

Hay fever and predictive value of prick test and specific IgE antibodies: A prospective study in children

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Little is known from population-based studies in children about the diagnostic values of allergen-specific IgE antibodies (RAST) and skin prick test (SPT) with respect to hay fever. We aimed to determine and compare the diagnostic values of SPT and RAST to aeroallergens with respect to the incidence of hay fever cases in schoolchildren at different cut-off points. A prospective cohort study was performed on 1100 school children (5–7 and 8–10 years). Information on a doctor's diagnosis of hay fever was obtained by questionnaire and allergic sensitization to grass and birch pollen, cat, and *Dermatophagoides pteronyssinus* were measured using SPT and RAST between September 1992 and July 1993. Thirty-eight children give a history of hay fever (3.5%) in 1992/93 and additionally 37 cases occurred until 1996. Allergic sensitization was present in 17.9% (SPT), 30.2% (RAST) and more frequent in children with a history of hay fever (SPT: OR 11.7, 5.5–24.7; RAST: OR 10.6, 4.3–26.4). This difference was most pronounced for sensitization to pollen allergens. The sensitivity, specificity, positive and negative predictive values (PPV, NPV) for SPT and RAST were 65.6, 83.7, 11.9, 98.6 and 79.3, 71.6, 9.3, 99.0, respectively, with differences for specificity being significant ($p < 0.001$). Whereas NPV were equally high for SPT (99.2) and RAST (99.3), the incidence of hay fever cases were predicted rather poorly though somewhat better by SPT than by RAST (PPV 16.7 vs. 9.8; $p < 0.001$) initially. With increasing cut-off point for RAST reactivity, the PPV increased and reached 25.0 at 17.5 kU/l, whereas the NPV decreased to 97.9, which was lower than that of SPT reactivity ($p < 0.01$). At the cut-off point of 1.5 kU/l almost identical predictive values for SPT and RAST were obtained. SPT and RAST perform better in the negative than positive prediction of hay fever cases in epidemiological studies. Differences in the predictive capabilities depend on the chosen cut-off point for RAST reactivity.

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The determination of allergen-specific IgE antibodies in the serum and skin prick test (SPT) is commonly used to diagnose atopic and especially IgE-mediated allergic diseases. Both techniques have also frequently been applied in epidemiological studies to assess the frequency of allergic sensitization in the population. However, little is known from population-based studies in children about the diagnostic value of both tests with respect to hay fever. The predictive capabilities of

the test results have hardly been studied systematically and prospectively.

Population-based studies performed in adults indicated a good correlation of SPT reactivity to aeroallergens and allergic rhinitis (1, 2). These findings were independent from total IgE levels, but specific IgE antibodies were not determined. Another epidemiological study in a younger age group (6–24 years) revealed strong associations of reactivity to single aeroallergens in prick test

and hay fever. RAST results again were also not available in this study (3). In a large Swiss study in adults, the diagnostic values of prick test and specific IgE antibodies with respect to current allergic rhinitis were evaluated (4). Because Phadiatop was used in this study, direct comparisons on individual allergen level were not possible. As part of the European Community Respiratory Health Survey, 20- to 70-year-old Dutch subjects were prick tested and allergen-specific IgE antibodies were determined (5). Strong associations of prick test reactivity and allergen-specific IgE antibodies with symptoms of allergic rhinitis were established for most aeroallergens. However, conclusions on the predictive value regarding the incidence of hay fever cases could not be drawn from this cross-sectional study.

We aimed to determine and compare the diagnostic value of prick test and RAST with four common aeroallergens with respect to hay fever in schoolchildren. Furthermore, the predictive value of these tests regarding the incidence of hay fever cases was investigated in this prospective cohort study taking different cut-off levels for RAST reactivity into account.

Methods

Study design

We performed a prospective cohort study in three areas of Saxony-Anhalt (East Germany). Children of three age groups (5–7, 8–10, and 11–14 years) from all schools in Zerbst and Hettstedt were invited to participate. In the larger area of Bitterfeld, schools were chosen to represent each regional district. Parents gave written consent after they had received an informational letter. The examinations took place at schools and kindergartens. Between September 1992 and July 1993, a total of 2470 (response 89.1%) children were investigated. Of these, 1566 who were 5–7 years or 8–10 years old were defined as cohort children and studied 3 years later following the same protocol. Complete data of 1100 (response 70.2%) cohort children were available for both points of investigation. The study design and results regarding health effects and the body burden of pollutants have been published elsewhere in more detail (6–10).

