

Original articles

Preschool wheezing and prognosis at 10

E S PARK, J GOLDING, F CARSWELL, AND S STEWART-BROWN

Department of Child Health, University of Bristol

SUMMARY Information was collected at birth and at 5 and 10 years of age on the national cohort of children born in one week of April 1970 (the Child Health and Education Study). For 11 465 children, information on wheezing attacks before 5 years was compared with reports of wheezing occurring in the 12 months before the interview at 10 years.

Of 2345 children who had had at least one wheezing attack before their fifth birthday, 80% (1869) were free of wheeze at 10 years; only 8% of children who had just one wheezing attack by 5 years wheezed in their 10th year. The more attacks the child had had by the age of 5 the higher the risk of continuing to wheeze at the age of 10, but there were no major differences in prognosis according to the age of the first attack. Half of the children who had been labelled asthmatic at the age of 5 were wheezing at the age of 10 compared with an eighth of those with wheezing not so labelled. There was little evidence to suggest that the prognosis of wheezing with bronchitis was markedly different from that of children with other episodes of wheezing provided they were not said to be asthmatic. A longer follow up is necessary to ascertain whether remission at the age of 10 is followed by relapse later.

Asthma in childhood is one of the commonest disorders to cause both acute and prolonged morbidity. Children labelled asthmatic constitute only a proportion of those with wheezing attacks. Data from the 1970 British National Cohort Study indicated that by the age of 5 years 21% of all children had had at least one episode of wheezing on the chest and by 10 years 27% had had such a history.¹

For the parents to understand the condition and for the physician to assess the value of his treatment,² knowledge of the natural history of childhood asthma is essential.

Blair followed two groups of asthmatic children prospectively for over 20 years, by which time 52% of both groups had stopped wheezing.³ The final prognosis was influenced by the severity of the asthma at onset but not by the age at onset or the results of skin tests. Other series disagree and imply that age of onset is the best determinant of severity.⁴

The present paper addresses the problem of predicting whether children who wheeze in the first five years of life will still be wheezing at the age of 10.

Subjects and methods

The data analysed for this study were collected on

all children born in the week beginning 5 April 1970 who were surveyed in the 1970 cohort study at both 5 and 10 years of age (The Child Health and Education Study).

Information was obtained by qualified midwives on 98% of these children at birth in the course of the British Births Survey. The surviving children were traced at the ages of 5 and 10 years. At both ages the parents were interviewed by their health visitors and a medical, social, and environmental history was taken.

At 10 years the national sample of children was studied again; a medical, social, and environmental history was taken and the child examined by a clinical medical officer.

In the 5 year study 2702 parents answered 'yes' to the question 'Has your child ever had one or more attacks or bouts in which he/she had wheezing on the chest regardless of the cause?' These parents were then asked (i) the age at onset, (ii) the number of attacks in the first 12 months of life, (iii) the number of attacks between the first and fourth birthdays, (iv) the number of attacks from the fourth birthday until the date of interview, (v) the number of hospital admissions for wheezing on the chest, and (vi) the diagnosis the parent thought had been made.

Of the 2702 parents who had given a history when the child was 5 of the child having wheezed, 2348 (87%) were interviewed again when the child was 10.

In the 10 year study the question asked was 'Has the child ever had one or more attacks or bouts in which there was wheezing or whistling in the chest?' Those who answered 'yes' were asked the diagnosis (asthma, wheezy bronchitis, other causes), the age of the child when the attacks had occurred, and about the presence or absence of attacks during the past 12 months.

The 10 year old children who had had a history of wheezing by the age of 5 were allocated to one of two groups defined as follows:

Group 1: Remission—children who had no evidence of current asthma at 10—that is, with no wheezing attacks in the past 12 months.

Group 2: Current asthma—10 year old children who had had at least one wheezing attack during the past 12 months.

Subcategories of wheezing identified at the age of 5 included; (a) asthma (the diagnosis being that volunteered by parents), (b) wheezing said to be associated with bronchitis, (c) wheezing said to be associated with croup, and (d) wheezing without any of these labels.

Results

Incidence and prevalence. Information was available at ages 5 and 10 for 11 465 children. Of these, 20.5% had been recorded at the age of 5 as having had at least one attack of wheezing. These comprised; (a) 238 (2% of the population) labelled asthma, (b) 567 (5%) wheezing with bronchitis, (c) 276 (2%) wheezing associated with croup, and (d) 1264 (11%) other wheezing.

Prognosis. Of the 2345 children who had had at least one wheezing attack before their fifth birthday, 476 (20%) had had at least one wheezing attack at the age of 9. Conversely, of the children who had not wheezed by the age of 5, 78 (4.2%) had wheezed at the age of 9.

