

Tree Pollen Allergy

II. Sensitization to Various Tree Pollen Allergens in Sweden. A Multi-Centre Study

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In a multi-centre study, comprising 16 clinics, 871 adult hay fever patients were studied. Most patients included had springtime hay fever. Skin prick tests were performed with 20 different tree or bush pollen (lignoses) allergens. RAST determinations were done with eight different tree pollen allergens in 590 patients. Birch pollen (BP) allergen gave the highest frequency of positive test results. The test results with the various tree pollen allergens in patients with BP allergy were compared with those in patients without BP allergy. With all the allergens a significantly higher frequency of positive test results was found in those with BP allergy than in those without. Only very small differences were noted between various parts of the country, and sensitization against various tree pollens was common even in regions where the corresponding trees do not grow. It was concluded that a high degree of cross-sensitization exists among tree pollens, and testing with BP allergen is sufficient for the diagnostic screening of tree pollen allergy.

Key words: allergen; birch pollen; cross-sensitization; hay fever; tree pollen.

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CLINICAL ASPECTS

Springtime hay fever patients in Sweden are most often sensitized against birch pollen (BP) and many show positive test results with other tree pollen allergens as well. In the absence of BP allergy, a clear-cut allergy against other tree pollens is seldom or never found. For diagnostic screening of springtime hay fever it is sufficient to use BP allergen.

Tree pollen allergens are often responsible for springtime hay fever reactions in Sweden. In some parts of the country tree pollen allergy seems to be as frequent as grass pollen allergy (7). Birch pollen (BP), has a high air concentration during a few weeks in May (13) and is the commonest cause of springtime hay fever, al-

though sensitization to other tree pollens is also common (5, 11, 15).

In clinical allergology it is important to know which allergens have practical significance. Because of cross-sensitization it is also important to know if one allergen can replace other allergens in diagnostic screening and immunothe-

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rapy. For this reason a large number of hay fever patients were diagnostically tested with tree pollen allergens from all large botanical families judged to be of allergological importance in Sweden. A botanical survey of the taxonomy has been given in a previous paper (13).

This paper reports on the results of the skin prick testings and Phadebas RAST® analyses with the tree pollens available. Cross-sensitization patterns will be presented elsewhere (8).

PATIENTS AND METHODS

Adult hay fever patients from 15 clinics in Sweden (from Malmö in the south, lat. 55.5°, to Gällivare in the north, lat. 68°) and one clinic in Norway (Sandefjord) took part in the study. The geographical locations of the clinics are seen on the map in Fig. 1. At each clinic about 50 patients with springtime hay fever and 10

patients with a non-springtime hay fever were selected, making a total of 872 patients (464 males and 408 females) with a mean age of 27 years (range 8–67 years). According to their histories, 734 of the patients had a springtime hay fever with a mean duration of 11 years (range 1–49 years).

Allergens

Skin prick tests (SPT) were performed with glycerinated Neohelisen 5000 PNU/ml prick test extracts (Allergopharma, Reinbek, DFR). The 20 tree and bush pollens used (see Table 1) represent all large botanical families of allergological interest in Sweden (13). The participating clinics also performed tests with grass and mugwort (*Artemisia vulgaris*) pollen, using their routine extracts from Allergologisk Laboratorium, Copenhagen, Denmark, Dome Hollister-Stier, Slough, England, Allergopharma,

Table 1
Prick test results (%) with various tree pollen allergens in BP+ and BP-.

Allergens ^a	Patient group BP+ (n=648)				Patient group BP- (n=55)			
	Prick test results (%)				Prick test results (%)			
	Neg.	1-2+	3+	≥4+	Neg.	1-2+	3+	≥4+
Birch (56577)	0	9	23	68	100	0	0	0
Alder (56924)	5	13	30	52	96	4	0	0
Hazel (56491)	6	19	30	45	90	10	0	0
Beech (56718)	6	18	33	53	88	8	2	2
Oak (56743)	18	33	28	21	92	6	2	0
Aspen (56374)	62	26	9	3	98	2	0	0
Sallow (56802)	53	25	9	3	94	6	0	0
Bog myrtle (TL 92518)	17	30	30	23	94	2	4	0
Elm (56338)	60	33	6	1	92	6	0	0
Maple (57024)	54	41	5	<1	98	2	0	0
Ash (56741)	54	36	7	3	94	6	0	0
Privet (92513)	60	34	5	1	98	0	2	0
Lime (56819)	40	48	9	3	84	12	2	2
Elder (56486)	22	54	19	5	60	34	4	2
Horse chestnut (92515)	28	55	13	4	84	12	4	0
Plane (56473)	43	45	10	2	86	14	0	0
Heather (TL 92517)	43	40	12	5	68	26	6	0
Juniper (TL 92516)	68	29	3	<1	94	6	0	0
Pine (56801)	85	12	2	1	100	0	0	0
Larch (TL 92514)	87	12	1	<1	100	0	0	0

