

Recurrent wheezing in relation to environmental risk factors in infancy

A prospective study of 276 infants

S. HALKEN¹, A. HØST¹, S. HUSBY¹, L. G. HANSEN², O. ØSTERBALLE² & J. NYBOE³

Departments of ¹Paediatrics, Odense University Hospital, ²Paediatrics, Viborg Hospital, and ³Statistical Unit, State University Hospital, Copenhagen, Denmark

Clinical course and environmental factors were recorded in a prospective study of 276 unselected infants followed from birth to the age of 18 months. The study was performed with a questionnaire at the age of 6 and 12 months and a physical examination at 18 months. Fifty-nine (21%) of the children had ≥ 2 episodes of wheezing before they were 18 months old. A total of 58 (21%) of the children belonged to the lowest social class V, 182 (66%) were daily exposed to passive tobacco smoking at home and/or in daycare, 164 (59%) were breastfed ≥ 3 months, 192 (70%) were in daycare, 62 (22%) lived in flats and 167 (61%) were in daily contact with furred pets at home and/or in daycare. In social class V a preponderance of children were exposed to passive tobacco smoking, a majority were living in flats and a minority were breastfed ≥ 3 months. Linear logistic regression analysis was used for the purpose of assessing the causal effect of environmental risk factors on the risk of recurrent episodes of wheezing before the age of 18 months. The study demonstrated that male sex and daily exposure to passive tobacco smoking were significant risk factors with estimated odds ratios 1.9 and 2.4, respectively. Maternal tobacco smoking seemed to be associated with the highest risk. There was a tendency - though not significant - indicating that breastfeeding ≥ 3 months had a protective effect. Low social status, daycare, daily contact with furred pets, having carpeted floor in bedroom, and living in a flat proved not to affect significantly the risk of recurrent wheezing.

Key words: environmental risk factors; infancy; linear logistic regression analysis; passive tobacco smoking; wheezing.

Accepted for publication 27 December 1990

CLINICAL ASPECTS

Significant correlation between daily exposure to passive tobacco smoking and recurrent wheezing in infancy has been demonstrated. Thus, daily exposure of infants to passive tobacco smoking should be avoided.

Wheezing, often associated with signs of upper respiratory tract infection, is a common disease among children in the first years of life. Recurrent episodes of wheezing are associated with increased risk of development of bronchial asthma (20, 25) and some authors argue, that recurrent wheezing should be considered

bronchial asthma until otherwise proven (9). In recent years several studies have indicated that the occurrence of asthma and allergic disorders are increasing in industrialised countries (1, 27). Various environmental factors such as exposure to tobacco smoking, daycare, damp housing, industrial pollution or poor social sta-

tus are reported associated with increased frequency of wheezing in children (1, 3, 5, 10). In these studies the diagnostic criteria, study populations and age groups vary, and moreover, most of the studies are retrospective with some uncertainty as to the information concerning early childhood. The aim of our study was to analyse the relationship between recurrent episodes of wheezing and some environmental factors in a prospective study of 276 unselected infants followed from birth to the age of 18 months.

MATERIAL AND METHODS

Study population

During 1985, 1758 infants were born alive at Odense University Hospital, nine of them died neonatally. A total of 276 infants of this cohort were chosen for this study, representing a random spot sample of 16% of newborns from the municipality of Odense, Denmark. In 1985 cord-blood IgE (Phadebas IgE PRIST) was determined as a routine.

The parents of the infants answered a standard questionnaire when the children were 0, 6 and 12 months old. The questionnaire included questions concerning family history of atopy (atopic dermatitis, allergic urticaria, asthma and hayfever), careful dietary history, various environmental factors, socioeconomic data, respiratory tract infections, wheezing, atopic dermatitis, adverse reactions to foods and other possible signs of allergic disease.

At the age of 18 months all the children underwent physical examination by one of three paediatricians (S. Halken, S. Husby and A. Høst) and the children's individual case history and data were recorded.

