

Short communication

Birch and ragweed pollinosis north of Milan: a model to investigate the effects of exposure to “new” airborne allergens

Background: The effects of sudden and massive exposure of the general population to novel airborne allergens are not known. This study aimed to investigate the clinical effects of two “new” allergens, ragweed and birch, in an area north of Milan during the last 15 years.

Methods: We reviewed the records of 2571 monosensitized patients seen during the last 10 years in two allergy units north of Milan. Data included age at onset of allergic symptoms, and family history of allergic diseases. In this sample, 500 were allergic to grass, mite, birch, and ragweed; 293 to pellitory; 167 to mugwort; 100 to *Alternaria*; and 11 to plantain.

Results: Birch pollen-allergic patients and ragweed pollen-allergic patients showed a similar mean age at onset (35.3 years vs. 35.1 years; $P = \text{NS}$), but were significantly older than all other groups of patients ($P < 0.001$). Patients allergic to ragweed and birch pollen, 304 and 323 respectively, were > 30 years at the onset of allergic symptoms. A family history of allergic disorders among first degree relatives was far less frequent among patients allergic to birch pollen (29%) or ragweed pollen (27%) than among patients sensitive to all other airborne allergens, except those allergic to mugwort pollen ($P < 0.001$). In both ragweed and birch groups, a positive family history was significantly more common among subjects < 30 years than in those > 30 years at onset of respiratory allergy (81/196 (41%) vs. 54/304 (18%), $P < 0.001$ for the ragweed group; 80/177 [45%] vs. 65/323 (20%), $P < 0.001$ for the birch group).

Conclusion: Exposure of the general population of this area to two new airborne allergens resulted in the onset of respiratory allergy in many older people who lacked any relevant predisposing factor. Although we cannot exclude the possibility that those who became allergic had been exposed to birch or ragweed pollen elsewhere, a more likely explanation is a specific susceptibility that remains viable until the subject encounters the “right” allergen.

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That atopic diseases have a strong genetic basis has been known for many years (1,2). However, genetics studies have been much complicated by variables such as polygenicity, genetic heterogeneity, incomplete penetrance, and by the complex interactions between environmental stimuli and genetic backgrounds. Despite the complex relationship between allergen exposure and sensitization, recent studies have shown a close association between levels of exposure and sensitization to a specific allergen (3). In Western countries, the general population is exposed to both environmental factors that have been shown to facilitate allergic sensitization (4) and to common airborne allergens from early infancy. Consequently, sensitization generally occurs in young people (5).

The concentration of outdoor airborne allergens shows great geographic variability (e.g. pellitory and olive pollen grains are mainly present in Mediterranean areas, birch

pollen in Northern countries, ragweed pollen in certain parts of the USA and Europe), which influences the patterns of allergen sensitization observed in different geographic areas.

Little is known about the effects of sudden and massive exposure of the general population in a certain geographic area to airborne allergens that have never been present in that area before; this is exactly what has happened in a suburban area north of Milan. In this area, birch trees became very popular ornamental plants in parks and private gardens during the 1970s and 1980s, causing the appearance of, and a significant increase in, allergic sensitization to tree pollen allergens (6–8). The marked difference in prevalence of birch pollen allergy in people attending allergy clinics in the area north of Milan, compared to those from the city of Milan (5 Km away) where birch trees have not been planted extensively, has been highlighted (9). Even more recently, the whole of the

area north of Milan was colonized by short ragweed. The first reports of ragweed allergy in this area appeared in the late 1980s (10,11), and it has gradually become the second most frequent pollinosis in the area (9). The reasons for such a sudden spread of ragweed are still debated. Concentrations of the pollen may reach peaks of > 200 granules/m³. The peak concentrations of birch pollen and ragweed pollen observed in this geographic area during the last few years are summarized in Table 1.

This study investigated the effect of the appearance of these "imported" plants by examining the clinical features of patients allergic to "old" and "new" airborne allergens of this area. The study followed the revised nomenclature for allergy of the EAACI (12).

