

Month of birth and allergic disease at the age of 10*

M. WJST†, S. DOLD‡, P. REITMEIR§, E. STIEPEL§ and E. VON MUTIUS†

†*von Haunersche Kinderklinik, Ludwig-Maximilians-Universität, München, Munich, Germany*, ‡*Institut für Umwelthygiene und Toxikologie, Munich, Germany* and §*GSF Forschungszentrum für Umwelt und Gesundheit, MEDIS, Neuherberg, Germany*

Summary

The relationship between month of birth and asthma, hay fever and skin sensitization to mixed grass pollen was analysed in a population-based cross-sectional study in Munich and Bavaria 1989–1990 of 6535 10-year-old children. The relative risk of developing atopic disease is calculated by comparing the prevalence in a single month with the prevalence of all other months. A slightly increased risk of developing allergic skin sensitization for grass pollen ($n=1128$) was found for February (odds ratio, 1.3, 95% confidence interval 1.0–1.6), May (1.4, 1.1–1.8) and June (1.3, 1.0–1.6). For hay fever ($n=379$) an increase was found for May (1.5, 1.0–2.1) and for allergic asthma ($n=277$) for August (1.4, 1.0–2.1). A protective effect was observed for certain months of birth; September for allergic sensitization (0.8, 0.6–1.0), October for asthma (0.6, 0.3–1.0) and November for hay fever (0.6, 0.3–0.9). The occurrence of hay fever and positive prick test is explained by the seasonal variation of atmospheric grass pollen and the peak in August of asthmatic patients by house dust. Date of birth appears therefore to slightly influence the risk of developing an allergic sensitization and allergic diseases.

Clinical and Experimental Allergy, Vol. 22, pp. 1026–1031. Submitted 11 March 1992; revised 29 May 1992; accepted 5 June 1992.

Introduction

During the last decade increasing attention has been paid to the incidence of atopic diseases which are now a widespread problem in child health [1]. The cellular mechanism of allergization has recently been described [2] but less is known about the *in vivo* process of allergic sensitization [3]. The occurrence of allergies is predominantly genetically determined [4]. Poor concordance in the development of allergic symptoms in twin studies, and the changing incidence of allergic diseases in immigrant populations illustrate that environmental factors are also of importance [5].

It has been suggested that the first few months of life constitute a sensitive period during which exposure to certain allergens may create a predisposition to the subsequent development of atopic disease [6]. As many

allergies show a seasonal variation, a relationship between the month of birth and the subsequent development of atopic disease might then be expected. Since there are only data of case studies available, we analysed the relationship between the month of birth of 6535 children and different atopic diseases in a population-based study.

Methods

The data reported in this paper were collected as part of the Munich Asthma and Allergy Survey from October 1989 to July 1990. The major objective of the study was to determine the prevalence of allergic and asthmatic diseases in children [7]. The survey comprised 9403 school children aged 9 to 11 years, including all fourth-grade children in 118 primary schools in Munich and 65 schools in Southern Bavaria. The schools in the rural districts were selected for lower air pollution. Questionnaires were sent home from the school with children, answered by their parents, returned to school, and collected by the investigators. The response rate was 87% (8204/9403) for questionnaires and 76% (7192/9403) for prick tests. Children of parents who did not answer the questionnaire did not differ significantly to the study population. This

Correspondence: Dr M. Wjst, von Haunersche Kinderklinik, Ludwig-Maximilians-Universität München, Lindwurmstrasse 4, W-8000 München 2, Germany.

* The Munich Survey on Asthma and Allergy was supported by the 'Bayerische Staatsministerium für Landesentwicklung und Umweltfragen' and carried out in cooperation with the 'Gesundheitsamt der Stadt München'.

was an informed consent study approved by the ethic commission of the 'Bayerischen Landesärztekammer'.

