

Position paper

Pollen-related allergy in Europe*

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The increasing mobility of Europeans for business and leisure has led to a need for reliable information about exposure to seasonal airborne allergens during travel abroad. Over the last 10 years or so, aeropalynologic and allergologic studies have progressed to meet this need, and extensive international networks now provide regular pollen and hay-fever forecasts. Europe is a geographically complex continent with a widely diverse climate and a wide spectrum of vegetation. Consequently, pollen calendars differ from one area to another; however, on the whole, pollination starts in spring and ends in autumn. Grass pollen is by far the most frequent cause of pollinosis in Europe. In northern Europe, pollen from species of the family Betulaceae is a major cause of the disorder. In contrast, the mild winters and dry summers of Mediterranean areas favor the production of pollen types that are rarely found in central and northern areas of the continent (e.g., the genera *Parietaria*, *Olea*, and *Cupressus*). Clinical and aerobiologic studies show that the pollen map of Europe is changing also as a result of cultural factors (e.g., importation of plants for urban parklands) and greater international travel (e.g., the expansion of the ragweed genus *Ambrosia* in France, northern Italy, Austria, and Hungary). Studies on allergen-carrying paucimicronic or submicronic airborne particles, which penetrate deep into the lung, are having a relevant impact on our understanding of pollinosis and its distribution throughout Europe.

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Pollen allergy has had a remarkable clinical impact in Europe (1, 2), and there is evidence that the prevalence of allergic reactions induced by pollen is increasing (3, 4). The mechanisms governing pollinosis are now better understood thanks to comparative epidemiologic, aerobiologic, and clinical studies conducted over the past 15 years.

The European continent, which stretches from the Atlantic Ocean to the Urals, is characterized by great diversity of climates, vegetation, and geographic features. The type of pollen allergy affecting diverse populations is, in large part, related to these macro-, and even microregional differences.

However, in terms of allergy type, Europe can be divided into five areas (Table 1).

Pollen seasons tend to be shorter and less intense with increasing latitude, although the severity of allergy to individual pollen species varies because climatic factors affect the production and dispersal of pollen grains. In fact, the onset, intensity, and duration of pollen seasons are related to yearly weather patterns. In other words, the start of the flowering season of an individual species in European areas and its progress northward or southward tend to vary from year to year. Consequently, seasonal maps of pollen counts are merely a "guide" to potential exposure in a given area and must be continuously updated. In this paper, we review the data from epidemiologic, aerobiologic, and clinical studies of pollinosis conducted in Europe. Drawing on these data, we also examine the potential causes of the increased prevalence of pollinosis.

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Table 1. Allergy-inducing plants in five main geographic areas of Europe

Arctic	Birch
Central	Deciduous forests
	Birch
	Grasses
Eastern	Grasses
	Mugwort
	Ragweed
Mountainous	Grasses
	Trees
Mediterranean	Grasses
	<i>Parietaria</i>
	Olive
	Cypress

Urban westernized lifestyle has been found to be associated with a greater risk of sensitization also to pollen allergens. Urban living means exposure to increased indoor and outdoor pollution, and, because of possible interactions between inhalant allergens (also pollen) and other environmental factors, it may enhance the risk of both atopic sensitization and aggravation of symptoms in already sensitized patients (5).

The relationship between allergen exposure, cellular infiltration, inflammation of the airways, and clinical symptoms is complex, and factors other than allergens may contribute to the asthmatic activity. In this context, it is interesting to recall that pollen allergens are carried mostly in pollen grains. Pollen grains penetrate into the upper respiratory tract but, because of their size, rarely reach the bronchial regions. The existence of allergen-carrying airborne particles much smaller than pollen grains ("paucimicronic" and "submicronic" particles) was postulated to explain bronchial symptoms affecting subjects during the pollen season. Given their potential impact on the epidemiology of pollen allergy, we also review the results of studies on minute allergenic particles.

