

Winter pollinosis in Paris

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Pollen is rarely investigated as a cause of winter respiratory symptoms. Infectious coryza and asthma are particularly common during winter, and it has been shown that environmental antigens can cause at least some cases in Paris. Recent experimental data from Calhoun et al. (1991) indicate that pollen may act synergistically with viral respiratory infections, which are particularly prevalent in winter. In the present study, we investigated, in 130 consecutive patients presenting with winter aggravation of asthma or rhinitis, winter pollinosis by skin test, radioallergosorbent test (RAST), and specific endonasal challenge test. Totals of 35, 24, and 21 patients reacted positively in skin, RAST (> 0.70 PRU/ml), and endonasal tests, respectively. Clinical features during the season established the diagnosis of winter pollinosis in 20 cases; it was due to alder pollen in 10 patients and hazel pollen in 12. The positive predictive value of the skin test was only 0.57, as compared with 0.86 for the specific endonasal test, which had a negative predictive value of 1. Our results indicate that hazel and alder pollens should be prick-tested for more often as causes of winter respiratory symptoms in Paris, even if similar manifestations were absent during previous winters, were previously present during spring or summer, or were both absent in previous winters and present in spring or summer.

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In Paris, pollinosis is usually caused by the Poaceae (grass) family. The main manifestations are rhinitis and asthma attacks, usually associated with bilateral conjunctivitis, between 15 May and 15 July (6). Birch (7), hornbeam, and ash pollinosis occurs earlier, at the beginning of spring. These three tree pollens cause respiratory symptoms similar to those caused by Poaceae, but the pollinosis of trees is usually distinguished by the time of onset. Most patients develop manifestations each year, the intensity of which may vary from one season to the next.

Most winter respiratory attacks in Paris are due to infectious agents, but an allergic factor should be suspected in patients with rhinitis or asthma attacks when other known causes have been ruled out. Although the principal allergens are perennial, e.g., those of the house-dust mite and animal hair, pollen may be implicated when a marked aggravation of asthma or rhinitis occurs during relatively mild or good weather without rain for several days, or in the presence of unusual signs at this season, e.g., bilateral conjunctivitis, associated with respiratory symptoms.

We conducted a systematic search for winter pollinosis, even in patients who had not presented typical or similar symptoms in previous winters. Our

results suggest that winter pollinosis is common in Paris.

Material and methods

Patients

Thirty-five patients (17 males, 18 females; mean age, 40 years, range, 11–59 years) were selected from among 130 patients presenting with recurrent respiratory conditions (rhinitis, asthma, or both) during the winter, on the basis of skin reactivity to the pollen of one of the trees flowering in winter in Paris (alder, cypress, and hazel). All 35 patients had presented with rhinitis, sometimes with bilateral conjunctivitis. Twenty-three of these patients also had asthma, which in three cases had required emergency admission to hospital during a previous winter. The median overall duration of the respiratory manifestations was 13.5 years (2–39). The diagnosis of asthma was established after detection of bronchial hyperreactivity by pharmacodynamic test. Moreover, 19 patients showed signs of hypersensitivity to various fruits and vegetables, generally presenting as an oral syndrome, and had skin reactivity to these food items. Moreover, 30 patients were symptomatic at exposure during spring or summer

to various other pollens; in particular, to birch or hornbeam, both members of the Betulaceae family, in 24 cases. Any tested patient was not receiving drugs or specific immunotherapy.

Methods

The severity, type, and period of onset of the respiratory manifestations were determined by interview.

Bronchial hyperreactivity. Bronchial hyperreactivity was established by 15% improvement in FEV₁ after administration of a β_2 -agonist (Salbutamol) when the basal level was under 80% of the predicted value, or a 20% decrease in FEV₁ after inhalation of histamine (20–1600 g) when the basal value was above 80% of the theoretic one.

Skin test. All 130 patients underwent prick tests (9% codeine and diluent were used as positive and negative controls) with alder, cypress, hazel, birch, ash, and grass pollen extracts and with common aeroallergens including those of mite, cat, and cockroach (unfortunately, only mite and grass, birch, alder, and hazel pollen extracts are standardized) (Laboratoires Allerbio, Varennes, France; Extraits Stallergènes-Pasteur, Fresnes, France), but only patients with positive prick test for alder, cypress, or hazel pollen extracts and 10 patients with negative prick test with these pollens were completely studied.

Total serum IgE assay. The total concentration of serum IgE was determined by the commercially available immunoradiometric assay (Pharmacia IgE RIA, Uppsala, Sweden), with normal upper limit of 200 kIU/l.