Definitions

We analysed the variables considered as possible risk factors for having at least two episodes of wheezing from 0 to 18 months of age. Wheezing was recorded when the child had a

history of expiratory wheezing lasting 2 or more days and the wheezing was diagnosed by a physician. The wheezing was nearly always associated with upper respiratory tract infection. Virus investigations were not performed routinely. The variables considered were atopic predisposition, social status, sex, exposure to passive tobacco smoking, breastfeeding, daycare, housing conditions, carpeted floor in bedroom, and contact with furred pets.

Social status was registered according to the social grouping system of the Danish Social Research Institute (13) when the child was 18 months old. This grouping system gave five social classes I-V according to education and employment on which the family income was made, with class V as the lowest.

Statistical methods

Statistical analysis was performed by simple contingency tables and χ^2 test. Moreover we used linear logistic regression analysis by use of the model:

$$\text{logit}(p) = \log_e(p/(1-p)) = a + b_1x_1 + b_2x_2 + \dots + b_nx_n$$

where p was the risk or probability of a child suffering from wheezing at least twice during the first 18 months of life. x_1 , x_2 , x_n were explanatory variables and the b_1 , b_2 , b_n indicated the amount of change in the transformed probability - the logit - when the corresponding variables changed one unit and all the other variables remained constant.

In this study the variables were binary. Estimates of the regression coefficients were obtained by using the principle of maximum likelihood (2). We have used the odds-ratios in the presentation of our results. Odds-ratio (OR) is the anti-logarithm of the estimated regression coefficient and is approximately the same as the relative risk when probabilities are low.

Many of the considered variables affected each other. To establish whether a variable had an effect of its own, this effect had to be demonstrated under conditions where the

variables affecting the variable in question were constant and the variables affected by the considered variable were excluded from the model. The relevant regression coefficient was estimated for constant values of the other variables in the model. To determine how the considered variables affected each other, they were arranged according to time on the following time scale:

Social status - Sex - Passive smoking - Age of weaning
Housing conditions
Pets
Daycare

Social status was positioned to the extreme left on the time scale, because it was assumed to affect many of the other variables, but not itself to be affected by any other of the variables. The last four variables all concerned the period after birth and it was impossible to tell which was first. The effect of the variables was analysed from the left to the right of this time scale and the last four variables had to be included in the model at the same time.

The linear logistic regression analysis was performed with the Biomedical Computer Program BMPD.

RESULTS

The frequency of the considered environmental factors is shown in Table 1. As shown, 182

Table 1.

Study population. Frequency of the considered environmental factors

Total	276	
Boys	126	
Girls	150	
Social class I-II *	57	(21 %)
Social class III-IV *	161	(58 %)
Social class V *	58	(21 %)
Passive smoking **	182	(66 %)
Breastfeeding $\geq$ 3 mo.	164	(59 %)
Daycare	192	(70 %)
Living in a flat	62	(22 %)
Living in a detached house	214	(78 %)
Carpeted floor in bedroom	224	(81 %)
Furred pets **	167	(61 %)

* Social class according to grouping system of the Danish Social Research Institute

**Daily exposure at home and/or in daycare

(66 %) of the children were daily exposed to passive tobacco smoking either at home or in daycare. A total of 160 (58 %) of the children were daily exposed to passive tobacco smoking at home and 22 (8 %) were exposed in daycare only. 105 of the mothers smoked every day during pregnancy and 115 when the children were 0 to 18 months old. Only one mother smoked during pregnancy but not when the child was 0 to 18 months old. In social classes I-II 53 % of the children were daily exposed to passive tobacco smoking compared with 69 % in social class V.

A total of 164 (59 %) of the children were breastfed 3 months or more, but in social class V it was 43 %. In social class V 55 % of the families lived in flats, whereas among the study population as a whole only 22 % had these housing conditions. According to this, children from the lowest social class were more exposed to passive tobacco smoking, were weaned at an earlier age and lived under other housing conditions than the children from higher social classes.

Table 2 shows the number of children with genetic predisposition to atopic disease (asthma, hayfever, atopic dermatitis or allergic urticaria) and / or cord blood IgE $\geq$ 0.5 kU/l. Double predisposition was here defined as double parental predisposition. Single predisposition was present when one parent and / or one or more siblings had atopic disease. Sixteen (6 %) of the study population had double parental predisposition or single predisposition combined with cord blood IgE $\geq$ 0.5 kU/l and seven (43 %) of these children had two or

Table 2.