Epidemiologic aspects of pollinosis in Europe

There is evidence that the prevalence of atopic diseases has increased over the last two decades (3, 4). However, very few studies have examined a large representative population at regular intervals for clearly defined disease entities diagnosed by a strictly defined hypersensitivity reaction. Unfortunately, the data at present available are not homogeneous as regards populations studied and diagnostic procedures.

Because of its typical signs and symptoms, which affect the conjunctiva, the nasal mucosa, and the

respiratory tract, and because of its annual seasonal recurrence, with exacerbation in warm, windy weather and relief after a rainy period, pollinosis can be detected also by means of a well-constructed questionnaire or by a personal interview (6–8), as well as by the study of atopic markers of allergen sensitization. In an epidemiologic survey conducted in Switzerland (9), objective atopic markers, detected by skin prick test and by the radio-immunoassay skin test Phadiatop®, were used to confirm hay fever diagnosed from the results of a computerized questionnaire. There was good agreement between self-reported hay fever symptoms and atopic markers. The Swedish study showed that between 1991 and 1993 the number of self-reported cases of current hay fever increased at least 10-fold, reaching 14.2% of the population.

In nine European countries, the prevalence of pollinosis estimated from replies to questionnaires and/or from parental and self-report varied from 4.9% in Spain to 16.5% in the UK (Table 2). In studies based on questionnaires plus objective testing and/or medical examination, the prevalence varied from 3.2% in Danish farmers to 19.6% in German conscripts (Table 3).

Aerobiologic and clinical aspects of pollen allergy in Europe

For a clearer understanding of the aerobiologic and clinical aspects of pollinosis, we shall examine grass, trees, and weeds separately.

Grasses

Grass pollen is the major cause of pollinosis in many parts of the world (35). Grass-induced pollinosis is the most common pollen allergy also in Europe, although its frequency differs regionally.

Table 2. Prevalence of hay fever in European countries. Studies based on questionnaire and/or parental and self-report

Country	Year	%	Subjects (ages in years)	Reference
Finland	1989–90	14.00	1712 students aged 15–16	10
France	1986	5.90	629 adults	11
Germany	1989–90	9.50	6135 children aged 9–11	12
UK	1986	10.90	5349 adults aged 16–65	13
UK	1981	16.50	17414 adults aged 23	14
UK	1989	11.90	3403 children aged 8–13	15
Norway	1987–8	10.00	4492 adults aged 15–70	16
Portugal	1995	7.30	5036 children aged 6–7	17
Portugal	1995	6.30	11427 children aged 13–14	17
Spain	1991	4.90	6996 schoolchildren	18
Sweden	1979	5.50	7163 children aged 7–9	19
Switzerland	1985	10	2524 adults aged 15–25	20
Switzerland	1986–7	16.8	2060 top athletes	21

Adapted from European Allergy White Paper (2).

Table 3. Prevalence of hay fever in European countries studies; based on questionnaire plus objective testing or medical examination*

Countries	Year	%	Subjects (ages in years)	Criteria and methods	Reference
Denmark	1989	3.20	187 farmers, mean age 43	Rhinitis, skin prick test, RAST, total IgE	22
Finland	1980	6.00	3649 children, aged 3–15	Diagnosis by physician, symptoms during previous year	23
France	1984–7	11.70	8261 adults, aged 18–65	Symptoms reported and positive skin prick test	24
France	1984	3.00	505 children, aged 4–14	Questionnaire, skin prick test, IgE level	25
France	1987	18.50	2067 adults, aged 20–60	Examination, interview, IgE level	26
Germany	1984	16.70	8771 children, aged 10–18	Questionnaire, skin prick test, nasal provocation	27
Germany	1985	19.60 ¹	511 men (conscripts), aged 18–23	Questionnaire, physical examination, total and specific IgE	28
Germany	1989	7.20 ²	581 children, aged 5–6	Questionnaire to parents, physical examination, skin prick test	29
Germany	1989–90	18.50 ³	8204 children, aged 9–11	Questionnaire, lung-function test, skin prick test	30
UK	1988	14.90	965 children, aged 12	Questionnaire, PEFR	31
Hungary	1993	11.00	1000 aged 5–75	Questionnaire, skin prick test, physical examination	32
Italy	1995	31.00	2841 children and adults, aged 8–75	The value of 31.00 is related to SPT+ (also in subjects without clinical symptoms)	33
Sweden	1971	4.40	165 624 adults aged 18–20	Questionnaire and interview at military enrollment examination	34
	1981	8.40		Questionnaire and interview at military enrollment examination	34
	1992	14.60		Questionnaire and interview at military enrollment examination	34
Switzerland	1991	12.8	8357 adults aged 18–60	Computerized questionnaire and interview, skin prick test, and Phadiatop	9