Significance of difference between BP+ and BP- with each of the allergens was $P < 0.001$

a. For latin names and botanical relationship see ref. 13. Figures in (parenthesis) indicate batch-number of Neohelisen allergen extracts.

negative tests with all remaining tree pollens. Ninety-four of the 141 patients with negative SPT against BP had positive (usually only 1+ or 2+) reactions to one or more of the remaining tree pollens.

Alder and beech succeeded birch in order of frequency of positive SPT (691), followed by hazel (686), oak (605), and bog-myrtle (598). The frequency of concordant positive SPT results with combinations of these tree pollens is shown in Table 2.

With the Phadebas RAST the rank order of tree pollens with regard to positive results was: birch, alder, oak, hazel, beech, willow, elm, and maple (box-elder).

Springtime symptoms versus SPT reactions to birch pollen

Some discrepancies were found between birch SPT results and a history of springtime symp-

toms (Table 3). Since provocation tests were not regularly recorded, the diagnosis of BP allergy had to be based on a combination of case history and SPT results. It has been shown earlier that a reliable diagnosis of BP allergy can be established when history and SPT are concordant (6). Thus the 648 patients with a positive history of springtime hay fever and a positive SPT with BP were regarded as being allergic to BP (BP+) and the 55 patients with a negative history and a negative SPT reaction were regarded as non-allergic to BP (BP-).

With respect to BP allergy, the status of the remaining 174 patients, who had discordant history and prick test results, had to be regarded as unknown.

Comparison between those with and without birch pollen allergy

Since there obviously exists a relationship between BP allergy and allergy to several other tree pollens, it was considered of interest to study the rate of sensitization to the various tree pollens employed in the groups of patients with and without BP allergy. The distribution of SPT results in the two groups is shown in Table 1. With all the allergens a statistically significant higher degree of sensitization was found among BP+ than among BP- ($P<0.001$). In those with BP allergy the highest frequency of positive SPT was found with alder (95%), hazel

Table 3

Relationship between patients' histories of springtime hay fever and prick test results with birch pollen allergen

Prick test results with birch pollen	Springtime season	
	No	Yes
Negative	55	86
Positive ($\geq 1+$)	83	648
Total	138	734

Table 4

RAST results (%) with various tree pollen allergens in BP+ and BP- patients.

Allergen	Patient group BP+ (n = 449)					Patient group BP- (n = 32)				
	Phadebas RAST® class					Phadebas RAST® class				
	0	1	2	3	4	0	1	2	3	4
Birch	16	5	22	39	18	100	0	0	0	0
Alder	18	7	26	31	18	97	3	0	0	0
Hazel	35	11	31	20	3	97	3	0	0	0
Beech	38	10	35	15	1	94	3	0	0	0
Oak	28	13	36	20	3	91	6	3	0	0
Willow	60	16	18	5	1	91	9	0	0	0
Maple (box-elder)	73	12	13	2	1	88	9	3	0	0
Elm	61	15	20	4	0	88	9	3	0	0

Significance of difference between BP+ and BP- with each allergen $P<0.001$.

