

Tree pollen allergy

III. Cross reactions based on results from skin prick tests and the RAST in hay fever patients. A multi-centre study

N. E. ERIKSSON,¹ J.-Å. WIHL,² H. ARRENDAL³ and S.-O. STRANDHEDE⁴

¹Dept. of Medicine, Länssjukhuset, Halmstad, ²ENT Dept. Malmö Almänna Sjukhus, Malmö, ³Research Dept., Pharmacia, Uppsala, and ⁴Dept. of Plant Taxonomy, University of Göteborg, Sweden

872 adult hay fever patients were investigated with skin tests, using 20 different tree pollen allergens, and Phadebas RAST®, using eight different tree pollen allergens. Correlation between test results with the different allergens were studied employing the Spearman's correlation coefficient (Rho). Most combinations showed statistically significant correlations. The highest values of Rho (0.8-0.9) were found for pollen from combinations of trees belonging to the families *Betulaceae*, *Corylaceae* and *Fagaceae* (birch, alder, hazel, beech and oak). High values were also found between pollens from aspen and sallow (belonging to *Salicaceae*). With several of the trees a high degree of pollen cross sensitization was found, even with trees from a different plant family. Since most of the patients were allergic to birch pollen, some of the reactions to other pollens could be due to allergens shared by birch. To exclude this possibility, a separate analysis was performed for patients having no birch pollen allergy. Even in these patients evidence of cross sensitization was found. It is concluded that cross reactions are common among tree pollens and are most pronounced within botanical families.

Key words: allergen; cross reactions; hay fever; RAST; skin test; tree pollen.

Accepted for publication 1 December 1986

CLINICAL ASPECTS

The study shows that patients with springtime hay fever often react to several tree pollens. To a large extent this is due to cross reactivity because of a partial immunologic identity among tree pollen allergens. Several tree pollens share allergens with birch pollen, which is dominant, and for diagnostic screening of tree pollen allergy in Sweden it is sufficient to use birch pollen extracts.

Besides the Authors, the following doctors took part in the study: Ulf Andsberg, ENT Dept., Växjö, Sweden. Göran Boethius, Chest Dept. Östersund, Sweden. Ulf Eilard, Dept. of Dermatology, Borås, Sweden. Gunnar Holmgren, ENT Dept., Boden, Sweden. Christina Irander, ENT Dept., Linköping, Sweden. Sten B. Lindgren, Dept. of Allergology, Sahlgren's Hospital, Göteborg, Sweden. Hans Matsols, Dept. of Medicine, Falun, Sweden. Maria Moberger, Dept. of Medicine, Gällivare, Sweden. Jan-Erik Nilsson, Dept. of Medicine, Kristianstad, Sweden. Kjell Orvar Pegelow, Dept. of Allergology, Huddinge, Sweden. Leif Rosenhall, Chest. Dept. Umeå, Sweden. Jan Sandström, ENT Dept. Västerås, Sweden. Odd Strømme, Sandefjord, Norway. Karl Bertil Tegner, Chest Dept. Gävle, Sweden.

Knowledge of cross reactivity among different pollens is of practical importance in diagnosing allergic diseases. The knowledge is useful when judging the significance of positive skin test (SPT) reactions or RAST results obtained with pollen allergens from non-indigenous plants. Moreover, it is a valuable tool for minimizing the number of allergen extracts used in diagnostic screening. It is also of great value when deciding which allergens should be included in a hyposensitization programme.

It is generally agreed that grasses, which represent one single family, are more antigenically related than trees. Cross reactivity does exist between different tree pollen allergens. However, the findings from various *in vitro* (2, 3, 4, 5, 13, 14)) and *in vivo* studies (8, 9, 10, 11, 20, 22, 23) are somewhat conflicting.

The purpose of the present study was to further analyse cross sensitization patterns among tree pollens by testing hay fever patients from various parts of Sweden with different tree pollen extracts. SPT and RAST results obtained with different tree pollen allergens were compared and correlation coefficients were calculated.

PATIENTS AND METHODS

These data come from a multi-centre study in which 16 clinics took part (11). The clinics were scattered all over Sweden from Malmö in the south to Gällivare in the north, covering regions with different tree pollen environments. The investigation comprised 872 hay fever patients with a mean age of 27 (range 8–67) years. Of the patients 464 were males and 408 females. The majority of the patients (734) had springtime symptoms and 600 patients had hay fever symptoms in summer.