* Adapted from European Allergy White Paper (2).

¹ Percentage refers to anamnesis/questionnaire.

² Percentage: results of questionnaire.

³ Cumulative prevalence.

Up to 95% of patients allergic to grass pollen possess IgE specific for group 1 allergens and 80% for group 5 allergens – the two groups that constitute the major grass-pollen allergens (36).

The antigens of grass pollen, like those of the other allergenic pollen grains, are rapidly released when allergen-carrying pollen comes into contact with the oral, nasal, or eye mucosa, thereby inducing the appearance of hay-fever symptoms in sensitized patients. As a consequence, the concentration of airborne grass pollen influences the degree of symptoms in pollinosis patients. In London (UK), the lowest atmospheric concentration of grass pollen able to induce the appearance of hay-fever symptoms was shown to be 10–50 grains/m³ (37). In Cardiff (Wales), 10% of pollinosis patients experienced symptoms in the presence of 10 grass-pollen grains/m³, and again in London, a concentration of more than 50 grains/m³ induced symptoms in all pollinosis patients (38). In Bilbao (Spain), 100% of pollinosis patients experienced symptoms when the pollen count was above 37 grass-pollen grains/m³ (39). In Turku (Finland), a count of less than 30 grass-pollen grains/m³ was significantly correlated with nasal symptoms at the start of the grass-pollen season (40).

The grass family (Gramineae) comprises more than 600 genera and over 10 000 species, of which more than 400 herbaceous, wind-pollinated plants are found in Europe (1). The most abundant airborne grass pollen originates from tall meadow grasses such as timothy (*Phleum pratense*), orchard grass (*Dactylis glomerata*), and meadow foxtail (*Alopecurus pratensis*). Cultivated rye (*Secale cereale*), which has a remarkably high pollen

production, is another potent source of allergens (41). However, with very few exceptions, all grass-pollen types show a very high degree of cross-reactivity (42, 43).

In northern, central, and eastern Europe, the main grass flowering period starts at the beginning of May and finishes at the end of July. In Mediterranean areas, flowering usually starts and ends 1 month earlier (44). Pollination occurs about 2–3 weeks earlier at sea level than in mountainous regions. As mentioned above, pollen seasons tend to vary from year to year because of fluctuations in climatic factors, but maximum atmospheric concentrations of grass pollen usually occur 1–2 months after the start of the main flowering season. On the whole, in Europe, grass flowering notoriously peaks in June.

Table 4 shows the prevalence of skin prick test positivity to grass allergens in various European countries. Notwithstanding a decreased annual total grass-pollen count, probably because changes in agricultural practices and land use have led to a reduction in grasslands, the frequency of allergic sensitization to grass pollen does not seem to be decreasing (57).

Grass allergens induce mostly nasal and conjunctival symptoms. Djukanovic et al. (58) provided evidence that natural exposure to grass pollen may exacerbate asthma, and so induce an inflammatory response involving T cells, mast cells, and eosinophils.

Trees

The most allergenic tree pollen is produced by birch (*Betula*) in north, central, and eastern Europe,

Table 4. Prevalence of skin prick test positivity to Gramineae allergens among pollinosis patients in nine European countries

Country	%	Reference
France	88	45
The Netherlands	90	46
Austria	72	47
Greece	50.2	48
Portugal	80	49
Spain	87	50
Sweden	16.9–44	34, 51, 52
Switzerland		
Zurich	81	
Locarno	71.6	53
Italy		
Campania	38	54
Liguria	29.5	55
Lombardia	80	56

and by olive (*Olea europaea*) and cypress (*Cupressus*) in Mediterranean regions.