Age at onset. There were slight differences in the risk of asthma at the age of 10 according to the age at which the first wheezing attack had occurred (Table 1). Children whose first attack was in infancy had the best prognosis and those with onset at the age of 2 had the greatest risk of wheezing at the age of 9. These differences, however, were not pronounced and are only significant at the 5% level.

Number of attacks in the first year of life. Even though children with wheezing in the first year of life were most likely to be free of wheezing at the age of 9, there was a significant variation in prognosis with the frequency of attacks during the first year. The greater the number of attacks in the first year of life the more likely the child was to have asthma at 10 years (Table 2).

Number of attacks in children aged 1–4 years. More important was the association between prognosis and the number of attacks during the period from 1 to 4 years of age (Table 3). Among the 935 children who had had less than four attacks, 789 children (84%) were free of wheezing at the age of 10. In contrast, of the 702 children who had had more than four attacks; 471 (67%) were free of wheezing at the age of 10 ($p < 0.001$).

Table 1 Age at onset of wheezing and prognosis at 10 years of age (excluding those in whom the age at onset was unknown). Values are No (%)

Asthma at 10	First episode of wheezing (years)					Total
	<1	1	2	3	4+	
Absent	806 (83)	263 (77)	259 (75)	250 (77)	225 (81)	1735 (79)
Present	170 (17)	79 (23)	85 (25)	76 (23)	52 (19)	452 (21)
Total	976 (100)	342 (100)	344 (100)	326 (100)	278 (100)	2187 (100)

$\chi^2_4 = 11.2$; $p < 0.05$.

Table 2 No (%) of attacks in the first year of life and prognosis at 10 years of age

Asthma at 10	No of attacks				Total
	1	2	3	4+	
Absent	384 (86)	172 (82)	109 (81)	141 (77)	806 (83)
Present	62 (14)	39 (18)	26 (19)	43 (23)	170 (17)
Total	446 (100)	211 (100)	135 (100)	184 (100)	976 (100)

The value 4+ includes cases with 'vague' responses such as 'several' and 'many'. $\chi^2_2 = 8.9$; $p < 0.05$.

Table 3 No (%) of attacks during the period from 1 year to fourth birthday and prognosis at 10 years of age

Asthma at 10	No of attacks				Total
	1	2	3	4+	
Absent	353 (87)	238 (82)	198 (82)	471 (67)	1260 (77)
Present	52 (13)	52 (18)	42 (18)	231 (33)	377 (23)
Total	405 (100)	290 (100)	240 (100)	702 (100)	1637 (100)

The value 4+ includes vague responses such as 'several' and 'many'. $\chi^2_3 = 71$; $p < 0.0001$.

Number of attacks after the fourth birthday. Between the fourth birthday and the interview at around the fifth birthday 550 children had had just one attack, of whom 79% were free of wheezing at the age of 10. Table 4 shows again that the more attacks that the child had had during this year the greater the possibility of wheezing attacks at 10 years.

Among those who had wheezing at an earlier age but who did not wheeze while aged 4, 91% (710/784) were free of wheezing at the age of 10.

A comparison of the information in Tables 2, 3, and 4 shows that within each period the more attacks the child had the worse the prognosis. Data on the total number of attacks in the first five years (Table 5) show that the child who had had only one attack in all had a fairly low risk of having asthma at the age of 10 (8%). Children who had had two attacks before the age of 5 were 50% more likely to have wheezing at the age of 10 (13%), and the predictive value increases thereafter with 38% of children who had had 10 or more attacks before the age of 5 having asthma at the age of 10.

Hospital admission before the age of 5. There was little difference in prognosis between children who had had a single hospital admission for wheezing before 5 years and those who had not. Altogether, 78% of those who had and 80% of those who had not had a hospital admission were free of wheeze at 10 years. (Table 6).

Diagnosis at the age of 5. Of 238 children aged 5 reported by their parents as asthmatic, 50% were free of symptoms at the age of 10 (Table 7). Of 567 reported as having wheezed with bronchitis, 80% were free of wheeze at the age of 10. Seventeen per cent of children with unspecified wheeze and 10% of those who had wheezed with croup had symptoms at the age of 10.

Children who were said by their parents to have wheezed with croup therefore had only twice the risk of wheezing at 10 compared with children who

Table 4 No (%) of attacks in children aged 4 and prognosis at 10 years of age

Asthma at 10	No of attacks				Total
	1	2	3	4+	
Absent	437 (79)	155 (70)	79 (64)	136 (49)	807 (71)
Present	113 (21)	67 (30)	45 (36)	140 (51)	365 (29)
Total	550 (100)	222 (100)	124 (100)	276 (100)	1172 (100)

The value 4+ includes vague responses such as 'several' and 'many'; 'aged 4' indicates period from fourth birthday to interview at around the age of 5. $\chi^2=79$; $p<0.001$.