Skin tests

SPT were performed on the volar side of the forearm or on the back as described elsewhere (11). The wheal reactions were measured after 10–20 min and designated as 3+ when the areas were of the same size as the positive histamine reference, 4+ when double the size

of the histamine-induced wheal, etc (1). Reactions larger than that of the negative saline buffer reference but smaller than the positive reference were graded as 1+ or 2+. All reactions > 1+ were defined as positive.

In vitro tests

Specific IgE as well as total IgE antibody concentrations were measured using Phadebas RAST® and Phadebas IgE PRIST®, respectively (Pharmacia Diagnostics AB, Uppsala, Sweden). All *in vitro* determinations were performed according to the instructions for use of the test procedures.

Allergens

A botanical survey of the pollen represented in the study has been given previously (19). All patients were skin prick tested with a standard allergen panel consisting of 20 different tree or bush allergens (see Table 3). Neohelisen glycerinated prick test extracts of 5000 PNU/ml strength (Allergopharma, Reinbek, GFR) with batch numbers given elsewhere (11) were employed. For determination of specific IgE antibody concentrations in the sera Phadebas RAST allergens were used (Table 4).

Statistics

The statistical significances of correlations were tested with Pitman's non-parametric permutation test (6). The Spearman's correlation coefficient (Rho) was also calculated in order to get a quantitative measurement of the degree of correlation. Phadebas RAST classes 0–4 and prick test results graded according to the number of plusses were used in the calculations.

Calculation of allergen panel for screening purposes

To find the allergen panel most suitable for screening purposes, if 1, 2, 3, etc. allergens were to be used for diagnosis of tree pollen allergy, the allergen giving the highest number of positive reactions was first calculated. All individuals having a positive reaction with that

allergen were then excluded from the following calculations. The allergen to which most of the remaining patients reacted was then searched for and all individuals showing a positive reaction to that allergen were excluded from the next calculations. The process was repeated until all individuals having a positive skin test reaction had been excluded. A similar calculation program has previously been used by Østerballe et al. (23).

RESULTS

Correlations in pollen sensitization found in the total patient material

Overall, a total number of 17,440 SPT (20 allergens in 872 patients) and 4,728 RAST-analyses (8 allergens in 591 patients) were performed. SPT results obtained with each of the 20 tree pollen allergens were compared with those of each of the others, making 190 cross-tables. As an example, one of these tables (the comparison between birch and beech) is shown in Table 1. Analogously, the Phadebas RAST results with eight different tree pollen allergens were compared two by two, making 28 tables, an example of which is shown in Table 2 (the comparison between birch and alder). Simplified results from all tables, with test results expressed only as negative or positive, appear in the upper right of Table 3 (SPT results) and Table 4 (Phadebas RAST results). In these tables the test result figures are given as percentages of the total number of patients. Noticeable is the high frequency of sensitization against birch and alder pollens. Very few cases with negative test results for these allergens show positive results for other allergens.

All different combinations of allergens, with the exception of that between pine and heather pollens, showed statistically significant correlations ($P < 0.001$). A simple measure of the strength of the correlations, the value of the Spearman's correlation coefficient (Rho), is given in the lower left of Tables 3 and 4. As seen from the tables, the strongest correlations (with $R > 0.80$) were found for birch/alder, alder/hazel, hazel/beech, beech/oak and oak/hazel.

Correlations in pollen sensitization found in patients without birch pollen allergy

A high degree of correlation in patient sensitization was found between birch pollen and other tree pollens. Correlations in patient sensitization between non-birch tree pollens could thus be due to the allergens they each share with birch pollen. To exclude the influence of birch pollen allergy a separate analysis was performed on the patients without signs of birch pollen sensitization. Table 5 presents 2×2 tables with Phadebas RAST results for seven tree pollens in 189 patients who had negative RAST results with birch pollens. Statistically significant correlations ($P < 0.001$) were found with all combinations.

Several of the combinations, e.g. alder/sallow, hazel/maple and oak/maple, showed Rho higher than corresponding Rho in the total patient group. However, with mutual combinations of alder, hazel, oak and beech the values of Rho were considerably smaller in the birch-negative group than in the total patient group.