Fagales. As in the grass family, there are high levels of allergenic cross-reactivity between the representative plants of the genera of the order Fagales (59). This order comprises three families: Betulaceae, including the genera *Betula* (birch) and *Alnus* (alder); Corylaceae, including the genera *Corylus* (hazel), *Carpinus* (hornbeam), and *Ostrya* (hop hornbeam); and Fagaceae, including the genera *Quercus* (oak), *Fagus* (beech), and *Castanea* (sweet chestnut).

Birch is the major pollen-allergen-producing tree in northern Europe (51). In western Europe, the main flowering period usually starts at the end of March, and in central and eastern Europe, from the beginning to mid-April. Going northward, the flowering seasons starts, depending on the latitude, from late April to late May (northern Europe) (44, 46). Pollen values peak 1–3 weeks after the start of the season. The duration of the main season is remarkably dependent on temperature and thus varies from 2 to as much as 8 weeks. Far shorter or longer periods, with yearly alternating low and high pollen production, have been observed in various European regions (60).

The Corylaceae trees hazel and alder are the first (December–April) to shed pollen in the outdoor air in Europe, followed by birch, hornbeam, and hop hornbeam. As a consequence of this early pollination and of the allergenic cross-reactivity, hazel and alder can act as primers of allergic sensitization to Betulaceae pollen allergens, so that clinical symptoms become more marked during the birch-pollen season.

Similarly, the onset of the oak season in spring, shortly before the beech-pollen season, which is usually quite mild, can prolong the birch season in

western, central, and eastern Europe. Sweet-chestnut pollen appears in June and July in western and central Europe and in the mountainous areas of southern Europe. In central Alpine regions, the highest concentrations of *Alnus viridis* pollen are found at the end of May and in early June (44, 46).

Birch, followed by alder and hazel, has the greatest allergenic potency in this group. In Europe, the percentage of subjects with a positive skin prick test to birch allergens ranges from 5% in The Netherlands to 54% in Zurich (Switzerland) (Table 5). In recent years, the popularity of *Betula* as an ornamental plant, particularly in northern Italy, has caused a significant increase in allergic sensitization to this allergen (56, 65, 66). In a large study of adult patients with asthma or rhinitis cross-sensitization, Eriksson & Holmen (51) found that sensitization to birch was frequently associated with other allergens, that it induced mostly nasal symptoms, and that respiratory symptoms started at 30 years of age. The Eriksson & Holmen study did not confirm the report by Björkstén et al. (67) of a correlation between birth during the months of *Betula* flowering and the subsequent development of respiratory allergy to the same pollen.

Among the genus *Castanea*, *C. saliva*, which is grown both for the food industry and for use in parklands (68), is mainly related to rhinitis, usually in concomitance with other more important seasonal spring pollen allergens such as those of grasses.

Oleaceae. In Spain, southern Italy, and Greece, olive pollen is one of the most common causes of pollinosis (69–75). The main pollen season is from April to June. The frequency of olive-induced pollinosis is increasing as a consequence of improved diagnostic procedures and as a result of changes in farming practices (69). The lowest prevalence among pollinosis patients in Europe of sensitization to *O. europaea*, as estimated by the skin prick

Table 5. Prevalence of skin prick test positivity to *Betula* (birch) pollen allergens among pollinosis patients in countries of Europe

Country	%	Reference
Austria	20	47
Switzerland		
Zurich	54	53
Locarno	46.1	
Finland	10	61
Sweden	24–38	51, 52, 62, 63
The Netherlands	5	64
Italy		
Liguria	4.6–16.8	65
Lombardia	10	56
Trentino	28.8	66

test, is 1.1% in Sweden, and the highest is 53.9% in Switzerland (Table 6).