Current and previous allergic diseases of the child and its relatives together with the date of birth were evaluated using a total of 58 questions. The information given by the parents saying that a physician had diagnosed asthma and that at least two episodes of wheezy bronchitis had occurred, was regarded as asthma. In the case of allergic ('extrinsic') asthma a seasonal variation of symptoms should also be present. Allergic rhinitis was assumed for a diagnosis of hay fever, if seasonal eye or nose symptoms were present and no asthma was diagnosed. A positive skin test was concluded if the mean diameter of skin reaction on the right forearm was at least 3 mm, 20 min after the application of a commercially available multitest applicator system containing six common allergens (Stallergenes, Lyon). Tested allergens were mixed grass pollen, hazel, birch, *D. pteronyssinus* allergen, cat and dog dander.

All the children with missing data (408) were excluded from analysis. Because of birth places outside Germany and possible language difficulties, only the 6535 German children were considered for evaluation: 4910 of these (75.1%) had not moved home since birth.

The child's sex, place of residence (Munich/Southern Bavaria), birth weight, parents' education, the number of cigarettes smoked at home, and the person who filled in the questionnaire were analysed as possible confounding variables.

Data were analysed in a case control design. The control subjects should have had neither a positive skin test, nor allergic nor asthmatic diagnoses or symptoms. The risk of developing allergic disease is given as an odds ratio (OR) with the corresponding 95% confidence interval of the analysed month to all the other months [9]. Frequencies are compared by cross-tabulation and compared for statistical significance with the chi-square test. All analyses were carried out with SAS.

Results

Table 1 shows the general characteristics of the allergic asthma group (277, 4.2% of the total population), the children with allergic rhinitis (379, 5.8%) and allergic skin reaction to grass pollen (1128, 17.3%) and the controls (2352, 36.0%). One-hundred-and-thirty-nine children (2.1%) were born before 1979, 3184 in 1979 (48.7%), 3210 in 1980 (49.1%) and two in 1981. Significant differences to control subjects measured by χ^2 -statistical test were observed for sex, place of residence, family history of atopy and education of child's father. After calculation of stratum specific ORs substantial confounding however could be excluded.

There is significant influence of the month of birth to allergic skin sensitization (d.f. = 11, $\chi^2 = 21.5$, $P = 0.029$) but not to asthma (d.f. = 11, $\chi^2 = 9.9$, $P = 0.542$) nor hay fever (d.f. = 11, $\chi^2 = 14.4$, $P = 0.205$). Table 2 shows the crude ORs of a single month compared to all the other months. Significant increased ORs were noted for allergic asthma in August (OR 1.4, 95%-CI 1.0–2.1), for allergic rhinitis in May (1.5, 1.0–2.1) and positive prick test in February (1.3, 1.0–1.6), May (1.4, 1.1–1.8) and June (1.3, 1.0–1.6). A protective effect was observed for certain months of birth; September for allergic sensitization of grass pollen (0.8, 0.6–1.0), October for asthma (0.6, 0.3–1.0) and November for hay fever (0.6, 0.3–0.9).

The analysis of different subgroups revealed the same results, especially in the high risk group as defined by a familial history of asthma or allergies. The age of onset was not influenced by the month of birth, and neither did breast feeding alter the results.

For hazel pollen sensitization, elevated risks were observed in February (1.4, 1.1–1.9); this is in keeping with the February peak of grass pollen sensitization by multiple sensitization. For the house dust antigen *D. pteronyssinus* the sensitive months were August (1.6, 1.1–2.3) and September (1.6, 1.1–2.4) thus also showing a seasonal pattern.

Discussion

The results show that allergic sensitization and allergic diseases are associated with the date of birth. This effect is in keeping with previous studies (Table 3). Differences may be due to varying causes, such as study design and selection of cases and control subjects. Most of them are case studies with the general population as control group. The case control or cross-sectional studies should be of more value, since the distribution of allergic diseases in the general population is not known.

The geographic conditions also present differences between studies. Most of the studies are from Europe, the remainder from Australia [14] and the U.S.A. [15,20]. The number of cases ranges from 58 [21] to 7796 [18] and the length of the survey from birth [21] to 38 years [10]. Therefore, an exact comparison of prevalence and relative risks is not possible.