Specific serum IgE assay. Patients with positive skin test results (wheal more than 5 mm larger than the negative control wheal) and 10 patients with negative prick test underwent specific IgE assays (positive if > 0.70 PRU/ml).

Nasal challenge test. A nasal challenge test with the suspect allergen was done by active anterior rhinomanometry (11, 22) (Rhinomanometer Difra Welkenraedt, AudiFrance, Paris, France). Briefly, total nasal resistance was measured 20 min after each allergen spray after first checking the patency of the nasal passages and reactivity to the normal saline (excipient) used to dilute the lyophilized allergenic extract of either alder, cypress, or hazel pollen (Laboratoire Allerbio, Varennes, France; Laboratoire des Stallergènes, Fresnes, France). The initial dilution was 1/1280e (w/v) or 1.5 BU/ml. The reaction was considered to be positive when total nasal resistance increased by 200% relative to the value

obtained with the excipient. When the reaction was negative, the dose was doubled and the same procedure applied, in order to identify an eventual dose-response relationship. Moreover, a clinical score was also calculated (graded 1–10, and independent of nasal obstruction) at each dilution of pollen extract.

Pollen counts. Pollen was counted after collection by Hirst trap during winter 1993 by M. R. Ickovic (Aerobiologie, Institut Pasteur, Paris).

Pollinosis diagnosis. The diagnosis was based on the results of these various tests and examination in succeeding winters during clinical manifestations. The diagnostic value of the prick test, RAST, and nasal challenge test was determined for the population from Paris with winter respiratory manifestations.

Results

The time of onset of the respiratory symptoms varied greatly during the first 3 months of the year (January, $n = 17$; February, $n = 19$; and 1–20 March, $n = 22$). Seven patients had respiratory symptoms for 3 months, 10 for 2 months, and 18 for 1 month. Thirty-four patients had rhinitis, 26 had bilateral conjunctivitis, and 23 had asthma.

Bronchial hyperreactivity. Bronchial hyperreactivity was demonstrated in 23 patients by salbutamol (eight patients) and histamine (dose 40–940 μ g).

Skin tests. Skin tests were positive for alder pollen in 30 cases, always negative for cypress pollen, and positive for hazel pollen in 21 cases.

Total serum IgE assay. Values were elevated in 23 cases (Tables 1 and 2).

Specific serum IgE assay. In patients with positive skin tests, values were elevated in 19 cases (10 times greater than 17.5 PRU/ml) for alder pollen and in 20 cases (eight times greater than 17.5 PRU/ml) for hazel pollen. RAST was negative for cypress pollen in the five patients with positive prick test for alder or hazel pollen. Moreover, RAST was negative for the three pollens in 10 patients with negative skin tests.

Nasal challenge test ($n = 41$). The rhinomanometry assay was positive for alder pollen in 13 of the 20 patients with positive skin test (titer, 1/1280 to 1/160) with a clinical score of between 3 and 8 (median, 6). Nasal challenge tests with cypress pollen were not done. The rhinomanometry assay was positive for hazel pollen in 14 of the 18 patients with positive

Table 1. Characteristics of 20 patients with winter pollinosis

Patient no.	Sex	Age (years)	Clinical manifestation	Duration (years)	IgE t kU/l	Skin test		RAST		Nasal P test	
						A	H	A	H	A	H
1	M	59	A + E + KJ	39	810	6/20	7/25	> 17.5	> 17.5	nd	320
2	M	57	A + R + KJ	38	322	7/20	6/25	> 17.5	17	nd	nd
3	M	54	A + R + KJ	16	167	3/5	5/15	1.59	15	nd	160
4	M	24	R + A	5	800	5/15	7/20	nd	16	nd	80
5	M	47	R + KJ	23	220	10/35	8/30	nd	2.5	nd	160
6	M	33	R + KJ	8	313	6/20	20/50	2.15	8.5	640	320
7	M	40	A + R + KJ	7	275	30/35	14/25	> 17.5	> 17.5	320	640
8	M	42	A + R + KJ	14	220	7/30	6/25	> 17.5	> 17.5	nd	160
9	F	47	A + R + KJ	16	786	8/20	12/25	92.9	> 17.5	1280	640
10	M	46	A + R + KJ	33	87	5/15	nd	0	nd	640	nd
11	F	18	A + R + KJ	2	200	8/30	nd	11.1	nd	640	nd
12	F	55	A + R + KJ	22	422	10/30	7/25	> 17.5	> 17.5	320	640
13	M	51	R + KJ	19	228	5/25	7/45	nd	1.8	nd	160
14	F	50	A + R + KJ	18	255	8/30	10/35	> 17.5	> 17.5	320	640
15	F	17	A + R + KJ	7	357	6/20	3/5	1.85	nd	160	nd
16	M	11	R + KJ	3	856	9/25	10/30	66.5	18.2	nd	160
17	F	37	A + R + KJ	14	182	10/40	2/10	6.3	7.1	320	nd
18	M	12	A + R + KJ	2	2450	7/30	8/25	> 100	> 17.5	640	nd
19	F	47	R + KJ	16	301	5/7	6/8	0	0	—	640
20	F	37	A + R + KJ	20	223	5/7	3/8	3.28	1.36	nd	nd