O. europaea pollinosis is clinically characterized by oculorhinitis and/or bronchial asthma. There is a higher prevalence of rhinoconjunctival symptomatology than bronchial asthma. Moreover, polysensitization to olive pollen is more frequent than monosensitization (69, 77).

In southern Italy, the frequency of positivity to *Olea* pollen allergens among all skin prick test-positive patients is 13.49% in adults and 8.33% in children (69). In pollinosis patients of the Naples area, monosensitization to olive pollen was identified in only 1.33% of children and in 2.28% of adults; in all the remaining patients, sensitization to olive pollen was associated with other allergens, mainly derived from pollen grains (69). Interestingly, children and adults with monosensitization to olive who live in the Naples area are frequently affected by year-long symptoms that usually do not increase during the olive-pollen season (80, 81). A similar finding has recently been described in Spanish patients (82), and could be due to differing allergenic contents of olive cultivars, as demonstrated in Israel (83, 84).

Pollen from other species of the Oleaceae family, e.g., *Fraxinus excelsior* and *Ligustrum vulgare*, rarely induce severe allergic respiratory symptoms (85–89).

Cupressaceae. The increasing epidemiologic impact of pollinosis induced by Cupressaceae plants is probably related to the increasing use of these species for gardening and reforestation (90, 91). The frequency of skin prick test positivity to Cupressaceae pollen antigens among pollinosis patients varies among the three European countries for which data are available (Table 7). It is highest (35%) in the Córdoba region of Spain.

Within the Cupressaceae family, which is found worldwide, the genus of main allergologic interest

Table 7. Prevalence of skin prick test positivity to Cupressaceae pollen allergens among pollinosis patients in countries of Europe

Country	%	Reference
Italy		
Tuscany	15	91
Liguria	5.7	55
Apulia	12	78
Campania	2	54
Spain		
Madrid	16	50
Córdoba	35	92
France		
Provence	29	91
Montpellier	15	45

is *Cupressus*, which includes 12 species. *C. sempervirens* and *C. arizonica* are common in southern Italy and France, *C. alba* is present in most parts of Italy, and *C. lawsoniana* is used in the UK as a fast-growing evergreen (57).

Charpin et al. (93) and Mari et al. (94) demonstrated that exposure to cypress pollen is a strong risk factor for allergic asthma. Moreover, Bousquet et al. (95), in a study conducted in southern France, showed that the incidence of conjunctivitis is very high (73.7–88.5%) and may be severe in patients sensitized to cypress pollen allergens. Because cypress pollen is present in the atmosphere in late winter, symptoms of cypress-pollen allergy could be mistaken for viral infections (94). Recently, Guerin et al. (96) described two cases of allergic rhinitis to trees of the Cupressaceae genus *Thuja*.

During the last 30 years, *C. arizonica* has been widely used for reforestation, for wind and noise barriers, and in gardens and parks. The vast distribution of *C. arizonica*, which pollinates in January and February and partially overlaps with the completely cross-reacting *C. sempervirens* (pollinating from February to the end of March), has led to an earlier onset of the Cupressaceae pollen season (97–100).

The genus *Juniperus* also exerts a sensitizing allergenic effect. In fact, IgE-mediated sensitization to *J. sabinoides* (mountain cedar) has been reported in a population from France (45, 93). Lastly, this tree seems to be responsible for the increasing prevalence and clinical impact of winter pollinosis (101).

Weeds

Urticaceae. *Parietaria* is the main allergenic genus of the Urticaceae (nettle) family. *P. judaica* grows mainly in coastal Mediterranean areas, but has also been found in the UK (102). Sensitization to

Table 6. Prevalence of skin prick test positivity to *Olea Europaea* pollen allergens among pollinosis patients in countries of Europe

Country	%	Reference
Southern France	15.2	45
Greece	37.2	76
Spain	36.3	77
Portugal	17.0	49
Switzerland		
Locarno	53.9	53
Sweden	1.1–2.3	51
Italy		
Liguria	15.4	55
Apulia	30	78
Campania (Naples)	13.4	79

Parietaria pollen varies greatly according to geographic area. Pollinosis caused by *Parietaria* is less frequent before the age of 10 years (72, 103, 104). The highest frequency of pollinosis caused by *Parietaria* occurs in subjects aged 10–30 years and is more frequent in populations of coastal towns than in those living in rural, noncoastal areas. In Europe (105, 106) and the USA (107), there is a greater frequency of reactivity to *Parietaria* pollen in women than in men. The prevalence of sensitization to *Parietaria*, as assessed by the skin prick test, in seven European countries is shown in Table 8.