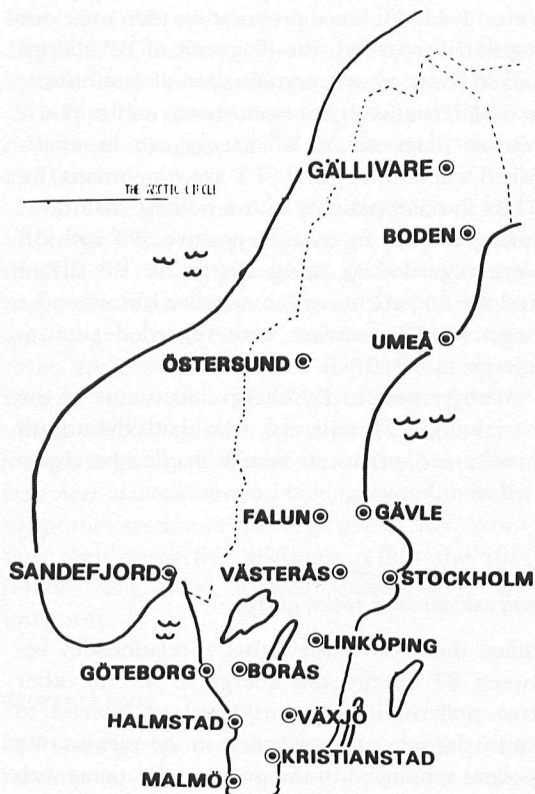


Fig. 1. Locations of clinics taking part in the study.

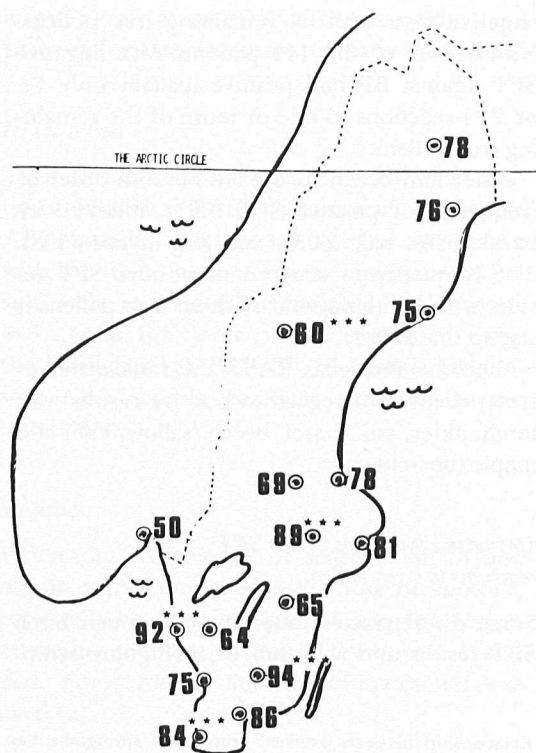


Fig. 2. Frequency of positive skin prick test results with beech pollen in patients with birch pollen allergy at various clinics. Clinics with test results significantly differing from those of other clinics are indicated; ** = $P < 0.01$, *** = $P < 0.001$.

(94%), beech (94%), bog-myrtle (83%) and oak (82%) allergens. In those without BP allergy the highest frequency of positive reactions was found with elder, heather, horse-chestnut, and linden. These reactions were usually weak, however, and of questionable clinical significance.

The findings with Phadebas RAST were similar to those with SPT (Table 4). With each of the allergens there was a significant difference between BP+ and BP- ($P < 0.001$). In those with BP allergy the rank order of tree pollens producing positive RAST was: birch, alder, oak, hazel, beech, willow, elm, and maple (box-elder). In the patient group without BP allergy elm, maple (box-elder) and willow topped the list.

In 174 patients with discordant history and SPT result with BP, the SPT and RAST results

with the various tree pollens lay intermediately between those of BP+ and BP-.

Springtime hay fever patients with negative test results with tree pollen

Of the 86 patients who had a springtime hay fever but negative prick test with BP, 19 had negative prick test and *in vitro* test results with the remaining tree pollens as well. Thus, in these patients no allergological explanation of their springtime symptoms could be found. They did not differ in sex or age from other patients but their mean total IgE was somewhat lower (73 ± 32 kU/l) than that of the other patients (259 ± 14 kU/l) (not significant). However, nine of these 19 patients had positive SPT with grass pollen extract.