A = asthma, R = rhinitis, KJ = conjunctivitis, A = alder, H = hazel, nd = not done, nasal P test = titer of allergen causing positive nasal provocation reaction.

skin test (titer, 1/1280 to 1/40), with a clinical score of between 1 and 8 (median, 4). Six patients had a positive nasal challenge test for both alder and hazel pollen (Table 1). Moreover, the nasal challenge test was negative with alder or hazel pollen in 10 patients with negative skin tests.

Pollen counts. Figs. 1 and 2 show the number of pollen grains per cubic meter from 6 January to 21 March 1993. The pollen rain was above 20 grains/m³ during 19 days for alder, 9 days for hazel, and 30 days for cypress. During the winter season, the

total counts reached 1355 grains/m³ for alder, 845 for hazel, 3266 for cypress, and 6831 for the total number of pollen grains.

Clinical diagnosis. Twenty of the 130 patients were diagnosed as having winter pollinosis. The pollinosis was caused by both alder and hazel pollen in six patients, alder alone in seven patients, and hazel alone in seven patients. No cases of cypress pollinosis were identified.

The prick test had a sensitivity of 1, a specificity of 0.86, a positive predictive value (PPV) of 0.57,

Table 2. Characteristics of 15 patients with positive skin test in whom diagnosis of winter pollinosis was not retained (see Table 1 notes for meaning of abbreviations)

Patient no.	Sex	Age (years)	Clinical manifestation	Duration (years)	IgE t kU/l	Skin test		RAST		Nasal P test	
						A	H	A	H	A	H
21	F	20	R	4	180	5/10	8/15	nd	5.86	nd	nd
22	F	55	R + KJ	20	272	nd	8/27	nd	13	nd	nd
23	M	51	A + R + KJ	11	79	18/30	8/25	13.8	15.6	160	nd
24	F	42	A + R	15	324	6/25	3/5	> 17.5	nd	320	nd
25	F	25	R + KJ	13	133	5/25	3/20	12.2	0.91	1280	640
26	F	31	A + R	2	198	5/8	nd	6.2	nd	—	nd
27	M	39	A + R	2	83	5/25	nd	0	nd	—	nd
28	M	23	A + R + KJ	13	328	7/15	3/10	nd	nd	—	nd
29	M	56	A	2	455	0	5/15	0	0	nd	—
30	M	28	R	6	165	5/7	0	0	0	—	nd
31	F	39	A + R + KJ	8	nd	6/6	0	nd	nd	—	nd
32	F	57	R + KJ	15	46	5/7	nd	nd	nd	—	nd
33	F	39	R	3	6	nd	5/7	nd	nd	nd	—
34	F	58	A + R	37	300	nd	6/8	nd	nd	nd	—
35	F	47	A + R	2	595	5/8	3/5	nd	0	nd	—

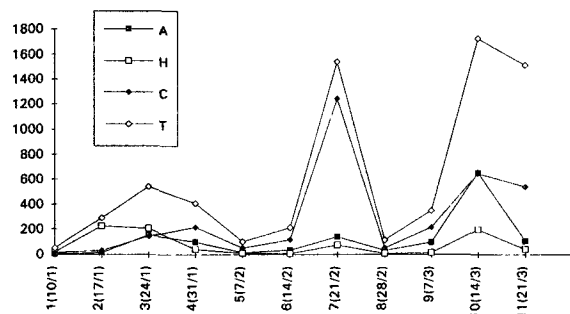


Fig. 1. Daily alder (A), hazel (H), cypress (C), and total (T) pollen counts expressed in number of grains per cubic meter of aspired air during each week from 6 January to 21 March 1993 (data kindly provided by Aerobiologie, Institut Pasteur, Paris, France).

and a negative predictive value (NPV) of 1. RAST had a sensitivity of 0.9, a specificity of 0.76, a PPV of 0.75, and an NPV of 0.90. The nasal challenge test had a sensitivity of 1, a specificity of 0.87, a PPV of 0.86, and an NPV of 1 (Table 3).