Questionnaire

Standardized instruments were mailed to the parents together with the invitational letter and checked for completeness at the time of exam-

ination. Beside basic demographic data, we obtained information on a doctor's diagnosis of hay fever (lifetime prevalence), parental history of hay fever, social class (approximated by parental school education) and other relevant confounders. The questionnaire was sent out a second time after 3 years.

Allergen-specific IgE antibodies

During the first examination (September 1992 – July 1993), additional venous blood samples were drawn and allergen-specific IgE antibodies to four common aeroallergens (*Dermatophagoides pteronyssinus*, grass pollen, birch pollen, and cat) were determined using standard laboratory procedures (RAST-CAP-FEIA, Pharmacia, Uppsala, Sweden). All analyses were done by Pharmacia (Germany, Freiburg) with the same batches of allergen caps. Differences in the numbers of measurements for the single allergens occurred due to insufficient amount of sera in some cases. The detection limit for RAST reactivity was set at 0.35 kU/l and further cut-off points were chosen according to the limits of RAST classes (0.7, 3.5, 17.5, and additionally 1.5 kU/l).

Skin prick test

Also, at the start of the study standard lancet prick tests were performed on the volar aspects of the forearms of the children using the same four aeroallergens as for the serological test (Allergopharma, Reinbek, Germany). Histamine and saline were used as controls and results were read after 15 min. Tests were considered positive when the wheal diameter reached at least 3 mm. Tests showing wheals >2 mm to saline or <3 mm to histamine were repeated the following day and excluded from further analyses when these findings were confirmed.

Statistical analyses

Besides descriptive statistics, we report the validity (sensitivity, specificity, positive and negative predictive values) of SPT and RAST results with respect to a positive history of hay fever at study entrance. The predictive values of both tests were also calculated with respect to children who developed hay fever between 1992/3 and 1995/6. Furthermore, the predictive values were calculated for different cut-off points of RAST reactivity. To compare SPT and RAST with respect to sensitivity and specificity we used a test proposed by Leisenring et al. (11). This is a generalization

of the McNemar test, which allows children with incomplete test results to be included (only one of two test results available). For the comparison of predictive values the score test proposed by Leisenring et al. in 2000 was applied (12). Statistical analyses were done using the software packages SPSS 10.0 (SPSS Inc, Chicago, IL, USA), EpiInfo 6.0 (Epi Info, Centers for Disease Control and Prevention Atlanta, Atlanta, GA, USA) and SAS (SAS Institute Inc, Cary, NC, USA) (1, 8) for the PROC GENMOD procedure.

Results

A total of 1100 children were investigated in 1992/93 (49% 5–7 years; 51% 8–10 years) and after a 3-year period. A history of a doctor's diagnosis of hay fever was obtained in 3.5% of the children (38/1100) in 1992/93. Three years later 37 new cases of hay fever were observed of which 22 were boys. These incident cases occurred equally in both age groups (5–7 years in 1992/93: $n = 18$; 8–10 years in 1992/93: $n = 19$). The demographic characteristics as well as the prevalence of possible confounders in the different study populations are given in Table 1. Children with a positive history of hay fever in 1992/93 were significantly older and had better educated parents than children who were not diagnosed with hay fever. A parental history of hay fever was significantly more frequent in

children with a present history as well as in those who developed hay fever during the following 3-year study. Smoking during pregnancy was avoided more often in children who had or developed hay fever. This might indicate differential preventive behavior in a high-risk group.

The number of performed tests and prevalence of allergic sensitization to the four aeroallergens tested by SPT and RAST are displayed for each study month in Table 2. Although some seasonality for the reactivity to single allergens was observed, only the peak of reactions to birch pollen during June and July as measured by SPT reached statistical significance. The pattern of reactions in SPT or RAST did not differ between children with and without a positive history of hay fever in 1992/93. The affected children also exhibited a significant effect of the season for birch pollen reactivity in SPT (data not shown). Data on the prevalence of SPT and RAST reactivity for the total group, those with a current history of hay fever, and those who developed hay fever within the following 3 years are shown in Table 3. In the total group, the prevalence of allergic sensitization as obtained by RAST was almost twice as high as that obtained by SPT. Children with a positive history of hay fever were sensitized significantly more often than those without such a history. Taking all allergens together this association was equally strong for SPT and RAST. Children with hay fever showed

Table 1. Basis characteristics of the study populations (%)

