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INCREASE OF RESPIRATORY ALLERGY TO THE POLLENS OF CYPRESSES IN THE SOUTH OF FRANCE

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A form of pollen allergy, which is uncommon in most parts of the world and in other Mediterranean countries where cypresses are abundant (Italy, Spain, Greece), with the exception of Israel, has become a problem since 1975 in our area. We have found 111 cases since 1975 compared with only a few cases from 1950 to 1975.

The period of pollination is between mid-February and the end of March. Diagnosis has been made by skin tests and, in some instances, by RAST with good correlation. In almost all the cases, cross-reactivity has been found between the members of the Cupressaceae family with Cupressus sempervirens, the commonest cypress in the South of France, associated most often with this allergy.

Clinically, allergy was of the oculo-nasal type with the association, in a few cases, of asthma or spasmodic cough. The unexpected increase of a particular allergy in a given population of atopic people raises several general problems. In this particular case it seems to us that the larger number of cypresses, which have been recently grown, is not the only explanation of the phenomenon.

Introduction

THE INCREASE in respiratory allergy to cypress pollen in the south of France is perhaps of limited clinical interest outside France. This increase has not been observed, as far as we know, in other Mediterranean countries except Israel¹ where cypresses are in abundance, eg, in Italy, Spain, Greece, Portugal, Turkey, Yugoslavia, Lebanon.²⁻⁸ This raises several questions that are at the core of a fundamental problem of our speciality, why a patient with a particular genetic background becomes allergic to some allergens and not to others?

The members of the Cupressaceae family and more especially the junipers (mountain cedar, western red cedar, incense cedar) in the USA have a well known role⁹⁻¹¹ but it does not seem that there is an increase of the cases of respiratory allergy to these pollens.¹² Cypress allergy has also been observed in South Africa^{13,14} but not in Brazil.¹⁵ In Japan, allergy to Japanese cedar

(sugi in Japanese) is very important, but this tree belongs to the Taxodiaceae family (Fig. 1).¹⁶⁻²⁰

One of us (Panzani R.) was the first in France to publish cases of cypress allergy which were, at that time, very rare.^{21,22} But since 1962 several studies on cypress pollen allergy have been published in France.²³⁻²⁵ It is interesting to add that, in some patients, wood from the Cupressaceae family (western red cedar or thuja plicata) can cause asthma with specific IgE antibodies.²⁶ Since 1976 we have identified 111 cases.

Results

Clinical Data

Cypress pollination starts mid-February and ends between mid-March and the end of March. Since cypresses (and junipers) are the only plants to pollinate during winter, clinical diagnosis was clear especially as the symptoms recurred every year at the same time. Diagnosis was confirmed by skin tests.

Clinically, there is nothing unusual about cypress allergy: patients suffer from allergic rhinitis and conjunctivitis; asthma appears only when other airborne allergens are associated (house dust, grass pollen, molds, wall pellitory pollens, *Parietaria officinalis*). In one

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case, conjunctivitis was the only symptom. There was no case of atopic dermatitis.

Allergy to cypress was isolated in 48 cases and associated in the other cases to house dust (and molds) and to pollens (grasses, parietaria, plane tree) (Table 1).

In France, *Cupressus sempervirens* is mainly found, although more recently *Cupressus arizonica* can also be found. We tested 77 patients with all the available pollens of the Cupressaceae family and with extracts of *Cupressus sempervirens* from different laboratories (Table 2).

Several facts emerge from these tables: (1) cross-reactivity very often occurs, as in other American and European studies, between the members of the Cupressaceae family.²⁷ For example, in the Cupressoideae family, *Cupressus arizonica* and *Cupressus macro-*

carpa; in the Juniperoideae family, *Juniperus communis* (*Genevrier commun*); and in the Thujoideae family, *Thuja orientalis*. But juniper is of only minor importance. (2) All the cypress pollen extracts are not antigenically identical and it is unlikely that all the antigen(s) of *Cupressus sempervirens* are present in any one extract.

It seems that there is a major antigen and others of minor importance, since a patient who has a positive test with the extracts of one laboratory failed to react to extracts from other companies and vice versa. So identification and isolation of the major allergen of *Cupressus sempervirens* is of first necessity. (3) There is, in general, no cross-reactivity with the Pinaceae (*Abietineae*) ie, fir tree, cedar, spruce-fir, pine tree, and larch tree although we found in about 10% of the cases a low positivity in skin test to pine tree, cedar, and fir tree. The relationship between the Taxodiaceae (*Taxus*: yew tree and *Cryptomeria japonica*) and the Cupressaceae are studied elsewhere. (4) In some cases, the skin test was negative in the scratch test and even intradermally with a 1/1.000 solution. This point raises the possibility of some cases of cypress allergy due to other antibodies such as IgG4.

Immunologic Data

For some cases we have tried to correlate the clinical data (clinical history, skin tests) with the RAST. Lyophilized sera were sent by air mail to Italy or Japan in order to use different antigens and techniques.

Venous blood was drawn from patients who had not been hyposensitized. The serum samples were lyophilized and sent by air mail for the RAST assays. The serum samples were reconstituted to their initial volume by adding distilled water and were kept at +4 °C during the period of analyses. It has been shown repeatedly that IgE and IgG are not altered by the process of lyophilization.