Discussion

This study of 130 patients with respiratory manifestations indicates that winter pollinosis does occur in Paris. Twenty cases of winter pollinosis were diagnosed by prick tests, RAST, nasal challenge tests, and clinical findings during winter. The most common manifestation was rhinitis, and the associated

Table 3. Comparison between skin tests, RAST, and nasal provocation test in diagnosis of winter pollinosis in Paris

130 Patients	Winter pollinosis		
	Dg ⁺	Dg ⁻	
Prick test ⁺	20	15	Se = 20/20 = 1
Prick test ⁻	0	95	Sp = 95/110 = 0.86
			PPV = 20/35 = 0.57
			NPV = 95/95 = 1
RAST ⁺	18	6	Se = 18/20 = 0.9
RAST ⁻	2	19	Sp = 19/25 = 0.76
			PPV = 18/24 = 0.75
			NPV = 19/21 = 0.90
Nasal P test ⁺	18	3	Se = 18/18 = 1
Nasal P test ⁻	0	20	Sp = 20/23 = 0.87
			PPV = 18/21 = 0.86
			NPV = 20/20 = 1

Se = sensitivity, Sp = specificity, PPV = positive predictive value, NPV = negative predictive value, Dg = diagnosis.

presence of bilateral conjunctivitis was highly suggestive of pollinosis. Asthma was also a very common manifestation in these patients. The fact that such respiratory manifestations can appear during other seasons in the same patient makes it difficult to diagnose winter pollinosis without specific tests. Moreover, asthma attacks may be severe, as witnessed by the fact that three of the patients in this series had been urgently admitted to hospital during previous winters.

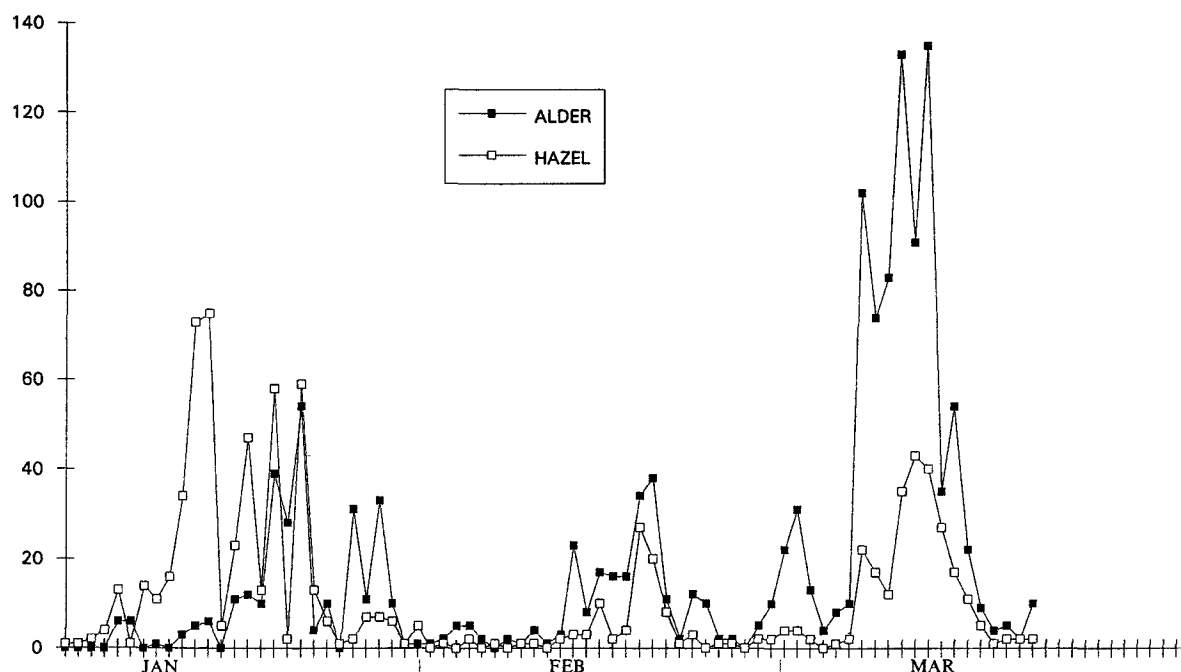


Fig. 2. Comparison of total daily alder (A) and hazel (H) pollen counts expressed in number of grains per cubic meter of aspired air during each day from 6 January to 21 March 1993 (data kindly provided by Aerobiologie, Institut Pasteur, Paris, France).