	Total $n = 1100^*$	Negative history of hay fever in 1992/3 and 1995/96 $n = 1018$	Positive history of hay fever in 1992/93 $n = 38$	Incidence of hay fever between 1992/3 and 1995/6 $n = 37$
Gender (female)	49.5	50.5	36.8	40.5
Age (years)				
5–7	48.9	49.4	28.9	48.6
8–10	51.1	50.6	71.1 ^{†a}	51.4
Parental school education				
≤10 years	53.8	54.4	35.1	54.1
>10 years	46.2	45.6	64.9 ^b	45.9
Parental history of hay fever	10.4	9.1	29.7 ^c	27.0 ^d
Pet keeping	64.5	64.5	64.9	62.2
Single child	22.2	22.5	12.5	30.3
Smoking				
during pregnancy	5.5	5.6	2.7	0 ^e
after birth	54.2	54.8	39.5	54.1
Traffic density (≥10 cars/day)	50.4	50.6	44.7	48.6

*Information on hay fever incomplete in $n = 7$.

†Denotes associations with a group of children with negative hay fever history in 1992/3 and 1995/6.

OR 95% CI

^a2.40 (1.18–4.89)

^b2.20 (1.11–4.37)

^c4.20 (2.01–8.79)

^d3.68 (1.73–7.85)

^e0.96 (0.95–0.97)

Table 2. Number of performed skin and serological tests and prevalence (%) of positive reactions by study month

	Jan 1993	Feb 1993	Mar 1993	Apr 1993	May 1993	Jun 1993	Jul 1993	Sep 1992	Oct 1992	Nov 1992	Dec 1992	tot	p
Prick (n)	68	83	128	90	41	90	15	135	106	30	89	875	
Grass	5.9	14.5	10.2	11.1	17.1	11.1	20.0	8.9	11.3	10.0	13.6	11.3	NS
Birch	2.9	8.4	4.7	3.3	4.9	10.0	20.0	0.7	5.7	3.3	7.9	5.0	0.026
<i>D. pter.</i>	7.4	7.2	7.0	6.7	9.8	3.3	0	5.9	9.4	16.7	4.5	6.5	NS
Cat	5.9	2.4	2.3	3.3	0	2.2	6.7	3.7	6.6	10.0	4.5	3.4	NS
Any	14.7	20.5	17.2	16.7	26.8	17.8	33.3	12.6	20.8	23.3	21.6	17.9	NS
RAST (n)	68	69	115	81	20	74	11	107	98	28	84	755	
Grass	16.2	19.8	24.4	19.1	27.6	24.4	23.1	17.9	24.3	32.3	32.2	22.7	NS
Birch	14.7	10.3	11.6	6.3	0	12.9	14.3	5.8	6.2	4.3	18.1	10.3	NS
<i>D. pter.</i>	16.2	16.0	10.9	16.7	19.4	9.9	28.6	11.3	20.4	23.3	10.3	13.9	NS
Cat	7.4	3.8	7.2	11.5	12.5	4.5	14.3	7.4	11.1	10.0	9.2	7.6	NS
Any	29.4	31.9	30.4	32.1	55.0	31.1	54.5	28.0	37.8	50.0	38.1	30.2	NS

Table 3. Prevalence of allergic sensitization to four aeroallergens in SPT and RAST in different groups characterized by disease status total

	Total n = 1100*		Negative history of hay fever in 1992/93 and in 1995/96 n = 1018		Positive history of hay fever in 1992/93 n = 38		The incidence of hay fever between 1992/93 and 1995/96 n = 37	
	SPT	RAST	SPT	RAST	SPT	RAST	SPT	RAST
Grass	11.3	22.7	7.8	19.2	59.4 ^{†ap}	75.8 ^{ar}	65.6 ^{fp}	65.6 ^{fr}
	112/993	216/953	72/923	169/882	19/32	25/33	21/32	21/32
Birch	5.0	10.3	4.2	8.1	18.8 ^{bp}	51.7 ^{br}	15.6 ^{gp}	30.8 ^{gr}
	50/993	85/824	39/923	62/765	6/32	15/29	5/32	8/26
<i>D. pter.</i>	6.5	13.9	6.1	12.3	6.3 ^{cp}	29.4 ^{cr}	21.9 ^{hp}	43.8 ^{hr}
	65/993	135/972	56/923	111/900	2/32	10/34	7/32	14/32
Cat	3.4	7.6	3.0	6.4	3.1 ^{dp}	27.3 ^{dr}	12.5 ^{ip}	18.8 ^{ir}
	34/993	72/952	28/923	56/881	1/32	9/33	4/32	6/32
Any	17.9	30.2***	14.1	26.5	65.6 ^{ep}	79.3 ^{er}	81.3 ^{kp}	84.6 ^{kr}
	178/993	249/824	130/923	203/765	21/32	23/29	26/32	22/26

*** (vs. SPT) $p < 0.001$.

*Information on hay fever incomplete in $n = 7$.