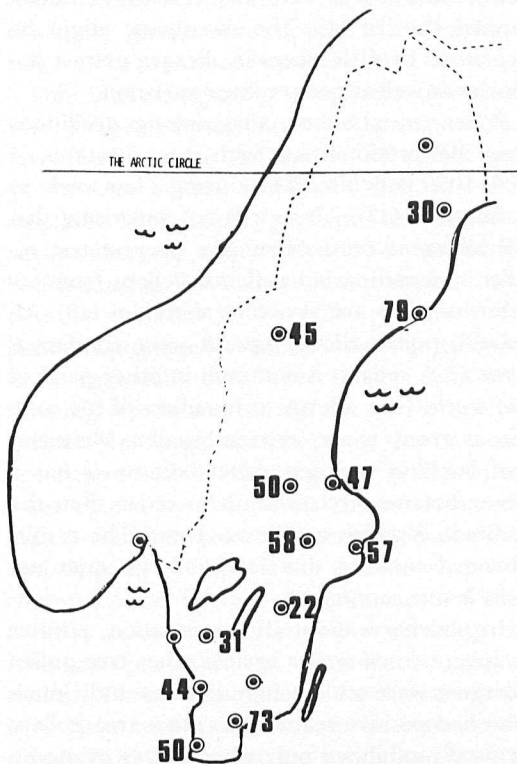


Fig. 3. Frequency of positive Phadebas RAST® results with beech pollen in patients with birch pollen allergy at various clinics.

Comparison between regions

When comparisons between various clinics were made, only patients who had lived in the region prior to the onset of their hay fever symptoms were included in the calculation. 539 patients fulfilled this criterion for comparisons of skin tests and 370 for comparisons of RAST results.

With Phadebas RAST very few differences were seen between clinics, whereas, at some of the clinics, most of the allergens used showed different degrees of SPT reactivity. The differences were small, however, and obviously reflected variations in patient selection and test methodology rather than differences in the patients' pollen environment. This is exemplified by the test results with beech pollen in Fig. 2 (SPT) and Fig. 3 (RAST). Although beech grows mainly in the southern most part of Sweden (Fig. 4), positive reactions with SPT as well

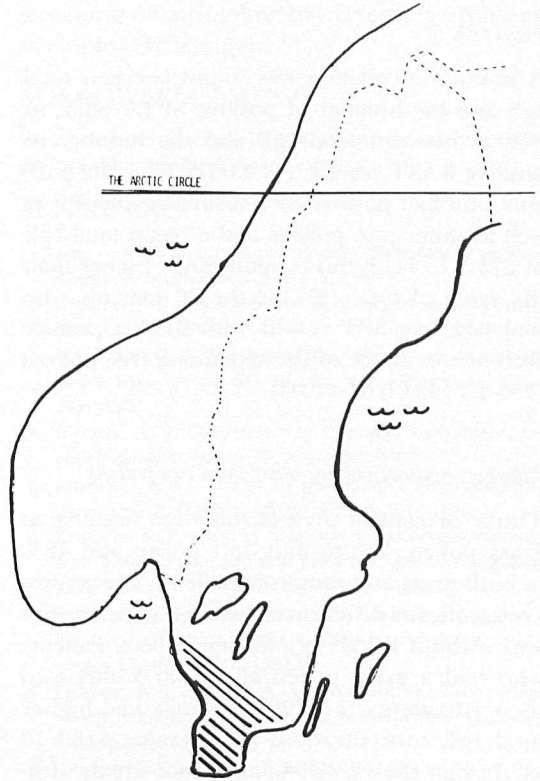


Fig. 4. Distribution of beech in Sweden.

as with RAST were seen with about the same frequencies in northern and southern clinics.

When the results of 187 patients with BP allergy from the six most northern clinics (Gällivare, Boden, Umeå, Östersund, Gävle, Falun) were compared with those of 170 patients from the four southern clinics (Malmö, Kristianstad, Halmstad, Växjö) very small but statistically significant differences were found in SPT reactivity with some allergens. Alder, hazel, beech, bog-myrtle, and elder, gave more positive SPT reactions among patients with BP allergy in the south than in the north.

With Phadebas RAST no significant differences were found between northern and southern Sweden.

Since variations in test methodology between the different clinics might have influenced the results of the SPT but not the RAST, the results of the latter are more reliable for comparisons between various parts of the country.

Total IgE

A positive correlation was found between total IgE and the number of positive SPT results, as well as between total IgE and the number of positive RAST results ($P < 0.001$). The 502 patients who had positive SPT results against BP as well as other tree pollens had a mean total IgE of 275 ± 15 kU/l; this is significantly higher than the value of total IgE for the 60 patients who had negative SPT results with BP but positive with one or more of the remaining tree pollens (155 ± 21 kU/l) ($P < 0.01$).

Allergies against pollens other than tree pollens

Thirty percent of the patients were sensitive to grass pollen, 7% to mugwort pollen and 42% to both grass and mugwort pollens. There were no significant differences between patients with and without BP allergy in this respect. Patients who had a grass pollen allergy in addition to their BP allergy ($n = 296$) generally had higher total IgE concentrations (mean value 318 ± 19 kU/l) than the 126 BP allergic individuals without grass pollen allergy (mean value 255 ± 23 kU/l) ($P < 0.001$).