The extraordinarily long persistence in the atmosphere of *Parietaria* pollen in the Mediterranean area is responsible for a multiseasonal symptomatology (108, 109). In some areas, some patients have year-long symptoms. Even in areas where the pollination period is shorter, late asthmatic reactions may be detected in patients in both summer and autumn (110, 111).

Bronchial asthma or its equivalent, such as cough (severe in some cases) associated with rhinoconjunctivitis, is present in 52% of the monosensitized *Parietaria* patients in central and southern Italy, reaching a peak of 60% in Naples and Rome (110). Although the correlation was not significant, a higher number of *Parietaria*-monosensitized subjects living in the Naples area were born during the *Parietaria* pollen season and underwent early exposure to the allergens of this pollen (104).

The frequency of positive skin prick tests to various types of pollen grains (particularly those of *Parietaria* spp.) implicated in pollinosis symptoms in atopic subjects has increased in the Naples area during the last 15 years (104). A study conducted in Genoa showed a reduction in the prevalence of skin prick test positivity to *Parietaria* allergens in Italian conscripts and an increase in the number of cases of allergic rhinitis and asthma (112). Recently, severe oral allergy syndrome after the ingestion of pistachio nuts was described in two patients with monosensitization to *Parietaria*; a slight degree of cross-reactivity between *Parietaria* allergens and the pistachio nut was detected in both cases (113).

The treatment of *Parietaria* hay fever is often a frustrating experience for both patients and clinicians because of the prolonged persistence of this pollen in the atmosphere.

Compositae *Artemisia* and *Ambrosia*. The most common species of *Artemisia* are *A. vulgaris* (mugwort), which grows throughout Europe (114), and *A. Annua* and *A. verlotorum*, which grow mainly in southern Europe. Mugwort is present in both urban and suburban areas. It flowers from late July

Table 8. Prevalence of skin prick test positivity to *Parietaria* pollen allergens among pollinosis patients in countries of Europe

Country	%	Reference
France	25	46
Spain	10–60	50
Greece	22	48
Switzerland		
Locarno	17.9	53
Southern Croatia	65	105
Sweden	0.2–3.4	52
Italy		
Northern	9–44	
Central	20–33	108
Southern	15–70	

to the end of August in northwest Europe, and about 3–4 weeks later in Mediterranean areas (44, 46). The later flowering of mugwort in southern Europe contrasts with the pollen season of other allergenic plants (e.g., grass) that flower earlier in Mediterranean areas than in central and northern Europe. *A. annua* and *A. verlotorum* usually flower from September to the end of October. The frequency of sensitization to mugwort among pollinosis patients in Europe is 3–10% (115). A common pollen-associated food allergy is known as the “mugwort–celery syndrome” (116).

Ambrosia (ragweed). Unlike in the USA, where *Ambrosia* pollen (in particular, *A. artemisiifolia* and *A. trifida*) is the etiologic agent in about half of all cases of pollinosis, in most parts of Europe it is not a major cause of pollinosis. However, ragweed sensitization is increasing in Europe (117), where the main species are *A. elatior* and *A. artemisiifolia*; some rare colonies of native species (*A. maritima* and *A. coronopifolia*) are also found. Ragweed was introduced into Europe at the beginning of this century. The plant was first limited to Hungary, but during the Second World War, it was introduced into France (118). Thereafter, it gradually expanded and is now abundant in the Rhone valley (France) (119), northern Italy (120, 121), eastern Austria (122), Hungary (123), and Bulgaria (124). Tall ragweed (*A. trifida*) is rare in Europe. The ragweed-flowering period, in Europe, as in North America, is from August to September (44, 46). Ragweed-pollen allergy is very often accompanied by severe asthma attacks.

