

Parietaria Pollinosis: Clinical and Epidemiological Aspects

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ABSTRACT

The aim of our study was the evaluation of clinical and epidemiological aspects of P pollen allergy, which is a very frequent cause of respiratory allergy in the Mediterranean area, in a homogeneous group of 442 monosensitive subjects (235 females and 207 males, mean age about 30 years) living in Naples. All patients underwent the following diagnostic procedures: anamnestic evaluation with an internal questionnaire, physical examination, SPT with commercially available allergenic extracts (DHS-Bayropharm Milan Italy); sNPT, NsBPT, and serum specific IgE determinations were also carried out in three groups of 50 different subjects. The results of our study show a highly relevant intensity of SPT positivity (++++ and +++ in about 95% of patients). The age of onset of clinical symptoms ranged between 20–25 years, and the majority of P monosensitized patients were born in the spring months, with an early exposure to P allergens. Rhinoconjunctivitis and bronchial asthma, alone or in association, represent the most common clinical manifestation of this allergy. The season in which patients experience clinical symptoms is prevalently spring (75, 12%). However, many people show a multiseasonal pattern (18, 55%). The frequency of SPT positivity to P allergens is increasing in the last 15 years, probably due to increased urban air pollution. In conclusion, the results of this study demonstrate the high frequency and severity of this pollinosis and seem to confirm some epidemiological aspects connected with other allergenic pollens (birth during the seasonal period of pollination and association with a high urban air pollution). (Allergy and Asthma Proc 17:23–29, 1996)

Parietaria (Pellitory) (P) pollen allergens are a prevalent cause of the so-called “hay fever” and/or “hay asthma”

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in the Mediterranean area.^{1–6} The genus *P*, together with the nonallergenic genus *Urtica* (nettle), belongs to the Urticaceae family.

P. officinalis and *P. judaica* are the most common species within the genus *P*. They grow respectively in hilly/mountainous and coastal Mediterranean areas of various European countries such as France,^{7–9} Spain,^{10,11} Albania and Greece,¹² former Yugoslavia,¹³ and some southwestern regions of the former USSR. *P* species have been found also in UK¹⁴ and in extra European countries (USA and Australia).^{15,16}

Although millions of people suffer from pollinosis due to *P* allergens, only relatively few reports on this allergy have been published, compared to articles on other inhalant allergens such as grasses, ragweed, birch, and mites.

Only in recent years have some studies demonstrated the characteristics of *P* major allergens (*Par J I*, *Par o I*)^{17–21} and cell response to *in vitro* stimulation with these allergens.²² The main *P* cycle of flowering in southern Italy, particularly in the Naples area, begins in March and continues until July. Peak pollination occurs in May and June. In September and October, a lower peak is detectable. In other words, in southern Italy *Parietaria*'s pollen season can persist from February to December, resulting in almost perennial symptoms.²³ Sensitization to other inhalant allergens associated with effects of some agents as cigarette smoke, viral infection, work-related irritants, etc., should constitute a masking factor of clinical symptoms of *P* pollinosis. For this reason it is necessary to evaluate the real aetiological significance of *P* sensitization including the possibility of late asthmatic reaction (LAR)²⁴ to obtain better management of this allergy (specific immunotherapy, preventive, and symptomatic medications, etc). The aim of our study was the evaluation of environmental and clinical aspects of allergic sensitization to *P* pollen by using an adequate and homogeneous group of monosensitized patients living in a well defined geographical area (Naples).

MATERIALS AND METHODS

Patients

From the population of 3857 subjects of both sexes ranging in age from 3 to 70 years, examined in our Allergological Center consecutively from January 1, 1990 to December 31, 1992 for a respiratory (nasal and/or bronchial) symptomatology of a suspected IgE mediated etiology, we selected a group of 442 subjects with immediate skin positive reaction only to *P* pollen extract (Table I). We excluded polysensitized subjects and those not living in urban and strictly suburban areas, in order to obtain a selected group of patients with homogeneous environmental conditions. Moreover, this district of Naples is included in the area of sampling of our volumetric pollen trap.

At the time of the study, patients were not under treatment with specific hyposensitization; antihistamines, corticosteroids, and β_2 agonists were not used in the week preceding the tests (6 weeks when Astemizole was used).

All patients were submitted to an accurate anamnestic procedure (by using an internal questionnaire) in order to determine clinical and environmental aspects of *P* sensitization and the possibility that specific factors could enhance nasal and/or bronchial hyperreactivity. Before challenge tests, informed consent was obtained from patients or their parents.