A similar analysis was performed using the SPT results with 19 different tree pollen allergens on 141 patients with negative SPT results against birch pollen. Of the 171 tree pollen combinations, 56 showed significant positive correlations in patient sensitization ($P < 0.001$). With some of the combinations, e.g. alder/sallow and oak/plane, the Rho values were higher in birch-negative patients (Table 6) than in the total patient group (Table 3).

Those tree pollens which most often gave positive SPT reactions in patients with a negative birch pollen SPT were elder, heather, linden, horse chestnut, bog myrtle, privet, and oak. Less than 1% of the birch pollen negative patients showed clearly positive ($> 3+$) SPT with alder, hazel, or aspen.

Correlations in pollen sensitization found in patients living in northern Sweden

The correlation between different tree pollens could depend on simultaneous sensitization to pollens occurring together in the patient's environment. Several of the trees do not grow

Table 1

Comparison of skin prick test results with birch and beech pollen

Prick test with birch	Prick test with beech number of plusses					Total
	0	1-2	3	4	≥ 5	
0	123	16	1	1	0	141
1-2	27	40	11	4	0	82
3	16	52	81	22	3	174
4	8	41	77	75	11	212
≥ 5	7	17	64	91	83	263
Total	181	167	234	193	97	872

Table 2

Comparison of RAST results with birch pollen and alder pollen allergen

Phadebas RAST class with birch	Phadebas RAST® class with alder					Total
	0	1	2	3	4	
0	162	17	9	1	0	189
1	15	9	8	0	0	32
2	18	19	63	7	0	107
3	0	0	48	118	16	182
4	0	0	0	19	64	83
Total	195	45	128	145	80	593

Table

Correlations between skin prick test results
The table is symmetrical. The upper right consists of 2 × 2 tables and the lower left gives

	Birch		Alder		Hazel		Beech		Oak		Aspen		Sallow		Bog-myrtle		Elm		Maple	
	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+
Birch	-	15	1	14	2	14	2	14	2	15	1	15	1	15	1	15	1	15	1	
	+	6	78	7	77	7	77	17	67	52	32	46	38	17	67	51	33	46	38	
Alder	0.83		-	18	3	17	4	17	4	20	1	19	2	19	2	19	2	19	2	
			+	4	75	4	75	13	66	48	31	42	37	12	67	46	33	42	37	
Hazel	0.76		0.86		-	17	4	18	3	20	1	20	1	19	2	20	1	20	1	
					+	3	75	13	66	47	32	42	37	12	67	46	33	41	38	
Beech	0.75		0.83		0.86		-	19	2	20	1	19	2	19	2	19	2	19	2	
							+	12	67	48	31	42	37	12	67	46	33	42	37	
Oak	0.59		0.71		0.75		0.75		-	29	2	27	4	24	7	28	3	27	4	
									+	38	31	34	35	7	62	38	31	34	35	
Aspen	0.22		0.28		0.34		0.33		0.39		-	56	12	29	39	58	10	51	16	
											+	5	27	2	30	8	24	10	23	
Sallow	0.24		0.29		0.34		0.34		0.36		0.71		-	28	33	53	8	49	12	
													+	3	36	12	27	11	27	
Bog-myrtle	0.62		0.75		0.79		0.76		0.77		0.40		0.41		-	29	2	29	3	
															+	37	32	32	36	
Elm	0.22		0.28		0.33		0.32		0.37		0.64		0.65		0.40		-	52	13	
																+		9	26	
Maple	0.32		0.36		0.40		0.40		0.42		0.48		0.52		0.46		0.58		-	
																			+	
Ash	0.24		0.29		0.32		0.34		0.37		0.60		0.61		0.39		0.57		0.54	
Privet	0.21		0.24		0.28		0.28		0.31		0.52		0.54		0.32		0.49		0.47	
Lime	0.22		0.21		0.26		0.28		0.31		0.44		0.49		0.28		0.45		0.45	
Elder	0.31		0.30		0.34		0.38		0.37		0.35		0.34		0.39		0.33		0.32	
Horse-chestnut	0.43		0.48		0.50		0.52		0.51		0.47		0.47		0.55		0.45		0.49	
Plane	0.28		0.28		0.31		0.32		0.36		0.55		0.55		0.37		0.50		0.50	
Juniper	0.16		0.16		0.20		0.20		0.25		0.40		0.41		0.21		0.39		0.35	
Larch	0.12		0.15		0.16		0.15		0.22		0.26		0.25		0.17		0.25		0.21	
Pine	0.16		0.19		0.18		0.16		0.19		0.15		0.22		0.21		0.24		0.25	
Heather	0.15		0.14		0.18		0.19		0.21		0.45		0.46		0.21		0.40		0.30	