†Denotes associations with a group of children with negative hay fever history in 1992/3 and 1995/6 of children with:

Positive history of hay fever in 1992/93 Incidence of hay fever between 1992/93 and 1995/96

OR 95% CI	OR 95% CI
^{ap} 17.3 (8.2–36.4)	^{fp} 22.6 (10.5–48.6)
^{ar} 13.2 (5.8–29.7)	^{fr} 8.1 (3.8–17.0)
^{bp} 5.2 (2.0–13.4)	^{gp} 4.2 (1.5–11.5)
^{br} 12.1 (5.6–26.3)	^{gr} 5.0 (2.1–12.1)
^{cp} 1.0 (0.2–4.4)	^{hp} 4.3 (1.8–10.5)
^{cr} 3.0 (1.4–6.4)	^{hr} 5.5 (2.7–11.4)
^{dp} 1.0 (0.1–7.8)	^{ip} 4.6 (1.5–13.9)
^{dr} 5.5 (2.5–12.5)	^{ir} 3.4 (1.3–8.6)
^{ep} 11.7 (5.5–24.7)	^{kp} 26.4 (10.7–65.5)
^{er} 10.6 (4.3–26.4)	^{kr} 15.2 (5.2–44.7)

significantly more often detectable specific IgE antibodies to all four allergens with differences being most pronounced for pollen allergens. In the skin prick test only sensitization to pollen allergens were found to be significantly higher in children with a history of hay fever, but for grass pollen the association was stronger than that for RAST. In general, children who had a negative history of hay fever at the time of investigation, but developed allergic rhino-conjunctivitis later on, showed a even higher frequency of sensitization than those who already had developed hay

fever. This difference was most pronounced for SPT results and true for all allergens but birch pollen. For RAST measurements these differences were true only for HDM and the overall reactivity. When comparing the sensitization of children with incident of hay fever to those with a persistent negative history, a significantly elevated prevalence of sensitization to all allergens measured by either SPT or RAST was obtained. The overall association was stronger for the SPT, which was mainly a consequence of differences in grass pollen reactivity.

Table 4. Validity of SPT and RAST with respect to a positive history of hay fever at the time of investigation (cross-sectional data analyses)

	Sensitivity		Specificity		PPV		NPV	
	SPT	RAST	SPT	RAST	SPT	RAST	SPT	RAST
Grass	59.4*	75.8	90.3***	79.2	17.0*	11.6	98.5	98.9
	19/32	25/33	862/955	724/914	19/112	25/215	862/875	724/732
Birch	18.8**	51.7	95.4***	91.2	12.0	17.7	97.2	98.1
	6/32	15/29	911/955	721/791	6/50	15/85	911/937	721/735
<i>D. pter.</i>	6.3**	29.4	93.4***	86.6	3.1	7.4	96.7	97.1
	2/32	10/34	892/955	807/932	2/65	10/135	892/922	807/831
Cat	3.1**	27.3	96.6***	93.2	3.0*	12.7	96.8	97.3
	1/32	9/33	923/955	851/913	1/33	9/71	923/954	851/875
Any	65.6	79.3	83.7***	71.6	11.9	9.3	98.6	99.0
	21/32	23/29	799/955	566/791	21/177	23/248	799/810	566/572

Denotes differences between SPT and RAST *p < 0.05, **p < 0.01, ***p < 0.001.