Total number of children and number with recurrent wheezing in relation to atopic predisposition and cord blood IgE

	Total <i>n</i> = 276 (%)	No. with RW <i>n</i> = 594
Atopic predisposition	88 (32)	19
Double parental predispos.	7 (2.5)	2
Single predispos.	81 (29)	17
Cord blood IgE $\geq$ 0.5 KU/l	35 (13)	12
Single predispos. + Cord blood IgE $\geq$ 0.5 KU/l	9 (3)	5

RW = recurrent wheezing in the period 0-18 months.

Table 3.

Raw data on cumulative prevalence of two or more episodes of wheezing (RW) in the period 0-18 months of age

	No. children	No. (%) cases with RW
Total	276	59 (21)
Boys	126	35 (28)*
Girls	150	24 (21)
Passive smoking	182	45 (25)
No passive smoking	94	14 (15)
Social class I-IV	218	43 (20)
Social class V	58	16 (28)
Social class I-IV, no smoking	77	9 (12)
Social class V, no smoking	20	5 (25)
BF ≥ 3 mo.	161	29 (18)
BF < 3 mo.	112	30 (27)
BF < 1 mo.	53	18 (34)*
BF ≥ 3 mo. (girls)		
soc. cl. I + II, no smoking	27	2 (7)
BF < 3 mo. (girls)		
soc. cl. I + II, no smoking	12	2 (17)
+ Daycare	192	43 (22)
- Daycare	84	16 (19)
+ Daycare, no smoking, BF ≥ 3 mo.	38	5 (13)
- Daycare, no smoking, BF ≥ 3 mo.	27	0
Flat	62	19 (31)*
Detached house	214	40 (19)
Flat, no smoking	16	3 (19)
Detached house, no smoking	80	11 (14)
+ Carpets in bedroom	224	46 (21)
- Carpets in bedroom	52	13 (25)
+ Pets at home/daycare	167	33 (20)
- Pets at home/daycare	109	26 (24)

BF = breastfeeding, * $P < 0.05$

Table 4.

Number of children with recurrent wheezing in relation to social status

Social class	No. children	No. cases (%)	Estimated OR (95% conf. limits)
I-II	57	12 (21)	
III-IV	161	31 (19)	1
V	58	16 (28)	1.6 (0.8-3.2)

 χ^2 test, $P = 0.176$ = n.s.

Table 5.

Number of children with recurrent wheezing in relation to sex, eliminating the effect of social status

Sex	No. children	No. cases (%)	Estimated OR (95% conf. limits)
Female	150	24 (16)	1
Male	126	35 (28)	1.9 (1.1-3.4)

 χ^2 test, $P < 0.05$

more episodes of wheezing before 18 months of age.

Raw data on cumulative prevalence of at least two episodes of wheezing at age 0-18 months is shown in Table 3. Fifty-nine (21%) of the study population had two or more episodes of wheezing before they were 18 months old. Using χ^2 -test, significantly more boys than girls had wheezing episodes twice or more. Further, breastfeeding ≥ 3 months seemed to be associated with a significantly lower prevalence of recurrent wheezing than breastfeeding < 1 month. Low social status and exposure to passive tobacco smoking also appeared to be associated with a higher cumulative prevalence of recurrent wheezing, but using simple 2×2 tables and χ^2 -test it was not significant.

Because many of the variables were related, it was necessary to use linear logistic regression analysis. Using this analysis, variables examined for an independent association with recurrent episodes of wheezing were: low social status = class V, sex, daily exposure to passive tobacco smoking, age of weaning, daycare, living in a flat versus a detached house, carpeted floor in the child's bedroom and furred pets at home or in daycare at least during the first year of life. These results are presented in Tables 4-8 with estimated odds-ratios and 95% confidence limits. χ^2 and P -values are derived from the likelihood ratio and when no values are written $P > 0.05$.