-: negative prick test; + : prick test results > 1 plus.

in northern Sweden, however, namely beech, oak, hazel, elder, horse chestnut, linden, plane, ash, elm, privet, maple, and larch (19). For this reason, those patients who lived in northern Sweden were studied separately, since they could not have been sensitized to the above trees by the natural route (patients who had hay fever before moving to northern Sweden were excluded from the calculations). Using the results from SPT and RAST the Rho values for most of the combinations were found roughly to be the same as corresponding values from the

total patient material. For some of the combinations somewhat lower Rho were found than in the total patient group.

Correlation studies using the SPT results from 45 patients living in northern Sweden and having a negative SPT result with birch pollen allergen showed significantly positive correlations for the following combinations: oak/plane, ash/privet, horse chestnut/plane, ($P < 0.001$) beech/plane, bog myrtle/privet, bog myrtle/lime, alder/plane and alder/heather ($P < 0.01$).

3

with various pollens in 872 patients.
the Spearman correlation coefficients (Rho). In the 2 × 2 tables figures indicate percentages

Ash		Privet		Lime		Elder		Horse- chest-nut		Plane		Juni per		Larch		Pine		Heather	
-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+
15	1	14	2	12	4	10	6	13	3	13	3	14	2	16	0	15	1	10	6
45	38	50	34	35	49	20	64	25	59	36	48	57	27	73	11	72	12	36	48
18	3	18	3	15	6	11	10	16	5	16	5	18	3	20	1	20	1	12	9
42	37	46	33	32	47	18	61	22	57	34	45	53	26	68	11	67	12	34	45
19	2	18	3	16	5	12	9	17	4	17	4	19	2	20	1	20	1	13	8
41	38	46	33	31	48	17	62	21	58	32	47	52	27	68	11	67	12	33	46
19	2	18	3	16	5	12	9	18	3	17	4	19	2	20	1	20	1	13	8
42	37	46	33	31	48	17	62	21	58	32	47	53	26	68	11	67	12	33	46
26	4	26	5	22	8	17	13	23	8	25	6	28	3	30	1	28	2	19	11
34	36	38	31	25	45	12	58	15	54	25	44	43	26	58	11	59	11	27	43
53	15	54	14	41	26	27	41	35	33	44	24	57	11	64	4	63	5	40	28
7	25	10	27	6	27	2	30	3	29	5	27	14	18	24	8	24	8	6	26
50	11	50	11	39	22	24	37	33	28	41	20	52	9	58	3	57	4	36	25
10	29	15	24	8	31	5	34	5	34	9	30	19	20	30	9	30	9	10	29
27	4	27	4	21	10	17	15	23	9	24	7	27	5	30	1	30	1	19	13
33	36	38	31	26	43	12	56	15	53	26	43	44	24	58	11	58	11	27	41
51	15	53	13	40	26	26	40	34	32	42	23	55	11	62	4	61	5	38	28
9	25	12	22	7	27	5	30	4	30	4	27	16	18	26	8	26	8	8	26
48	13	49	12	38	23	25	36	34	27	48	21	51	10	58	3	57	4	34	27
12	27	15	24	9	30	5	34	4	35	9	30	20	19	31	8	30	9	12	27
	-	52	8	40	20	25	35	33	27	41	19	52	9	57	3	56	4	36	24
	+	13	27	7	33	4	36	5	35	8	32	19	21	31	9	31	9	10	30
0.63			-	43	22	26	38	33	31	42	22	55	10	62	3	61	4	38	27
			+	4	31	3	33	5	31	8	28	16	19	27	9	27	8	8	27
0.57		0.61			-	25	22	29	18	34	13	42	5	45	2	44	3	30	17
					+	4	49	9	44	16	37	29	24	43	10	44	9	16	37
0.40		0.44		0.53		-		22	7	23	6	26	3	38	1	27	2	23	6
					+			17	54	26	45	45	26	60	11	60	11	23	48
0.50		0.47		0.48		0.56		-		31	7	34	4	37	1	37	1	25	13
						+				19	43	37	25	51	11	50	12	21	41
0.56		0.56		0.52		0.47		0.56		-		44	5	47	3	47	3	33	17
										+		27	24	41	9	40	10	13	37
0.42		0.45		0.46		0.34		0.42		0.46		-		68	3	66	5	41	30
												+		21	8	21	8	5	24
0.24		0.26		0.20		0.16		0.28		0.18		0.39		-		82	6	44	44
														+		5	7	2	10
0.24		0.20		0.17		0.16		0.28		0.21		0.23		0.39		-		43	44
																+		3	10
0.42		0.43		0.44		0.48		0.41		0.51		0.46		0.22		0.08			