The pollens responsible for these respiratory symptoms are produced by trees belonging to the Betulaceae family (hazel and alder). No cases of pollinosis caused by cypress were identified in this series, unlike the situation in Marseille (5).

Winter pollinosis should therefore be borne in mind, particularly in patients with hypersensitivity to fruit or a history of pollinosis caused by pollens of other Betulaceae trees, which cause respiratory symptoms in April or May in Paris (1, 7, 17). Of the diagnostic methods, the prick test is the simplest to do, but it has a relatively low positive predictive value. The sensitization to winter pollens was clear in our series, particularly because almost half the patients concerned had RAST values greater than 17.5 PRU/ml. In fact, the nasal challenge test appears to be the most reliable method for identifying respiratory hypersensitivity. The specific endonasal test had the best predictive value, reproducing the effect of the pollen on the respiratory mucosa. However, three patients with positive nasal test were not considered to have winter pollinosis, given the absence of clearly specific respiratory signs and absence of respiratory signs during systematic examination(s) during the winter period; it is likely that these three patients had not been sufficiently exposed and may develop pollinosis in the future, because the quantity of pollen used in the nasal challenge was small.

Winter pollinosis was thought to be confined to southern France, where mimosa (1) and trees of the Cupressaceae family (5) have been shown to be responsible, particularly in Nice and Marseille. D'Amato & Lobefalo (9) have reported similar observations in Naples and elsewhere in the Mediterranean basin. Moreover, Garcia-Ortega et al. have described pollinosis caused by *Mercurialis annua* in Spain (14), a newly discovered allergen of the winter period. Winter pollinosis has also been reported in Texas and Florida, caused by mountain cedar (*Juniperus sabinooides*), a member of the Cupressaceae family (3, 15, 20). Winter pollinosis can, however, be encountered in northern France, as underlined by Ott et al. (19) and Bessot et al. (2) in Strasbourg. These authors showed that early respiratory manifestations of pollinosis were mainly due to Betulaceae, particularly alder and hazel. The incidence of bronchial symptoms for this pollinosis in Strasbourg was 30%, a figure lower than that observed in Paris, while the severity varied from season to season according to climatic conditions. Ott et al. also raised the possibility of cross reactions with other members of the Betulaceae family (birch and hornbeam) and with the Fagaceae family, which belongs to the same botanic order, Fagales (21). The results we obtained were similar, although the time of onset was earlier, possibly because of the milder winter in Paris.

An association between Betulaceae pollinosis and

allergy to fruit and vegetable allergens has been described by Juhlin & Dannfelt (16) and studied by Eriksson et al. (12). We observed this type of hypersensitivity in 11 of the patients with winter pollinosis, generally presenting as an oral syndrome similar to that initially described by Lessof & Wraith (18). The fruits or nuts most often implicated are hazelnut, apple, peach, kiwi, and strawberry. There is therefore an analogy with birch pollinosis (16), which is common both in Scandinavia and in the Paris area (7). Food-related reactions should, in our opinion, be sought routinely in patients with asthma attacks or spasmodic coryza during winter; such reactions are suggestive of hypersensitivity to alder or hazel pollen.

Winter pollinosis differs from pollinosis occurring in other seasons, by a marked variability in its intensity and time of onset from year to year (according to climatic conditions). Alder, hazel, and birch start to produce catkins in autumn, and this explains the massive shedding of pollen when the weather becomes milder, even so early in the season.

The possible synergistic effect of pollen and viral respiratory infections is particularly interesting. Calhoun et al. reported a lowering of the sensitivity threshold and an increase in the specific bronchial reaction to ragweed pollen after experimental infection with rhinovirus 16 (4). The bronchial hypersensitivity reaction to winter pollens could, in certain cases, be favored by recent viral infections. This suggests that skin hypersensitivity to alder and hazel pollens should be sought more frequently in patients with respiratory manifestations during winter, even if the clinical presentation is not typical of pollinosis. In addition, this early pollinosis induces inflammation of the respiratory mucosa. After initial contact during winter with hazel and alder pollen, patients are very rapidly exposed to birch and hornbeam pollen at the end of March and during April. Most such patients have been sensitized to these pollens, probably because of the presence of common antigenic epitopes, because these trees belong to the same family (Betulaceae) (13, 24, 25). Exposure of the inflammatory, hyperreactive mucosa may, in part, explain the intensity of the further pollinosis (8), even in the absence of viral infection. Of course, climatic conditions in winter can reduce pollen dissemination, but they can also favor release from pollen grains of starch granules, which contain most of the antigenic determinants and can penetrate deep into the human respiratory tract (10, 23).

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