Material and methods

Patients

The records of all patients diagnosed with respiratory allergy between 1 January 1990 and 30 September 2001 at the allergy units of two towns 5 km north of Milan (Bollate and Paderno Dugnano) were reviewed. The following clinical data was obtained: age at onset of allergic symptoms (rhinoconjunctivitis and/or asthma); family history of respiratory or food allergy among at least one first-degree relative (one parent and/or one sibling), diagnosed by an allergy center by skin prick test (SPT) and/or radioallergosorbent test (RAST).

Admission criteria

To avoid bias caused by overlapping pollen seasons (e.g. grass/pellitory, ragweed/mugwort), by sensitization to crossreacting allergens such as profilin (13,14), or to common allergens in ragweed and mugwort pollen (15) or grass and plantain pollen (16), the

Table 1. Peak concentrations of birch and ragweed pollen grains 1986–2001 in the area north of Milan

Year	Pollen counts (number of grains/m ³ air)			
	Birch	Date	Ragweed	Date
1986	192	Apr 19	48	Sep 07
1987	350	Apr 21	28	Sep 07
1988	113	Apr 13	75	Sep 01
1989	447	Mar 28	186	Aug 30
1990	983	Mar 20	120	Aug 30
1991	497	Apr 04	114	Aug 26
1992	408	Apr 04	156	Aug 30
1993	347	Apr 07	143	Aug 25
1994	361	Mar 26	50	Aug 16
1995	56	Mar 27	69	Sep 07
1996	249	Apr 15	198	Aug 24
1997	321	Mar 16	119	Aug 26
1998	65	Mar 19	96	Aug 27
1999	1650	Apr 02	37	Aug 25
2000	NA		203	Aug 27
2001	393	Mar 30	97	Sep 13

NA = Not available.

study included only monosensitized patients (with a single positive SPT in keeping with the clinical history).

The main airborne allergens in this area were considered. They included grass, pellitory, ragweed, mugwort, plantain, birch, *Alternaria*, and house-dust mite. The study aimed to investigate the effects of "novel" allergens on the general population, so allergens that only limited numbers of people are exposed to (e.g. cat or dog dander) were not considered. People who are monosensitized to cypress and olive pollen are very rare in the area and were therefore excluded.

Clinical recordings were reviewed in alphabetical order; the maximum number of patients per group was 500.

Skin tests

All patients underwent SPT with a standard panel of commercial extracts (Allergopharma; Reinbeck, Germany) of airborne allergens including: grass, mugwort, ragweed, pellitory, plantain, birch, cypress, olive, *Alternaria*, house dust mite, cat dander, and dog dander. Skin tests were carried out and read following established methods (17).

Statistics

Means were compared by the two-tailed Student's *t*-test. Proportions were compared by chi-squared test with Yates' correction. Probability values less than 5% were considered significant.

Results

A total of 2571 patients (500 allergic to grass, mite, birch, and ragweed; 293 to pellitory, 167 to mugwort, 100 to *Alternaria*, and 11 to plantain) were studied. Results are shown in Table 2. Birch pollen- and ragweed pollen-allergic patients had a similar mean age at onset (35.3 years vs. 35.1 years; $P = \text{NS}$), but were significantly older than all the other groups ($P < 0.001$). The age at onset of allergic symptoms showed a nearly normal distribution in both ragweed pollen- and birch pollen-allergic patients, whereas in all other groups the distribution was markedly skewed towards younger ages (Table 3). Patients allergic to ragweed and birch pollen > 30 years old at the onset of respiratory allergy were 304 and 323 respectively.

A family history of allergic disorders among first degree relatives was significantly less frequent for patients allergic to birch pollen (29%) or ragweed pollen (27%) than among those sensitive to all other airborne allergens except those allergic to mugwort pollen ($P < 0.001$; Table 2). In both ragweed- and birch-hypersensitive groups, a positive family history was significantly more common among those aged < 30 years than those aged > 30 years (81/196 (41%) vs. 54/304 (18%), $P < 0.001$ for the ragweed group; 80/177 (45%) vs. 65/323 (20%), $P < 0.001$ for the birch group). The subgroups did not show any relevant difference in the clinical features of respiratory allergy (asthma and/or rhinoconjunctivitis) at onset.