Allergens suitable for diagnostic screening of tree pollen allergy

Because of cross-allergenicity as well as simultaneous concomitant sensitization to several tree

pollens, only a few of the allergens should be necessary for diagnostic screening of tree pollen allergy (see Methods). If only birch pollen was used, 89% of the 785 patients with positive SPT to any of the 20 tree or bush pollen

Table 4

Correlations between RAST results with various pollens in 591 patients. The table is symmetrical. The upper right consists of 2 × 2 tables. The figures indicate percentages. The lower left gives the Spearman correlation coefficients (Rho). All correlations are statistically significant (*P* < 0.001) according to Pitman's test. In the statistical analyses RAST classes 0-4 were used

	Birch	Alder		Hazel		Beech		Oak		Sallow		Elm		Maple	
		-	+	-	+	-	+	-	+	-	+	-	+	-	+
Birch	-	27	4	29	3	29	3	23	9	22	10	23	9	26	6
	+	6	63	18	50	21	47	14	54	40	28	40	28	49	19
Alder	0.90		-	31	2	31	2	26	7	26	7	26	7	29	4
			+	15	52	18	49	12	55	37	30	38	29	46	21
Hazel	0.78		0.84		-	42	5	33	14	36	10	36	11	40	7
					+	7	46	4	49	27	27	28	25	35	18
Beech	0.75		0.80		0.86		-	34	15	38	11	38	11	43	7
							+	3	48	25	26	26	25	32	18
Oak	0.69		0.78		0.81		0.80		-	32	5	32	5	35	2
									+	31	32	32	31	40	23
Sallow	0.23		0.33		0.43		0.42		0.51		-	54	9	57	5
											+	10	27	18	20
Elm	0.19		0.27		0.38		0.39		0.47		0.70		-	58	6
													+	17	19
Maple	0.17		0.25		0.29		0.32		0.40		0.61		0.56		

- = RAST class 0; + = RAST class 1-4.

Table 5

Correlations between RAST results with various pollens in 189 patients with negative RAST to birch pollen. The table is symmetrical (for explanations see Table 4)

	Alder	Hazel		Beech		Oak		Sallow		Elm		Maple	
		-	+	-	+	-	+	-	+	-	+	-	+
Alder	-	83	3	81	4	69	16	66	20	69	17	76	10
	+	8	6	8	6	4	11	4	10	4	10	5	9
Hazel	0.61		-	86	4	72	19	67	23	71	20	78	12
			+	4	6	1	8	3	7	2	7	3	7
Beech	0.50		0.54		-	72	18	67	23	73	16	77	13
					+	1	9	3	7	4	7	4	6
Oak	0.56		0.49		0.52		-	62	11	64	9	68	5
							+	8	19	9	18	13	14
Sallow	0.59		0.43		0.35		0.66		-	62	8	65	5
									+	11	19	16	14
Elm	0.54		0.49		0.37		0.67		0.62		-	67	6
											+	14	13
Maple	0.55		0.49		0.45		0.61		0.57		0.59		

allergens used would be detected. The allergen giving most positive test results in the remaining 85 patients was elder. If elder and birch pollen were used, 95% of the tree pollen allergic patients could be detected. Table 7 shows that 99% of the patients with positive SPT to any tree pollen could be detected by screening with five allergens only.

Table 8 shows the corresponding findings when the RAST was used for screening 438 patients with positive RAST to any of the eight trees used in the RAST.