Allergenic Extracts For Skin Prick Test (SPT)

SPT was carried out by using a commercially available *S* allergenic extract standardized as AUR/mL (DHS-Bayrofarm, Milan, Italy). We used a kit of aeroallergens (Dust mites, cat and dog hair, *Alternaria tenuis*, *Cladosporium*

herbarum, *Parietaria*, Grasses, *Artemisia vulgaris*, *Olea europaea*, *Cupressus sempervirens*, *Betula pendula*, *Corylus avellana*) considered as more frequently causative agents of respiratory allergic symptomatology in the Naples area.

Skin Prick Test (SPT)

Patients were tested by the same operators by prick puncture by using a standardized pricker (DHS-Bayrofarm, Milan, Italy). In all patients we used the volar surfaces of both forearms, and allergenic extracts were placed in the same site in order to obtain comparable SPT results. Only reactions ≥ 3 mm of diameter were considered as positive.

Reactions were read at 15 minutes by using a millimeter ruler. The wheal diameters were compared to the size of a positive histamine control (10 mg/mL) and to a negative control (extraction solution without allergen).

According to the Aas and Belin method,²⁵ a wheal of the same size as that induced by the histamine control is indicated as +++ and a reaction similar to that induced by the negative control is indicated as -.

The grading + and ++ are used for reaction sizes between the negative and the positive controls.

For a reaction larger than +++, a plus is added for each doubling of the average diameter.

Allergenic Extract for Specific Nasal Provocation Test (sNPT)

P Alphabase, a sterilized form of lyophilized alpha fraction extract, was reconstituted in normal saline to give a stock solution of 1000 AUR/mL. Fivefold serial dilution was prepared (1000, 200, 40, 8, and 1.6 AUR/mL).

Specific Nasal Provocation Test (sNPT)

A group of 50 subjects with only nasal symptoms and a SPT positivity of almost +++ was evaluated by using sNPT. Nasal challenge was carried out outside of the *Pj* pollination season. One drop (0.5 mL) of saline was placed in each nostril as a control. If no symptoms occurred in 15 minutes, 0.05 mL of the weakest concentration of the test material was placed in each nostril. If no response occurred in 15 minutes, the next most concentrated solution was administered.

TABLE I

Demographic data		
	Pj Monosensitized	Skin Negative Controls
No. of patients	442	836
Age range (years)	5-65	3-70
(Mean)	(30.1)	(40.6)
Sex (M/F)	207/235	406/430

TABLE II

Results of Ns BPT in a Group of 50 Subjects with a Prevalent Bronchial Symptomatology and SPT Positivity of Almost+++					
	Hyperreactivity			Normal	Total
PD20FEV1 (mcg) values	≤ 200 very high	$\geq 200 - \leq 400$ moderate	$\geq 400 - \leq 800$ low	≥ 800 normal	
Patients					
Number	21	20	9	—	50
Percent	42	40	18	—	100

A response was defined as positive if there were at least three of the following: sneezing, itching, increased nasal secretions, increased nasal congestion, increased edema, or increased nasal pallor. To avoid the deposition of allergen into the lower airways, the patients were asked to avoid deep inhalation.²⁶

Serological IgE Specific Assay

A group of 50 rhinitis and/or asthmatic subjects with a SPT positivity of almost +++ were submitted to serological determinations. The analyses of *Pj* serum specific IgE was carried out by using commercially available allergenic extracts and reagents (Phadebas-RAST, *Pharmacia Diagnostics*, Uppsala, Sweden).^{27,28} All *Pharmacia* Phadebas RAST determinations were performed at the same time. The results are expressed as classes ranging from 0 to 4 according to the manufacturer's specifications.

Nonspecific Bronchial Provocation Test (Ns BPT)

The evaluation of nonspecific bronchial hyperreactivity in a sample of 50 *Pj* sensitized subjects with bronchial asthma was carried out by using a methacholine inhalation challenge.

This test was performed using a standardized method at the end of *Pj* pollen season²⁹ and a spirometer (Pulish Spiroscope Zenith Data Systems Corporation, St. Joseph, Michigan).

Inhaled B2 agonists, rapid-release theophylline, and ipratropium bromide were discontinued at least 12 hours before the challenge. Oral B2 agonists and slow-release theophyl-

line preparations were discontinued for at least 24 hours, disodium cromoglycate and Ketotifene for at least 48 hours, antihistamines for at least 72 hours, and oral steroids for at least 1 week.