Three out of four studies reveal an effect of birth month on asthma [6,9,17], three out of six on hay fever [5,13,18] and 12 out of 13 an effect on skin sensitization [1,5,10–14,16,17,19,21,23]. Maximal relative risks are comparable to the results presented here. The ORs of the greatest effect for asthma recalculated by published data are 1.2 [6], for skin sensitization 1.2 [20], 1.3 [12,16], 1.4 [10], 1.8 [1] and 2.0 [11] and for hay fever 5.1 [13]. Peak months for grass sensitization are May [1,5,10,11,16–19] and June

Table 1. General characteristics of the study groups compared to the control group

	Allergic asthma group	Hay fever group	Prick-test grass pollen positive group	Control group
<i>Total*</i>	277 (100.0)	379 (100.0)	1128 (100.0)	2352 (100.0)
<i>Sex</i>				
Male	172 (62.1)	222 (58.6)	619 (54.9)	1111 (47.2)
Female	105 (37.9)	157 (41.4)	509 (45.1)	1241 (52.8)
	$P < 0.001$	$P < 0.001$	$P < 0.001$	
<i>Year of birth</i>				
1979	141 (50.9)	181 (47.8)	528 (46.8)	1146 (48.7)
1980	127 (45.6)	189 (49.9)	584 (51.8)	1159 (49.3)
	n.s.	n.s.	n.s.	
<i>Place of residence</i>				
Munich	227 (82.0)	295 (77.8)	1003 (88.9)	1606 (68.3)
Upper Bavaria	50 (18.0)	84 (22.2)	125 (11.1)	746 (31.7)
	$P < 0.001$	$P < 0.001$	$P < 0.001$	
<i>Family history</i>				
None	166 (59.9)	199 (52.5)	739 (65.5)	1936 (82.3)
Mother hay fever	59 (21.3)	113 (29.8)	207 (18.4)	197 (8.4)
Mother asthma	28 (10.1)	16 (4.2)	57 (5.1)	62 (2.6)
Father hay fever	32 (11.6)	66 (17.4)	148 (13.1)	161 (6.8)
Father asthma	26 (9.4)	16 (4.2)	48 (4.3)	47 (2.0)
	$P < 0.001$	$P < 0.001$	$P < 0.001$	
<i>Education—father</i>				
Primary School	92 (35.0)	103 (27.2)	333 (29.5)	854 (36.3)
High School	50 (19.0)	77 (20.3)	233 (20.7)	383 (16.3)
University	95 (36.1)	127 (33.5)	388 (34.4)	754 (32.1)
	n.s.	$P < 0.01$	$P < 0.001$	
<i>Responder to the questionnaire</i>				
Mother	203 (74.1)	280 (73.9)	848 (75.2)	1676 (71.3)
Father	13 (4.7)	14 (3.7)	55 (4.9)	170 (7.2)
Both	57 (20.8)	81 (21.4)	215 (19.1)	479 (20.4)
	n.s.	n.s.	$P < 0.05$	

* Percentages do not always add to 100 because of incomplete categories or rounding errors

[5,10,13,14,16,17,19] followed by April [1,11–13,18,19] and March [1,11–13,18,19].

In explaining some of the inconsistencies, it is necessary to consider several problems. A geographical area combining town (Munich) and countryside (Bavaria) seems suitable to test the hypothesis that the date of birth influences the later development of allergies. Munich is located at 530 m above sea-level, has 1.9 million inhabitants and has a mild climate. The length of day, climatic conditions, infection incidences and other possible factors

undergo considerable seasonal variations. The concentration of grass pollen is low in April, August and September and high in May, June and July. Unfortunately no systematic measurements of grass pollen are available for 1979 and 1980. The increased risk of hay fever in May, however, corresponds well with a peak of grass pollen sensitization and the seasonal pollen count in May (Fig. 1). The higher risk of children born in August of developing asthma could be due to the elevated risk in August and September of developing a sensitization