DISCUSSION

There are two principal methods of studying cross reactions among allergens: to perform *in vitro* inhibition studies on a limited number of individuals, or to study sensitization frequencies in relatively large numbers of patients and correlate the test results with each other. The first method will give a more accurate answer to the question: Do cross reactions occur or not? It is exceedingly difficult, however, to study large numbers of patients with these laborious methods, and even then the results will depend on the specific sensitization patterns of the patients studied.

Table 6

Correlation coefficients (Rho) for skin prick test results with the tree pollen combinations giving the highest Rho values in 141 patients with negative prick test to birch pollen allergen

Allergen combination		Correlation coefficient (Rho)
Alder	- sallow	0.67
	- privet	0.49
Oak	- aspen	0.47
	- plane	0.59
	- heather	0.44
Aspen	- plane	0.45
Elm	- maple	0.60
Ash	- privet	0.54
	- lime	0.48
Privet	- lime	0.46
	- juniper	0.58
Horse-chestnut	- plane	0.56
	- juniper	0.56
	- larch	0.52
Plane	- juniper	0.47

In the present study a great number of hay fever patients were tested with SPT and Phadebas RAST. Several tree pollen allergens were employed and cross-sensitization patterns were studied. Simultaneous sensitization to two different allergens can be due to true cross reactivity between these allergens or to both occurring together in the same region and coincidentally sensitizing the same individual. For this reason it is only possible to draw firm conclusions about cross reactions between two allergens when they occur in separate regions. Even when two allergens occur in the same region, however, a high level of the correlation coefficient suggests a high degree of cross allergy (12).

Sixteen clinics took part in the study. As far as RAST-results are concerned this does not imply any problems, as all the *in vitro* work was done at one centre and all determinations were performed simultaneously. Skin test results, however, will be influenced by variation in test technique among different investigators. For

Table 7

Allergens found most useful for the screening of tree pollen allergy when skin test was performed with 20 different tree pollen allergens in 785 patients

Chosen number	Allergen	Proportion (%) of patients detected	No. of patients left
1.	Birch	89	85
2.	Elder	95	49
3.	Heather	97	16
4.	Lime	98	5
5.	Hazel	99	4

For explanation of calculations, see Methods.

Table 8

Allergens found most useful for the screening of tree pollen allergy when RAST was performed with eight different tree pollen allergens on 438 patient sera

1.	Birch	85	65
2.	Oak	94	37
3.	Elm	97	13
4.	Sallow	98	7
5.	Maple	99	3

For explanation of calculations, see Methods.

this reason comparisons of skin test results between clinics is of limited value. Comparisons between different pollen allergens can, however, safely be done, as each test result is compared with another in the same individual.

In an earlier paper (11), we measured patient sensitization rates to 20 trees. We found that the rates were almost the same in southern as in northern Sweden, despite the fact that 12 of the trees studied do not grow in northern Sweden. These findings strongly indicate a high degree of cross-reactivity among tree pollens.

In the present study, we further analysed the sensitization of patients to a panel of tree pollens and compared all the different pollens two-by-two. We found strong (as measured by Rho) and statistically significant correlations in patient sensitization between the various tree pollens tested. Since several hundred significance tests were performed, the problem of mass significance must be considered. Of the 380 comparisons performed in Table 3, 379 showed a significant correlation with $P < 0.001$. A few of these could depend on the mass significance but most of them obviously should be regarded as truly significant. These findings give further support to the existence of common allergenic determinants among tree pollens.

The correlations found could result from the pollens being truly cross reactive or from being present together in a region and each sensitizing the patients studied. To exclude the latter possibility, a separate analysis was performed for patients from northern Sweden, where many of the trees tested are not found. Even in this group of patients statistically significant correlations were found for most of the tree pollens.

Our results do not agree with those of Kurata et al. (12) who, using SPT results with tree pollen, found Pearson's correlation coefficient ranging from 0.20 to 0.57. Their abstract does not state which tree pollen allergens were included in their test panel. The results of the present study, in which five botanical families (*Betulaceae*, *Fagaceae*, *Salicaceae*, *Oleaceae* and *Pinaceae*) were represented by two or more species, are in agreement with other earlier studies, indicating that cross reactions are most pro-

nounced between pollen from trees belonging to the same family (8, 18, 20).