Other allergenic pollen in Europe

The most relevant of the other allergy-inducing pollen in Europe (Table 9) is that of *Platanus*, which accounts for a prevalence of allergic sensitization of 56% in Madrid (130).

Table 9. Prevalence of skin prick test positivity and/or number of case reports of other less important allergenic pollens in Europe

Country	Pollen	%/no. of cases	Reference
Switzerland		22–28%	
Sweden		3.3–7.3%	
The Netherlands	<i>Artemisia vulgaris</i>	4%	
France		9%	
Italy			
Naples		17%	
Poland		42%	
Italy	Birch bonsai	1 Case	125
France	<i>Ficus Benjamina</i> /latex	2 Cases	126
Spain	<i>Mercurialis annua</i>	8.5%	127
Italy		0.9%	128
Italy	Mimosa (<i>Acacia floribunda</i>)	1.2%	129
Spain	<i>Platanus</i>	56%	130
Spain	Australian pine (<i>Casuarina</i>)	2.8%	131

Small particles carrying pollen allergen

Secondary allergen carriers

Pollen grains are the primary carriers of pollen allergens, a fact which explains why the symptoms typical of hay fever are located in the eyes, nose, and nasopharynx. Basically, intact pollen grains, which have (aerodynamic) sizes of 15–40 nm, probably cannot enter the lower, thoracic regions of the respiratory tract; instead, they affect the nasal or nasopharyngeal mucous membrane (132, 133). However, symptoms of the bronchial regions, such as cough or wheezing, are not infrequently seen in pollen-allergic patients. Among the various hypotheses put forward to account for the thoracic afflictions in hay fever is the existence of secondary pollen-allergen-carrying particles of much smaller sizes, capable of penetrating the lower respiratory tract. In fact, as early as 1873, Blackley (134) speculated that “free granular matter” floating in the air causes “hay asthma”.

Although it is plausible that, in spite of aerodynamic principles, a small number of pollen grains may penetrate into the lower respiratory tract (136–138), particularly by mouth breathing (138), there is now strong evidence of the atmospheric presence of pollen-allergen-carrying particles of sizes much smaller than intact pollen grains (139–141).

In the early 1970s, Busse et al. (142) were the first to demonstrate the presence of specific ragweed allergens carried by small particles. By different techniques, this observation was confirmed and extended, first for ragweed-pollen allergen (143–145). Subsequently, the same phenomenon was observed for grass-pollen allergen (146–148), red oak-pollen allergen (149), Japanese cedar-pollen allergen (150), and birch-pollen allergen (151). With cascade impactors or other instruments that

fractionate the sampled airborne matter into several size classes, it was established that these small particles range from some micrometers, i.e., 2–10 μm (paucimicronic), to less than 1 μm (submicronic) sizes (144, 145, 148, 150, 151).

Three aspects of the atmospheric presence of pollen-allergenic, paucimicronic, or submicronic particles are of particular interest; i.e., the consequences for the localization of pollinosis-related symptoms, the relationship between the atmospheric pollen concentration and pollen-allergen quantities, and the nature and origin of these small pollen-allergen carriers. Although research and discussion on these aspects have not been concluded, some observations and data are worth considering here.

Pollinosis symptoms in the lower respiratory tract

Several hypotheses have been proposed to account for pollinosis-related symptoms in the lower respiratory tract, at the level of the bronchi and bronchioli; e.g., absorption of allergen in the nose and subsequent transportation to the bronchi, or reflex mechanisms inducing bronchial involvement after a nasal reaction. Discussion of these hypotheses is beyond the scope of this paper, but it is clear from an aerodynamic point of view that the inhalation and penetration of small particles carrying pollen allergen into the lower respiratory region is a rather direct and not unlikely cause of pollinosis-related symptoms in that region (140, 141).