Three reproducible spiograms with FEV1 (Forced Expiratory Volume) that did not differ >5% from the highest value were obtained before beginning the challenge. Methacholine solution (supplied by Lofarma Laboratories, Milan, Italy) in buffered saline or buffered saline solution alone were nebulized using a MB3 dosimeter (MEFAR Elettromedical, Brescia, Italy). The nebulizer was connected directly to a mouthpiece, a clip was applied on the nose of the patient, and the aerosol was inhaled through the mouth by tidal volume breathing for 2 minutes. The solution without methacholine was inhaled first, followed at variable intervals by twofold increasing concentrations of methacholine. The first dose was 20 mcg and doubled with each inhalation until reaching a maximum cumulative dose of 1260 mcg or a fall in FEV1 of 20% or more in comparison with basal values.

Results were expressed as the provocative concentration of methacholine required to induce a 20% fall in FEV1 (PD 20 FEV1). This was calculated from the log dose-response curves by linear interpolation of the two adjacent data points.³⁰

We consider as hyperreactive every subject with a PD 20 FEV1 ≤ 800 mcg methacholine (≤200 mcg very high, ≥200 mcg ≤ 400 mcg moderate, and ≥ 400 mcg ≤ 800 mcg low hyperreactivity).

TABLE III

Results of Serum Specific IgE Determinations in a Group of 50 Subjects with Nasal and Bronchial Symptoms and a SPT Positivity of Almost+++

Phadebas RAST Classes	1	2	3	4	Total
Patients					
Number	—	3	28	19	50
Percent	—	6	56	38	100

TABLE IV

Clinical Symptoms

	C + R	A or E	A or E R + C	C	A + R	Total
<i>Pj</i> ms						
n.	240	21	41	4	136	442
%	54,30	4,75	9,28	0,90	30,77	100
SPT np						
n.	311	236	31	39	219	836
%	37,20	28,23	3,71	4,66	26,20	100

A = Asthma; R = Rhinitis; C = Conjunctivitis; E = Asthma Equivalent Symptoms (Cough); *Pj* ms = *Pj* monosensitive subjects; SPT np = SPT negative patients.

Pollen Counts

Aerobiological data were obtained by using a Hirst-type, 7-day volumetric air sampler (VPPS-2000 Lanzoni, Milan, Italy) placed on the A. Cardarelli Hospital, about 25 m above street level. The technical procedures have been described elsewhere.³¹ The atmospheric presence of *P* pollen grains was expressed as daily mean concentration/m³ of air.

Statistical Analysis

Pj monosensitive and control patients have been grouped according to their month of birth in order to evaluate the correlation between the month of birth and development of *P* sensitization. Statistical significance has been researched by using the X_2 test.

RESULTS

From a population of 3857 subjects examined for three consecutive years (1990–1992), we selected two groups of patients: 442 *Pj* monosensitive and 836 skin prick negative (as control) (Table I).

The results of our clinical findings are shown in Tables II–VII and in Figure 1. *Pj* sensitized patients experience a prevalent seasonal pattern of clinical symptoms (75, 12%), and many subjects (18, 55%) also show a perennial type of symptomatology. In the control group, a perennial pattern is prevalent (49, 40%). *Pj* sensitization is characterized by a high degree of skin prick test positivity (95, 03% of patients show a response of +++ and ++++), and specific nasal

TABLE V

Working Activities

	Students	Housewives	Workmen	Employees	Professionals	Traders	Teachers	Farmers	Other	Total
<i>Pj ms</i>										
Number	99	102	52	39	23	11	22	10	84	442
Percent	22,40	23,08	11,76	8,82	5,20	2,49	4,98	2,26	19,01	100
SPT np										
Number	344	169	63	57	24	19	22	13	125	836
Percent	41,15	20,21	7,53	6,82	2,87	2,27	2,63	1,57	14,95	100

Pj ms = *Pj* monosensitive subjects; SPT np = SPT negative patients.

TABLE VI

Month of Birth

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
<i>Pj ms</i>													
No.	40	34	47	36	43	42	35	38	39	28	37	23	442
%	9,05	7,69	10,63	8,14	9,73	9,50	7,92	8,60	8,82	6,33	8,37	5,22	100
SPT np													
No.	80	52	87	65	68	78	65	77	71	64	59	60	836
%	9,57	6,22	10,41	7,77	8,13	9,33	7,77	9,21	8,49	7,65	7,06	7,18	100

Pj ms = *Pj* monosensitive subjects; SPT np = SPT negative patients.