Among the trees belonging to *Betulaceae* and the closely related family *Corylaceae* (birch, alder, and hazel) Rho reached very high values (0.8–0.9), which is consistent with a high degree of cross allergy. Van Dalen & Voorhort (8), using SPTs with three 10-fold dilutions of the allergen extracts, found correlation coefficients of the same magnitude. This strongly suggests true cross allergy, since with the same test method for two identical extracts they got a correlation coefficient of 0.74. Similar results have been reported by Dirksen & Østerballe (9). Furthermore, close antigenic relationships between *Betulaceae* pollens have been shown by Belin (2) using immunodiffusion and haemagglutination inhibition technique, by Löwenstein et al. (13, 14) employing crossed radioimmuno-electrophoresis technique and by Bessot et al. (4), using RAST inhibition technique.

We found a Rho correlation value of 0.8 for the correlation between beech and oak pollens, indicating a high degree of cross reaction within the *Fagaceae* family, corroborating the findings of Van Dalen & Voorhorst (8). Furthermore, in agreement with these authors (8), we got test results indicating a pronounced cross allergy between pollen from trees belonging to *Betulaceae* and those belonging to *Fagaceae*, i.e. among trees belonging to the order *Fagales*. *In vitro* studies, however, do not support this finding (4, 13).

Like Van Dalen & Voorhorst (8) we also found a high Rho value (0.7) for the correlation between trees belonging to *Salicaceae* (aspen and willow).

The family *Oleaceae* was represented in our study by privet and ash, and a relatively high Rho value (0.6) was found for their correlation. These results are in accordance with those of Bousquet et al. (5) who, through RAST inhibition experiments and iso-electric focusing, showed a high degree of similarity among pollens from four species belonging to the *Oleaceae* family (olive, ash, privet and Phillyrea).

Pollen from the *Pinaceae* family, represented in our study by larch and pine, gave very few positive SPTs. The coefficient for the corre-

lation between larch and pine pollen sensitization (0.4) was smaller than that for correlations within families discussed above, and smaller than Rho for their correlations with some deciduous trees. The correlation between larch and juniper pollen sensitization (both belonging to the order *Coniferales*) also showed a Rho value of 0.4. Cross reactivity between members of one family among the coniferous trees (*Cypressaceae*) have earlier been reported (21).

Besides the high degree of correlation found within botanical families, some high Rho values were also found between pollens from trees not belonging to the same family. Thus pollen from bog myrtle (belonging to *Myricaceae*) had Rho values of 0.6–0.7 for correlations with pollen from trees belonging to *Betulaceae* and *Fagaceae*. Pollen from elm (belonging to *Ulmaceae*) as well as ash (belonging to *Oleaceae*) showed a Rho value > 0.6 for correlations with pollen from trees belonging to *Salicaceae*. These findings indicate that cross reactions may exist between different families as well as within families.

Most of our patients were sensitized to birch pollen. Earlier studies have shown that birch pollen contains major allergens of some other trees (2, 14). Some of the cross sensitizations found in our study could be due to a concomitant birch pollen allergy. The results of correlation tests in patients without signs of birch pollen allergy (Tables 5, 6) indicate, however, that at least some cross reactions depend on allergens not related to birch pollen allergens.

The existence of cross reactions among tree pollens has implications for the choice of allergens in immunotherapy. One study indicates that a mixture of birch pollen, alder and hazel might give somewhat better results than treatment with birch pollen alone (15), although in another study treatment with birch pollen extract gave as efficient protection as the combined tree pollen extract (7).

CONCLUSIONS

Cross reactions are common among tree pollens and are most pronounced within botanical families (of which *Betulaceae*, *Fagaceae*, *Salicaceae*, *Oleaceae* and *Pinaceae* were studied in this investigation).

Birch pollen shares allergens with several other tree pollens, but cross reactions not dependent on birch allergen probably also exist.

Because of cross reaction as well as the dominance of birch pollen allergy in Sweden, birch pollen extracts are sufficient for allergy diagnosis in springtime hay fever in our country.