DISCUSSION

A large number of patients with springtime hay fever underwent allergological investigation (SPT and Phadebas RAST) with pollen allergens from 20 different trees, representing all large botanical families of potential allergological importance in Sweden (13). The results of the study confirm the clinical experience that only deciduous, and not coniferous trees, constitute allergological problems in Sweden. Like other Scandinavian investigations (4, 5, 11, 15), this study shows that birch is the outstanding tree pollen allergen, eliciting higher frequencies of positive SPT and RAST results than any other tree. Very often, alder, beech, hazel, oak, and bog-myrtle also give positive test results in patients with springtime hay fever, a finding in accord with an earlier study (15). The rank order of positive SPT was slightly different in a large Danish multi-centre study, in which birch,

hazel, alder, beech, ash, maple, willow, and oak topped the list (4). The discrepancy might be explained by differences in allergen extract potencies as well as geographical variation.

Pollen counts show that among deciduous trees BP predominates with concentrations of 100–1000 pollen/m³/24 h during a few weeks in springtime (13). Thus, it is not surprising that BP allergens most often give positive test results in Scandinavian patients. Pollens from coniferous trees are also very abundant (13). Although pollen allergy against some coniferous trees (e.g. cedars) is common in other parts of the world (16), allergy to members of the coniferous group is very rare in Sweden. We included larch in our test panel because it has a closer botanical relationship to cedar than the common Swedish coniferous trees. The results obtained indicate that larch allergy does not exist in our country.

In patients without BP sensitization, positive *in vivo* or *in vitro* tests against other tree pollen allergens were seldom found. Those individuals who had positive reactions to other tree pollens generally exhibited only a low degree of sensitization (SPT 1–2+ and Phadebas RAST class 1). In Sweden, clinically relevant tree pollen allergies, i. e. allergies caused by ordinary exposure to native tree pollens, are extremely rare in patients without BP allergy (5), although one of us (J.-Å. W.) has seen two patients with an isolated allergy against elm (not published). The conclusion for practical clinical work is that in patients with springtime hay fever testing with BP allergen should suffice for the initial diagnostic screening.

Although the tree flora in northern and southern Sweden to some extent differ (13), the sensitization rates for the various tree pollen allergens were almost the same. Some trees tested, e. g. beech and ash, do not grow in the north and others, e. g. plane, do not grow in Sweden at all, except rarely when cultivated. Nevertheless, sensitization to these pollens was found, as well as to other pollens that are never or seldom detected in the pollen counts (13). The most probable explanation for this phenomenon is the existence of cross-sensitization between tree pollen allergens, as found by several

earlier studies (3, 5, 12, 14, 15). Results from this study, giving more support to this explanation, will be presented elsewhere (8).

One interesting group of patients are those who, in spite of their history of springtime hay fever, had negative SPT and RAST results with all the tree pollens employed. Are they true atopics? They could perhaps be sensitized against allergens not included in our test panel. Pollen causing seasonal symptoms should, however, be detected in the pollen counts if the pollen is produced in sufficiently large amounts to be regionally distributed. Pollen from low-growing weeds and shrubs are not commonly spread over large distances and, thus, are underrepresented in the regional pollen spectrum shown by the pollen counts. However, such pollen may have an intense local distribution. A good example is the well-known pollen allergy caused by rape (*Brassica napus*) found mainly among the farmers cultivating it. Another possibility is sensitization against molds (10). In some patients the clinical history may have been false. Hay fever, erroneously reported to appear during springtime, may in fact occur in summer, with grass pollens as a probable cause. For most patients, however, the probable explanation for springtime symptoms without any signs of sensitization to springtime pollen allergens is that they are non-atopics with a high degree of hyperreactivity of the airways. Another investigation has shown that non-atopic individuals may have symptoms from birch twigs with or without catkins nearly as often as atopics (9). Probably some substances, originating from the springtime vegetation, evoke symptoms by their odour or irritating properties.

Conclusions

Springtime hay fever patients in Sweden are most often sensitized against BP, and many show positive test results with other tree pollen allergens as well. Differences in sensitization pattern between various parts of the country are very small or absent. In the absence of BP allergy, a clear-cut allergy against other tree pollen is seldom or never found. For diagnostic

screening of springtime hay fever it is sufficient to employ BP allergen.

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