Table 2. Age at onset of respiratory symptoms and family history in 2571 mono-sensitized allergic patients

Allergen	No. patients	Age at onset (years)			Family history
		Mean (SD)	Range	Median	
Birch	500	35.3 (13.3)*	3–71	35	29%*
Ragweed	500	35.1 (12.4)*	5–76	33	27%*
Grass	500	18.6 (9.8)	2–58	17	47%
Mite	500	18.4 (11.3)	2–73	16	46%
Pellitory	293	26.2 (11.6)	3–66	25	45%
Mugwort	167	27.4 (11.9)	8–69	25	31%*
<i>Alternaria</i>	100	15.1 (8.1)	2–40	13	51%
Plantain	11	22.5 (7.2)	12–32	26	44%

* $P < 0.001$.

Table 3. Distribution of 2571 monosensitized patients with respiratory allergy by age and allergen

Allergen	Age at onset (years); number (%)				
	0–15	16–30	31–45	46–60	> 60
Birch	38 (8%)	139 (28%)	215 (43%)	87 (17%)	21 (4%)
Ragweed	22 (4%)	174 (35%)	209 (42%)	78 (16%)	17 (3%)
Grass	216 (43%)	224 (45%)	53 (11%)	7 (1%)	0 (0%)
Mite	240 (48%)	194 (39%)	47 (9%)	16 (3%)	3 (1%)
Pellitory	48 (16%)	165 (56%)	65 (22%)	13 (4%)	2 (1%)
Mugwort	20 (12%)	93 (56%)	38 (23%)	13 (8%)	3 (2%)
<i>Alternaria</i>	54 (54%)	40 (40%)	6 (5%)	0 (0%)	0 (0%)
Plantain	3 (30%)	7 (60%)	1 (10%)	0 (0%)	0 (0%)

Discussion

It is well known that most patients develop respiratory allergy before the age of 20, and that initial symptoms appear only occasionally in middle to old age (5). The observation that allergy to pellitory pollen appears some years later than allergy to grass pollen is not surprising (8); but the finding, that in this area the average age of onset for both birch and ragweed allergy is 35 years, was unexpected. Interestingly, ragweed-allergic people were significantly older than those allergic to mugwort (a member of the *Compositae* family, sharing some minor allergens with ragweed, which has always been in this area). There is some possibility that the later age of onset for birch and ragweed allergy relates to the fact that older people have traveled more widely, perhaps being exposed to these allergens elsewhere. A more reasonable explanation for these findings, however, could be a strictly specific genetic predisposition of some people for developing respiratory allergy.

Both ragweed pollen- and birch pollen-allergic subjects in this area have spent their whole lives in contact

with mites, moulds, grass, pellitory and mugwort pollens, and most of them had never traveled abroad, but they became allergic at older ages, only after being exposed for long enough to the “new” allergens. It is tempting to speculate that if these people had lived in areas where both birch trees and ragweed were not present, they would not have developed any respiratory allergy. Such speculation would also suggest that, in general, a genetic predisposition to allergic disease is more common than believed, and that many people do not develop clinically relevant respiratory allergies simply because they have not been exposed to the “right” specific allergen(s) for long enough. An alternative explanation may be that exposure to high levels of a “new” allergen induces sensitization also in people with a low disposition for atopy. In previous studies, adult immigrants from Asia and Turkey developed birch pollen allergy after spending a few years in Sweden, and the prevalence of this allergy was related to the time spent in Sweden (18). Similarly, the introduction of blankets in Papua New Guinea was associated with a 70-fold increase of asthma (19). The immigrant model is characterized by exposure to a native allergen that has been stable for a long time and by subsequent sensitization within a few years. However, this model might not fit well the situation described here, with concentrations of birch and ragweed pollen probably increasing over many years.

The family histories were also interesting. Possibly the results were influenced by the exclusion of people with multiple hypersensitivities to airborne allergens (a subset that is more likely to develop respiratory allergy at a young age and to show a family history of allergic diseases). However, a family history of atopic disorders was significantly less frequent in both birch and ragweed pollen-allergic patients than in most other groups. Surprisingly, in younger patients the prevalence of a positive family history did not differ from that observed in most of the other groups.

In conclusion, this study shows that exposure of the population living in this area to two new airborne allergens resulted in the onset of respiratory allergies in older people who seemed to lack relevant predisposing factors. The existence of a specific susceptibility that remains viable until the “right” allergen is encountered cannot be excluded.

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