 1-mm-tip lancet. Neither the physicians nor the patients knew the content of the home-made bee pollen extracts.

Results were recorded after 15 minutes. The results of SPT were considered positive if the wheal diameter was at least 3 mm greater than the negative control. The positive results thus obtained were expressed as a ratio of allergen wheal diameter to histamine-induced wheal diameter. The SPT responses to the aforementioned 6 extracts (olive, grasses mix, *Parietaria* mix, mugwort, and 2 house dust mites) were chosen to be compared with the bee pollen skin test results, because they are consistently observed in most ($>90\%$) of our atopic population (as single sensitivity or more commonly in various combinations).¹⁵

Statistical Analysis

The nonparameter Spearman correlation coefficient was used to evaluate the correlation of bee pollen extract SPT results with commercial extract SPT results. Statistical analysis was performed using the software program Statistica, version 5.0 (StatSoft, Inc, Tulsa, OK).

RESULTS

Bee Pollen Analysis

The results of the quantitative and qualitative bee pollen analysis are given in Table 1. Each different spherule contained mainly a unique type of pollen, typically accounting for 99% of the total pollen content; this was usually true for samples of bee pollen from the inland (Lamia, Preveza, Kiato), whereas in samples of island origin (Crete, Skiros), 4 to 5 spherules of different constitution were identified. The explanation of this difference is that the samples of inland origin were acquired from beekeepers and were products of a specific location, whereas the samples of island origin were bought from stores and were mixes of different local producers.

Jasmin, of the Oleaceae family, was found in various concentrations in all samples analyzed. Surprisingly, the major pollen in 1 of the 5 spherules from Crete's bee pollen was

Table 1. Plant Pollen Content in Bee Pollen Samples From 5 Greek Districts*

	Kiato	Crete	Lamia	Preveza	Skiros
Pollen grains per gram	2.6×10^6	$2-4.5 \times 10^6$	4.6×10^5	2×10^6	6.4×10^6
Major pollen	<i>Robinia pseudoacacia</i> (2×10^6)	Oleaceae (2.8×10^6) <i>Avena sativa</i> (1.3×10^6) Rosaceae (1.3×10^6)	Oleaceae (3.5×10^5)	Oleaceae (2×10^6)	<i>Daucus</i> sp (4.7×10^6)
Minor pollen	Grasses (4.8×10^5), Oleaceae (1.2×10^5)	Compositae, Chenopodiaceae, Myrtaceae, <i>Olea europea</i> (total = 1.7×10^6)	Vitaceae (1×10^5)	<i>Cladosporium</i> (1.4×10^4)	Compositae (2×10^6), Oleaceae (1.7×10^6)

* The quantity of bee pollen is expressed as the absolute number of pollen grains per gram of bee pollen. Major pollen represents more than 50% of the total identified pollen; less than 50% is considered minor pollen. In the samples from Crete, 3 different major pollen were found. In the Preveza bee pollen sample, the mold *Cladosporium* was also present.

oat (*Avena sativa*) of the grasses family. Smaller amounts of pollen grains from grasses were also found in other samples. The rest of the minor pollen grains identified, originating from anemophilous and amphiphilous plants, included *Olea europea*, *Eucalyptus*, *Chenopodium*, and Compositae. Pollen from Urticaceae or Gymnosperm plants (Pinaceae, Cupressaceae) was not detected in any of the samples.

SPT Results and Correlation

Among 202 individuals examined, 145 (71.8%) were atopic (67 male and 78 female; mean age, 31.9 years; age range, 14–71 years) with symptoms of rhinitis and rhinoconjunctivitis and/or asthma. The remaining 57 nonatopic control subjects (28.2%) (19 male and 38 female; mean age, 39 years; age range, 14–70 years) were personnel or patients who presented with drug allergy, nonallergic rhinitis, or idiopathic urticaria or angioedema. Most atopic patients were sensitive to grasses (63%), *Parietaria* (62%), and olive (58%), which are the 3 most common airborne pollen allergens in Greece. A total of 36% were mugwort sensitive, whereas 29% were sensitive to *D. pteronyssinus* and 27% to *D. farinae*.

None of the control group subjects exhibited positive SPT results to bee pollen extracts. However, 73% of atopic patients reacted to one or more extracts of bee pollen. The results of sensitivities to both airborne allergens and bee pollen extracts are shown in Figure 1. Six atopic individuals who were only mite sensitive and 9 *Parietaria*-monosensitive individuals displayed no bee pollen sensitivity. In contrast, 3 of 5 individuals monosensitive to grasses had positive SPT results to all bee pollen extracts. Similarly, 5 of 8 olive-monosensitive patients had positive SPT results to bee pollen extracts. A statistically significant positive correlation was found between sensitivity to bee pollen extracts and olive ($P < .00001$), Gramineae ($P < .0005$), and mugwort ($P < .001$), whereas no correlation was found to *Parietaria* and mites (Fig 1).

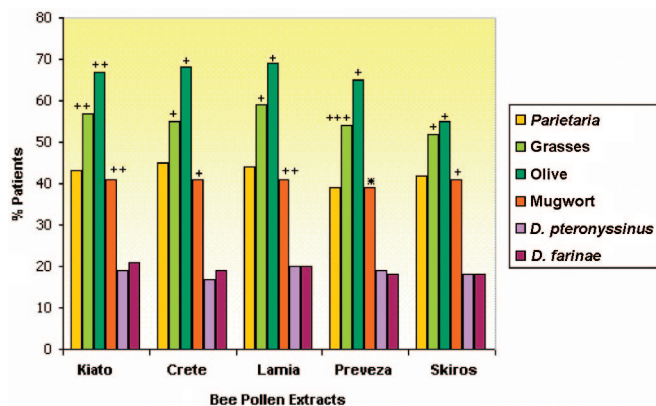


Figure 1. Patients with positive skin prick test results to both bee pollen and airborne pollen allergens. The y-axis represents the percentage of airborne allergen sensitive patients who also present with positive skin prick test results to bee pollen extracts. Bee pollen extracts are named after the district of origin (x-axis). The positive correlation between bee pollen extracts and airborne allergens is marked over the relative pollen. + $P < .000001$; ++ $P < .00001$; +++ $P < .0005$; * $P < .001$.