Table 2. Crude odds ratios of the individual month compared to all remaining months of developing allergic asthma, hay fever and skin sensitization

	Allergic asthma group	Hay fever group	Prick-test grass pollen positive group
Total	277 (100.0)	379 (100.0)	1128 (100.0)
January			
No Cases	19 (6.9)	31 (8.2)	100 (8.9)
OR (CI)	0.8 (0.5-1.3)	1.0 (0.6-1.4)	1.0 (0.8-1.3)
February			
No Cases	18 (6.5)	37 (9.8)	106 (9.4)
OR (CI)	0.9 (0.5-1.4)	1.3 (0.9-1.9)	1.3 (1.0-1.6)
March			
No Cases	31 (11.2)	28 (7.4)	91 (8.1)
OR (CI)	1.4 (0.9-2.1)	0.9 (0.6-1.3)	1.0 (0.7-1.2)
April			
No Cases	25 (9.0)	35 (9.2)	98 (8.7)
OR (CI)	1.0 (0.6-1.5)	1.0 (0.7-1.4)	0.9 (0.7-1.2)
May			
No Cases	23 (8.3)	41 (10.8)	115 (10.2)
OR (CI)	1.1 (0.7-1.8)	1.5 (1.0-2.1)	1.4 (1.1-1.8)
June			
No Cases	20 (7.2)	31 (8.2)	117 (10.4)
OR (CI)	0.9 (0.5-1.4)	1.0 (0.7-1.4)	1.3 (1.0-1.6)
July			
No Cases	20 (7.2)	32 (8.4)	85 (7.5)
OR (CI)	0.9 (0.6-1.4)	1.1 (0.7-1.6)	0.9 (0.7-1.2)
August			
No Cases	32 (11.6)	29 (7.7)	88 (7.8)
OR (CI)	1.4 (1.0-2.1)	0.9 (0.6-1.3)	0.9 (0.7-1.2)
September			
No Cases	26 (9.4)	33 (8.7)	80 (7.1)
OR (CI)	1.0 (0.7-1.6)	0.9 (0.6-1.4)	0.8 (0.6-1.0)
October			
No Cases	12 (4.3)	35 (9.2)	78 (6.9)
OR (CI)	0.6 (0.3-1.0)	1.2 (0.8-1.8)	0.9 (0.7-1.2)
November			
No Cases	23 (8.3)	18 (4.7)	88 (7.8)
OR (CI)	1.0 (0.6-1.6)	0.6 (0.3-0.9)	0.9 (0.7-1.2)
December			
No Cases	28 (10.1)	29 (7.7)	82 (7.3)
OR (CI)	1.2 (0.8-1.8)	0.9 (0.6-1.3)	0.8 (0.6-1.1)

Table 3. Literature review

Author/year	Reference	Type	Age	No.	Effect on asthma	Hay fever	Prick test
Anderson 1981	[9]	CA	8-9	3676	(Yes)	—	—
Beck 1987	[10]	CA	0-14	210	—	—	Yes
Björkstén 1980	[11]	CA	> 5	2149	—	—	Yes
Björkstén 1976	[12]	CA	0-29	2171	—	—	Yes
Businco 1988	[1]	CC	1-14	2124	—	—	Yes
Carosso 1986	[13]	CA	—	304	—	Yes	(Yes)
David 1985	[6]	CA	< 16	4520	Yes	—	—
Kemp 1979	[14]	CA	3-14	86	—	—	Yes
Kleiner 1975	[15]	CA	—	210	—	—	No
Korsgaard 1983	[16]	CA	15-30	456	—	—	Yes
Morrison-Smith 1979	[17]	CA	5-15	1715	Yes	No	(Yes)
Pearson 1977	[5]	CA	—	476	—	Yes	Yes
Pedersen 1983	[18]	CA	—	7796	No	Yes	—
Quoix 1988	[19]	CA	0-38	1301	—	—	Yes
Reed 1958	[20]	CA	> 15	150	—	No	—
Soothill 1976	[21]	PC	0-1	58	—	—	Yes
Troise 1989	[23]	CA	5-35	264	—	—	Yes

—, Not stated. CA, Case study. PC, Prospective cohort study.