TABLE VII

Variation of Frequency of Skin Positivity to Some Common Aero Allergens in Three Samples of 2000 Atopic Patients, Over Three Biennial Periods

Allergens	Percent 1976–77		Percent 1981–82		Percent 1988–89	
	Children	Adults	Children	Adults	Children	Adults
Dermatophagoides	90,64	60,31	77,52	38,80	83,14	37,77
Parietaria spp	16,84	30,83	27,82	64,58	25,28	66,61
Gramineae	11,75	14,10	18,96	31,56	17,18	32,80
Mugworth	2,81	—	6,49	9,72	4,37	6,25
Olea Europaea	3,95	—	5,27	9,77	8,13	15,19

From Liccardi et al. 1994⁴⁵.

reactivity (prevalently with 40 and 200 AUR/mL of allergen concentration).

A high degree of bronchial hyperreactivity (Table II) and serum specific IgE determinations (Table III) were also

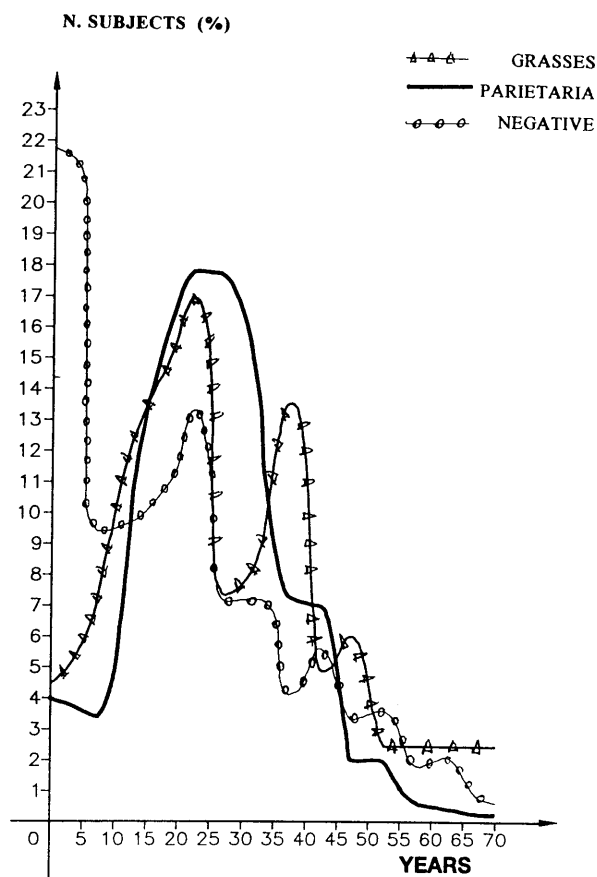


Figure 1. Age of onset of allergic symptoms.

demonstrated. Rhinitis and bronchial asthma represent the most common clinical symptoms (Table IV). Students and housewives represent the most common working categories in allergic and control group (Table V). The age of onset of clinical symptoms in *Pj* monosensitive patients reaches the maximum rate at about 20–25 years (Fig. 1). These findings are in agreement with our previous studies.³² The higher number of births in *Pj* allergic subjects is found in spring (Table VI). However, these results are not statistically significant ($P > 0.1$) and are in agreement with our previous studies.³³ Figure 2 shows urticaceae pollen counts during 3 consecutive years (1990–92).

DISCUSSION

Among the various *P* species, *Pj* is the most common in Mediterranean coastal areas. *P* pollen, which has very strong allergenic properties, appears first at the beginning of the spring and persists throughout the spring and summer months, often reaching peak levels of about 500 grains/m³ of air in the beginning of June.³⁴ A shorter pollination period is observed from the end of August to October.

A prodigious output of pollen, which ensures the reproduction success of the plant, is responsible for frequently severe respiratory symptoms. In Naples, the prevalence of sensitization to *P* as an isolated allergen or in association with other allergens, is about 80% of all pollinosis patients.⁴ Moreover, the pattern of skin prick test and serological responses to *Pj* allergenic extract is characterized by a high degree of positivity. Also, sNPT and NsBPT show a high degree of specific and aspecific airways responsivity, even though they were carried outside *P* pollen season.