Table 5. Predictive values of SPT and RAST with respect to the incidence of hay fever cases (cohort data analyses)

	PPV		NPV	
	SPT	RAST	SPT	RAST
Grass	22.6***	11.1	98.7	98.5
	21/93	21/190	851/862	713/724
Birch	11.4	11.4	97.0	97.5
	5/44	8/70	884/911	703/721
<i>D. pter.</i>	11.1	11.2	97.2	97.8
	7/63	14/125	867/892	789/807
Cat	12.5	9.7	97.0	97.0
	4/32	6/62	895/923	825/851
Any	16.7***	9.8	99.2	99.3
	26/156	22/225	793/799	562/566

***Denotes differences of PPV (SPT vs. RAST) p < 0.001.

Table 6. Predictive values of SPT and RAST with respect to the incidence of hay fever cases (cohort data analyses) for different cut points of RAST reactivity

	PPV	NPV
SPT (any)	16.7	99.2
	26/156	793/799
RAST (any)		
Cut-off point (kU/l)		
0.35	9.8***	99.3
	22/225	562/566
0.7	13.0	99.4
	22/169	618/622
1.5	16.0	99.1
	20/125	660/666
3.5	20.2	98.7
	17/84	698/707
17.5	25.0	97.9**
	(10/40)	(735/751)

Denotes differences of PPV or NPV (RAST vs. SPT) **p < 0.01, ***p < 0.001.

The validity with respect to a positive history of hay fever at the time of investigation for both diagnostic tests is given in Table 4. As indicated by the differences in the prevalence of positive findings, RAST compared with SPT showed in general a higher sensitivity, which was significant for all allergens and a lower specificity, which was also significant for all allergens and overall. Both tests had an equally high negative predictive value and overall the positive predictive value was low and slightly higher for the SPT, which was mainly the result of a significantly better prediction by grass pollen sensitivity.

The prognostic capabilities of both tests were evaluated by calculating the prognostic values taking the test results of 1992/93 into account. On the basis of all children with a negative history of hay fever in 1992/93, we compared those whose history remained negative to those

who developed hay fever within the observation period of 3 years. Details are given in Table 5. In summary, the negative predictive value is very high for both tests and all allergens. The positive predictive value again is rather low and higher for the SPT than for RAST. This was true for all allergens but house dust mite (HDM) and significant for grass pollen and the overall reactivity.

We further analyzed how far the PPV and NPV changed with increasing cut-off points for overall RAST reactivity. The data are given in Table 6. It became clear that the predictive values of RAST reactivity depend highly on the chosen cut-off point. With increasing cut-off point the PPV increases constantly from 9.8 to 25.0, thereby exceeding the PPV for SPT reactivity. Simultaneously the NPV for RAST reactivity dropped from 99.3 to 97.9, which is

significantly lower than the NPV of SPT reactivity. When choosing a cut-off point around 1.5 kU/l for RAST reactivity, almost identical results for PPV and NPV of RAST and SPT were achieved.

The prevalence-derived probabilities of overall SPT and RAST reactivity together with the corresponding hay fever histories in 1992/93 and 1995/96 are displayed in Figs 1 and 2. These figures allow us to estimate conditional probabilities under different assumptions, e.g. the probability of having a positive hay fever history in 1995/96 while having a negative history 3 years before is in the group of children with positive RAST $p = 0.907 \times 0.098 = 0.089$. The corresponding probability for SPT-positive children would be $p = 0.881 \times 0.167 = 0.147$, indicating a better positive prognostic value of SPT.

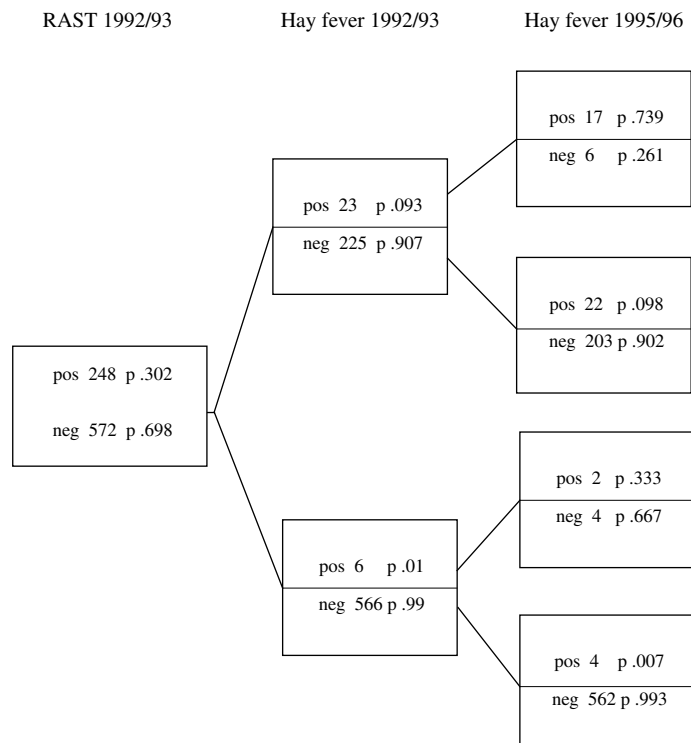
Discussion

In this epidemiological study, we have demonstrated that both SPT reactivity and RAST are highly associated with a history of hay fever and that this association is most pronounced for pollen allergens. According to these results, SPT had a significantly higher specificity compared with RAST, whereas the serological test was more sensitive with respect to a positive history of hay fever. Concerning the prediction of future hay fever cases, SPT showed a significantly