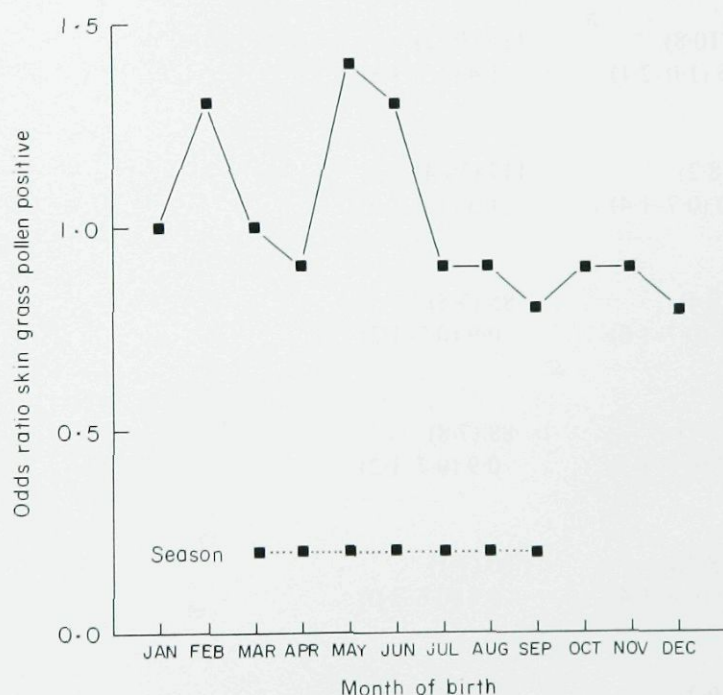


Fig. 1. Grass pollen sensitization and grass pollen season.

against *D. pteronyssinus*.

The second problem relates to the validity of the diagnoses elicited during an epidemiological survey. To avoid uncertain diagnoses, the corresponding symptoms are also requested. Further misclassification is difficult to quantify. Recall bias concerning the date of birth is

unlikely, since nearly all parents remember their children's date of birth correctly.

It is possible that the month of birth and the allergic sensitization are related to some common factors, which results in a secondary association. For example, the birth month may vary according to certain social and economic factors which are of aetiological importance [9]. This would appear unlikely since no relationship between social class and birth month could be demonstrated. Exposure varies also according to the microenvironment of neonate [12]. Systematic research is needed there.

In conclusion it is likely that there is a slight relationship between the month of birth and the prevalence of allergic sensitization. Further studies of early environmental factors and parallel monitoring of markers of atopic disease should lead to useful suggestions for prevention of the disease.

Acknowledgments

We thank Ms F. Lynch for correcting the manuscript. Our thanks also to Prof Dr W. Lehmacher, Dr T. Nicolai, Dr Frfr. von Loeffelholz-Colberg, Dr B. Berbig, Dr K. Winter for the planning and organizing the study; Dr A. Hillebrecht, Dr K. Beck, Dr R. Frentzel-Beyme-Bauer, A. Becker, W. Bialas, S. Braun, A. Fuger, C. Griehl, H. Hörnlein, J. Kohle, H. Kroker, G. Lindl-Agiolopolus for examining the children, C. Malin, M. von Mutius, T. Kreyssig, A. Provelegios, R. Berbig, A. Jensen for the

transport provided, Mr Kienle for technical assistance, G. Röhl for statistical advice and A. Wulff for medical documentation, J. Rohe, S. Funk, A. Stankiewicz and L. Pritscher for data typing, the Public Health Office, the Supervisory School Authority, the principals and teachers of the 182 participating schools for their interest and all the children and parents who volunteered for this study.