Table 5 Total No (%) of attacks of wheezing in the first five years

Total No of attacks	Asthma at 10			All
	Absent	Present		
1	573 (92)	53 (8)		626 (100)
2	229 (87)	33 (13)		262 (100)
3	209 (85)	38 (15)		247 (100)
4	147 (77)	44 (23)		191 (100)
5	108 (79)	29 (21)		137 (100)
6	106 (79)	29 (21)		135 (100)
7	56 (67)	27 (33)		83 (100)
8	42 (72)	16 (28)		58 (100)
9	45 (75)	15 (25)		60 (100)
10+	272 (62)	164 (38)		436 (100)
All	1787 (80)	448 (20)		2235 (100)

The value 10+ includes cases with vague responses such as 'several' and 'many'. $\chi^2=130$; $df=6$; $p<0.0001$.

Table 6 No (%) of times admitted to hospital for wheezing (children with history of wheezing in first five years only)

Asthma at 10	No of times admitted			Total
	0	1	2+	
Absent	1654 (80)	174 (78)	41 (64)	1869 (81)
Present	404 (20)	49 (22)	23 (36)	476 (19)
Total	2058 (100)	223 (100)	64 (100)	2345 (100)

$\chi^2=10.6$; $p<0.01$.

Table 7 Diagnosis at 5 years of age and prognosis at 10 years of age. Values are No (%)

Asthma at 10	Diagnosis at 5				All
	Asthma	Wheeze and bronchitis	Croup and wheezing	Wheeze not otherwise stated	
Absent	120 (50)	452 (80)	247 (90)	1050 (83)	1869 (80)
Present	118 (50)	115 (20)	29 (10)	214 (17)	476 (20)
Total	238 (100)	567 (100)	277 (100)	1264 (100)	2345 (100)

$\chi^2=151$; $p<0.0001$.

were said not to have wheezed at all during the period.

Discussion

In this national prospective study we have determined the outcome, by the age of 10, of wheezing in the first five years of life in terms of age at onset, frequency of attacks, number of hospital admissions, and diagnosis at 5 years of age. The study is limited as the information used is largely dependent on the parents' memory.⁵ Nevertheless, studies that have been undertaken to validate parental questionnaires on wheezing have shown good reliability.⁶ The present study is particularly useful because of the large sample size (11 465) and the high follow up rate (87%).

Age at onset. Derrick showed the significance of the age at onset of asthma by observing the hospital admissions of asthmatics of ages up to 60.⁷ He found that the risk of admission to hospital was highest for those whose asthma had begun before the age of 10 and fell rapidly thereafter with increasing age of onset. Buffum, found that the onset of symptoms before 2 years influenced the prognosis,⁸ and Williams and McNicol in a well devised prospective study in Australia found a highly significant correlation between early age of onset and the persistence of asthmatic episodes up to the age of 10.⁹

Unlike the studies of Williams and McNicol,⁹ we have found that within the first five years there was no evidence that the earlier the age of onset the worse the prognosis, in terms of persistence of wheezing or asthma. Our results are consistent with other studies.^{3 10}

In infancy wheezing is commonly associated with viral infection and presents as part of the clinical picture of bronchiolitis. One explanation that has been advanced for wheezing in this age group is that it is a specific response to particular viral infections, which is peculiar to infancy, and that it is unrelated to atopy and allergy. We found that children who first wheezed in infancy were less likely than other groups to be wheezing at the age of 10 (17% compared with 23% for children first wheezing aged 1–4 years) but that the difference was not very great. These results would be compatible with a hypothesis suggesting that a subset of children who wheeze in infancy are not atopic and have no predisposition to asthma in later life. They would not support a hypothesis suggesting that most children who wheeze in infancy are manifesting a non-allergic specific response to viral infection.

Severity of early symptoms. The number of attacks

or frequency of hospital admission can generally be accepted to represent the severity of the disorder. Though the measure to express the severity of symptoms was different, Williams and McNicol showed that there was a highly significant correlation between the frequency of episodes in the first year of symptoms and the persistence of asthma.^{4 9} Blair agreed with the correlation between the severe onset of symptoms and predisposition to chronic asthma.³

Johnstone showed, however, in his prospective follow up study of a group of American children with perennial asthma, that the likelihood of a child 'out growing' his asthma was not significantly influenced by severity of symptoms when first seen.¹⁰

In this series the more wheezing attacks children had had, regardless of age at onset, the less likely they were to be free of wheeze at 10 years. Nevertheless, the number of attacks in the first year was far less predictive than the number of attacks after the first year.

Prognosis by diagnosis at the age of 5. Many doctors have been blamed for being reluctant to use the word 'asthma'. Underdiagnosis and undertreatment of asthma in childhood are indicated by more and more authors,^{11 12} strongly suggesting that any wheezing child should be watched and treated as having asthma.