DISCUSSION

Respiratory allergy is mainly caused by plants such as grasses that produce airborne pollen (anemophilous) and less commonly by those using both insect and wind vectors (amphiphilous; eg, willow). Pollen from entomophilous plants (which produce flowers that attract insects) and amphiphilous plants may potentially sensitize professionals who cultivate or handle them.

Honeybees, attracted to entomophilous plants, display plant stability. In other words, each bee prefers to assemble pollen from a specific type of plant; thus, each spherule contains pollen of homogeneous constitution, whereas the various spherules that are usually contained in a single sample of bee pollen are from different bees and may be of different content and color. One would expect that bee pollen contains only pollen from entomophilous plants. However, the presence of pollen from anemophilous or amphiphilous plants is not rare. In addition, molds (*Alternaria*, *Cladosporium*) may also be detected.⁸

The present study showed that bee pollen contains significant amounts of airborne pollen. In alternative medicine, the usually recommended dose of bee pollen is usually “one to two teaspoonfuls (approximately 2 to 5g, respectively), 1 to 3 times daily,”¹² which may represent an enormous amount of airborne pollen. In our analyses, 1 g of bee pollen contained a mean of 0.4 to 6.4×10^6 plant pollen. As a consequence, a pollen-sensitive person who ingests bee pollen that contains the relevant airborne pollen, may be at risk for the development of an allergic reaction.

The rich flora of Greece (6,000 different species of plants) is also accountable for the diversity in the constitution of the bee pollen samples used in this study. Pollen grains that belonged to 5 different botanic families (Gramineae, Leguminaceae, Oleaceae, Rosaceae, and Umbelliferae) were detected.

Although bee pollen came from beehives of geographically different districts, it mainly contained pollen grains from entomophilous plants (Leguminaceae, Rosaceae, Umbelliferae, and some Oleaceae); a significant amount of airborne pollen (Gramineae, Oleaceae), which constitute major allergens for the Hellenic area, was also found (in 3 samples as primary pollen and in 2 as secondary). The presence of oat pollen as the prevailing type, in spherules from a sample that came from the island of Crete, was an unexpected finding.

Complementary and alternative medicine practitioners promote honeybee products as antiallergic remedies.¹⁶ These products are typically administered in gradually increasing doses, similar to allergen immunotherapy, with a premise that it may result in desensitization to pollen. Our data show that this practice is misguided and risky, since each spherule typically contains pollen of different gender and thus provides unpredictable amounts of allergens. Lack of preservatives for protein stability also affects the dose of allergenic proteins in bee pollen. Finally, no controlled clinical trials have been performed to determine efficacy and safety of bee pollen therapy.

Allergic reactions after consumption of honey and royal jelly have also been reported.^{17–19} Allergy to honey has been attributed to the airborne pollen, as well as to the enzymes

from bee glands (salivary and pharyngeal) or other allergenic particles from the bee's body. The amount of plant pollen in honey is reported to range from 10,000 to 20,000 pollen grains per gram of honey. According to our measurements and those of other laboratories,¹⁹ bee pollen contains up to 2,000 times more grains than honey. This finding suggests that bee pollen may have a much higher potential for causing allergic reactions on ingestion than honey.

Theoretically, an allergic reaction to bee pollen may be the result of sensitization via ingestion of bee pollen. However, atopic patients who are sensitized to pollen via the respiratory tract may also develop an allergic reaction on ingesting bee pollen for the first time.⁸ Pollen grains of plants that belong to the same botanic family often share common antigenic epitopes,²⁰ which explains the cross-allergenicity between bee pollen (that mostly contains entomophilous pollen; eg, dandelion) and anemophilous pollen (eg, ragweed). Thus, a ragweed allergic person is at great risk when ingesting bee pollen that contains pollen from cross-reacting plants, such as dandelion, sunflower, or chrysanthemum.¹⁸ Furthermore, cross-reactivity is also observed between pollen of different botanical families because of the existence of common panallergens, such as profilin.²¹

The correlation noted between bee pollen and mugwort (of the Compositae family) is probably due to Compositae pollen contained in bee pollen. On the contrary, no correlation was observed between *Parietaria* and bee pollen; this is probably because of the absence of Urticaceae pollen in our samples of bee pollen. Sensitivity to mites was evaluated as a control of the methods; as expected, there was no correlation with bee pollen.

In conclusion, bee pollen contains an enormous amount of allergenic plant pollen. In our study, most atopic patients showed sensitivity to the bee pollen extracts, indicating the potential risk of allergic reactions after ingestion of bee pollen. Pollen allergic persons should, therefore, be warned accordingly before ingesting bee pollen. In Australia and New Zealand, an allergy surveillance label on the packages of foods that contain bee pollen is already obligatory, according to the national Food Standards Code (www.foodstandards.gov.au).

ACKNOWLEDGMENTS

We thank the fellows Dr Nikolaos Lyris and Dr Konstantinos Petalas for performing SPT.

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