Atmospheric pollen grains and pollen allergen

The traditional way to measure the presence and quantity of pollen allergen in the atmosphere is to assess the airborne pollen concentration. With the demonstration of substantial quantities of airborne pollen allergen outside the pollen grain, the question arises as to whether or not the traditional pollen count is a correct measurement of atmospheric pollen allergen. This point is still being debated because the conclusions drawn by different researchers are not in agreement. Studies on red oak-pollen allergen (149) and birch-pollen allergen (151, 152) revealed a discrepancy between the numbers of pollen grains and quantities of pollen allergen in the atmosphere. In fact, substantial airborne pollen-allergenic activity has been found, not only after, but even before, the period of the presence of pollen grains. On the contrary, there is a good correlation between the presence of grass-pollen grains and grass-pollen allergens, with very little airborne pollen allergen outside the grass-pollen season. The discrepancies detected during the pollen season have been attributed to

the occurrence of rainstorms (146, 147, 155, 156). Probably, the final conclusion will depend on the appreciation of the incidental presence of atmospheric allergen outside the pollen season, and its significance for pollinosis symptoms (154). This topic should be investigated, and perhaps studies on the relationship with clinical symptoms of pollinosis will contribute to the discussion.

Nature and origin of small allergenic particles

The nature and origin of paucimicronic and submicronic allergen-carrying particles also have yet to be conclusively defined. Four suggestions or hypotheses have been proposed (140, 141, 154): pollen-grain fragments, starch granules, nonpollen plant parts, and nonplant environmental particles.

Pollen fragments. Because pollen grains generally resist fragmentation, it is unlikely that pollen-grain fragments make a major contribution to the pollen-allergen-carrying particulate matter in the atmosphere, although abrasion (139), particularly from echinate pollen grains, cannot be ruled out completely.

Starch granules. It has been shown that, under wet conditions, pollen grains may rupture and release part of their content into the atmosphere. An important element of pollen-grain content is starch granules, which range in size from 0.5 to 2–5 µm. Starch granules appear to be carriers of specific pollen allergen (155, 156). However, the process of the release of allergenic starch granules from pollen grains cannot account for the presence, also under dry conditions, of the larger fraction of the paucimicronic allergenic particles, which range between 5 and 10 µm in size.

Nonpollen plant parts. Several authors have suggested that pollen-allergenic particles originating from plant parts other than pollen can occur in the atmosphere. Parts from inflorescences and/or leaves (145, 149, 157), as well as the so-called orbicules, or Ubisch bodies (less than 0.2 µm in size), are capable of carrying specific pollen antigens responsible for the presence of allergenic activity in the atmosphere.

Nonplant particulate matter. Allergen from the surface of the pollen grain could be transferred to other small particles present in the direct environment of the pollen grain; e.g., through physical contact or by leaching (155, 160–162). This process of transfer could take place both in the air and after the pollen has settled on the ground. Particularly in regions with an extra atmospheric load

of particulate matter as a result of air pollution (160–162), this process could be of great clinical importance in view of the possible synergistic effect of exposure to allergen and air pollution (140, 160, 163). The process of transfer of pollen allergen from pollen grains to nonspecific environmental particulate matter might explain the wide range of sizes (from submicronic to paucimicronic) of these secondary pollen-allergen carriers (154).

Concluding remarks

Despite the vast amount of expertise and funding devoted to the study of pollen respiratory allergy in Europe, the data available are still fragmentary and difficult to compare from one country or region to another. While respiratory allergy has been “mapped” as to prevalence, triggers, seasonality, symptoms, and treatment in some European countries, very little is known of others. Therefore, it is still difficult to draw a clear picture of Europe as a whole. Coordinated, well-structured studies are required to fill the gaps in our knowledge. In particular, we need to know more about the interaction between air pollution and aeroallergens in terms of allergenicity. Despite much considered speculation, no definitive conclusions have been drawn. In this context, it has been suggested that air pollutants can interact with pollen grains to make them more allergenic (164, 165). Moreover, atmospheric pollutants, such as O₃, are known to reduce plant fertility (166).

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