One of us (G. Centanni) using the RAST technique with an Italian extract insolubilized on the disks found

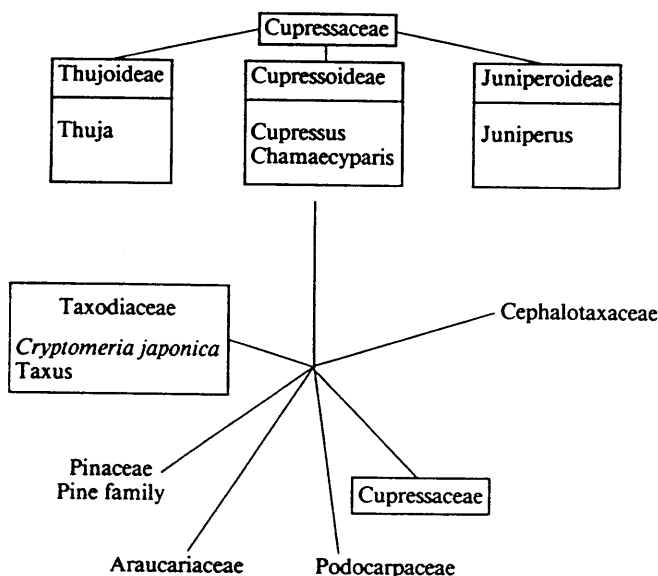


Figure 1. Reproduced from *Relations botaniques et réactions croisées immunologiques dans l'allergie aux pollens*. Copyright © 1982, by Pharmacia France (pp 7 and 24).

Table 1. Clinical Data on 111 Patients

	Sex	Age			Symptoms				Other Allergies				Home	
		Under 15	15-50	Over 50	Asthma	Allergic Rhinitis	Conjunctivitis	Spasmodic Cough	Grass Pollens	Parietaria	Plane Tree	House Dust Molds	Town	Countryside
F	55	4	44	7	16	37	1	1	25	2	2	29	25	30
M	56	7	43	6	13	42	4	1	25	4	5	28	27	29

Table 2. Cross Reactivity Among the Cupressaceae Family Using Allergens from Different Laboratories

Stallergenes, France				Berkeley Biologicals USA			Lofarma, Italy				
<i>Cupressus sempervirens</i>	Pin	Genevrier	Sapin	<i>Cupressus arizonica</i>	<i>Cupressus macrocarpa</i>	<i>Cupressus sempervirens</i>	<i>Abies alba</i>	<i>Cedrus</i>	<i>Pinus sylvestris</i>	<i>Thuja orientalis</i>	<i>Cupressus sempervirens</i>
62	7	36	5	72	68	71	8	7	8	37	50

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Table 3. RAST on 40 Patients (Dr Yasueda)

Negative	8
Positive	32
1° Phadebas ref A	1
2° Phadebas ref B	14
3° Phadebas ref C	14
4° Phadebas ref D	3

that in 27 cases of allergy to cypress pollen, 21 had a positive RAST with the following scores:

1	: 8
2	: 7
3	: 6
4	: 0

In a second series of experiments, 40 sera were sent to Japan and RAST was also done using the Phadebas technique with an extract from Berkeley Biological and we had the following results (Table 3) (Dr H. Yasueda). In both series, a rather good correlation was found but there were some false positives and false negatives. Unfortunately, all the patients having doubtful skin tests have not been checked by RAST. The RAST did not give more information than the routine skin testing.

Discussion

We have no precise answer to the question raised at the beginning of this paper. According to Carbonnel,²⁴ the increase in cypress allergy in France is due to two causes. A minor one is the fact that in France many people living in towns often go to the countryside during the weekend and the major one is the increase of cypresses in private and public gardens and parks. The large number (52 out of 111) of our patients live in major cities and we should add that the pollen count of *Cupressus sempervirens* has not increased from 1975 to 1984.²⁸

Probably we must look for other reasons either in the genetic make-up of the patient or in the environment. First there is the possibility of a change in this level of pollution in the environment with pollutants such as aluminum silicate having an adjuvant effect.^{29,30} Second, the fact that the increase is observed only in the South of France (if we exclude Jerusalem where many of cypresses have been recently grown) could prompt us to look more deeply into the genetic background of our patients. A recent paper from Kaufman et al³¹ raises the possibility of a racial difference in antigen recognition when he found that "Chinese and Japanese patients react more frequently to juniper cypress and cedar than did Caucasians." Third, a modification of the pollens themselves can possibly explain the phenomenon. Studies by Bousquet et al³² on the role of enzymes, may help in understanding this problem. This opinion is also shared by Sullivan.³³ Although we know that pollens do not penetrate into the lung, it is now well documented that under the influence of heat and humidity, pollen grains liberate glycoproteins that are the allergens, and are being closely investigated for

ragweed, grasses, and some trees. We may hypothesize that the change in climate observed recently could result in a change in antigenic composition which could explain the increase in antigenicity.

A combination of all three potential factors may explain the phenomenon.

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Searching an infinite where,
Probing a bottomless when,
Dreamfully wandering,
Ceaselessly pondering,
What is the wherefore of men

*Lapsus Calami. The Philosopher
and the Philanthropist, Stanza 1*
by J. K. Stephen (1859-1892)