References

- Businco L, Cantani A, Farinella F, Businco E. Month of birth and grass pollen or mite sensitization in children with respiratory allergy: a significant relationship. *Clin Allergy* 1988; 18:269–74.
- Holt PG, McMenamin C, Nelson D. Primary sensitisation to inhalant allergens during infancy. *Ped Allergy Immunol* 1990; 1:3–13.
- Kjellmann NIM. Prediction and prevention of atopic allergy. *Allergy* 1982; 37:463–74.
- Dold S, Wjst M, Mutius von E, Reitmeir P, Stiepel E. Genetic risk of asthma, allergic rhinitis and atopic eczema. *Archiv Dis Child* 1992; 67:
- Pearson DJ, Freed DLJ, Taylor G. Respiratory allergy and month of birth. *Clin Allergy* 1977; 7:29–33.
- David TJ, Beards SC. Asthma and the month of birth. *Clin Allergy* 1985; 15:391–5.
- Mutius E v, Dold S, Wjst M, Stiepel E, Reitmeir P, Frentzel-Beyme-Bauer R, Beck K, Hillebrecht A, Nicolai T, Leh-macher W, Löffelholz-Colberg E, Adam D. Münchner Asthma- und Allergiestudie. Prävalenzen atopischer und asthmatischer Erkrankungen im Kindesalter. *Münchner Medizinische Wochenschrift* 1991; 133:675–9.
- Henneken CH, Buring JE. *Epidemiology in medicine*. Boston: Little, Brown and Company, 1987.
- Anderson HR, Bailey PA, Bland JM. The effect of birth month on asthma, eczema, hay fever, respiratory symptoms, lung function, and hospital admissions for asthma. *International Journal of Epidemiology* 1981; 10:45–51.
- Beck HI, Hagdrup HK. Atopic dermatitis, house dust mite allergy and month of birth. *Acta Dermatol Venereol Stockh* 1987; 67:448–51.
- Björkstén F, Suoniemi I, Koski V. Neonatal birch pollen contact and subsequent allergy to birch pollen. *Clin Allergy* 1980; 10:585–91.
- Björkstén F, Suoniemi I. Dependence of immediate hyper-sensitivity on the month of birth. *Clin Allergy* 1976; 6:165–71.
- Carosso A, Ruffino C, Bugiani M. The effect of birth season on pollinosis. *Ann Allergy* 1986; 56:300–3.
- Kemp AS. Relationship between the time of birth and the development of immediate hypersensitivity to grass pollen antigens. *Med J Austr* 1979; 1:263–4.
- Kleiner H, Arkins JA, Lauwasser M. Correlation between date of birth and pollen sensitivity. *Ann Allergy* 1975; 34:310–14.
- Korsgaard J, Dahl R. Sensitivity to house dust mite and grass pollen in adults. Influence of the month of birth. *Clin Allergy* 1983; 13:529–35.
- Morrison Smith J, Springett VH. Atopic disease and month of birth. *Clin Allergy* 1979; 9:153–7.
- Pedersen PA, Weeke ER. Month of birth in asthma and allergic rhinitis. *Scand J Prim Health Care* 1983; 34:97–101.
- Quoix E, Bessot JC, Kopferschmitt-Kubler MC, Fraisse P, Pauli G. Positive skin tests to aero allergens and month of birth. *Allergy* 1988; 43:127–31.
- Reed CE. The failure of antepartum of neonatal exposure to grass pollen to influence the later development of grass sensitivity. *J Allergy* 1958; 29:300–1.
- Soothill JF, Stokes CR, Turner MW. Predisposing factors and the development of reagenic in infancy. *Clin Allergy* 1976; 6:305–19.
- Sporik R, Holgate ST, Platts-Mills TAE, Cogswell JJ. Exposure to house dust mite allergen (*Der pI*) and the development of asthma in childhood. *New Engl J Med* 1990; 323:502–7.
- Troise C, Voltolini S, Delbono G, Ebbli A, Negrini AC. Allergy to Parietaria pollen and month of birth. *Allergol Immunopathol Madrid* 1989; 17:201–4.

Copyright of Clinical & Experimental Allergy is the property of Blackwell Publishing Limited and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.