higher, although rather low positive predictive value than RAST and for both tests an equally high negative predictive value was determined. The population-based and prospective setting and the possibility to directly compare two diagnostic procedures on the level of individual allergens may account as strengths of this study. The rather high response will allow the results to be generalized to a broader children population.

Of the study group, 3.5% initially gave a positive history of a doctor's diagnosis of hay fever, which is rather low compared with other epidemiological studies. According to the ISAAC protocol, the lifetime prevalence of reported symptoms of allergic rhinitis were 14.9% and 36.5% for 6–7 and 13–14 years olds in West and 11.8% and 38.0% in East Germany (13). However, when compared with studies, which also estimated the frequency of a doctor's diagnosis of hay fever in East German children at the time our study was performed, similar results were obtained. A doctor's diagnosis of hay fever was found to be as low as 2.4% in 9- to 11-year-old school children in Leipzig (14) and 1.4% in 5- to 6-year-old preschool children in Halle a.d. Saale in 1991 (15). We decided to analyze the data on the basis of a doctor's diagnosis of hay fever in order to enhance the specificity of our outcome measure. Thereby cases, which were not seen by a doctor, may have been missed, which would affect a valid population-based frequency

Fig. 1. Probability tree of RAST reactivity in 1992/93 and history of hay fever in 1992/93 and 1995/96 (pos/neg: number of children being positive or negative to the characteristic of the column heading; p: probability with respect to the absolute numbers).



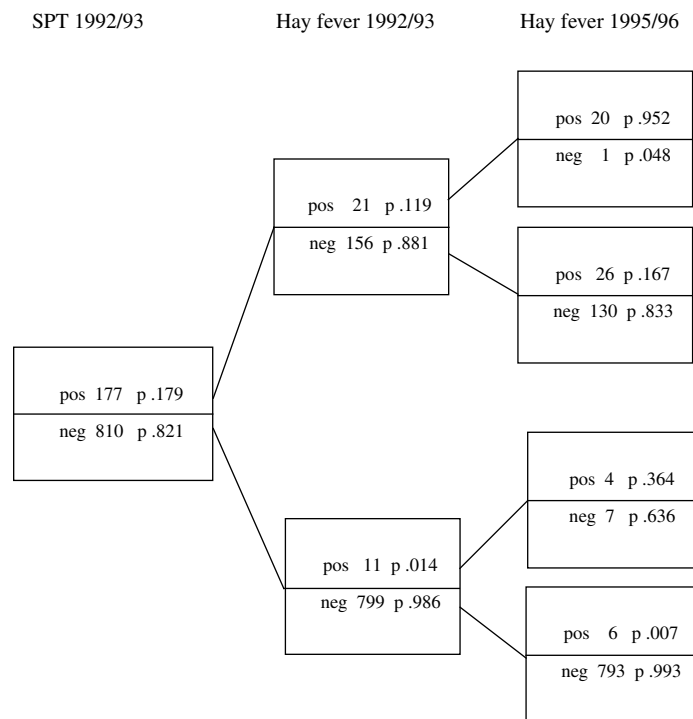


Fig. 2. Probability tree of SPT reactivity in 1992/93 and history of hay fever in 1992/93 and 1995/96 (pos/neg: number of children being positive or negative to the characteristic of the column heading; p: probability with respect to the absolute numbers).