Half of the children who were reported as having asthma at 5 still had wheezing attacks in their 10th year. On the other hand, most children who had had wheezing attacks before 5, but who were not labelled as asthmatic, had grown out of their symptoms; few of them had asthma (as defined by a wheezing attack in their 10th year).

Recent studies have suggested that asthma and wheezy bronchitis constitute part of a single entity differing only in degree,⁹ that they share a common genetic defect,¹³ show the same characteristics of bronchial hyper-reactivity and allergy,¹⁴ and should all be treated as asthma.¹¹ Our results (Table 5), however, show that children said to have asthma at the age of 5 had a quite different prognosis from those who at 5 had had attacks of wheezing with bronchitis. They suggest that a useful prognostic subdivision had been made on clinical grounds within the omnibus group of children who had had wheezing attacks. Our study did not identify the clinical criteria that were used in labelling these children asthmatic, and in extrapolating the results of this study for use in 1985 it is important to consider the possibility that these criteria may have changed.

This study, so far, has a fairly short term follow

up. Martin has described subjects with apparent remission in childhood and at 14 years who subsequently had a recurrence of wheezing and indicated that follow up studies that do not go beyond early adolescence may give a false impression of the true natural history of childhood asthma.² Balfour-Lynn agreed with this point but showed that children whose illness improved before any sign of puberty had developed could be confidently predicted to 'grow out' of their disease.¹⁵ Information from later follow ups of this cohort will provide a valuable picture of the further long term natural history of childhood asthma.

We are extremely grateful to all the health personnel who made the Child Health and Education Study possible. In particular, we thank the health visitors who were responsible for interviewing the parents of the children at the ages of 5 and 10 and especially the parents themselves for their cooperation. The 5 year contact with this cohort was funded by the Medical Research Council and the questions on health at the age of 10 by the Department of Health and Social Security. The analyses for the present paper were funded by the Chest Heart and Stroke Association. Jean Golding is a Wellcome Senior Lecturer, funded by the Wellcome Trust. We are especially grateful to Yasmin Iles and Yvette Coles who typed many versions of the manuscript and Peter Thomas who was responsible for the computing. The Director of the survey was Professor Neville Butler and principle research officers included Dr Sue Dowling, Dr Albert Osborn, Dr Mary Haslum, and Mr Brian Howlett.

References

- ¹ Butler NR, Golding J. Wheezing and stress? In: Butler NR, Corner BD, eds. *Stress and disability in childhood: the long-term problems*. Bristol: Wright, 1984.
- ² Martin AJ. The natural history of childhood asthma to adult life. *Br Med J* 1980;**280**:1397-400.
- ³ Blair H. Natural history of childhood asthma: 20 year follow-up. *Arch Dis Child* 1977;**52**:613-9.
- ⁴ McNicol KN, Williams HB. Spectrum of asthma in childhood. I. Clinical and physiological components. *Br Med J* 1973;**iv**: 7-11.
- ⁵ Hamman RE. Asthma in schoolchildren. *British Journal of Preventive Social Medicine* 1975;**29**:228-38.
- ⁶ Holland WW, Bailey P, Bland JM. Long-term consequences of respiratory disease in infancy. *J Epidemiol Community Health* 1978;**32**:256-9.
- ⁷ Derrick EH. The significance of the age of onset of asthma. *Med J Aust* 1971;**115**:1317-9.
- ⁸ Buffum WP. Prognosis of asthma in childhood. *Am J Dis Child* 1966;**112**:214-7.
- ⁹ Williams H, McNicol KN. Prevalence, natural history and relationship of wheezing bronchitis and asthma in children, an epidemiological study. *Br Med J* 1969;**iv**:321-5.
- ¹⁰ Johnstone D. A study of the natural history of bronchial asthma in children. *Am J Dis Child* 1968;**115**:213-6.
- ¹¹ Lee DA, Winslow NR, Speight ANP, et al. Prevalence and spectrum of asthma in childhood. *Br Med J* 1983;**286**:1256-8.
- ¹² Colyer AF. Community campaign against asthma. *Arch Dis Child* 1984;**59**:449-52.
- ¹³ Sibbald B, Horn MEC, Gregg I. A family study of the genetic basis of asthma and wheezing bronchitis. *Arch Dis Child* 1980;**55**:354-7.
- ¹⁴ Price J. Asthma in children. *Journal of Maternal and Child Health* 1981;**6**:27-33.
- ¹⁵ Balfour-Lynn L. Childhood asthma and puberty. *Arch Dis Child* 1985;**60**:231-5.

Correspondence to Dr J Golding, Department of Child Health, Royal Hospital for Sick Children, Bristol BS2 8BJ, England.

Received 17 March 1986