Table 4 shows the relation between social status and recurrent wheezing and it is seen that in our study population low social status was not a significant risk factor. A significant relationship between male sex and the risk of recurrent wheezing (OR 1.9) was found

(Table 5). Table 6 shows that exposure to passive smoking was a significant risk factor for recurrent wheezing. If the child was exposed to daily passive tobacco smoking at home or in daycare the estimated OR was 2.4 and OR was 2.6 when the child's mother smoked tobacco every day. The frequency of maternal smoking during pregnancy did not differ from that during the period 0-18 months post partum. Thus, in this study we cannot distinguish between the influence of exposure to maternal tobacco smoking before and after birth. The relation between the risk of recurrent wheezing and the age of weaning is shown in Table 7. There was a tendency indicating that children breastfed <1 month had a higher risk of recurrent wheezing than children breastfed for a longer period, but the difference was not significant.

Finally, the last four variables are presented in Table 8. Neither daycare, living in a flat, having carpeted floor in the bedroom nor daily contact with furred pets were noted to have a significant effect on the risk of recurrent wheezing.

DISCUSSION

In this prospective study 21% of the children had two or more episodes of wheezing before the age of 18 months. This figure is comparable to the corresponding figure of a previous Danish study (20) where Storm et al. found that 15% of 1210 unselected Danish school

children had three or more episodes of wheezy bronchitis before the age of 4 years. This study however, was retrospective and the children were 7 years old when the data were collected. Hence, the real cumulated prevalence of wheezy bronchitis may have been higher. Bisgaard (3) only found 2% of 5953 children having at least one episode of wheezing before 1 year of age, but those children were born in 1959-61 and the data were not collected for this specific purpose, so probably the real prevalence was higher. In a prospective study from 1987 Cogswell (5) found that 23% of 73 newborn infants had at least two episodes of wheezing from 0 to 5 years of age, but those children were all predisposed to atopy with at least one parent with asthma or hayfever.

Our study population consists of unselected infants, and does not represent any high risk group with regard to atopic heredity. A total of 88 (32%) of these infants had atopic predisposition with at least one atopic parent or sibling. This figure is a normal finding in a large Danish population (20).

Previous studies (3, 15) described low social status as a risk factor for wheezing, but in a large prospective study Burchfield (4) found no influence of social status on this risk. In an extensive Swedish study (1) it was shown that children living in damp houses and children living in areas with moderate industrial pollution had higher incidences of bronchial hyperactivity and allergic asthma than other

Table 6.
Number of children with recurrent wheezing in relation to daily exposure to passive smoking,
eliminating the effect of social status and sex

Exposure to passive smoking	No. children	No. cases (%)	χ^2 test <i>P</i>	Estimated OR (95% conf. limits)
None	94	14 (15)		1
Mother during pregnancy	105	32 (30)	< 0.01	2.4 (1.3-4.4)
Mother 0-18 mo.	115	35 (30)	< 0.01	2.6 (1.4-4.8)
Mother/father/daycare	182	45 (25)	< 0.05	2.4 (1.2-4.9)

Table 7.

Number of children with recurrent wheezing in relation to duration of breastfeeding, eliminating the effect of social status, sex and passive smoking

Breastfeeding months	No. children	No. cases (%)	Estimated OR (95% conf. limits)
0	23	8 (35)	1.6 (0.9-2.8)*
0-1	30	10 (33)	2.0 (1.0-4.0)*
1-3	59	12 (20)	1.0 (0.5-1.3)*
3-6	63	13 (21)	1.0 (0.5-1.9)*
≥ 6	101	16 (16)	1.0

* $P > 0.05$

children. The definition and significance of low social status vary in different areas and in different studies, and many factors could explain the possible effect of low social status, for example tobacco smoking, industrial pollution, damp housing and nutrition. Thus it is difficult to interpret the results concerning the effect of low social status. In the present study we found no effect of low social status on its own, but the reason for this might be that our study population was too small to demonstrate a significant effect.

Our data showed that recurrent wheezing occurred more frequently in boys than in girls, and this is in accordance with previous studies (3, 8, 20).

In the past decade evidence has shown that exposure to passive tobacco smoking is associated with increased incidence of lower respiratory infections, wheezy bronchitis, bronchial asthma and diminished pulmonary function. Recent studies (1, 3, 4, 5, 10, 11) have demonstrated a higher incidence of wheezing in children exposed to passive tobacco smoking, especially in the first years of life and especially if they were genetically predisposed to allergic disease. In general, it is found that maternal smoking is more strongly correlated with respiratory dysfunction in the children than is paternal smoking (4, 12, 22, 24). The explanation might be that fathers spend less time at home than mothers and that most children spend more time in their first years of life with their mother than with their father. Thus maternal smoking means more exposure

Table 8.