estimate. This, however, was not the primary purpose of this analysis. On the other hand, a low frequency may decrease statistical power. This must be discussed, although we were able to prove most important absolute differences as being statistically significant. Furthermore, differential selection must be discussed, if severe cases and that implies cases with a higher percentage of allergic sensitization, tend to be diagnosed by a doctor more frequently. Selection bias, leading to false associations by participation differential for both disease and sensitization cannot be ruled out completely. However, it seems unlikely that this happened differentially for both diagnostic tests. It can be argued that a symptom-oriented outcome would have been an outcome with better predictive capability. We obtained data on two corresponding symptoms of the past 12 months: sneezing attacks and an itchy and runny nose without having a cold. In order to respond to this argument, we performed the following analysis without showing these data in the result section of the paper. The specificity and NPV remained basically unchanged for all allergens tested by either method whether taking a doctor's diagnosis of hay fever or reporting both symptoms as endpoints. The PPV increased for perennial allergens in SPT (e.g. HDM: 3.1–7.7) but not in RAST (e.g. HDM: 7.4–6.7). For seasonal aeroallergens, a decrease of the PPV was observed in SPT (e.g. grass pollen 17.0–7.9) and RAST (e.g. grass

pollen 11.6–5.1). We therefore believe that taking the doctor's diagnosis, as an endpoint did not lead to a substantial loss of validity information.

Seasonality may have influenced the results. We therefore described the reactivity to all allergens in SPT and RAST for each study month in the overall group and the children with a positive history of hay fever in 1992/93. Only the reactivity to birch pollen in SPT revealed a significant influence of the season, with distributions not being different between groups. We therefore conclude that seasonality has an effect in general but no strong differential effect, which may have influenced the validity data.

There is an argument that the predictive capacity of the diagnostic tests depends on the family history. This is certainly true and might also be true for other factors, which are known to be associated with the outcome (e.g. SES, family size). In this context one would ask, what the sequence of diagnostic tests should be and which tests should be included. This, however, is beyond the scope of this study. We have analyzed the capacity of the tests to predict a history of hay fever in 1992/93 separately for children with and without a positive parental history of hay fever. As expected PPV increases almost uniformly in the group of predisposed children (data not shown). The number of predisposed and affected children, however, is quite low ($n = 10$) and does not allow for more detailed and reliable analyses.

Whether the prevalence of hay fever and allergic sensitization has increased in East German children is still discussed controversially. No significantly different time trend for a doctor's diagnosis of hay fever was reported for 5- to 8-year-old school children from several locations in East and West Germany between 1991 and 1995 (16). In contrast, von Mutius et al. reported a significant increase in a doctor's diagnosis of hay fever and allergic sensitization measured by SPT in 9- to 11-year-old school children from the City of Leipzig between 1991/92 and 95/96 (17). Heinrich and colleagues found no change in a doctor's diagnosis of hay fever prevalence and allergic sensitization as measured by RAST in 5- to 7-year-old school children in rural areas of East Germany between 1992/93 and 1995/96 (18). It remains to be clarified whether the observed differences in time trends of allergic sensitization are due to incomparable study designs or differences in the assessment of allergic sensitization.

There are hardly any epidemiological studies of hay fever in children, which compare the diagnostic value of SPT and RAST on an individual allergen level. Chinn et al. (19) reported high associations of allergen-specific IgE antibodies to cat, HDM, and grass pollen with bronchial responsiveness in adults. Similarly a strong association of inhalant-specific IgE and upper-airway allergy (RR = 5.0) was seen in high-risk children (20). Significant associations of SPT reactivity to common aeroallergens, but not total IgE and hay fever were reported from two US studies in adults (1, 2).

The National Health and Nutrition Examination Survey compared SPT reactivity with aeroallergens with reported symptoms or a doctor's diagnosis of hay fever in 4295 US Americans (6–24 year olds) (3). After adjustment for age, sex, smoking, region, and other allergen reactivity, sensitization to ryegrass (OR = 2.8) and house dust (OR = 2.5) appeared to be significantly associated with hay fever, whereas sensitization to cat (OR = 1.0) revealed no significant result. In our study, SPT reactivity only to seasonal allergens was significantly associated with hay fever. We did not report adjusted odds ratios, because age, gender, and location showed no significant influence in logistic regression models of SPT and RAST reactivity and did not affect the magnitude of the effect estimates for sensitization or its significance.