The extraordinarily long persistence in the atmosphere of *P* pollen in the Mediterranean area is responsible for a multiseasonal symptomatology and sometimes also for a

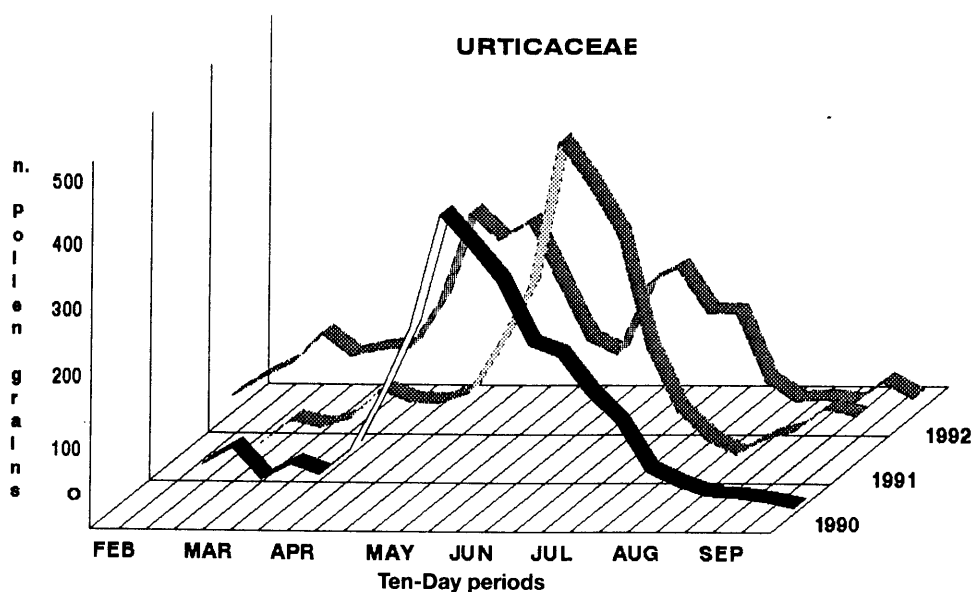


Figure 2. Airborne concentrations of urticaceae (*Parietaria*) pollens in Naples during 1990–92. Results are expressed as 10-day running means based on daily observations.

perennial pattern. In skin negative patients a perennial type of symptoms is prevalent. Recently we have demonstrated a positive effect of specific immunotherapy, with either traditional³⁵ or inhalant³⁶ route, on respiratory symptoms in *Pj* allergic patients. In *Pj* monosensitized subjects, the association of conjunctivitis and rhinitis as clinical symptoms is more frequent than bronchial asthma. The association of nasal and bronchial symptomatology has been demonstrated in about 85% of allergic patients.

In the nonallergic group, there were a high number (57, 94) of asthmatic subjects (Table IV).

The results of this study show that the age of onset of clinical symptoms in *Pj* monosensitive subjects is about 20–25 years as demonstrated in previous research. This suggests the necessity of an adequate period of exposure to allergens before completing the sensitizing process. The onset age of respiratory symptoms in mite-allergic individuals is frequently under 10 years.³² Some studies confirm that a risk factor for development of an allergic sensitization in the later years may be the birth in a certain period of the year when there is a high level of an allergen in the environment.^{37–39}

Only two previous studies have been carried out by Troisi et al.⁴⁰ and Liccardi et al.³³ in patients with *P* allergy. Even though there is not a statistically significant correlation, we have found that a higher number of *Pj* monosensitized subjects were born during *P* pollen season and consequently underwent an early exposure to pollen allergens.

We have also demonstrated an increasing frequency of skin prick test positivity to different pollen grains involved in pollinosis symptoms in our area during the last 15 years⁴¹ (Table VII). Our results are in agreement with those of other authors.⁴²

According to the opinion of most authors,⁴³ the increased air pollution in Naples may be the main factor of the increase of respiratory allergic diseases, especially those induced by pollen allergens.⁴⁴

Our research has been carried out by using a selected group of subjects with sensitization only to *Pj* allergens living in a relative restricted area in which atmospheric concentration of *P* pollen grains and environmental air pollution are homogeneous.

In our opinion, this selection is very important to distinguish the clinical effects of allergic sensitization to *Pj* allergens from those induced by other environmental conditions that may change from an area to another. Our research points out the relevant sensitizing capacities of *Pj* allergens on the respiratory tract that are evident in severe nasal and/or bronchial symptomatology. Moreover, some epidemiological aspects demonstrated for other pollens (grasses, birch, etc.) by several authors (early exposure during birth, increasing frequency of sensitization in areas with a high environmental air pollution, etc.) may be associated also with *P* allergy. In conclusion, only an adequate environmental control (on the wide growth of this plant and on the increasing rate of

air pollution) in association with antiinflammatory medications may constitute an adequate approach to management of this allergy.

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