Number of children with recurrent wheezing in relation to other environmental factors, eliminating the effect of social status, sex, passive smoking and breastfeeding

	No. children	No. cases (%)	Estimated OR (95% conf. limits)
Daycare	192	43 (22)	1.4 (0.6-1.9)*
Living in a flat	62	19 (31)	1.4 (0.6-3.0)*
Carpeted floor in bedroom	224	46 (21)	0.1 (0.1-0.3)*
Furred pets	167	33 (20)	0.6 (0.3-1.2)*

* $P > 0.05$

to passive tobacco smoking than does paternal smoking. In our study we demonstrated a significantly increased risk of developing recurrent wheezing when the child was daily exposed to passive tobacco smoking, especially when exposed to maternal smoking. In the present study we could not draw any conclusion concerning the influence of maternal smoking during pregnancy.

Studies of the relationship between recurrent episodes of wheezing and the duration of breastfeeding are conflicting (14). However prospective studies (6, 7, 10, 26) have demonstrated a protective effect in children predisposed to allergic disease, when the period of breastfeeding was 3 months or more. Regarding raw data, the present study demonstrated a significant higher risk of recurrent wheezing when the period of breastfeeding was <1 month compared with ≥ 3 months. When using logistic regression analysis there was a tendency towards a higher risk when the child was breastfed for <1 month, but using this analysis the difference was not significant. The explanation for this could be that this unselected study population was too limited to demonstrate this effect when other more powerful risk factors were present.

Recent studies (17, 18, 19, 21, 23) have demonstrated a positive correlation between exposure to furred pets in the first year of life and later development of asthma and allergy to these pets.

However, children seldom develop clinical allergy to animal dander during their first years of life. As shown in Table 8 we did not find any correlation between daily exposure to furred pets⁷ and recurrent wheezing when the children were 18 months. This does not exclude the possibility of showing a correlation between early exposure to furred pets and asthma and allergy to pet dander when the children grow up.

Regarding raw data (Table 3) there appeared to be an increased risk for recurrent wheezing when living in a flat, but as seen from Table 8 this effect disappeared when using logistic regression analysis. The reason for this is probably because children living in a flat were also more exposed to other risk factors (passive tobacco smoking, earlier weaning, etc.), and when eliminating the effect of these factors, "living in a flat" proved not to have an effect on its own.

Table 8 also shows that daycare and having carpeted floor in the child's bedroom were not significant risk factors, when the effect of social status, sex and passive tobacco smoking was eliminated.

Thus, we can conclude that in our prospective study of 276 unselected infants, male sex and daily exposure to passive tobacco smoking were significantly associated with an increased risk of recurrent wheezing until the age of 18 months. Moreover, there was a tendency indicating a protective effect of breastfeeding for 3 months or more.