In a cross-sectional Swiss study (Swiss Study on Air Pollution and Lung Disease in Adults) in adults, (18–60 year olds) current self-reported hay fever or related symptoms were methodo-

logically compared with overall SPT (comprising cat, dog, *D. pter.*, grass, birch, parietaria, alternaria, cladosporium) or RAST (Phadiatop: pollen, HDM, molds, mammals) reactivity (4). With respect to current allergic rhinitis the sensitivity, specificity, PPV, and NPV for SPT and Phadiatop were found to be 68.4, 85.9, 48.7, 93.3 and 77.1, 80.5, 43.5, and 94.7, respectively. With the caveat that in the Swiss study adults were examined and 16.3% were identified with current allergic rhinitis as opposed to 3.5% with doctor's diagnosed hay fever in our study, the PPV were found to be higher. The results for sensitivity, specificity, and NPV accord well with our findings and underline that SPT has a higher specificity than RAST whereas the sensitivity of RAST is higher compared with that of SPT. The latter is in accordance with the higher overall prevalence of positive RAST findings whereas the higher specificity of SPT agrees with the lower prevalence of positive findings there. One might also speculate in how far the methodological differences of the tests in detecting IgE-mediated allergic sensitization (free floating vs. cell-bound IgE) contribute to differences in test validity.

In another cross-sectional Dutch study as part of the European Community Respiratory Health Survey, 2167 adults (20–70 year olds) were tested by SPT and RAST with a set of allergens comparable to that in our study. According to the ECHRS protocol, symptoms of allergic rhinitis were recorded with respect to exposure to perennial or seasonal allergens or both. In the group of subjects with nasal symptoms to seasonal allergens, significant associations with SPT reactivity were observed after control for age, gender, location, and smoking status with grass pollen (OR 6.6), birch pollen (OR 4.1), and cat (OR 4.2), whereas HDM was not significantly associated (OR 0.7). With the exception of cat allergen this result pattern is comparable to our study. In the same study, allergen-specific IgE levels (cut point 0.7 kU/l) to all allergens which were also used in our study were significantly associated with hay fever symptoms: birch pollen (OR 4.0), grass pollen (OR 3.8), cat (OR 7.8), and HDM (OR 2.9). Similarly, in our study significant association of RAST reactivity and hay fever were observed with all four allergens. Whereas the strength of association with cat and HDM was comparable to that of the Dutch study, we observed a much stronger association with reactivity to pollen allergen. This might indicate that the outcome assessment by a doctor's diagnosis of hay fever leads to a more precise identification of cases.

Little is known about the diagnostic value of SPT and RAST with respect to the identification of future hay fever cases. We could show that both techniques have an equally high NPV, but positive prediction is quite low although better for SPT than RAST. That was true for all aeroallergens and significant for grass pollen. Data from a German birth cohort study indicates that persistent sensitization to food allergens, especially hen's egg, is a good predictor for later sensitization to aeroallergens and allergic airway disease (21). A recent study from Denmark (22) investigated the association of sensitization in SPT and an IgE screening test (Magic Lite SQ, ALK-Abelló A/S, Hørsholm, Denmark) with respect to hay fever cases, which occurred during a 6-year follow-up in a population of 7- to 17-year-old subjects. The authors reported a significant association between the SPT sensitization to grass (RR = 2.6) and HDM (RR = 2.7) or a positive IgE screening test (RR = 2.4) and the development of hay fever. The associations with sensitization to cat (RR = 1.0) and birch (RR = 1.1) were not significant. Beside crude parameters of association, no further data on test validity were given. The associations between sensitization and the incidence of hay fever in our study were all significant and much higher (SPT: grass OR = 22.6, birch OR = 4.2, cat OR = 4.6, HDM OR = 4.3; any RAST: OR = 15.2). This might in part be explained by different outcome assessments. Whereas the Danish study recorded nasal symptoms, we obtained data on a doctor's diagnosis of hay fever.

Methodological studies in patients with inhalative allergies demonstrated that the results of SPT and RAST are not interchangeable (23). It was shown that the validity and predictive capability of RAST depend on the chosen cut-off level. According to a study in symptomatic patients, the optimal cut-off level to discriminate sensitized patients without symptoms was determined to be 11.7 kU/l (24). Similar studies were performed with regard to SPT reactivity (25). We primarily categorized RAST reactivity according to the detection level of 0.35 kU/l. With increasing cut-off points, however, a consistently increasing PPV of RAST reactivity and a corresponding slight decrease of NPV was observed. With a cut-off point of 1.5 kU/l the predictive capabilities of SPT and RAST had equalized, indicating a comparable performance of both tests.

We conclude that both SPT and RAST are valid techniques to identify or exclude current hay fever cases in epidemiological studies. Thereby SPT and especially reactivity to pollen aller-

gens have a better specificity as compared with RAST. SPT and RAST perform better in the negative than positive prediction of hay fever cases. The capability in predicting hay fever cases depends highly on the chosen cut-off point for RAST reactivity and is similar for both tests with a cut-off point of 1.5 kU/l.

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