REFERENCES

1. Aas, K. & Belin, L.: Standardization of diagnostic work in allergy. *Acta Allergol.* 27, 439–468, 1972.
2. Belin, L.: Immunological analyses of birch pollen antigens with special reference to the allergenic components. *Int. Arch. Allergy Appl. Immunol.* 42, 300–322, 1972.
3. Bernstein, I. L., Perera, M., Gallagher, J., Michael, J. G. & Johansson, S. G. O.: *In vitro* cross allergenicity of major aeroallergenic pollens by the radioallergosorbent technique. *J. Allergy* 5, 363–373, 1975.
4. Bessot, J. C., Ott, W., Thierry, R. & Pauli, G.: Cross allergenicity of tree pollens (Fagales order) as determined by direct RAST and RAST inhibition. Abstract No. 237 in Abstracts from the XI International Congress of Allergology & Clinical Immunology, London, 1982.
5. Bousquet, J., Guerin, B., Hewitt, B., Lim, S. & Michel, F. B.: Allergy in the Mediterranean area. III: cross reactivity among *Oleaceae* pollens. *Clin. Allergy* 15, 439–448, 1985.
6. Bradly, J. V.: Distribution-free statistical tests. Prentice Hall, London, 1968.
7. Böwadt, H., Ipsen, H., Jannicke, H., et al.: A double blind hyposensitization study on tree pollen allergic patients treated with standardized pollen extracts from birch or with patient-tailored combinations of alder, birch and hazel. (Abstr.) XII International Congress of Allergology & Clinical Immunology, London, 1982: abstract 297.
8. van Dalen, G. & Voorhorst, R.: Allergen community in pollen from certain tree species. *Ann. Allergy* 46, 276–278, 1981.
9. Dirksen, A. & Østerballe, O.: Common components in pollen extracts. *Allergy* 35, 611–616, 1980.
10. Eriksson, N. E.: Allergy to pollen from different deciduous trees in Sweden. *Allergy* 33, 299–309, 1978.
11. Eriksson, N. E., Wihl, J.-Å., & Arrendal, H.: Tree pollen allergy. II. Sensitization to various tree pollen allergens in Sweden. A multi-centre study. *Allergy* 39, 610–617, 1984.
12. Kurata, J. H., Kaplan, M. & Glovsky, M. M.: Computer assisted study of the cross reactivity of pollen allergens. *Ann. Allergy* 38, 384, 1977.
13. Ipsen, H., Böwadt, H., Jannicke, H., et al.: Immunochemical characterization of reference alder (*Alnus glutinosa*) and hazel (*Corylus avellana*) pollen extracts and the partial immunochemical identity between the major allergens of alder, birch and hazel pollens. *Allergy* 40, 510–518, 1985.

14. Löwenstein, H.: Cross reactions among pollen antigens. *Allergy* 35, 198-200, 1980.
15. Möller, C. & Dreborg, S.: Cross-reactivity between deciduous trees during immunotherapy. I. In vivo results. *Clin. Allergy* 16, 135-143, 1986.
16. Rackelmann, F. M. & Wagner, H. C.: The desensitization of skin sites passively sensitized with serum of patients with hay fever. Crossed reactions of different pollens. The variations in the recipient. *J. Allergy* 4, 319-332, 1930.
17. Schatz, M.: An approach to diagnosis and treatment in the migrant allergic population. *J. Allergy* 59, 254-262, 1977.
18. Segal, A. T., Kemp, P. & Frick, O. L.: An immunologic study of tree pollen antigens (Abstr.). *J. Allergy* 45, 120, 1970.
19. Strandhede, S. O., Wihl, J.-Å. & Eriksson, N. E.: Tree pollen allergy. I. A botanical survey. *Allergy* 39, 602-609, 1984.
20. Weber, R., Nelson, H.: Pollen allergens and their interrelationships. *Clin. Rev. Allergy* 3, 291-318, 1985.
21. Yoo, T.-J., Spitz, E. & McGerity, J. L.: Conifer pollen allergy: Studies of immunogenicity and cross antigenicity of conifer pollens in rabbit and man. *Ann. Allergy* 3, 87-93, 1975.
22. Zetterström, O., Fagerberg, E. & Wide, L.: An investigation of pollen extracts from different deciduous trees in patients with springtime allergy in Sweden. *Acta Allergol.* 27, 15-21, 1972.
23. Østerballe, O., Dirksen, A., Weeke, B. & Weeke, E.: Cutaneous allergy in a Danish multicentre study. *Ugeskr. Laeger*, 143, 3211-3218, 1981.

Address:

Nils E. Eriksson

Dept. of Medicine

Länssjukhuset

S-30185 Halmstad

Sweden

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.