REFERENCES

- Andrae S, Axelsson O, Björkstén B, Frederiksson M, Kjellman N-IM. Symptoms of bronchial hyperreactivity and asthma in relation to environmental factors. *Arch Dis Child* 63, 473-478, 1988.
- Armitage P, Berry G. Statistical methods in medical research, pp. 387-399, 2nd ed. Blackwell Scientific, London, 1987.
- Bisgaard H, Dalgaard P, Nyboe J. Risk factors for wheezing during infancy. A study of 5953 infants. *Acta Paediatr Scand* 76, 719-726, 1987.
- Burchfield CM, Higgins MW, Keller JB, Howatt WF, Butler WJ, Higgins ITT. Passive smoking in childhood. Respiratory conditions and pulmonary function in Tecumseh, Michigan. *Am Rev Respir Dis* 133, 966-973, 1986.
- Cogswell JJ, Mitchell EB, Alexander J. Parental smoking, breast feeding, and respiratory infection in development of allergic diseases. *Arch Dis Child* 62, 338-344, 1987.
- Chandra RK, Singh G, Shridhara B. Effect of feeding whey hydrolysate, soy and conventional cow milk formulas on incidence of atopic disease in high risk infants. *Ann Allergy* 63, 102-106, 1989.
- Chandra RK, Pari S, Cheema PS. Predictive value of cord blood IgE in the development of atopic disease and role of breastfeeding in its prevention. *Clin Allergy* 15, 517-522, 1985.
- Davis JB. Asthma and wheezy bronchitis in children. *Clin Allergy* 6, 329-338, 1976.
- Faden H, Eliot E. Acute bronchopulmonary infections. In Bierman CW, Pearlman DS (eds): Allergic diseases of infancy, childhood and adolescence. Saunders, Philadelphia 1980.
- Geller-Bernstein G, Kenett R, Weiglass L, Tsur S, Lahav M, Levin S. Atopic babies with wheezy bronchitis. Follow-up study relating prognosis to sequential IgE values, type of infant feeding, exposure to parental smoking and incidence of lower respiratory tract infections. *Allergy* 42, 85-91, 1987.
- Gortmaker SL, Walker DK, Jacobs FH, Ruch-Ross Holly. Parental smoking and the risk of childhood asthma. *Am J Public Health* 72, 574-579, 1982.
- Greenberg RA, Bauman KE, Glover LH, et al. Ecology of passive smoking by young infants. *J Pediatr* 114, 774-780, 1989.
- Hansen EJ. Social groups. Introduction to a study of one of the analytical tools for social research (in Danish). *Societ Tidskr* 53, 1-18, 1977.
- Kramer MS. Does breastfeeding help protect against atopic disease? Biology, methodology, and a golden jubilee of controversy. *J Pediatr* 112, 181-190, 1988.
- Leeder SR, Corkhill RT, Irwig LM, Holland WW, Colley JRT. Influence of family factors on asthma and wheezing during the first five years of life. *Br J Prev Soc Med* 30, 213-218, 1976.
- Nordvall SL, Eriksson M, Rylander, Schwartz B. Sensitization of children in the Stockholm area to house dust mites. *Acta Paediatr Scand* 77, 716-720, 1988.
- Popp W, Raucher H, Sertl K, Wanke T, Zwick H. Risk factors for sensitization to furred pets. *Allergy* 45, 75-79, 1990.
- Rugvitt J. Environmental factors in the first months of life and the possible relationship to later development of hypersensitivity. *Allergy* 45, 154-156, 1990.
- Sear MR, Herbison GP, Holdaway MD, Hewitt CJ, Flannery EM, Silva PA. The relative risks of sensitivity to grass pollen, house dust mite and cat dander in the development of childhood asthma. *Clin Exp Allergy* 19, 419-424, 1989.
- Storn K, Haahr J, Kjellman N-IM, Österballe O. The occurrence of asthma and allergic rhinitis, atopic dermatitis and urticaria in 1 year cohort of Danish children (in Danish). *Ugeskr Laeger* 148, 3295-3299, 1986.
- Suoniemi I, Björkstén F, Haahela T. Dependence of immediate hypersensitivity in the adolescent period on

- factors encountered in infancy. *Allergy* 36, 236-268, 1981.
22. Taylor B, Wadsworth J. Maternal smoking during pregnancy and lower respiratory tract illness in early life. *Arch Dis Child* 62, 786-791, 1987.
23. Vanto T, Koivikko A. Dog hypersensitivity in asthmatic children. *Acta Paediatr Scand* 72, 571-575, 1983.
24. Weitsman M, Gortmaker S, Walker DK, Sobol A. Maternal smoking and childhood asthma. *Pediatrics* 85, 505-511, 1990.
25. Wilson NM. Controversy. Wheezy bronchitis revisited. *Arch Dis Child* 64, 1194-1199, 1989.
26. Wright AL, Holberg CJ, Martinez FD, Morgan WJ, Taussig LM and Group Health Medical Associates.: Breast feeding and lower respiratory tract illness in the first year of life. *Br Med J* 299, 946-949, 1989.
27. Åberg N. Allergic disease in childhood and adolescence, in relation to background factors. Göteborg University Medical Dissertation, Göteborg, Sweden, 1988.

Address:

S. Halken

Department of Paediatrics
Odense University Hospital
5000 Odense C
Denmark

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.